OBESITY, PHYSICAL ACTIVITY
AND ACADEMIC ACHIEVEMENT IN
SCHOOLCHILDREN.

Departamento de Enfermería, Fisioterapia y Terapia Ocupacional

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OBESITY, PHYSICAL ACTIVITY AND ACADEMIC ACHIEVEMENT IN SCHOOLCHILDREN.

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CRF: Cardiorespiratory fitness

LBW: Low Birth Weight

PA: Physical Activity
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1. ABSTRACT
ABSTRACT

Cognition is a term that includes a high number of underlying mental processes related with acquiring knowledge and understanding through life-long experience; including attention, memory, working memory, judgment and evaluation, reasoning, problem solving, decision making, comprehension and production of language. It could also include academic achievement and classroom behaviours.

In the recent years, understanding cognition and its development has become an important health goal. Life expectancy has been increased during last years and this could have a negative effect on individuals’ cognition due to the accumulative effect of diseases and biological changes. This cognitive decline could be partially determined by the early childhood development, in such a way that this status tracks from infancy through adolescence to adulthood. Moreover, the optimal development and acquisition of cognition have been related with proper physical and mental health during childhood. This is why recent research has been focused on how to improve and boost cognitive development since childhood.

Physical activity is included among the modifiable environmental factors that could influence the development of children’s cognition, and school-based physical activity programs have been the most worldwide accepted interventions, understanding that school is the ideal place to promote children’s health behaviours and to try to make of them “healthier adults”. Additionally, other factors related to mothers’ and children’s behaviours and characteristics such as pre-pregnancy overweight/obesity, sedentary behaviour during pregnancy, birth weight and children’s cardiorespiratory fitness, have been related with children’s cognition development.

Several questions in this regard remain unclear: i) which cognition areas are the most benefited from school-based physical activity programs; ii) which are the physical
activity characteristics most closely related to success on promoting cognitive skills
development; iii) is there any association between pre-pregnancy weight status or
physical activity during pregnancy with offspring’s cognition; iv) are birth weight and
cardiorespiratory fitness associated with cognition development in preschool children;
and v) is there any mediation role of fitness in the relationship between birth weight and
cognition.

The objective of this doctoral dissertation is to provide scientific evidence aimed to
clarify these important questions, due to the importance of brain development during
pregnancy and childhood period.

With this aim, several systematic reviews and meta-analysis have been conducted, as
well as some analyses of empirical data coming from the MOVI-KIDS project, a cluster
randomized trial involving 21 schools from the provinces of Cuenca and Ciudad Real.

As result of these research works, this doctoral dissertation allows us to conclude that: i)
some cognitive skills, including classroom behaviours and academic achievement, are
sensitive to school-based physical activity interventions; ii) the most effective physical
activity interventions are those aimed at increase the time of daily exercise, those
integrating physical activity during classroom lectures and those aimed at being
cognitively demanding; iii) pre-gestational obesity weight status seems to negatively
influence on offspring’s neurocognitive development, but a small negative effect on
general intelligence. Also, children from active mothers during pregnancy scored better
on general intelligence and cognitive skills; and iv) low birth weight and low
cardiorespiratory fitness are negatively related with cognition in preschool children, and
this relationship is fully and/or partially mediated by children’s birth weight.

The research was designed by Vicente Martínez Vizcaíno and Celia Álvarez Bueno,
researchers of the Health and Social Research Center (Centro de Estudios
Sociosanitarios –CESS–, from Cuenca, Spain. The analysis of the results was coordinated by Caterina Pesce, from the University of “Foro Italico”, Rome, and Celia Álvarez Bueno. Celia Álvarez Bueno has been awarded a scholarship for the completion of this dissertation by the Spanish Ministry of Education, Culture, and Sport (FPU13/03137).
2. RESUMEN
RESUMEN

Cognición es un término que incluye un gran número de procesos mentales relacionados con la adquisición de conocimiento y la comprensión a través de la experiencia; incluyendo atención, memoria, memoria de trabajo, juicio y evaluación, razonamiento, resolución de problemas, toma de decisiones, comprensión y producción del lenguaje. Puede incluir también las notas y los comportamientos en clase.

En los últimos años, el estudio de la cognición y su desarrollo se ha convertido en uno de los temas más relevantes en investigación. La esperanza de vida se ha incrementado en los últimos años, pudiendo tener efectos negativos en las capacidades cognitivas de las personas debido al efecto acumulativo de enfermedades y cambios biológicos. Esta disminución puede estar parcialmente determinada por el desarrollo desde la infancia, de forma que este estado se extiende desde la infancia hasta la adolescencia y la edad adulta. Además, el desarrollo y adquisición óptimos de las capacidades cognitivas se ha relacionado con el adecuado desarrollo físico y mental en la infancia. Por ello, las investigaciones recientes se han centrado en cómo mejorar y fomentar el desarrollo de las capacidades cognitivas desde la infancia.

La actividad física está incluida entre los factores ambientales modificables que pueden influenciar en el desarrollo de la cognición en niños, y los programas de actividad física en el entorno escolar son las intervenciones más aceptadas para promover su desarrollo, entendiendo que las escuelas son el sitio ideal para promover comportamientos saludables e intentar hacer de esos niños, adultos saludables. Además, otros factores relacionados con los comportamientos y características de las madres y los niños, como obesidad y sobrepeso pre-gestacional, sedentarismo durante el embarazo, peso al nacer y capacidad aeróbica de los niños.
Algunas cuestiones continúan sin respuesta en relación a estos aspectos: i) qué áreas de cognición son las que más se benefician de los programas de actividad física en el entorno escolar, ii) cuáles son las características de los programas de actividad física que más efectivamente promocionan el desarrollo de las capacidades cognitivas, iii) cuál es la fuerza de asociación de la relación entre estatus ponderal pre-gestacional y el desarrollo de actividad física durante el embarazo con las capacidades cognitivas de los niños, y iv) cuál es la fuerza de la asociación entre el peso al nacer y la capacidad aeróbica de los niños en edad pre-escolar con sus capacidades cognitivas, así como la posible relación de mediación existente entre las tres.

El objetivo de esta tesis doctoral es proporcionar evidencia científica para clarificar estas cuestiones debido a la importancia del embarazo y la infancia en el desarrollo cerebral.

Con este objetivo, varias revisiones sistemáticas y meta-análisis se han llevado a cabo, así como algunos análisis de datos empíricos del proyecto MOVI-KIDS, un ensayo clínico por clusters llevado a cabo en 21 colegios de las provincias de Cuenca y Ciudad Real.

Como resultado de este trabajo, esta tesis doctoral podemos concluir que: i) algunas capacidades cognitivas, incluyendo comportamientos en clase y notas académicas son sensibles a las intervenciones de actividad física; ii) las intervenciones de actividad física más efectivas son las destinadas a aumentar el tiempo diario de ejercicio, las intervenciones de actividad física integrada en el aula y las cognitivo-demandantes; iii) la obesidad pre-gestacional parece influenciar negativamente el desarrollo cognitivo de los niños, teniendo un pequeño efecto negativo en la inteligencia general de los mismos. Además, los niños de madres que han desarrollado actividad física durante el embarazo puntúan mejor en test de inteligencia general y otras variables cognitivas; and iv) el bajo
peso al nacer y la capacidad aeróbica de los niños se relaciona negativamente con las variables de cognición en niños en edad pre-escolar. Adicionalmente, la capacidad aeróbica juega un papel de mediador total y/o parcial en la relación entre peso al nacer y determinadas variables cognitivas de estos niños.

3. INTRODUCTION
INTRODUCTION

3.1 UNDERSTANDING COGNITION

Cognition is understood as a general term that reflects the number of underlying mental processes of acquiring knowledge and understanding through life-long experience.\(^1\)

Under the umbrella of this concept\(^2\) are included terms such as: core executive functions metacognition and academic performance.\(^3,4\) Executive functions is a term describing the cognitive processes that regulate thought and action, especially in non-routine situations.\(^5\) This term includes functions such as problem solving, planning, sequencing, selective and sustained attention, inhibition, utilization of feedback, multi-tasking, cognitive flexibility and ability to deal with novelty.

We used the term metacognition as the higher-order mental processes involved in learning that include making plans for learning such as planning, reasoning and problem solving. Finally, academic performance is referred to the acts related to how students try to achieve a target by learning efforts.

The process of brain development, from the gestation period through childhood to adult life, is essential for the acquisition of core executive functions, metacognition, and life skills later in life, since some cognitive skills have their expression early in life with rapid improvements during preschool and early school years, while other more complex tasks do not mature until adolescence or even early adulthood.\(^5\) Additionally, there is a close relationship between the proper acquisition of these neurocognitive dimensions with academic achievement and classroom behaviours such as on-task behaviours.\(^6,7\)

Cognitive skills have been also related to mental and physical health during the life span. Some aspects of cognition have been identified as positive markers of mental health (stress, sadness, and rest) during childhood.\(^8\) It seems that these markers could be
tracked into adulthood and that they could be predictors of some health parameters. In this regard, lower levels of cognition have been associated with psychological disorders, risk of cancer, and higher morbidity and mortality during adulthood.\textsuperscript{9-11}

Figure 1. "The ACE Pyramid". Atlanta, Georgia: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, Division of Violence Prevention. May 2014. Archived from the original on 16 January 2016.

1. Core executive functions

There is a general agreement in the recognition regarding which are the three core executive functions: inhibition (including self-control and interference control), working memory, and cognitive flexibility.\textsuperscript{12} One of the characteristics of these functions is that they are really fast tasks and usually could be performed within seconds, therefore the test designed to measure them are aimed to reflex the on-line processing and the capacity to adapt rapidly to changes of a person.\textsuperscript{13}

These three basic executive functions are related to the later development in the life of more complex cognitive functions such as higher-level executive functions.\textsuperscript{7} They are key in the latter expression of everyday life activities such as academic achievement and classroom behaviours, and are essential for school and work success.\textsuperscript{13}
Additionally, core executive functions have been linked to mental and physical health status. Lower levels in these functions have been observed in many mental disorders such as depression and attention deficit hyperactivity disorder (ADHD)\(^\text{14,15}\) and have been related to the development of obesity and metabolic disorders\(^\text{16,17}\) as well as with risk behaviours such as substance abuse\(^\text{18}\).

Even though the three terms are closely related, a definition can be provided for each one.

\textit{a. Inhibition:}

This is the executive function that helps us to focus our attention on a given task, behaviour, thought and/or emotion, by repressing external impulse and internal stimuli/distractions\(^\text{19}\).
This ability allows our brain to manipulate the information we have in mind, to manage different options, to think how to combine them in order to find the best way of solving a problem or achieving a specific objective.\textsuperscript{2,7}

Two tests are commonly used for measuring core executive function: The Flanker task test and the Color-Word Stroop test, which psychometric properties have been repeatedly proven.\textsuperscript{20,21} Basically, these tests try to measure one’s ability to suppress the first impulse, but it is necessary to take into consideration that all ways of measuring inhibition require a minimum of working memory implication in order to maintain a rule in mind to express the inhibition process.\textsuperscript{6}

During “Flanker task” test a set of arrows are presented and the participant has to determine if the direction of the central arrow is left or right. The trial could be congruent when all the arrows are in the same direction, incongruent when the central arrow is in the opposite direction of all the rest arrows or neutral if only the central arrow is presented.\textsuperscript{20}

In “Color-Word Stroop” test, a set of words are presented printed in colors as different trials: names of colors appeared in black ink, names of colors in a different ink than the color named, and squares of a given color. During the first task, the participant needs to read the name of colors printed in black. The second task requires the participant to read the written color names of the words independently of the color of the ink (for example, they would have to read "purple" no matter what the color of the font). In the third task, squares in color are shown and the participant speaks the name of the color.\textsuperscript{21}
b. Working memory:

It is the executive function that helps us to temporally hold limited amount of information on mind and mentally working with it.\textsuperscript{2} The exertion of working memory requires that either the verbal storage system (i.e., the phonological loop) or the visuo-spatial storage system (i.e., visuo-spatial sketchpad) work coordinated to a greater or lesser degree.

Working memory allows us to relate the events across the time keeping in mind their sequence and helping us to establish time-relationships among them.\textsuperscript{22,23} It has been closely related to reasoning and problem-solving because it allows us to reorder items in mind and/or reorganize the information to search the best solution.\textsuperscript{24} Additionally, it has been related to general intelligence and academic achievement.\textsuperscript{25,26}

The tests aimed to measure this core executive function assess the ability to keep in mind a small amount of information during a short time period. Two widely used tests for measuring working memory are the “Stenberg task” or “Digit Span task”.\textsuperscript{27,28}
During “Stenberg task”, the participant is presented with a list of random letters of the alphabet. It is needed to read and remember the letters presented. Once the letter set has been removed from the screen, a single letter is presented on the screen and the participant has to indicate whether the single letter presented was present in the previous letter set or not as quickly as possible.27

During “Digit Span” task participants see or hear a sequence of numerical digits and are asked to recall the sequence correctly, with increasingly longer sequences being tested in each trial. Digit-span tasks can be given forwards or backwards, meaning that once the sequence is presented, the participant is asked to either recall the sequence in normal or reverse order.28

**c. Cognitive flexibility:**

This executive function helps us to change the demands and priorities, adapt our perspective, think from another point of view and adapt the thought to the needs. It is the ability to mental switch between two different concepts and to think in multiple concepts at the same time.29 It is a skill that requires to be mentally flexible and to adapt to different priorities, anticipate changes and be aware of opportunities, adding novelty to the way of thinking.30

There is a part of cognitive flexibility that overlaps with some higher-level executive functions and life skills such as creativity, task switching and set shifting. In fact, this cognitive skill is complemented with other core executive functions to be.31

This core executive function could be measured by using tests such as “A-B trial making” test or “Wisconsin Card Sorting” test, which are aimed at measuring mental flexibility, it means the ability to switch between thoughts and actions.
During “A-B trial making” test the participant needs to connect a sequence of 25 consecutive targets on a sheet of paper or computer screen, in a similar manner to a child connects the dots of a puzzle. The targets are numbers and letters and the participant needs to connect them in sequential order alternating between numbers and letters (1, A, 2, B, etc.).

During “Wisconsin Card Sorting” test a number of stimulus cards are presented to the participant, who is invited to match the cards, but not how to match. Participant has different ways to classify a card, according to: the color of its symbols, the shape of the symbols, or the number of the shapes on each card. The only feedback is whether the participant did it correctly or not. The classification rule changes every 10 cards, and this implies that once the participant has figured out the rule, the participant will start making one or more mistakes when the rule changes.

Figure 5. A-B trial making test example.

Figure 6. Screenshot from a computerized version of the Wisconsin Card Sort.
2. Metacognition:

The core executive functions are related to the development of metacognition later in life. Metacognition is higher order thinking by using all of these mental resources to achieve a goal or solve a problem, it is understood as the “control of cognition”. This term could reflect the individual’s understanding of how one thinks and knows and how to use knowledge to regulate behaviours, supervising and managing cognitive processes in order to regulate own cognition and maximize potential to think and learn.

It could be understood as “thinking about thinking”. Some ways of metacognition come from the understanding of your own abilities; for example, when a student evaluates his/her knowledge of a subject in a class, how he/she perceives the difficulty of the task and how self-evaluates his/her skills to overcome this.

These mental processes take more time to be coordinated than core executive function processes and encompass: high-level executive functions, which is referred to these executive functions more complex and related to fluid intelligence, reasoning, problem-solving and planning, and cognitive life skills, which is referred to abilities needed for adaptive and positive behaviours that enable us to deal effectively with the demands and challenges of everyday life such as planning, reasoning and problem solving.

Furthermore, the development of these skills in life is needed to transfer cognitive functions to academic achievement, and essential for preparing children for their changing social circumstances, socialization, and healthy development. Thus, they are crucial to self-regulate behaviour and successfully adapt it to everyday requirements.
Strategies for evaluating metacognition include checklists about self-questioning or decision-making, making graphics representations of one’s thoughts. Planning could be evaluated by using the Tower of London test and the Self-beliefs for the ability of goal setting, could be used to evaluate problem-solving and positive thinking by a 10-items” scale.

During the “Tower of London” test, two boards with pegs and several beads with different colors are presented. Several problem-solving tasks are presented to the participants that should be solved using the beads and the boards.40
Figure 8. Tower of London initial configuration and possible target configurations.

The “Self-beliefs for the ability of goal setting, problem-solving and positive thinking 10-items” is a scale in which 5 items are used to assess participants’ perception of goal setting ability (e.g., “I am very good at setting goals for myself”), while the other five are used to assess participants’ perception of positive thinking (e.g., “I am very good at thinking positively for myself”).

3. Academic achievement

Also termed academic performance, is referred to an educational construct related to the acts throughout students try to achieve a goal by doing learning efforts. Under this term, we could include not only academic scores but also other factors that may influence students’ success at schools such as academic behaviours: time on-task, understood as the verbal or motor behaviour that follows class rules and is appropriate to the learning situation or attendance; and some cognitive skills, such as verbal ability or memory.

The academic performance goals are closely related with academic field and with the cognitive, emotional, social and physical demands. Therefore, getting metacognition abilities and life skills during childhood is essential for the success in school
performance. Additionally, core executive functions have been demonstrated important processes underlying academic performance.\textsuperscript{14,31}

Academic achievement could be evaluated by using individual grades of different subjects such as Mathematics, Language, Science, History or Foreign Language (the two first are the most common); using an average of the specific subjects (usually Mathematics and Language) or using grade point averages (GPA) as an average of all examinable subjects.\textsuperscript{43}

On-task behaviour could be measured using systematic direct observation. A behaviour is considered “on-task” if the participant is attentive to the teacher or actively engaged in the appropriate task assigned by the teacher. “Off-task” behaviours can include: participants gazing off, placing their head on the desk, reading or writing inappropriate or unassigned material, talking to or looking at other students when not part of a given task, and leaving the desk without receiving permission from the teacher.\textsuperscript{44}

4. How to improve cognition?

In the recent years, several studies have tried to elucidate how to improve children’s and adolescents’ executive functions and metacognition, and how to translate these improvements into academic achievement. All the interventions aimed at improving executive functions and metacognition have consistently reported that:

- Children scoring worst in cognition measurements are those that most could benefit from any intervention program.\textsuperscript{45}

- Training one isolated cognitive function seems to be no possible since improvements in one of them are transferred to the others.\textsuperscript{46}

- The challenging tasks are those that more improve cognitive functions; otherwise, the task could get boring and not challenging.\textsuperscript{47}
The practice seems to be the most important point in the improvement of cognitive functions.²

3.2 PHYSICAL ACTIVITY.

1. Concepts

*Physical activity* (PA) is defined as a complex behaviour that could be understood as “any body movement produced by skeletal muscles that requires energy expenditure”.⁴⁸ Everyone performs daily PA since it includes all the processes needed to sustain the life, but the extra amount and the intensity of PA that everyone exert is a personal decision that could change across the life span.

Following this assumption, *exercise* should be considered a subcategory of PA instead of being considered as a synonymous. Exercise is a planned, structured, repetitive and purposive body movement aimed at improving or maintain physical fitness components.⁴⁹

<table>
<thead>
<tr>
<th>Physical activity</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Body movement via skeletal muscles</td>
<td>1. Bodily movement via skeletal muscles</td>
</tr>
<tr>
<td>2. Results in energy expenditure.</td>
<td>2. Results in energy expenditure.</td>
</tr>
<tr>
<td>3. Energy expenditure varies continuously from low to high</td>
<td>3. Energy expenditure varies continuously from low to high.</td>
</tr>
<tr>
<td>4. Positively correlated with physical fitness</td>
<td>4. Very positively correlated with physical fitness</td>
</tr>
<tr>
<td></td>
<td>5. Planned, structured, and repetitive bodily movement.</td>
</tr>
<tr>
<td></td>
<td>6. An objective is to improve or maintain physical fitness component(s).</td>
</tr>
</tbody>
</table>

*Table 1.* Physical activity and exercise characteristics. Adapted from J. Landsbaugh Kaar; 2007. (A longitudinal Study examining the relation of physical activity on weight status during adolescence, Doctoral dissertation, University of Pittsburgh).
Finally, physical fitness has been defined as “the ability to carry out daily task with vigor and alertness, without undue fatigue and with ample energy to enjoy leisure-time pursuits and to meet unforeseen emergencies”.\textsuperscript{48} This is a set of attributes that includes the components of cardiorespiratory endurance, muscle strength and endurance, flexibility and body composition.\textsuperscript{49,50}

In other sense, PA and exercise are positively linked to physical fitness but exercise is the only one which aim is to maintain or improve it since it is a voluntary activity.\textsuperscript{51}

![Figure 9](image)

**Figure 9.** Components of physical fitness. Adapted from Carpensen et al; 1985 (Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public health reports, 100(2), 126)

2. Physical activity and health

Recent evidence has shown health benefits of regular PA in children and adolescents, among them these could be highlighted:

*Cardiovascular.*

Physical activity has been related to better levels of high-density lipoprotein cholesterol, blood pressure and diabetes mellitus’s risk indicators,\textsuperscript{52-54} in a way that moderate-to-vigorous-intensity PA seems to maintain healthier children’s cardiovascular and metabolic profiles.
Additionally, children’s participation in PA has been proved as a way of enhancing cardiopulmonary fitness (CRF), muscle strength and other components of physical fitness, through increasing oxygen consumption, ventilation processes and saturation of hemoglobin.

Osteoporosis

Physical activity during childhood and adolescence has a positive influence on bone health during the life span. This could be caused because a high level of PA during youth can prevent natural decline of bone mineral density and could increase the peak bone mineral density; both of them postponed the start of osteoporosis. As peak bone mineral accrual rate occurs at puberty, the period before it could represent a window in which increasing peak bone mass.

In this relationship, the PA including mechanical demands or high impacts forces (as jumping, skipping or running) seems to be more important than the exertion of energetic exercise.

Weight status

Overweight/obesity in childhood has been related to worst motor coordination scores as well as with lower PA, increasing the risk of higher levels of blood pressure and other parameters of metabolic syndrome.

Research has described that normal-weight youth involved in higher levels of PA have lower levels of adiposity as compared with those with lower levels of PA. Additionally, it has been observed a reduction in overall adiposity and visceral adiposity among overweight/obese youth exposed to regular PA.

Mental health
For children and adolescents, PA has been associated with good mental health, higher self-perceptions (e.g., self-esteem, self-efficacy, self-concept)\textsuperscript{66} and improved emotional regulation (e.g., anxiety, depression, stress).\textsuperscript{67,68} Furthermore, these effects could be observed across the life span in terms of brain health and mental function.\textsuperscript{69}

![Diagram showing the relationship between physical activity, wellbeing, and health.](image)

**Figure 10.** Directs and indirect links between physical activity and well-being. Source: AH Obadiora et al; 2016. (The influence of sport participation on quality of life perceptions among inmates in Nigerian prisons, 4(6))

### 3. Recommendations

The recommendations of being physically active should be followed by all population regardless the age, gender, race, ethnicity and income level; also, children with disabilities should be encouraged to meet these recommendations.\textsuperscript{70-74} Considering that physical inactivity has become a global pandemic that affects to every age range, being one of the most important mortality contributors,\textsuperscript{75} it is important to develop effective PA strategies to profit from its physical and mental benefits since childhood.\textsuperscript{76}

For children, the international recommendations encourage to achieve the goal of accumulating at least 60 min of moderate to vigorous intensity PA per day, considering
that most of the daily PA should be aerobic. Additionally, exercises aimed at enhancing muscular strength and vigorous-intensity activities should be incorporated at least 3 times per week.\textsuperscript{74}

<table>
<thead>
<tr>
<th>Age group</th>
<th>Physical activity recommendations</th>
<th>Sedentary behavior and screen time recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants (0-1 year)</strong></td>
<td>Physical activity should be encouraged from birth, especially supervised floor-based play.</td>
<td>No sedentary, restrained or kept inactivity for more than 1 hour, with the exception of sleeping</td>
</tr>
<tr>
<td><strong>Toddlers (1-3 years) and preschoolers (3-5 years)</strong></td>
<td>Accumulate at least 3 hours of physical activity every day.</td>
<td>Children less than 2 years, should not take part in screen activities.</td>
</tr>
<tr>
<td><strong>Children (5-12 years) and young people (13-17 years)</strong></td>
<td>Accumulate at least 60 minutes of moderate to vigorous intensity physical activity every day Including aerobic activities. Strengthen muscles and bones physical activities should be included at least 3 days per week. For additional health benefits, more physical activity should be engaged.</td>
<td>Should minimize time spent being sedentary and break up long periods of sitting. Should limit screen time to no more than 2 hours per day.</td>
</tr>
</tbody>
</table>

**Table 2.** Physical activity recommendations for children and adolescents. Adapted from Australian Government's physical activity guidelines; 2014.

Although a dose-response relationship has been established, the most health benefits are reported after 60 min of moderate-to-vigorous-intensity PA per day.\textsuperscript{53,74} The appropriate activities that should be considered for children in order to achieve this goal include: play games, sports, transportation, recreation, physical education, planned exercise developed in the context of family, school and community activities.\textsuperscript{55}

4. How to improve physical activity?

For promoting PA among children and adolescents, some strategies have been proposed.\textsuperscript{55}

- Promote walking and cycling through cities planning and environmental policies, also with the aim to promote active school transportation.
• Provide local playing facilities for children (e.g. building walking trails).
• Provide advice or counsel in primary care.
• Create social networks that encourage PA.
• Provide schools with safe and appropriate spaces and facilities in order to facilitate that students can spend their time actively.
• Ensure that school policies support the provision of opportunities and programs for PA.

The aim of these recommendations is to get children be engaged in a minimal amount of PA instead of hopping great behaviour changes,\textsuperscript{53} to create healthy habits and to profit from health PA benefits. Also, considering that both, healthy behaviours and their effects on health, could be tracked into adulthood\textsuperscript{55} and that because of their rapid development and maturation, children are thought to be especially affected by routine PA.\textsuperscript{51}

Following the international recommendations of PA, interventions developed in school setting have been one of the most extended strategies to achieve the total amount of daily children’s PA and as consequence obtain the health benefits of it.\textsuperscript{64}
3.3 PHYSICAL ACTIVITY AND COGNITION

Physical activity has been associated with positive values in multiple cognitive domains such as better cognitive functioning (eg, information processing, memory, attention) and students’ success in academic achievement and on-task behaviours.\textsuperscript{77,78} Among PA types, some of them have demonstrated to improve psychosocial domains such as goal setting, problem solving and self-regulation, closely related to cognitive skills and life skills.\textsuperscript{39} The development of these skills have been proved elements to consider in the transference from PA to cognition, academic behaviour and achievement.\textsuperscript{79}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{conceptual_framework.png}
\caption{Conceptual framework illustrating relationships among physical activity, physical fitness, health, and academic performance. Source: https://www.nap.edu/read/18314/chapter/5#98}
\end{figure}

The effects of PA programs on cognition seem to be possible through the effects of PA on fitness. Several mechanisms induced these effects including angiogenesis, oxygen saturation, glucose delivery, cerebral blood flow and neurotransmitter levels.\textsuperscript{80} These produce structural changes in brain volumes,\textsuperscript{81} and could improve brain functioning\textsuperscript{82} as measured by resonance imaging and electrical activity recordings.

In line of these findings, research has reported that higher fitness children scored better in academic achievement and cognition tests than their peers with lower fitness children.\textsuperscript{83,84} Also better CRF levels have been associated with greater volume of some brain structures such as basal glia and gray and white matter.\textsuperscript{85}
Schools represent a crucial setting for boosting the development of cognition among children and adolescents throughout PA programs, providing a supportive classroom environment where conducting the practice and reinforce of cognitive skills.\textsuperscript{37}

Several reasons reinforced the use of PA strategies for improving children’s cognition in school setting for:\textsuperscript{37,38} i) sport is a universal activity throughout our society and most students are familiarized with it; ii) many of the skills learned in sports are transferable to other life domains (the abilities to perform under pressure, to solve problems, to meet deadlines and/or challenges, to set goals, to communicate, to handle both success and failure, to work with a team and within a system, and to receive feedback and benefit from it); and iii) life and physical skills are learned in a similar way, through demonstration and practice.

1. Characteristics of physical activity

In the search for the mechanisms that could influence this relationship, evidence consistently supports that not all forms of PA programs influence cognition equally.\textsuperscript{86} Therefore, changes in the qualitative and quantitative characteristics of the interventions result in different effects, is such a way that different types of PA could influence on different cognition domains.\textsuperscript{87} Also, these characteristics might be interrelated through mediation pathways linking the increase in executive function to improvements in metacognition and academic achievement.\textsuperscript{41}
Among the quantitative characteristics of PA, we can include all those variations related with intensity, frequency, and session or intervention duration.\textsuperscript{13}

The quantitative characteristics of PA that researchers have included in the school setting through PA programs have mostly been aimed at enhancing PA sessions, increasing the amount of time devoted to PA. This type of interventions are usually classified as interventions into school-time and after school-time. Among the former, we distinguish: curricular physical education, integrated PA (active breaks or teaching subjects as math with physically active tasks), and extracurricular PA (active recess or lunch time PA). The latter includes after-school PA or sports programs.

Against the current trends to reduce PA time in favor of other subjects, previous studies have demonstrated that increasing the amount of weekly-time dedicated to physical education in the scholarship curricular enhances, or at least does not adversely affect, the academic performance of children, even if after-school time for studying is reduced.\textsuperscript{89,90} Furthermore, it has been suggested that integrating exercise in an interdisciplinary learning strategy, with some other specific subjects such as
mathematics or language could have beneficial effects on children’s academic performance. Some PA programs have added modifications in intensity or frequency. Also, including PA specialist teacher who manages the program could be an effective method of control these parameters. The importance of professionals responsible for translating these evidence to program design and teaching strategies has been pointed as essential, in order to better integrate PA programs into school schedules. The teachers’ increased confidence in teaching physical education, teachers’ learned ways to manage children during PA, the trust relationship stabilized between pupils and teachers and/or teacher’s ability to manage peer-to-peer interactions during PA, could are some reasons behind these findings.

b. Qualitative characteristics.

The interest in the effect of qualitative characteristics of PA has been growing during the last years in the search for further mechanisms beyond the increase in metabolic and neuromuscular demands of physical exercise tasks. Evidence consistently supports that exercises requiring complex, controlled, and adaptive cognition and movement have a greater impact on executive functions. This PA involves not only physical effort but also emotional and socially engaging, developing physical activities that could impact on core cognitive functions, as well as on a broader range of cognitive skills, such as goal setting, problem-solving and self-regulation.

The qualitative characteristics of PA could be modified by promoting PA programs aimed at enriching PA sessions (increasing deliberately the non-physical—coordinative and/or cognitive—demands of PA tasks). The role played by qualitative exercise characteristics for cognitive development promotion includes coordinative and cognitive task complexity, novelty and diversification.
3.4 OTHER DETERMINANTS

1. Mother’s behaviours

   a. Pre-pregnancy weight status

Maternal overweight and obesity have been related with negative outcomes for the mother’s health, including some parameters of delivery, and for the foetus.\textsuperscript{98} For the mother, overweight/obese weight status increases the risk of infertility, gestational diabetes, preeclampsia, thromboembolism, preterm delivery and caesarean section. For the fetus, it increases the risk of death, congenital anomalies, macrosomia, and foetal and offspring neurodevelopment.\textsuperscript{99}

These effects might influence the mother’s and child’s health later in life. Women could be at increased risk of heart disease, diabetes, and hypertension, and children could be at increased risk of developing future obesity and heart disease.\textsuperscript{100}

Previous studies have related pre-gestational maternal obesity with worst offspring’s cognition scores. The relationship between pre-gestational weight status and children’s cognition is complex and some variables have been considering as playing a role in this relationship. In this regard, some gestational complications more common among obese mothers should be considered (congenital abnormalities, preeclampsia or gestational diabetes mellitus) due to they increase the risk of iatrogenic preterm delivery, labour induction and caesarean deliveries,\textsuperscript{101,102} or/and have a negative influence on mental neurodevelopment in children.\textsuperscript{103-105}
Figure 13. The relationship between maternal pre-pregnancy body mass index (BMI) and g scores in children at 5 and 7 years of age. Source from E. Basatemur et al; 2013. (Maternal pre-pregnancy BMI and child cognition: a longitudinal cohort study. Pediatrics, 131(1): 56-63)

Some socioeconomic factors should be also considered as confounders in this relationship such as home conditions, family income, or maternal and paternal educational or intelligence levels.\textsuperscript{103-105}

Hypothesis

The physiological mechanisms behind these long-term negative consequences in offspring are unclear and some hypothesis have been described:

i) Some psychological conditions such as personality characteristics, increased stress levels or stress sensitivity in obese mothers could produce a negative impact on children’s cognition.\textsuperscript{106}

ii) The foetal programming hypothesis suggests that the exposure of the foetus to an adverse intrauterine environment would be sufficient to produce permanent programming changes in tissue function and, as a result, long-term adverse effects on offspring neurodevelopment.\textsuperscript{107,108}
iii) The epigenetic hypothesis proposes that the foetus receives a set of information related to environmental factors from the mother, which is capable of producing changes in gene expression responsible not only for metabolic diseases but also for psychiatric disorders across the life span. These effects might be the consequence of interaction between genes and increased levels of fatty acids, glucose, leptin and inflammatory markers that might have an influence on plasticity and cognitive function.

iv) Pregravid obesity has been associated with a high risk of vitamin D deficiency that could have a direct impact on the nutritional status of the neonate.

v) Maternal obesity produces an inflammatory uterine environment with increases insulin concentrations, leptin levels and other low-grade inflammatory markers (such as oxidative stress and endothelial dysfunction). This environment could produce errors in brain maturation during gestation and, produce neurodevelopmental impairment in offspring.

Due to the worldwide continuous increment of the excess of weight (including obesity and overweight) prevalence, there is a growing concern regarding the possible negative effects of pre-pregnancy maternal weight status on children’s cognitive development and the strength of this relationship.

Additionally, recent research has focused also on the relationship of inadequate gestational weight gain and children’s neurological development.\textsuperscript{119} It has been proposed that the gestational weight gain over the International recommendations could cause impairment on children’s brain development thought the same mediation chain mechanisms.\textsuperscript{120,121}

\textit{b. Maternal physical activity during pregnancy}

It has been defined that unhealthy behaviours during pregnancy such as sedentary habits could negatively affect fetuses’ and children’s development.\textsuperscript{122}

The latest recommendations of the American College of Obstetrics and Gynaecology (ACOG) for pregnant women without complications indicated that they should accumulate at least 30 minutes of moderate-intensity PA on most days of the week.\textsuperscript{123}

In spite of these recommendations, the worldwide prevalence of pregnant women who do not meet the ACOG’s physical activity recommendations is steadily rising, reaching 33.9%.\textsuperscript{124} Never mind if we consider only the leisure PA (including sports and exercise during free time), or the general PA (including occupational and household activities).\textsuperscript{125}

Any type of PA during pregnancy could have a positive effect on neonatal and maternal outcomes. For the mother, PA has been related to less incidence and better management of postpartum depression, mood, gestational diabetes and maternal weight gain.\textsuperscript{126-129} For the children, it has been related to better gestational age and higher scores in Apgar
test, orientation, state regulation, academic achievement, cognition and classroom behaviours. These findings have been supported by clinical trials reporting that children from active mothers have more mature brains and better fine motor performance.

_Hypothesis_

Different pathways have been proposed behind this relationship, including:

i) Improvements in the **intrauterine environment**, PA that could modify the environment in which the fetus has grown.

ii) Better circulation and **higher placental volumes** could play a critical role in the supply of oxygen to the fetus and the increase of blood circulation that seem to be crucial for the fetus’ neurologic development, and the BDNF transferred from mother to child.

iii) **Maternal behaviours** like sedentary behaviour may increase the risk of depression and anxiety disorders during pregnancy, that has been associated with worse children’s behaviours and psychological development.

iv) The **epigenetic hypothesis** proposed for explaining the link between pre-gestational maternal weight and children cognition tries also to explain this relationship. Some aspects such as gestational diabetes, hypertension or elevated insulin levels could influence child development through epigenetic modifications. Physical activity might help control or mitigate these gestational disorders in such a way that children from active mothers could be at lower risk of developing some non-communicable diseases.
2. Children’s characteristics

a. Birth weight

Low birth weight (LBW) has been not only related with increased risk of short stature, metabolic disorders, and neonatal morbidity and mortality, but also to neurosensory impairments, emotional problems, and poorer general health compared with normal birth weight.\textsuperscript{143}

Additionally, using magnetic resonance imaging, LBW has been associated with smaller brain volumes, particularly those related with executive attention and motor control.\textsuperscript{144} These findings are in agreement with those that have related LBW with impairs on executive functions such as flexibility, planning, working verbal, visuospatial memory and inhibition.\textsuperscript{145}

These neurocognitive deficits could be extended to general intelligence levels, academic and behavioural problems, because of the close relationship between cognition domains, observing that LBW had poorer school performance, learning difficulties and behavioural problems.\textsuperscript{144,146}

Some compensatory brain mechanisms could be developed by LBW children to cope with these functional deficits.\textsuperscript{147} In spite of that, research has suggested that some structural brain alterations might be behind these cognitive impairments in LBW infants,\textsuperscript{148} and that the negative effects be observed from perinatal state could be tracked from infancy to adulthood.\textsuperscript{149}

Additionally, birth weight and physical fitness parameters have been related,\textsuperscript{150} in a way that LBW children are at risk of lower aerobic and neuromuscular fitness, although these differences also seem to become less apparent as children get older.\textsuperscript{151}
Considering the relationship described between physical fitness, birth weight and academic achievement in children, it seems reasonable to think that fitness could play a mediator role in the relationship between birth weight and academic performance,152 but the dimensions of cognition influenced by both birth weight and CRF remain unclear, and also the relationship between birth weight and which cognitive dimensions are mediated by CRF in preschool children.
4. BASIS FOR THIS DISSERTATION
BASIS FOR THIS DISSERTATION

This doctoral dissertation is based on the following statements:

1. Physical activity programs on school setting improve children’s cognition and metacognition.

Physical activity in the school setting has been related to improvements in cognitive functions. It seems important to know which cognitive and metacognitive functions are the most benefited from PA interventions, and how qualitative and quantitative characteristics could modify these effects.

2. Physical activity programs on school setting improve children’s academic achievement and behaviours.

The effectiveness of PA interventions on children’s and adolescents’ academic achievement has been previously established. It is needed to explore the role of PA interventions on different areas of academic achievement and behaviours, and identify the effect of the qualitative and quantitative characteristics on these effects.

3. Pre-gestational mother’s weight status affects offspring’s cognition.

A negative relationship between pre-pregnancy overweight/obese weight status on children’s cognitive skills has been previously described. Since the steadily worldwide rising of women’s obesity prevalence, it seems necessary to quantify this effect.

4. Birth weight mediated the relationship between CRF and children’s cognition.

Birth weight and physical fitness parameters have been previously related described, in such a way that low weight status has been related to increased risk of lower aerobic and neuromuscular fitness. Conversely, higher levels of physical fitness have been related to better cognition function and academic achievement in children. From the
public health perspective, it is needed to determine the nature of the relationship among the three parameters.


Previous studies have reported that PA programs during pregnancy are associated with children’s higher scores in academic achievement and cognition. Since the worldwide prevalence of pregnant women who do not meet the ACOG’s physical activity recommendations is steadily rising, it seems necessary to estimate the effect of mothers’ sedentary behaviours on children’s cognitive development.

Thus, due to the growing worldwide interest in cognition functions and the variables that could improve or modify their development and acquisition across the life span, it seems logical that:

- It is needed to determine the effects of PA programs on children’s and adolescent’s cognitive function, distinguishing the effects on core executive functions (attention/inhibition, working memory and cognitive flexibility), metacognition (higher-level executive functions, including planning, reasoning, and problem-solving; and like skills, including decision making, goal setting), academic achievement (including mathematics-related skills, language-related skills, reading and total scores) and school behaviours.

- It is needed to discern the individual and PA programs characteristics that could modify the relationship between PA programs and cognitive children’s function.

- It seems essential to measure the effect of pre-gestational weight status on children’s cognitive function.
- It is needed to clearly determine the relationship between birth weight, CRF and children’s cognition. Also, to establish the potential mediator effect of CRF in the relation of birth weight and cognition.

- It is needed to determine the effects of maternal leisure PA during pregnancy on offsprings cognition.
5. AIMS
AIMS

The main objective of this dissertation was to summarize the evidence regarding the relationship of cognition with some variable.

The specific aims of this dissertation were:

1) To provide a novel protocol designed to review interventional studies addressing the chronic exercise–cognition interaction in children and adolescents for obtaining relevant information for policymakers and decision makers particularly in, but not limited to, the education sector. (Manuscript 1)

2) To assess the effect of physical activity interventions on children’s and adolescents’ cognition, distinguishing between core executive functions and metacognition. (Manuscript 2)

3) To determine which individual and physical activity program characteristics are most favourable to aid the development of cognitive and metacognitive functions. (Manuscript 2)

4) To assess the effect of physical activity interventions on children’s and adolescents’ academic achievement and classroom behaviours (Manuscript 3)

5) To determine the individual and physical activity programs’ characteristics that are most favourable to aid the development of academic performance (Manuscript 3).

6) To assess the effect of pre-pregnancy overweight and obesity on children’s neurocognitive development. (Manuscript 4)

7) To assess the effect of leisure physical activity during pregnancy on children’s neurocognitive development (Manuscript 5).
8) To examine differences in cognition parameters by birth weight categories controlling for potential confounders or mediators (Manuscript 6)

9) To analyze whether the relationships between birth weight and cognitive functions are mediated by cardiorespiratory fitness in schoolchildren (Manuscript 6).
6. OBJETIVOS
OBJETIVOS

El objetivo principal de esta tesis doctoral es resumir la evidencia científica existente en la relación las capacidades cognitivas y a algunas variables que pueden influir en su adquisición y desarrollo.

Los objetivos específicos de esta tesis fueron:

1) Proporcionar una metodología novedosa diseñada para revisar los estudios de intervención en relación a la relación entre ejercicio crónico y cognición en niños y adolescentes con la finalidad de obtener información relevante para los encargados de formular y tomar decisiones políticas a este respecto, particularmente en el sector de la educación. (Manuscrito 1)

2) Evaluar el efecto de las intervenciones de actividad física en la cognición de niños y adolescentes, distinguiendo entre funciones ejecutivas centrales y metacognición. (Manuscrito 2)

3) Determinar qué características individuales y de los programas de actividad física son las más favorables para ayudar al desarrollo de funciones cognitivas y metacognitivas. (Manuscrito 2)

4) Evaluar el efecto de las intervenciones de actividad física sobre el rendimiento académico de los niños y adolescentes y los comportamientos en el aula. (Manuscrito 3)

5) Determinar las características individuales y de los programas de actividad física que son más favorables para el desarrollo del rendimiento académico. (Manuscrito 3)

6) Evaluar el efecto del sobrepeso y la obesidad antes del embarazo en el desarrollo neurocognitivo de los niños. (Manuscrito 4)
7) Evaluar el efecto de la actividad física en el tiempo libre durante embarazo en el desarrollo neurocognitivo de los niños. (Manuscrito 5).

8) Examinar las diferencias en distintos parámetros cognitivos por categorías de peso al nacer, controlando por potenciales factores de confusión o mediadores. (Manuscrito 6)

9) Analizar si las relaciones entre el peso al nacer y las funciones cognitivas están mediadas por capacidad cardiorrespiratoria en los escolares. (Manuscrito 6).
7. MANUSCRIPTS
1. **Manuscript 1**: Association of physical activity with cognition, metacognition and academic performance in children and adolescents: a protocol for systematic review and meta-analysis
Association of physical activity with cognition, metacognition and academic performance in children and adolescents: a protocol for systematic review and meta-analysis

Celia Álvarez-Bueno,1 Caterina Pesce,2 Iván Cavero-Redondo,1 Mairena Sánchez-López,1,3 María Jesús Pardo-Guijarro,1,4 Vicente Martínez-Vizcaíno1,5

ABSTRACT

Introduction: Schools provide a relevant context for improving children’s and adolescents’ physical and mental health by increasing physical activity during school hours and/or beyond. The interest in the relationship between physical activity programmes and cognition during development has recently increased, with evidence suggesting a positive association. We present a protocol of systematic reviews and meta-analysis of intervention studies that, by determining the effects of chronic physical exercise on children’s and adolescents’ cognitive and metacognitive functions, cognitive life skills, academic behaviours and achievement, aims to ensure procedural objectivity and transparency, and maximise the extraction of relevant information to inform policy development.

Methods: This protocol is guided by Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) and by the Cochrane Collaboration Handbook. Databases to be utilised for a thorough selection of the pertinent literature are MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science, PsycINFO and ERIC. Selection is proposed to encompass an international and a national publication level, with inclusion of experimental studies written in English or in Spanish, respectively. Also, relevant references included in the selected studies will be considered suitable for review as supplemental sources.

We present an integrated approach to the methodological quality assessment of the selected studies, including the Jadad Scale for the assessment of the quality of randomised controlled trials and the Quality Assessment Tool for Quantitative Studies for pre–post studies and non-randomised controlled trials. The pre–post interventions mean differences will be the primary indicator of the intervention outcome.

Statistical analysis: A subgroup analysis is proposed based on cognitive functions and their neural correlates, metacognitive functions and cognitive life skills, academic achievement areas and academic behaviours.

Trial registration number: PROSPERO
CRD42015029913

INTRODUCTION

In the last decades, scientific evidence on the relationship between chronic physical activity and cognitive/academic performance in childhood and adolescence has attracted increasing attention.1 Chronic physical activity interventions have been defined as long lasting repeated bouts of exercise aimed to improve physical fitness.2 Chronic physical activity participation has been associated with several mental health benefits in school children, such as improved self-perceptions
(eg, self-esteem, self-efficacy), emotional regulation (eg, anxiety, depression) and cognitive functioning (eg, information processing, memory, attention).3

Owing to the relevant implications for educational policies, many researchers have investigated the effects of chronic physical activity participation on students’ success in academic performance at school.1–3 The latter is pooled in classroom behaviour (eg, on-task behaviours during learning activities) and academic achievement (eg, school notes and performance in test on school subjects). Attention has also been focused on cognitive executive functions, since their development early in life has been proven predictive of school and lifelong achievement, health and quality of life.9 Diamond6 distinguishes between core executive functions—inhibitory control, working memory and cognitive flexibility—and higher-level executive functions such as reasoning, planning and problem solving. This higher-level cognition largely overlaps with what is termed metacognition, that is, the ability to supervise and manage cognitive process and to use knowledge to regulate behaviours.2

Chronic exercise–cognition research has experienced a progressive shift towards a biochemical and neuroscientific perspective from both, exercise and cognition researchers,7–8 as well as developmental neuroscientists.9 The positive influence of chronic physical activity has been related to angiogenesis, increasing oxygen saturation and glucose delivery, improving cerebral blood flow and increasing neurotransmitters levels.10 Differences in structural brain volumes, as measured by MRI,11 and brain function, as measured by electrical activity recordings.12

Previous systematic reviews and meta-analysis have synthesised evidence of the influence of exercise interventions on children’s and, less frequently, adolescents’ cognition and success in school, focused on quantitative exercise characteristics (intensity, frequency and session duration).13–16 Of these, one regarded experimental studies only and considered cognitive and psychosocial outcomes jointly.15 No study presented results distinguishing between cognitive and metacognitive functions, academic behaviour and achievement. Indeed, this distinction has recently been deemed relevant to understand the potential mediational paths that underlie the relationship between physical activity and academic achievement.2

In the search for further mechanisms beyond the neurobiological that may explain the link between chronic physical activity and children’s cognition, recent narrative or meta-analytic reviews have focused on the qualitative characteristics of the physical activity interventions.8–18 The difficulty in operationalising the breadth of the exercise quality construct in exercise and cognition research, beyond the mere metabolic and neuromuscular demands of physical exercise tasks,19 is a main cause for the underinvestigation of the role played by qualitative exercise characteristics such as coordinative and cognitive task complexity, novelty and diversification, for cognitive development promotion.20 Also, developmental neuroscientists interested in interventions aiding children’s cognition are increasingly shifting attention towards qualitative forms of physical activity that are not only physically effortful, but also emotionally and socially engaging.9 These kinds of interventions often involve physical activities that impinge on core cognitive functions, as well as on a broader range of cognitive skills, such as goal setting, problem solving and self-regulation.1 These are cognitive in nature and therefore fall into the field of cognitive sciences, but they are also investigated in psychosocial and social-cognitive research as essential life skills to self-regulate behaviour and successfully adapt it to everyday requirements.21 Since they are proven sensitive to designed physical activity interventions,22 it has been recently proposed that cognitive life skills may represent a further element to be considered in the relationship between physical activity, cognition and academic behaviour and achievement.8

In sum, scientific evidence on the relationship between physical activity and cognitive/academic performance, particularly in regard to its possible moderators and mediators, is still currently insufficient to obtain a comprehensive view that may be useful to inform policies and decision-making. Discrepancies persist regarding the effects of chronic exercise interventions on children’s cognition and success in school and life, and reviews still lack consideration of evidence at relevant intersection points between different research areas. Moreover, whereas several narrative and meta-analytic reviews have provided evidence syntheses that are mainly useful for setting future research priorities, they still leave open questions concerning how this evidence can be translated into good practices in ecological settings such as the educational.23

Thus, the general aim of the present methodological article is to provide a novel protocol designed to review interventional studies addressing the chronic exercise–cognition interaction in children and adolescents for obtaining relevant information for policymakers and decision makers particularly in, but not limited to, the education sector. To this aim, the proposed protocol encompasses different facets of cognitive function and academic performance that, to the best of our knowledge, should be jointly considered to facilitate transitioning evidence of the cognitive benefits of physical activity for children and adolescents into good practices.

OBJECTIVES
This systematic review and meta-analysis has three objectives: (1) to estimate the effects of chronic physical exercise interventions on different facets of cognitive function and academic performance of children and adolescents; (2) to determine which of those variables benefit most from physical activity; (3) to identify the
individual, task-related and contextual moderators that may amplify physical activity effects on cognition/academic performance, with particular focus on the qualitative and quantitative characteristics of the physical activity interventions.

Specifically, this systematic review and meta-analysis protocol presents an objective and clear procedure to maximise the extraction of information from experimental studies (randomised controlled trials—RCTs, non-RCTs and controlled pre–post studies), in which data for cognition, metacognition, cognitive life skills, academic behaviour and achievement have been separately or jointly reported as outcomes.

METHODS AND ANALYSIS

This systematic review and meta-analysis protocol is based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P)24 and the Cochrane Collaboration Handbook.25 This trial has been registered in PROSPERO (registration number: CRD42015029913).

Inclusion/exclusion criteria for study selection

Type of studies

Randomised control trials (RCTs), non-RCTs and controlled pre–post studies written in international language (English) or in the national language (Spanish) of interest.

Type of participants

Studies assessing the relationship, at developmental age, between chronic physical exercise interventions and cognition, metacognition, cognitive life skills and academic performance variables will be included regardless of sex, weight, ethnicity and socioeconomic status. Studies including participants aged from 4 to 18 years will be considered for inclusion. Among exclusion criteria, the one regarding participants will be the presence of children with any physical condition or any diagnosed disorder of cognition that would impede or limit their ability to participate in school physical activity programmes. If participants are assessed more than once in the same study, data will be extracted and analysed from the different measurements as independent samples.

Type of interventions

Studies reporting any type of chronic physical exercise intervention, defined as repeated bouts of exercise over time aimed to improve physical fitness and involving multiple sessions over a number of training weeks, months or years, will be eligible for inclusion. Studies reporting the transient effects of single bouts of acute physical exercise will be excluded. Studies comparing different types of chronic physical exercise interventions or examining a chronic physical exercise intervention with or without a control group are considered eligible for inclusion.

Among chronic physical exercise interventions, we will include those defined as: school-based physical exercise interventions, recess time interventions, classroom-based physical activity interventions and extracurricular physical activity interventions. Studies combining physical exercise with other health interventions, such as nutritional interventions, will be excluded when data concerning the effectiveness of physical activity programmes on cognitive or academic performance variables could not be extracted separately.

Type of outcome assessments

In the attempt to provide a comprehensive view of physical activity effects on the different facets of children’s and adolescents’ cognition, a broad array of cognitive outcome assessments is warranted, ranging from neural correlates of cognitive functioning to performance measures and observational or self-reported evaluations of cognition, metacognition, cognitive life skills and academic performance.

Indicatively, but not exhaustively, common performance measures for cognitive function assessment are provided by tests such as the Eriksen flanker task, Stroop Colour-Word task, Cognitive Assessment System (CAS), or the Stenberg task. Examples of performance measures for metacognitive function assessment are the Tower of London test and creativity assessment tools such as the Alternate Uses Test. Academic performance assessments regard: (1) academic achievement by curriculum-based marks or specific scales such as the Canadian Achievement Test, Terra Nova test, or Metropolitan achievement test; and (2) academic behaviours by measures such as on-task behaviours, organisation, or attendance. The assessment of cognitive life skills outcomes (goal setting, problem solving, self-regulation) can include self-report measures such as the Life Skills Self Beliefs test, or multisource assessment scales that triangulate self-reports with ratings by significant others (peers, teachers). When cognitive, metacognitive or academic performance outcomes are paralleled by biochemical, brain functional and structural correlates, such measures will also be considered, as they may inform about the biochemical and neural mechanisms underlying physical activity effects on cognition.

Search methods for the identification of studies

Electronic search

The search will be conducted in the MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science, PsycINFO and ERIC databases from their inception. Study records will be managed by means of the Mendeley reference manager.

The following search terms (and related truncations, eg, ‘cognit’ to tap cognition and cognitive) will be used: (1) physical activity, physical education, exercise, fitness, sport; (2) cognition, executive, executive function, cognitive control, intelligence, memory, attention,
metacognition; (3) life skills, goal setting, problem solving, self-regulation; (4) academic, academic achievement, academic grades, academic behaviour, academic performance, classroom behaviour; (5) brain development, brain health, neural, neuroelectric, neurotrophic, neurotrophin, hormone; (6) children, childhood, preschooler, schooler, preadolescent, adolescent, adolescence and (7) trial (see online supplementary appendix I for MEDLINE database search strategy).

Previous reviews and meta-analyses will be checked for additional references and relevant references cited in the selected studies will be screened as supplemental sources.

Data collection and analysis
Selection of studies
After excluding duplicated records, two reviewers will independently screen titles and abstracts to identify eligible studies according to the inclusion and exclusion criteria. Then, the potential eligible studies will be comprehensively reviewed and their reference list checked for additional relevant studies. Any discrepancies will be resolved by discussion with a third reviewer.

Two authors will independently extract data on publication year, number and age of participants (control and intervention groups), physical exercise intervention characteristics and (meta)cognition/life skills/academic performance variables.

Any disagreement will be resolved by discussion and consensus. If necessary, the authors of the included studies will be contacted to obtain additional relevant information.

Assessment of risk of bias in included studies
Two researchers will conduct a quality assessment according to the Cochrane Collaboration Handbook. Any disagreement will be resolved by discussion. A third reviewer will resolve the disagreement if consensus is not reached.

Methodological quality of the RCT will be assessed with the Jadad Scale. The risk of bias will be evaluated according to three domains: randomisation, double blinding and description of withdrawals and dropouts. Each domain will receive a score of one when the studies satisfy its description. Randomisation will score one extra point if the method to generate the sequence is appropriate. A double blind study will score one extra point if the double blind method is appropriately described. Based on these domains, scores can range from 0 to 5.

The Quality Assessment Tool for Quantitative Studies is proposed to assess the quality of pre–post studies and non-RCTs. This tool evaluates seven domains: selection bias, study design, confounders, blinding, data collection method, withdrawals and dropouts. Each domain could be considered strong, moderate or weak, and studies could be classified as strong (with no weak ratings), moderate (with one weak rating) and weak (with two or more weak ratings). If there are insufficient or unclear data describing the required domains, the study authors have to be contacted for more details.

Data synthesis
Key characteristics and important questions, such as sample size, age of participants, quantitative and qualitative intervention characteristics, and cognitive outcome relevant to the aim of the review, will be summarised in tables (see online supplementary appendix II). Reviewers will determine whether a meta-analysis is possible when data have been extracted. At least five observations addressing the same specific outcome will be required to conduct a meta-analysis.

If it is possible to carry out a meta-analysis, STATA V.13 software will be used to combine the pooled mean differences with 95% CIs. A fixed-effect model will be used if there is no evidence of heterogeneity; otherwise, a random-effects model will be used. The study heterogeneity will be assessed with an I² statistic. Usually, I² values of <25%, 25–50% and >50% represent small, medium and large amounts of heterogeneity, respectively. Studies with insufficient data to perform the analyses will be omitted from the data synthesis. If there is substantial heterogeneity among the studies and a meta-analysis is not possible, a descriptive analysis will be conducted.

The measure of mean pre–post intervention difference will be the primary indicator of the intervention outcome. Mean differences (standard error (SE)) and standardised mean differences (standard deviation (SD)) will be calculated for each specific skill or area included in the tests. For example, when the SE is provided, the SD will be calculated according to the following formula: $SD = SE \times \sqrt{N}$. The pooled effect size on the physical intervention and control groups will be compared using the mean differences and SE weight for the number of participants. Last, publication bias will be assessed by means of the method proposed by Egger, as well as visually on a funnel plot.

Subgroup analyses
Subgroup analyses will be performed based on the main factors that may cause heterogeneity, grouped as individual, task and contextual constraints. Main individual factors that could act as moderators of the exercise–cognition relation are age, weight status and skill level. Main types of task-related factors are qualitative and quantitative intervention characteristics, the type of cognition assessed and the stability of the intervention outcomes over time. Well-established quantitative parameters of the interventions are intensity, frequency and overall session duration. The qualitative characteristics of chronic exercise interventions to aid children’s and adolescents’ cognition have been tentatively classified in different ways in recent reviews. One classification primarily links the physical activity type to its
specific context of practice: physical education at school, active commuting in the urban route environment and individual versus team sport participation, indoors or outdoors. Another classification attempts to distinguish studies primarily focused on the metabolic demands of physical activity from those focused on or with deliberate manipulation of the coordinative and cognitive demands: aerobic training, skill-based training, cognitively demanding/enriched physical activity, traditional physical education or combinations of them.

The broad array of facets of cognitive functioning that may be differentially influenced by chronic exercise interventions include: (1) non-executive functions, such as non-verbal ability, spatial ability; (2) core executive functions, which are inhibition, working memory, cognitive flexibility; (3) metacognitive functions (ie, higher-level executive functions), such as abstract reasoning, planning, problem solving; (4) cognitive life skills, such as goal setting, self-regulation; (5) academic achievement areas, such as mathematics, language, reading, total scores; (6) academic behaviours, such as on-task behaviours, organisation, attendance. Finally, the time of cognitive assessment after intervention cessation influences the effect size and may inform on the outcome stability.

The main contextual factor that may cause heterogeneity of results is the intervention setting: school, out-of-school or laboratory setting. Also, in school-based studies, whether the physical activity intervention enhanced/enriched physical education, classroom-based activity breaks during curricular time, or active play during recess time, must be taken into account.

Sensitivity analysis
Sensitivity analyses will be conducted excluding studies from the analysis one by one. It needs to be proved that the findings from the meta-analysis are not dependent on arbitrary or unclear decisions. The main argument for carrying out a sensitivity analysis in the present review protocol is the existence of large differences in (1) study design and (2) type of specific assessment tools used. (1) As regards the study design, as indicated under the subheading ‘Type of studies’, we propose to include RCTs, non-RCTs and control pre-post studies, which may largely differ in their ability to truly tap intervention outcomes. (2) As concerns the specific assessment tools used, they may differ in the extent to which they specifically tap the cognitive function of interest, or may lead to spurious results. For example, academic grades represent final outcome of achievement behaviours that are affected not only by cognitive, but also by motivational, emotional and social factors of the learning context. Furthermore, there also may be differences due to the sensitivity issue, among more narrowly focused cognitive test outcomes. For example, inhibitory control—one of the most commonly studied cognitive functions in developmental exercise–cognition studies—is multifaceted and has been therefore studied with different tests that tap inhibition of thoughts and memories (eg, Random Number Generation), inhibition as perceptual interference control challenging attention (eg, Eriksen flanker task, Stroop Colour-Word task, expressive attention scale of the Cognitive Assessment System), or inhibition at the behavioural response level (eg, stop-signal task).

DISCUSSION
A positive association between physical exercise programmes and academic performance has been reported more or less consistently by recent systematic reviews and meta-analyses that analysed this relationship. The commonality of the abovementioned systematic reviews and meta-analyses is that they all included academic performance outcomes that represent a key variable for policymakers of the education sector. On the other hand, they largely differed as regards other characteristics that must be considered to reach relevant conclusion. Several differences among studies can render the evidence base more or less useful and the take-home message more or less meaningful and generalisable for policymakers. They regard: study design; acute/chronic exercise research type; intervention type and length of follow-up period; type and specificity of outcome measures; type of individual, task-related, and contextual moderators acting on the relationship between physical activity and cognition/academic performance.

First of all, some reviews included not only interventional studies, but also those with cross-sectional or observational designs; this limits the strength of causal conclusions and of the call for more physical activity in school and in out-of-school settings as a means to aid cognitive development and successful academic achievement. A narrative review that was exclusively focused on interventional research included both, acute and chronic exercise studies, having each of them a different take-home message for policymakers. The transient cognitive benefits of an acute bout of exercise support the call for more physically active breaks interspersed during the sitting learning time and for more physically active academic lessons (eg, ‘moved maths.’). On the other hand, the cognitive benefits of a longer-lasting chronic exercise programme support the call for legislative changes in favour of enhanced physical education and physical activity promotion in out-of-school settings.

To the best of our knowledge, only one systematic review included a RCT. It considered a broad range of outcomes of aerobic exercise programmes including cognition, academic behaviour and achievement, as well as psychosocial functioning outcomes. However, this review did not provide data for the impact of aerobic exercise programmes on each academic performance component, nor did it include, among the studies with psychosocial outcomes, those regarding physical activity...
effects on cognitive life skills that are linked to successful academic behaviour and achievement.

The lack of separate subgroup analyses of data according to the different academic performance areas or types of cognitive function assessed is common to most of the existing reviews. This limits the possibility to obtain a differentiated view on what type of physical activity interventions work best to reap specific cognitive/academic benefits. Also, the applied conclusions that can be drawn from many of the existing reviews are limited, as explicitly acknowledged, by the use of different measurement tools and the paucity and diversity of follow-up periods.

The present protocol is aimed at overcoming these limitations by performing subgroup analyses that take into account these issues in combination. Particularly, we follow the call by Tomporowski et al to distinguish between cognitive and metacognitive outcomes of physical activity in order to investigate their role in a hypothesised mediational chain linking chronic physical activity and academic performance. The authors state that cognitive assessments in developmental exercise and cognition research prioritise tools that test the cognitive functions of interest during ‘on-line’ processing.

To explain how exercise impacts children’s metacognitive processes and academic performance that develop along a wider time scale, they recommend expanding the view on exercise–cognition relations to encompass cognitive–social factors that underlie the personal awareness of own skills in achieving short-term and long-term goals. The present protocol provides an attempt in this direction, expanding the usual framework for exercise–cognition reviews to encompass cognitive life skills and separately analyse cognitive, metacognitive and academic performance outcomes.

As an outlook for future research, CDC encouraged analysing the same variables in any given category, to make a summary statement about the magnitude of the effect of physical exercise on academic performance variables. Singh et al recognised the inclusion of different study designs and outcome measures as a limitation of conclusions. Tomporowski et al recommended improving the information regarding the qualitative and quantitative characteristics of physical activity programmes that enhance children’s neurocognitive performance, and to consider the possible moderators and mediators acting on the relationship between chronic exercise and cognition/academic performance during development. Since it is common that moderator variables are included in interventional studies, it will be possible to apply the subgroup and moderation analyses proposed in the Methods section. However, there is still a paucity of studies addressing mediation, which remains an issue in need of further research before meta-analytic conclusions can be drawn.

The proposed protocol also presents limitations that derive from the deliberate choice of a given trade-off setpoint between inclusion and exclusion criteria to reach relevant conclusions for policymakers of the education and health sectors. Specifically, the broad and heterogeneous array of relevant outcomes that will be included has costs as well as benefits. It offers the possibility to tap different—from biological to behavioural—aspects related to cognitive functioning and academic performance. Nevertheless, the fact that included studies can broadly differ in assessed outcomes or tests used for assessing the same outcome might lead to underestimation of overall effect size, or to highly variable effect sizes among outcome subsets. On the other hand, heterogeneity of studies will be limited regarding participants’ characteristics, since studies involving participants with atypical development will be excluded. Nevertheless, in this way, the generalisability of results will be lowered, being traded for a higher comparability of intervention outcomes.

Given the importance of the entire developmental period—from infancy to late adolescence—for brain development and therefore for academic performance, a more detailed and comprehensive view on the exercise–cognition relation during development is needed for education and health professionals to orient policy efforts. This protocol provides a clear and structured procedure for maximising the extraction of relevant information and provides summarised information regarding the impact of long-term physical activity programmes on children’s cognition and academic performance.

**Ethics and dissemination**

Ethical approval will not be needed to apply this review protocol because data will be extracted from published studies and there will be no concerns about privacy. The results of such reviews can be best disseminated by publication in a peer-reviewed journal that broadly reaches researchers interested in hypotheses testing and policymakers interested in the translatability of scientific evidence into good practices.

Developing programmes and strategies to promote physical activity is justified by the international physical activity guidelines, which recommend that children participate in at least 60 min of daily physical activity. Nonetheless, the prevalence of overweight children and the total sedentary time that children daily accumulate have risen substantially in the past three decades in most countries. Therefore, schools and communities are encouraged to implement children’s physical activity time. However, it is necessary to further our understanding of how to capitalise on physical activity effects on cognitive function and life skills relevant to successful academic performance. The conclusions of the proposed type of systematic review and meta-analysis may support the decisions of school boards, school administrators and policy developers with scientifically grounded arguments on why to maintain or increase the time devoted to curricular or extracurricular physical activity.
and on what type of activities help reap largest cognitive and academic benefits.

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Contributors VM-V and CA-B designed the study. VM-V was the principal investigator and guarantor. MS-L, CA-B and VM-V were the main coordinators of the study. MS-L, CA-B, MJ-P and IC-R conducted the study. IC-R, CP and MJ-P provided statistical and epidemiological support. VM-V wrote the article with the support of MS-L, CP and CA-B. All the authors revised and approved the final version of the manuscript.

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REFERENCES

The Effect of Physical Activity Interventions on Children’s Cognition and Metacognition: A Systematic Review and Meta-Analysis

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Objective: The objective was twofold: to assess the effect of physical activity (PA) interventions on children’s and adolescents’ cognition and metacognition; and to determine the characteristics of individuals and PA programs that enhance the development of cognitive and metacognitive functions.

Method: We systematically searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, and PsycINFO databases from their inception to October 16, 2016. Intervention studies aimed at examining the exercise–cognition interaction at a developmental age were included in this systematic review and meta-analysis. Random-effects models were used to calculate pooled effect size (ES) values and their corresponding 95% CIs. Subgroup analyses were conducted to examine the effect of participants’ and PA programs’ characteristics.

Results: A total of 36 studies were included in this systematic review and meta-analysis. Pooled ES estimations were as follows: nonexecutive cognitive functions 0.23 (95% CI = 0.09–0.37); core executive functions 0.20 (95% CI = 0.10–0.30), including working memory (0.14 [95% CI = 0.00–0.27]), selective attention—inhibition (0.26 [95% CI = 0.10–0.41]), and cognitive flexibility (0.11 [95% CI = −0.10 to 0.32]); and metacognition 0.23 (95% CI = 0.13–0.32), including higher-level executive functions (0.19 [95% CI = 0.06–0.31]) and cognitive life skills (0.30 [95% CI = 0.15–0.45]).

Conclusion: PA benefits several domains of cognition and metacognition in youth. Curricular physical education interventions and programs aimed at increasing daily PA seem to be the most effective.

Key words: cognition, metacognition, physical activity, exercise

mainly focused on describing the characteristics of interventions in terms of intensity, frequency, and session or intervention duration. Two previous meta-analyses have examined the role of the qualitative characteristics of PA interventions in the relationship between exercise and children's cognition, although they did not distinguish between the cognitive outcomes that improved and those that did not.

To our knowledge, no review has evaluated the independent PA effects on each core cognitive executive function (inhibition, working memory, and cognitive flexibility) and metacognition, extending the later construct to encompass a neuroscience perspective on higher-level executive functions and a social-cognitive perspective on cognitive life skills. Tomporowski et al. proposed that the benefits of quantitatively and/or qualitatively different PA interventions in multiple cognitive subdomains might be interrelated through mediation chains that link increased executive function to improvements in metacognition and academic achievement. However, current mediation evidence is only cross-sectional in nature and has not yet addressed the potential role of metacognition, that is, the ability to supervise and manage cognitive processes and to use knowledge to regulate behaviors, and distinguish it from cognition, which is understood as the set of mental processes that contribute to perception, memory, intellect, and action. In sum, scientific evidence on the relationship between PA and cognitive performance in childhood and adolescence, particularly with regard to possible moderators and mediating mechanisms, is clearly insufficient to explain how and why PA may have an impact on academic achievement.

Thus, the aims of this systematic review and meta-analysis were: to assess the effect of PA interventions on children's and adolescents' cognition, distinguishing between core executive functions and metacognition; and to determine which individual and joint PA program characteristics are most favorable to aid the development of cognitive and metacognitive functions.

METHOD

This systematic review and meta-analysis was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement and the Cochrane Collaboration Handbook. The protocol for this systematic review and meta-analysis was registered on PROSPERO (CRD42015029913) and is published elsewhere.

Search Strategy

A literature search was independently performed by two reviewers (C.A. and C.P.), and studies were identified through a combination of resources. First, a systematic search was performed in MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science, and PsycINFO databases from their inception to October 16, 2016. The search strategy combined the following relevant terms: "physical activity," "physical education," "exercise," "fitness," and "sport"; "cognition," "executive," "executive function," "cognitive control," "intelligence," "memory," "attention," and "metacognition"; "life skills," "goal setting," "problem solving," and "self-regulation"; "brain development," "brain health," "neural," "neuroelectric," "neurotrophic," "neurotrophin," and "hormone"; "children," "childhood," "pre-schooler," "schoolchildren," "preadolescent," "adolescent," and "adolescence" and "trial" and "effect." Second, the reference lists of the included articles in this review, and the list of those included in previous systematic reviews and meta-analyses, were reviewed for any additional relevant study.

Eligibility

Studies concerning the relationship between PA interventions and children's and adolescents' cognition were included in the meta-analysis. Inclusion criteria were as follows. Regarding participants, studies included healthy children from 4 to 18 years of age (whose target population was not preterm children or with disorders that could limit the generalization of the data). Regarding intervention characteristics, studies included PA programs aimed at enhancing (referring to an increased amount of time devoted to PA) or enriching (referring to a deliberate increase in nonphysical, that is, coordinative and/or cognitive, demands of PA tasks) PA sessions. We classified the interventions into school-time and after-school-time PA. Among the former, we distinguished the following: curricular physical education, integrated PA (active breaks or teaching subjects such as mathematics with physically active tasks), and extracurricular PA (active recess or lunch time PA); the latter included after-school PA or sports programs. Regarding outcomes, studies included cognitive performance assessments of nonexecutive cognitive functions, core executive functions, and/or metacognition. Finally, regarding study design, studies included randomized controlled trials (RCTs), non-RCTs, and controlled pre-post studies.

Studies were excluded when they met the following exclusion criteria: included an adult population; were based on the acute measurement of the effect of PA on cognition (i.e., those measuring cognition during or immediately after the exertion of single bouts of physical activity); included children with any physical or mental disorders that could impede or limit their participation in the intervention program activities; and were not published in English or Spanish.

Search and Data Extraction

Two researchers (C.A. and C.P.) independently screened all abstracts of the retrieved articles, excluding those studies that did not meet eligibility criteria. The full texts of selected studies were retrieved, and the same two authors independently collected the following data of each study meeting the previously defined criteria: year of publication, country of the study, number of participants (in control and intervention groups), age of participants, control condition and PA intervention(s) duration, school time when PA interventions took place and task characteristics of the intervention, intervention design, length of intervention in weeks, and main outcomes and instruments for their measurement (Tables S1 and S2, available online). The authors of the included studies were contacted when a lack of information was detected. Disagreements in data collection were settled by consensus. Cohen’s κ was used to assess agreement between reviewers.

Studies were classified into three groups according to their measured outcomes: nonexecutive cognitive functions; core executive functions including: working memory, cognitive flexibility, and inhibition, with the latter including response inhibition and interference control for selective attention; and metacognition, including higher-level executive functions (planning, fluid
intelligence–abstract reasoning, and problem solving)\textsuperscript{29} and cognitive life skills.\textsuperscript{30}

Quality Assessment
After concealing information about authors, affiliations, date and source of each manuscript, two investigators (C.A. and I.C.) independently assessed their methodological quality. Disagreements were solved by consensus.

The Jadad scale\textsuperscript{37} was used to assess the methodological quality of RCTs. The scale included the evaluation of three domains: randomization, double blinding, and description of withdrawals and dropouts. Each item could be scored as “1” or “0” if the study did or did not satisfy it. Randomization and double blinding could score one extra point if they were described in detail. Based on this, each study could score between 0 and 5.

The Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies\textsuperscript{38} was used to assess the quality of non-RCTs and controlled pre–post studies. Studies were evaluated in seven domains: selection bias, study design, confounders, blinding, data collection method, and withdrawals and drop-outs. Each domain could be scored as strong, moderate, or weak, and studies could be classified as strong (with no weak domains), moderate (with one weak domain), or weak (with two or more weak domains).

Statistical Analysis
Detailed statistical procedures used in this meta-analysis have been reported elsewhere.\textsuperscript{39} A standardized mean difference score was calculated for each specific variable using Cohen’s d index,\textsuperscript{39} in which positive ES values indicate higher scores in outcomes in favor of the intervention group. The pooled ES was estimated using a random-effects model based on the DerSimonian and Laird method. Heterogeneity across studies was assessed using the I\textsuperscript{2} statistic. Values of <25%, 25% to 50%, and >50% are considered to represent small, medium, and large amounts of inconsistency, respectively. The influence of each study in the pooled ES estimates was examined using sensitivity analyses. For assessing publication bias, the Egger regression asymmetry test\textsuperscript{40} was used. The trim-and-fill\textsuperscript{41} computation was used to assess the effect of publication bias on the interpretation of results. Only those studies providing complete data for pre- and post-intervention measurements and including a control group were included in the meta-analysis.

Some additional statistical aspects that should be detailed here were as follows. First, when studies included two cohorts or two intervention groups, their data were analyzed as independent samples. Second, when studies used two or more tests for measuring the same variable, the average effect size was calculated. Third, when studies reported two or more follow-up measurements, only the last measurement was considered. Finally, an interference outcome for a Stroop-like test or Flanker-like test was calculated as follows: incongruent test–congruent test or commission test–omission test.

A pooled ES was calculated for the following three groups of cognitive domains: nonexecutive cognitive functions; core executive functions; and metacognition. In addition, subgroup analyses were conducted considering individual tasks within each domain: core executive function (working memory, cognitive flexibility, and selective attention–inhibition [for the last, an additional analysis was conducted by considering selective attention and inhibition measurements separately]); and metacognition (higher-level executive functions [including planning, fluid intelligence, e.g., reasoning and problem solving, and creativity] and cognitive life skills [including self-awareness of goal setting, problem solving, and positive thinking skills]).

Subgroup analyses were performed based on different aspects of the intervention: the school time when PA intervention took place, distinguishing between curricular physical education, integrated or extracurricular PA, and after-school PA and sports programs; and task characteristics, distinguishing between quantitative and qualitative characteristics of the PA intervention, considering whether the interventions were designed as enhanced or enriched PA. Interventions could be both enhanced and enriched when the manipulation included additional physically active times, and deliberately increased coordinative and cognitive task requirements.

Other subgroup analyses were performed based on some variables that could act as confounders: children’s weight status, comparing the effectiveness of studies considering when studies provided the effectiveness of the interventions on overweight and obese children; and time and accuracy of cognitive test performance, considering the papers that reported the effect of the intervention on accuracy, time, or both separately.

In addition, random-effects meta-regression analyses were performed to determine whether the children’s age (in years), the length of the intervention (in weeks), and the study quality could be related with the effectiveness of the intervention on each outcome.

Statistical analyses were performed using StataSE software, version 14 (StataCorp, College Station, TX).

RESULTS
The search retrieved a total of 4,582 articles. Of those, 777 were removed as duplicates, and 3,805 were screened based on the title and the abstract (Figure S1, available online). The overall percentage of agreement between the reviewers on data extraction, as assessed using Cohen’s k statistic, was 0.91.

A total of 36 papers were included in this systematic review,\textsuperscript{5,6,9,10,19,20,42,52} of which only five were non-RCT designs.\textsuperscript{42,44,59,64,66} Characteristics of the included studies are displayed in Table S1 (available online). Studies were conducted in 15 countries: United States (10 studies), India (5), Italy (5), Australia (2), Germany (2), Greece (2), the Netherlands (2), Denmark (1), Iran (1), South Africa (1), Spain (1), Switzerland (1), Taiwan (1), Turkey (1), and the United Kingdom (1). The total sample included 5,527 children and adolescents (2,308 in control group), who were 4 to 14 years of age. Three studies included only overweight and obese children,\textsuperscript{48,49,57} and three studies addressed the moderating role of children’s weight status.\textsuperscript{10,47,53}

The interventions, which were mostly performed during curricular school time, were aimed at increasing the amount of PA or qualitatively enriching PA,\textsuperscript{9,10,19,20,43,46,47,51,53,54,61,62,64–67,69} and at adding classroom-based PA during daily lessons targeted to learning various subjects through being physically active (integrated PA),\textsuperscript{50,60,63,68} unrelated to subject learning (active breaks),\textsuperscript{52,71} or PA during recess (e.g., active lunch).\textsuperscript{70} Furthermore, several studies developed after-school PA programs,\textsuperscript{6,42,44,45,48,49,55–57,72} two of them during summer camp.\textsuperscript{58,59}
Overall, the interventions resulted in an increase in PA time from 15 to 120 minutes per day, except one intervention study that included 480 minutes per day, 7 days per week, but was limited to the time of summer camp vacations. Only three studies included data from two cohorts and 14 studies included more than one intervention group, four of them without a control group. For those studies with more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group. Studies including more than one intervention group, experimental groups differed in exercise intensity, duration, PA type, or the moderate intensity group.

Systematic Review
Table S2 (available online) describes the relevant characteristics of the included studies. Seven studies reported information regarding the efficacy of PA interventions on cognitive domains that do not or only minimally rely on executive function. In all of them, nonexecutive functions improved as a result of the intervention. Four of those studies included two experimental groups that differed in exercise intensity, duration, PA type, and yielded controversial results. Two studies did not find dose–response relationships; however, two other studies found that increases in the duration and intensity of the sessions was associated with greater improvements in nonexecutive functions. A total of 29 studies reported improvements in core executive functions. Eleven studies included more than one intervention group: three did not find differences between intervention groups, and the remaining eight studies reported differences in favor of aerobic exercise, yoga, or both. One study failed to find significant differences in improvements.

Study Quality
Of the 31 RCTs in which quality was assessed using the Jadad scale, only two scored four points, and 13 scored three points. Of the 26 studies included information regarding the randomization method, and only two did not provide information about the withdrawals and drop-outs. However, only four studies properly described the double-blinding method used (Table S3, available online). Of the five non-RCTs in which quality was assessed using the EPHPP tool, four scored as weak and one as moderate. The worst-scored items were the following: data collection, because the tools for primary outcomes were not described as reliable and valid; and the descriptions of the withdrawals and drop-outs, because the papers did not describe the number and/or the reasons for the withdrawals and drop-outs (Table S3, available online).

Meta-Analysis
Nonexecutive Cognitive Functions. The pooled ES estimation for PA intervention effects on cognitive performances not, or only minimally, relying on executive functions was 0.23 (95% CI = 0.09–0.37). There was small heterogeneity among the studies (I^2 = 21.9%; p = .199) (Figure 1A).

Core Executive Functions. For core executive functions (including performance on selective attention tests requiring executive interference control), the pooled ES estimation was 0.20 (95% CI = 0.10–0.30). There was large heterogeneity between the studies (I^2 = 70.0%; p < .001) (Figure 1B).

Data for the working memory subgroup analysis showed a pooled ES of 0.14 (95% CI = 0.00–0.27). There was medium heterogeneity among the studies (I^2 = 48.0%; p = .027).

The pooled ES for selective attention–inhibition subgroup analysis, including the outcomes of selective attention tests requiring executive interference control, was 0.26 (95% CI = 0.10–0.41). There was large heterogeneity among the studies (I^2 = 76.0%, p < .001). When a complementary analysis was performed for measures of inhibition process and selective attention separately, the pooled ESs were 0.38 (95% CI = 0.13–0.63) and 0.13 (95% CI = -0.07 to 0.33), respectively. There was large heterogeneity in both groups of studies (I^2 = 86.2% and 66.8%, respectively).

Finally, for the cognitive flexibility subgroup, the pooled ES was 0.11 (95% CI = -0.10 to 0.32), with large heterogeneity across studies (I^2 = 68.7%; p = .013).

Metacognition. The pooled ES for PA programs on metacognition was 0.23 (95% CI = 0.13–0.32), with small heterogeneity between studies (I^2 = 4.7%; p = .398) (Figure 1C).

The pooled ES for the subgroup of higher-level executive functions was 0.19 (95% CI = 0.06–0.31), and heterogeneity was small (I^2 = 12.9%; p = .315).

For cognitive life skills, the pooled ES estimation was 0.30 (95% CI = 0.15–0.45) with no heterogeneity among the studies (I^2 = 0.0%, p = .549).

Subgroup Analysis. Subgroup analysis by the school time when PA interventions took place (curricular physical education, integrated or extracurricular PA, and after-school PA) showed that curricular physical education programs broadly benefited the following: nonexecutive cognitive functions (ES = 0.42; 95% CI = 0.14–0.70); the selective attention–inhibition component of core executive functions (ES = 0.41; 95% CI = 0.15–0.67); and higher-level executive functions (ES = 0.25; 95% CI = 0.06–0.43). On the other hand, no PA intervention influenced working memory or cognitive flexibility. This subgroup comparison could not be performed for cognitive life skills, which were measured only in curricular physical education programs (ES = 0.30; 95% CI = 0.15–0.45) (Table S4, available online).

Subgroup analysis based on task characteristics of the intervention (quantitatively enhanced PA, qualitatively enriched PA, or both) (Table S4, available online) showed that nonexecutive cognitive functions were improved mostly
in enhanced PA programs (ES = 0.21; 95% CI = 0.07–0.35). With regard to core executive functions, working memory benefited mostly from enhanced PA programs (ES = 0.28; 95% CI = 0.04–0.52), whereas selective attention—inhibition benefited mostly from enriched PA programs (ES = 0.49; 95% CI = 0.05–0.93), and cognitive flexibility did not benefit from any type of intervention. Finally, higher-level executive functions improved through enhanced PA (ES = 0.21; 95% CI = 0.07–0.35).

Subgroup analysis by children’s weight status could be performed only for the selective attention—inhibition sub-domain. Six overweight and/or obese children comparison groups were extracted from four studies. The pooled ES estimation when considering only overweight and/or obese children was 0.02 (95% CI = 0.00 to 0.02).

When subgroup analyses were conducted based on the individual and joint effects on cognitive performance time and accuracy, only inhibition and cognitive flexibility could be considered (Table S5, available online). The pooled ES for studies focused on accuracy outcomes was 0.15 (95% CI = 0.01–0.29), for those focused on reaction time, or time to test completion −0.25 (95% CI = −0.45 to −0.04), and for those including both accuracy and performance time, the pooled ES for accuracy was 0.29 (95% CI = 0.04–0.54), whereas the pooled ES for time was −0.05 (95% CI = −0.20 to 0.11).

Random-Effects Meta-Regression Model. The random-effects meta-regression model showed that the effect of PA interventions on children’s nonexecutive functions was positively associated with children’s age (β = 0.08; 95% CI = 0.00–0.15; p = .036) and on children’s working memory was negatively associated with length of intervention (β = −0.01; 95% CI = −0.02 to −0.01; p = .023) (Table S6, available online).

Moreover, this model showed that study quality was also not related to the heterogeneity observed across the studies.

Sensitivity Analyses. Sensitivity analyses suggested that the pooled ES estimation for working memory was modified only when removing studies by Fisher et al.,51 Kamijo et al.,55...
Publication Bias. Funnel plots indicated significant publication bias for the pooled subgroup analyses of working memory only ($p < .10$) (Figure S2, available online). In addition, trim-and-fill computation showed that six studies were needed for removing publication bias from working memory subgroup ($p = .628$).

**DISCUSSION**

To our knowledge, this is the first systematic review and meta-analysis that separately summarizes evidence regarding the effectiveness of PA interventions on children’s and adolescents’ nonexecutive cognitive functions, core executive functions, and metacognition. Overall, this review shows that PA programs benefit multiple facets of nonexecutive (ES = 0.23), executive (ES = 0.20), and metacognitive (ES = 0.25) functions and skills in children and adolescents. In addition, our data showed that curricular physical education and programs aimed at increasing the amount of exercise seem to be the most effective.

Subgroup analyses showed that the domains of cognition most sensitive to exercise were working memory (ES = 0.14), inhibition (ES = 0.26), higher-level executive functions (ES = 0.19), and cognitive life skills (ES = 0.30). However, individual and task characteristics, as well as the school time when the PA interventions took place, have some influence on these effects. Participants’ age seems to uniquely act as an amplifier of the size of intervention effects in nonexecutive functions. With regard to the context in which PA interventions were conducted, curricular physical education...
lessons seem to be the most appropriate framework to improve children’s cognition. The influence of the nature of activities included in the PA programs seems to be greater on core and higher-level executive functions. Although increasing the amount of PA appears to improve children’s working memory and higher-level executive functions, enriched PA programs with flexible cognitive-oriented tasks implying greater coordinative and cognitive demands seem to particularly improve inhibitory efficiency.

Developmental evidence concerning the beneficial effects of PA interventions on cognition has been growing during the last decades. However, not all exercise produces the same results, in such a way that animal studies have shown that complex and random activities result in greater neural growth in the hippocampus, cerebellum, and cerebral cortices than simple and repetitive actions. Thus, at present, evidence consistently supports that not all forms of exercise influence cognition equally, and that exercises requiring complex, controlled, and adaptive cognition and movement have a greater impact on executive functions.

In this meta-analysis, we classified as “enriched” only those PA interventions in which the coordinative and cognitive demands were deliberately manipulated. Such kinds of deliberate cognitive enrichment of exercise programs seem to be useful for promoting the development of inhibitory functions, which plays a crucial role in the achievement of academic goals and life skills that are essential to positive youth development.

In addition, our meta-analysis shows that when speed and accuracy in tasks tapping core executive functions are considered, only accuracy is improved by PA interventions.

### Table: Enriched PA Interventions

<table>
<thead>
<tr>
<th>References</th>
<th>Effect size (95% CI)</th>
<th>%</th>
<th>Weight</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arroyo et al 2014 (EG1) (43)</td>
<td>0.15 (-0.80, 0.60)</td>
<td>2.02</td>
<td>IGF-M: Abstract/Verbal Reasoning</td>
<td></td>
</tr>
<tr>
<td>Arroyo et al 2014 (EG2) (63)</td>
<td>1.14 (0.42, 1.86)</td>
<td>1.66</td>
<td>IGF-M: Abstract/Verbal Reasoning</td>
<td></td>
</tr>
<tr>
<td>Davis et al 2007 (EG1) (48)</td>
<td>0.07 (-0.43, 0.57)</td>
<td>3.38</td>
<td>CAS Planning</td>
<td></td>
</tr>
<tr>
<td>Davis et al 2007 (EG2) (48)</td>
<td>0.28 (-0.23, 0.78)</td>
<td>3.31</td>
<td>CAS Planning</td>
<td></td>
</tr>
<tr>
<td>Davis et al 2011 (EG1) (49)</td>
<td>0.06 (-0.31, 0.42)</td>
<td>6.15</td>
<td>CAS Planning</td>
<td></td>
</tr>
<tr>
<td>Davis et al 2011 (EG2) (49)</td>
<td>0.18 (-0.19, 0.54)</td>
<td>6.15</td>
<td>CAS Planning</td>
<td></td>
</tr>
<tr>
<td>Fisher et al 2011 (51)</td>
<td>0.00 (-0.52, 0.52)</td>
<td>3.13</td>
<td>CAS Planning</td>
<td></td>
</tr>
<tr>
<td>Reed et al 2013 (1) (64)</td>
<td>-0.03 (-0.44, 0.37)</td>
<td>5.06</td>
<td>Standard Progressive Matrices: Fluid intelligence</td>
<td></td>
</tr>
<tr>
<td>Reed et al 2013 (2) (64)</td>
<td>0.32 (-0.09, 0.73)</td>
<td>4.94</td>
<td>Standard Progressive Matrices: Fluid intelligence</td>
<td></td>
</tr>
<tr>
<td>Reed et al 2013 (3) (64)</td>
<td>0.39 (-0.01, 0.79)</td>
<td>5.18</td>
<td>Standard Progressive Matrices: Fluid intelligence</td>
<td></td>
</tr>
<tr>
<td>Reed et al 2013 (4) (64)</td>
<td>0.29 (-0.12, 0.70)</td>
<td>4.94</td>
<td>Standard Progressive Matrices: Fluid intelligence</td>
<td></td>
</tr>
<tr>
<td>Subramanian et al 2015 (67)</td>
<td>0.26 (0.02, 0.50)</td>
<td>13.17</td>
<td>RFFT Designs/Reactions: Creativity</td>
<td></td>
</tr>
<tr>
<td>Van der Nat 2016 (70)</td>
<td>-0.07 (-0.46, 0.35)</td>
<td>5.30</td>
<td>Tower of London: Planning</td>
<td></td>
</tr>
<tr>
<td>Overall (I-squared = 12.9%, p = 0.315)</td>
<td>0.19 (0.06, 0.31)</td>
<td>64.38</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Figure 1 (continued)

![Figure 1](https://www.jaacap.org)
Behind this finding could be the fact that children are not able to independently control their speed and accuracy in response to an impulse, but they could be able to control the speed–accuracy trade-offs; therefore, the sensory performance (accuracy) could be improved without improving the motoric stage (reaction time).

There has been a growing concern about the worldwide alarming increase in overweight and obesity prevalence rates in children. Physical inactivity and changes in eating habits have been identified as key factors for this dramatic change in children’s body composition. Evidence suggests a negative complex relationship between weight status and motor and cognitive development, although changes in the anatomy and function of the brain of overweight and obese children have also been highlighted. Mediation analyses suggest that motor development mediates the relationship between weight status and cognitive performance, and therefore it seems important to elucidate whether it would be expected that overweight and/or obese children involved in PA programs reap greater benefits in terms of cognitive development and academic achievement than their normal-weight peers. Our results did not show a significantly higher ES in overweight and/or obese children in the intervention groups than the overweight and/or obese children in the control groups. Nevertheless, these results should be considered with caution, because most of the studies did not provide effect data by weight status, and only six presented separate data for overweight and/or obese children.

The main point of our findings is that they consistently support that curricular PA programs seem to be the most effective interventions for promoting the development of a broad range of cognitive and metacognitive functions and skills. Therefore, increasing physical education curricular time does not negatively affect but also even promotes cognitive development and academic achievement. Moreover, it should be taken into account that although this review has exclusively focused on school-based structured PA interventions, the benefits on health and cognition of any of these programs would presumably be extended far beyond the school. Thus, scientific evidence on the effectiveness of interventions that jointly include motor and cognitive stimulation in school-based activities, along with that on the promotion of complementary outdoor free-play experiences, is necessary to amplify the benefits of school-based enriched PA programs.

Nevertheless, it should also be noted that there is a lack of information regarding school-based interventions design; therefore, studies should describe in more detail the methodologies, cognitive variables involved in the interventions, and the compliance and acceptability of the programs in order to make definitive conclusions regarding their effectiveness. Furthermore, considering the importance of early brain development processes in the acquisition of core executive functions, metacognition, and life skills later in life and their relation to academic achievement, it seems essential to gather information regarding the maintenance of the beneficial effects of PA interventions on children’s and adolescents’ cognition over time, after intervention cessation. We have not been able to state how long the benefits of school-based PA programs could be maintained over time, as there is a lack of follow-up studies measuring outcomes after intervention cessation.

The design of PA and motor learning interventions for children and adolescents with contents and delivery strategies tailored to specifically enhance their executive function is emerging as a promising way to promote motor and cognitive development. However, well-designed PA programs joining motor and cognitive stimulation should be complemented with the great variety of outdoor free-play experiences that seem to amplify the benefits of school-based enriched PE programs.

The limitations of this study are those common to systematic reviews and meta-analyses. In addition, we should highlight the following aspects that could limit the robustness of our results. First, we found significant publication bias only for working memory; however, we cannot affirm that publication bias did not affect other variables due to poor results being unpublished because we did not search for unpublished studies or include grey literature. Second, the results of this meta-analysis were obtained after some data manipulation, which could generate some bias. Third, less than 50% of the studies included in the systematic review scored as good quality; conversely, meta-regression models showed that study quality was not related to heterogeneity among studies. Fourth, cognitive performance was measured across the studies using a wide variety of tools, but measurements were standardized by calculating the ES. Finally, participants’ age and the length or type of interventions could influence our estimations; thus, subgroup analysis and meta-regressions were performed to minimize this possible source of bias and heterogeneity.

In conclusion, this systematic review and meta-analysis supports that PA interventions are useful strategies to foster the development of children’s cognition (nonexecutive cognitive functions, core executive functions, and higher-level executive functions). Moreover, this study shows that curricular exercise and programs aimed at increasing the time dedicated to PA are more likely to produce an effect on children’s and adolescents’ cognition. This information should be jointly considered with previous research that has highlighted the positive effects of physical activity on children’s health. It also might be relevant for policy and decision makers in order to design new strategies not only for promoting children’s cognitive development, and, as a consequence, better academic performance, but also for improving mental health (reducing anxiety/depressive disorders, improving self-esteem) and preventing cardiovascular disease. Including this evidence in good practice guidelines in education and public health might lead to counteracting the current school trend of PA reduction. For this purpose, qualified professionals are essential in designing PA strategies tailored to enhance children’s and adolescents’
executive functions, and thereby motor and cognitive development promotion.14,80,81 Future reviews should address the efficacy for children’s cognitive development, of environment-based programs tailored to create favorable surroundings for playground games and PA.

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REFERENCES


3. **Manuscript 3**: Academic achievement and physical activity: a meta-analysis.
Academic Achievement and Physical Activity: A Meta-analysis

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CONTEXT: The effect of physical activity (PA) on different areas of academic achievement and classroom behaviors and how different characteristics of PA interventions could modify the effect remain unclear.

OBJECTIVE: The objective was twofold: (1) to assess the effect of PA interventions on academic achievement and classroom behaviors in childhood and (2) to determine the characteristics of individuals and PA programs that enhance academic performance.

DATA SOURCES: We identified studies from the database inception to October 16, 2016.

STUDY SELECTION: We selected intervention studies aimed at examining the effect of exercise on academic achievement and classroom behaviors at developmental age.

DATA EXTRACTION: Random-effects models were used to calculate pooled effect size for all primary outcomes (language- and mathematics-related skills, reading, composite score, and time in on-task behavior). Positive values represent a direct relationship between PA programs and academic achievement scores or on-task behaviors.

RESULTS: A total of 26 studies (10,205 children, aged from 4 to 13) were included. Pooled effect size (95% confidence interval) estimates were as follows: (1) 0.16 (−0.06 to 0.37) for language-related skills; (2) 0.21 (0.09 to 0.33) for mathematics-related skills; (3) 0.13 (0.02 to 0.24) for reading; (4) 0.26 (0.07 to 0.45) for composite scores; and (5) 0.77 (0.22 to 1.32) for time in on-task behaviors.

LIMITATIONS: Limitations included the variety of tools used to measure academic achievement and the limited number of studies that reported the effect of after-school PA interventions.

CONCLUSIONS: PA, especially physical education, improves classroom behaviors and benefits several aspects of academic achievement, especially mathematics-related skills, reading, and composite scores in youth.
The development of core executive functions (inhibition, working memory, and cognitive flexibility) and metacognition have been closely related with academic achievement and classroom behaviors and are essential for healthy child development.1–4 Several aspects of cognition have been identified as positive markers of mental health (stress, sadness, and rest) during childhood.5 Furthermore, lower levels of cognition during childhood and adolescence are predictors of worse health parameters during adulthood such as psychological disorders, risk of cancer, and higher morbidity and mortality.6–9

In the last decade, a growing interest has emerged in studying the potential influence of physical activity (PA) on children’s cognitive functioning.10,11 This relationship seems to be mediated through enhanced angiogenesis, increased oxygen saturation and glucose delivery, improved cerebral blood flow, and increased neurotransmitter levels.12 Changes in structural brain volumes after PA programs as measured by MRI have also been observed13 as well as brain functioning determined by electrical activity recordings.14 Considering the importance of the brain’s development process in the acquisition of core executive functions, metacognition, and life skills later in life and the relationship of improvements on these neurocognitive dimensions with academic achievement, it seems essential to determine the beneficial effects of PA interventions on children’s and adolescents’ academic achievement and classroom behaviors and identify the characteristics of PA interventions that could modify the effect on these areas.

Thus, our aims with this systematic review and meta-analysis were the following: (1) assess the effect of PA interventions on children’s and adolescents’ academic achievement and classroom behaviors and (2) determine the individual and PA programs’ characteristics that are most favorable to aid the development of academic performance.

METHODS

This systematic review and meta-analysis was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement21 and the Cochrane Collaboration Handbook.22 The protocol of this systematic review and meta-analysis has been published elsewhere.23

SEARCH STRATEGY

Two reviewers independently performed a literature search (C.A.B. and C.P.). A combination of sources was used to identify the studies. First, a systematic search was performed in Medline, Embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science, and PsycINFO databases from their inception to October 16, 2016. The search strategy combined the following relevant terms: (1) “physical activity,” “physical education,” “exercise,” “fitness,” and “sport”; (2) “cognition,” “executive,” “executive function,” “cognitive control,” “intelligence,” “memory,” “attention,” and “metacognition”; (3) “academic,” “academic achievement,” “academic grades,” “academic behavior,” “academic performance,” and “classroom behavior”; (4) “children,” “childhood,” “preschooler,” “schoolchildren,” “preadolescent,” “adolescent,” and “adolescence”; and (5) “trial” and “effect.” Second, the reference lists of the included articles in this review and the list of those included in previous systematic reviews and meta-analyses were reviewed for any additional relevant studies.

STUDY SELECTION

Studies on the relationship between PA interventions and children’s and adolescents’ academic achievement and on-task behaviors time were included in the systematic review and meta-analysis. Inclusion criteria were as follows: (1) Participants included healthy children and adolescents at developmental age. (2) Intervention characteristics included exercise programs aimed at enhancing (referring to an increased amount of time devoted to PA) or enriching (referring to a deliberate increase in nonphysical [coordinative and/or cognitive] demands of PA tasks) PA sessions. We classified interventions into schooltime and after schooltime PA. Among the former, we distinguished the following: curricular physical education (PE), integrated PA (active breaks or teaching subjects such as math with physically active tasks); and extracurricular PA (active...
recess or lunch time PA); the latter included after-school PA or sports programs. (3) Outcomes included academic achievement assessed by curricular-based marks or a specific test and on-task behaviors’ time. (4) Finally, study design, which included randomized controlled trials (RCTs) and quasiexperimental and controlled pre-post studies.

Studies were excluded when they had any of the following characteristics: (1) adult populations were included, (2) studies were based on acute PA programs, (3) children with any physical or mental disorders that could impede or limit their participation in the intervention program activities were included, and/or (4) studies were published in languages other than English or Spanish.

Search and Data Extraction

Two researchers (C.A.B. and C.P.) independently screened all abstracts of the retrieved articles, excluding those studies that did not meet eligibility criteria. The same 2 authors independently collected the following data from each selected study: (1) year of publication, (2) country of the study, (3) number of participants (in control groups [CGs] and intervention groups [IGs]), (4) age of participants, (5) control condition and PA intervention(s) duration, (6) schooltime when PA interventions took place and task characteristics of the intervention, (7) intervention design, (8) length of intervention in weeks, and (9) main outcomes and instruments for their measurement (Tables 1 and 2).

When researchers detected a lack of information, the authors of the included studies were contacted. Disagreements among researchers in data collection were settled by consensus.

Risk of Bias

After concealing information about authors, affiliations, date, and source of each manuscript, 2 investigators (C.A.B. and I.C.R.) independently assessed their methodological quality. Disagreements were solved by consensus.

The Jadad Scale was used to assess the methodological quality of RCTs. The scale included the evaluation of 3 domains: randomization, double-blinding, and description of withdrawals and dropouts. Each item could be scored as “1” or “0” if the study satisfied it or not. Randomization and double blinding could score 1 extra point each if they were described in detail. On the basis of these extra points, each study could score between 0 and 5.

The Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies was used to assess the quality of quasiexperimental and controlled pre-post studies. Seven domains were evaluated: selection bias, study design, confounders, blinding, data collection method, withdrawals, and dropouts. Each domain could be scored as strong, moderate, or weak, and studies could be classified as strong (with no weak domains), moderate (with 1 weak domain), or weak (with 2 or more weak domains).

Statistical Analysis

Detailed statistical procedures used in this meta-analysis have been reported elsewhere. Briefly, a standardized mean difference score was calculated for each specific variable by using Cohen’s d index, in which positive effect size (ES) values indicate higher scores in outcomes in favor of the IG. The pooled ES was estimated by using a random-effects model based on the DerSimonian and Laird method. Following the Cochrane recommendation, we assessed heterogeneity across studies by using the I² statistic. Depending on I² values, heterogeneity might be considered as the following: not important (0%–40%), moderate (30%–60%), substantial (50%–90%), and considerable (75%–100%); moreover, the corresponding P values were also taken into account. For assessing publication bias, Egger’s regression asymmetry test was used. Only studies in which researchers provided complete data for pre- and postintervention measurements and included a CG were included in the meta-analysis.

Some additional statistical aspects need to be clarified: (1) when 2 cohorts or 2 IGs were included in studies, their data were analyzed as independent samples; (2) when 2 or more tests for measuring the same variable were included in studies, the average ES was calculated; and (3) when 2 or more follow-up measurements were reported in studies, only the last measurement was considered. Finally, when there was 1 study in which results from >1 IG were shown, a pooled estimate was calculated to create a single pairwise comparison for this study to control nested effects, and an additional pooled ES was calculated.

For academic achievement, a pooled ES was calculated for 4 areas according to their measured outcomes: (1) language-related skills, (2) mathematics-related skills, (3) reading, and (4) composite scores. A pooled ES was also calculated for time spent in on-task behavior.

Subgroup analyses for the areas of academic achievement were performed according to the schooltime during which the PA intervention took place, distinguishing between the following: (1) curricular PE, (2) integrated or extracurricular PA, and (3) after-school PA and sports programs.

Sensitivity analyses were conducted by removing the following from the pooled ES estimations: (1) studies 1 by 1 to assess the robustness of the summary estimates and to detect whether any particular study...
<table>
<thead>
<tr>
<th>Author and Publication Year</th>
<th>Country</th>
<th>N (CG, IG1, IG2)</th>
<th>Age (SD)</th>
<th>CG, IG1, IG2</th>
<th>Place in the School Plan</th>
<th>Task Characteristics</th>
<th>Intervention Design</th>
<th>Length (wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahamed et al (2006)</td>
<td>Canada</td>
<td>288 (73, 214)</td>
<td>9–11</td>
<td>CG: usual PE; IG: 15 min 5 d/wk</td>
<td>Extracurricular PA</td>
<td>Enhanced PA</td>
<td>Skipping, hip-hop dancing, playground circuits, and resistance exercises with bands (included in the classroom, hallway, or playground)</td>
<td>36</td>
</tr>
<tr>
<td>Arroyo et al (2014)</td>
<td>Spain</td>
<td>67 (18, 24, 23)</td>
<td>13 (0.82)</td>
<td>CG: 55 min 2 d/wk (usual PE)</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>CG: fitness and health, games and sports, motor skills, corporal expression, and activities in the natural environment</td>
<td>16</td>
</tr>
<tr>
<td>Chaya et al (2012)</td>
<td>India</td>
<td>180 (90, 30)</td>
<td>7.8 (0.9)</td>
<td>IG1: 55 min 4 d/wk</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>IG1: as CG, but doubled the No. of sessions and performed at a higher intensity</td>
<td>12</td>
</tr>
<tr>
<td>Coe et al (2005)</td>
<td>United States</td>
<td>214 (100, 114)</td>
<td>11.5 (0.4)</td>
<td>IG2: 45 min PE</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>IG2: pranayama, sithilikarna vyayama, asanas PE classes</td>
<td>40</td>
</tr>
<tr>
<td>Davis et al (2011)</td>
<td>United States</td>
<td>171 (60, 55, 56)</td>
<td>9.3 (1.0)</td>
<td>CG: sedentary activities</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>IG1: low-dose exercise: running games, jump rope, modified soccer, and basketball</td>
<td>13 ± 1.6</td>
</tr>
<tr>
<td>Donnelly et al (2009)</td>
<td>United States</td>
<td>203 (86, 117)</td>
<td>7.8</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>PE + 60 min 1 d/wk of motor skills development as a ground for learning method</td>
<td>9 y</td>
</tr>
<tr>
<td>Erwin et al (2013)</td>
<td>United States</td>
<td>29 (13, 16)</td>
<td>8.87 (0.54)</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fredericks et al (2006)</td>
<td>South Africa</td>
<td>53 (13, 13, 13)</td>
<td>5.5–6.5</td>
<td>CG: usual PE</td>
<td>Extracurricular PA</td>
<td>Enhanced and enriched PA</td>
<td>IG1: free play</td>
<td>IG2: educational toys</td>
</tr>
<tr>
<td>Gao et al (2012)</td>
<td>United States</td>
<td>375; cohort 1: (123, 85); cohort 2: (112, 51)</td>
<td>10.30 (0.91)</td>
<td>CG: usual PE</td>
<td>Extracurricular PA</td>
<td>Enhanced PA</td>
<td>Aerobic dance, jump rope, or similar types of activities</td>
<td>2 y</td>
</tr>
<tr>
<td>Käll et al (2013)</td>
<td>Sweden</td>
<td>1965 (408, 1557)</td>
<td>Grade 5 (10–11)</td>
<td>CG: no extra PA</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>Different sports and games and play and motion activities</td>
<td>5 y</td>
</tr>
<tr>
<td>Katz et al (2010)</td>
<td>United States</td>
<td>1214 (559, 655)</td>
<td>7–9</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Warm-up, aerobic activities (hopsotch, lunge, squats, star jumps, jogging, walking, hopping, dancing, skipping) and cool-down</td>
<td>32</td>
</tr>
<tr>
<td>Author and Publication Year</td>
<td>Country</td>
<td>N (CG, IG1, IG2)</td>
<td>Age (SD)</td>
<td>CG, IG1, IG2</td>
<td>Place in the School Plan</td>
<td>Task Characteristics</td>
<td>Intervention Design</td>
<td>Length (wk)</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>---------------</td>
<td>------------------</td>
<td>----------</td>
<td>--------------</td>
<td>--------------------------</td>
<td>----------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Lakes and Hoyt* 2004</td>
<td>United States</td>
<td>193 (89, 104)</td>
<td>Grade 5 (10.5)</td>
<td>CG: 45 min 4 d/wk (usual PE)</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>Martial arts: blocks, kicks, punches, martial arts movement, broad-breaking techniques, complete body-stretching techniques, and deep-breathing relaxation techniques</td>
<td>28</td>
</tr>
<tr>
<td>Mahar et al* 2006</td>
<td>United States</td>
<td>245 (108, 135)</td>
<td>Grade 5 (0.9)</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Short classroom-based PAs</td>
<td>12</td>
</tr>
<tr>
<td>Mullender-Wijnsma et al* 2015</td>
<td>Netherlands</td>
<td>81</td>
<td>8.2 (0.65)</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Marching, jogging, hopping in place, included in mathematics and language problem solving</td>
<td>22</td>
</tr>
<tr>
<td>Mullender-Wijnsma et al* 2016</td>
<td>Netherlands</td>
<td>498 (250, 249)</td>
<td>8.0 (0.72)</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Physical exercise integrated on math and language activities, from moderate to vigorous intensity</td>
<td>44</td>
</tr>
<tr>
<td>Reed et al 2010</td>
<td>United States</td>
<td>155 (75, 80)</td>
<td>4.42–9.45</td>
<td>IG: 30 min 3 d/wk</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Integrated PA (running, hopping, walking, etc) into core lessons</td>
<td>16</td>
</tr>
<tr>
<td>Resaland et al* 2016</td>
<td>Norway</td>
<td>1129 (533, 598)</td>
<td>10.2 (0.72)</td>
<td>IG: 30 min 3 d/wk</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>90 min/wk of PA + 5 min/d of active breaks + 10 min/d of PA homework; 29% of the total PA was vigorous intensity</td>
<td>28</td>
</tr>
<tr>
<td>Riley et al* 2016</td>
<td>Australia</td>
<td>240 (98, 142)</td>
<td>11.13 (0.73)</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>PA involved in mathematic classes</td>
<td>6</td>
</tr>
<tr>
<td>Sallis et al* 1999</td>
<td>United States</td>
<td>754; cohort 1: (124, 147, 59); cohort 2: (141, 165, 118)</td>
<td>9.49–9.62</td>
<td>IG: usual PE</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>—</td>
<td>72 (2 y)</td>
</tr>
<tr>
<td>Spitzer and Hollmann* 2013</td>
<td>Germany</td>
<td>44 (20, 24)</td>
<td>12.5–13</td>
<td>IG: 30 min 3 d/wk</td>
<td>Curricular PE</td>
<td>Enhanced and enriched PA</td>
<td>IG1: SPARK program developed by trained teachers: 15 min of health fitness activity (aerobic dance, running games, jump rope) + 15 min of sport fitness activity (soccer, basketball)</td>
<td>16</td>
</tr>
<tr>
<td>Tarp et al* 2016</td>
<td>Denmark</td>
<td>632 (458, 194)</td>
<td>12.7 (0.9–13.1 (0.8)</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>PA + promotion of daily PA; PA in subjects; PA homework, and active transport + weekly schedules PA during recess</td>
<td>20</td>
</tr>
<tr>
<td>Telford et al* 2012</td>
<td>Australia</td>
<td>620 (308, 312)</td>
<td>Grades 3–5 (8–10)</td>
<td>CG: usual PE, IG: 45–50 min 2 d/wk + 50–60 min 2–3 d/wk</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>90 min/wk of specialist PE, moderate to vigorous PA: walks, runs, and traditional games, teaching skills (catching, throwing hitting, kicking) + 50–60 min/wk of general classroom teachers PE</td>
<td>75–80 (2 y)</td>
</tr>
<tr>
<td>Vazou* 2016</td>
<td>United States</td>
<td>224 (118, 106)</td>
<td>Grades 4–5 (10)</td>
<td>CG: no classroom-based PA, IG: 10–12 min 5 d/wk</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Jumping, skipping, animal-like walking integrated in math classes of moderate intensity</td>
<td>8</td>
</tr>
<tr>
<td>Wilson et al* 2016</td>
<td>Australia</td>
<td>116 (52, 52)</td>
<td>11.2 (0.8)</td>
<td>CG: no classroom-based PA, IG: 10 min 5 d/wk</td>
<td>Extracurricular PA</td>
<td>Enhanced PA</td>
<td>Tag or chasing games or invasion-type games</td>
<td>4</td>
</tr>
</tbody>
</table>
accounted for a large proportion of heterogeneity among academic achievement, (2) data from children with overweight or obesity cohorts, and (3) data from studies scoring as weak in the EPHPP quality evaluation scale.

Additionally, random-effects meta-regression analyses were performed to determine if the children’s age and the length of the intervention could be related to the effectiveness of the intervention on each academic achievement area.

Statistical analyses were performed by using Stata/SE software, version 14 (SPSS Inc, Chicago, IL).

RESULTS

Study Characteristic

The search retrieved a total of 4582 articles. After removing 777 duplicates, 3805 were screened on the basis of the title and the abstract (Fig 1).

A total of 26 studies, reflecting 26 unique interventions, were included in this systematic review,24–49 of which 8 were quasiexperimental design studies.30,33–35,38,39,44,45,48 Characteristics of the included studies are displayed in Table 1. Studies were conducted in 11 countries: the United States (12 studies), Australia (3), the Netherlands (2), Sweden (2), and 1 in each of the following countries: Canada, Denmark, Germany, India, Norway, South Africa, and Spain. The total sample included 10 205 children and adolescents (4133 in the CG) aged 4 to 13 years. Authors of 1 study included only children with overweight and obesity.28

The PA interventions were aimed at the following: (1) increasing the amount or qualitatively enriching PE25–27,35,37,44,45,47; (2) adding classroom-based PA during daily lessons as integrated PA, targeted to learning various subjects through being physically active*; (3) extracurricular PA, offering active breaks or PA during recess24,32,33,49, and (4) after-school PA programs.28,30

Overall, the interventions resulted in an increase in PA time from 10 to 60 minutes per day. In only 3 studies did researchers include data from 2 cohorts,33,44,45 and in 5 studies, researchers included more than 1 IG,25,26,28,32,44 1 of them without a CG.26 For studies with >1 IG, experimental groups differed in exercise intensity,25,28 duration,28,32 PA type,26,32 or educators who delivered the intervention activities (generalist versus specialist teachers).44 The length of interventions ranged broadly from 4 weeks49 to 9 school years30 (Tables 1 and 2).

Systematic Review

In a total of 23 studies,24–33,35–37,39–48 researchers reported information regarding the efficacy of PA interventions on academic achievement. In these studies, researchers included information on marks for the following: (1) language-related skills, such as language, vocabulary, spelling, and writing; (2) mathematics-related skills, such as mathematics, numeracy, and arithmetic; (3) reading; (4) composite scores; and (5) other subjects, such as English (as a foreign language), science, and social studies.

In 9 studies,† researchers reported information regarding the efficacy of PA interventions on language-related skills. In only 4 of these studies,26,29,35,44 researchers found significant improvements in the IG; in particular, improvements were higher in

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†Refs 25,26,29,35,40,41,44,45,47.
TABLE 2 Academic Achievement Parameters Measured and Test Used in the Included Studies

<table>
<thead>
<tr>
<th>Author and Publication Year</th>
<th>Academic Achievement Parameters Measured and Test Used in the Included Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahamed et al(^{34}) 2007</td>
<td>CAT-3: Total score</td>
</tr>
<tr>
<td>Ardoy et al(^{25}) 2014</td>
<td>Curriculum-based marks, Language, Mathematics, Total score, Other subjects mean score, Average of all subjects, Average of all subjects excluding PE, Spanish overall and IGF-M, Verbal ability, Numerical ability</td>
</tr>
<tr>
<td>Chaya et al(^{35}) 2012</td>
<td>MISC: Arithmetic, Vocabulary, Reasoning (comprehension)</td>
</tr>
<tr>
<td>Coe et al(^{37}) 2006</td>
<td>Individual grades and standardized test score, Combined score</td>
</tr>
<tr>
<td>Davis et al(^{28}) 2011</td>
<td>TerraNova standardized test scores, Mathematics, Reading</td>
</tr>
<tr>
<td>Donnelly et al(^{29}) 2009</td>
<td>WIAT-III test, Mathematics, Reading, Spelling, Total scores</td>
</tr>
<tr>
<td>Ericsson and Karlsson(^{30}) 2012</td>
<td>Curriculum-based marks, Total scores</td>
</tr>
<tr>
<td>Erwin et al(^{11}) 2012</td>
<td>Curriculum-based fluency test, Mathematics, Reading</td>
</tr>
<tr>
<td>Fredericks et al(^{32}) 2006</td>
<td>Curriculum-based marks, Mathematics, Reading, ASB: Numerical, Verbal comprehension</td>
</tr>
<tr>
<td>Gao et al(^{35}) 2013</td>
<td>Utah Criterion Reference Test, Mathematics, Reading</td>
</tr>
<tr>
<td>Käll et al(^{35}) 2013</td>
<td>Regional child care and education department, Mathematics, Language (Swedish), English (foreign language)</td>
</tr>
<tr>
<td>Katz et al(^{36}) 2010</td>
<td>MAP: Mathematics, Reading</td>
</tr>
<tr>
<td>Lakes and Hoyt(^{37}) 2004</td>
<td>WISC-III FD, Arithmetic</td>
</tr>
<tr>
<td>Mullender-Wijnsma et al(^{39}) 2015</td>
<td>Tempo Test Rekenen (speed test, arithmetic), Mathematics, Eén-Minuut-Test (1-min test), Reading</td>
</tr>
</tbody>
</table>

From the 18 studies\(^1\) in which researchers reported data regarding the effect of PA programs on mathematics-related skills,\(^{25,26,29,31–33,40,42–44,47,48}\) positive significant differences between the IG and the CG after the intervention were found in 13 studies.\(^6\) In the studies that included >1 IG, researchers showed that differences were greater for IGs with higher PA exertion and that were developed by trained or specialist teachers.

In 10 studies,\(^7\) researchers reported information regarding the efficacy of PA interventions on reading. In 5 studies,\(^{29,31,32,42,44}\) researchers found significant improvements, with researchers in 1 study\(^44\) showing the greatest improvement in the trained teacher IG.

In only 5 studies\(^{24,27,29,42,44}\) did researchers include information regarding composite score measurements. Researchers in 2 studies\(^{29,44}\) found significant differences; for 1\(^44\) of them, differences were for the IG conducted by trained teachers.

In 3 studies, researchers reported information regarding other subjects such as English as a foreign language,\(^5,42\) and science.\(^41\) Researchers in only 1 study\(^35\) found significant improvements after PA intervention.

In 5 studies,\(^{34,38,39,43,49}\) researchers presented information about time in on-task behaviors, and researchers in all but 1 study\(^49\) showed that the on-task time increased after PA

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\(^1\)Refs: 25, 26, 28, 29, 31–33, 36, 37, 40–48.
\(^3\)Refs: 28, 29, 31–33, 36, 40, 42, 44, 47.
intervention in comparison with postcontrol lessons.

**Study Quality**

Of the 18 RCTs whose quality was assessed by using the Jadad Scale, only 1 scored 5 points, 4 scored 4 points, 10 scored 3 points, ** and 3 scored 2 points. In all of the studies, researchers included information regarding the randomization method, and in only 1, researchers did not provide information about the withdrawals and dropouts. However, in only 3 studies did researchers properly describe the double-blinding method used (Supplemental Table 3).

From the 8 quasiexperimental studies in which quality was assessed by using the EPHPP tool, 6 scored as weak and 2 as moderate (Supplemental Table 4). The worst scored items were as follows: (1) confounders, because researchers did not report the differences between groups before intervention; and (2) the description of the withdrawals and dropouts, because articles did not provide the number and/or the reasons for withdrawals and dropouts (Supplemental Table 3).

**Meta-analysis**

The pooled ES (95% confidence interval [CI]) estimates for PA intervention effects on academic achievement areas were the following: language-related skills – 0.16 (−0.06 to 0.37), mathematics-related skills † † 0.21 (0.09 to 0.33), reading † 0.13 (0.02 to 0.24), and composite scores 0.26 (0.07 to 0.45). Heterogeneity among studies was substantial for language-related skills (I² = 71.7%; P = .002), moderate for mathematics-related skills (I² = 57.8%; P = .002) and for reading (I² = 25.5%; P = .209), and considerable for composite scores (I² = 75.6%; P = .000). The pooled ES (95% CI) for time in on-task behaviors was 0.77 (0.22 to 1.32), and there was substantial heterogeneity among studies (I² = 62.69%; P = .006) (Fig 2).

When pooled ESs (95% CI) were calculated (controlling the nested effect), estimates were as follows: (1) language-related skills, 0.12 (0.02 to 0.23; I² = 73.3%); (2) mathematics-related skills, 0.17 (0.10 to 0.24; I² = 67.5%); (3) reading, 0.13 (0.04 to 0.23; I² = 10.9%); and (4) composite scores, 0.10 (0.01 to 0.19; I² = 55.5%).

**Subgroup Analysis**

Subgroup analysis by the schooltime when PA interventions took place (curricular PE, integrated or extracurricular PA, and after-school PA), revealed that curricular PE...
programs benefited the following: (1) mathematics-related skills (ES: 0.16; 95% CI: 0.00 to 0.32), (2) reading (ES: 0.21; 95% CI: 0.05 to 0.37), and (3) composite scores (ES: 0.30; 95% CI: 0.03 to 0.56). Mathematics-related skills were also benefited by integrated or extracurricular PA (ES: 0.29; 95% CI: 0.07 to 0.51). On the other hand, no specific intervention benefited language-related skills (Supplemental Table 5).

**Sensitivity Analyses**

With the sensitivity analyses, we suggested substantial modifications in the pooled ES for language-related skills and reading and composite scores after removing 1 by 1 the cohorts from Sallis et al.\textsuperscript{24} fifth grade students, Sallis et al.\textsuperscript{25} second grade students, and Ardoy et al.\textsuperscript{25} high-intensity PA, respectively (Supplemental Table 6).

Sensitivity analysis by children’s weight status could only be performed for mathematics-related skills and reading because only these areas included children with overweight and obesity cohorts. After removing the children with overweight or obesity comparison...
groups, the pooled ES estimation was not modified for mathematics-related skills (ES: 0.21; 95% CI: 0.09 to 0.34) and minimally modified for reading (ES: 0.16; 95% CI: 0.03 to 0.28).

Sensitivity analysis by removing from the pooled ES the data from studies that scored as weak in EPHPP quality evaluation scale could only be performed on mathematics-related skills and reading because only these areas included studies scoring as low quality. The pooled ES and its heterogeneity were modified for mathematics-related skills (ES: 0.12; 95% CI: 0.03 to 0.18; $I^2 = 94.9\%$) but not for reading (ES: 0.13; 95% CI: 0.03 to 0.23; $I^2 = 21\%$).

**Random-Effects Meta-Regression Model**

With the random-effects meta-regression model, we showed that the effect of PA interventions on academic achievement was not associated with children’s age or to the length of the intervention (Supplemental Table 7).

**Publication Bias**

Funnel plots only indicated significant publication bias for the pooled subgroup analyses of composite scores ($P < .10$) (Supplemental Fig 3).
DISCUSSION

To our knowledge, this is the first systematic review and meta-analysis in which the evidence regarding the effectiveness of PA interventions on children’s and adolescents’ academic performance is summarized. Overall, with this review, we show that PA programs significantly benefit multiple facets of academic achievement: mathematics-related skills (ES: 0.21), reading (ES: 0.13), and composite scores (ES: 0.28). Additionally, we show that classroom behaviors are improved after PA interventions (ES: 0.77).

The schooltime when the PA interventions took place has some influence on these effects, in such a way that curricular PE lessons seem to be the most appropriate framework to improve children’s academic achievement, although integrating PA in classroom lessons also benefited mathematics-related skills. On the other hand, because of the scarcity of studies in each group, we could not determine which characteristics of the PA interventions (enriched, enhanced, or both PA designs) are associated with higher effects.

In previous studies, researchers have demonstrated that increasing the amount of weekly time dedicated to PE in the scholarship curricula enhances (or at least does not adversely affect) the academic performance of children, even if after-school time for studying is reduced. Furthermore, it has been suggested that integrating exercise in an interdisciplinary learning strategy with some other specific subjects such as mathematics or language could have beneficial effects on children’s academic performance. With our meta-analysis, we support the idea that children’s academic achievement and classroom behaviors improve after increasing the schooltime dedicated to PE and that the performance in some subjects such as mathematics could be improved by integrating PA programs into lessons.

The greater positive effect of integrating PA in mathematic-related skills lessons could be attributed to the fact that the design of these types of interventions fits better with solving mathematics problems, and interventions focused on introducing PA in other subjects such as reading and language are not as well designed. However, mathematics-related skills benefited from both curricular and integrated PE and also from extracurricular PA, suggesting that mathematics-related skills are susceptible to be modified by PA. Nevertheless, these findings should be cautiously taken into account because of the lack of after-school PA interventions aimed at improving academic achievement.

A negative complex relationship between weight status and motor and cognitive development has been described. In this sense, worse scores among children with overweight or obesity have been related to worse motor performance as well as the effects of these motor performance levels on PA exertion. With our results after removing the children with obesity and overweight samples, we support previous researchers who suggested that benefits of PA programs in cognitive domains of children with obesity and overweight are at least as great as those from normal-weight children. With the sensitivity analyses, we suggested that heterogeneity across studies was only modified after removing some subgroups in which specialists conducted the intervention. This might be attributed to greater changes in outcomes in studies in which specialists conducted the intervention because they have better training but also because the specialists conducted the PA interventions at a higher intensity.

Some limitations that might limit the robustness of our estimates should be acknowledged: (1) although we have only found significant publication bias for the composite scores subgroup analysis, we cannot rule out that publication bias does not affect other outcome estimates because studies with poor results are usually less likely to be published; (2) academic achievement was measured across the studies by using a wide variety of tools, and although the effect measurement was standardized by calculating the ES, the validity and reliability of these instruments varies substantially; (3) researchers in few studies reported the effect of after-school PA interventions, and thus estimates of their effect on academic achievement should be taken cautiously; and (4) the pooled ES estimation for mathematics-related skills and its heterogeneity was modified after removing articles that scored as low quality. Additionally, after controlling the nested effect, it was shown that some pooled ES and/or heterogeneity estimations were slightly modified in areas including fewer studies with a single IG. This should be cautiously considered when planning PA programs aimed to improve these academic achievement-related outcomes.

Given the importance of the brain’s development process in the acquisition of core executive functions, metacognition, and
life skills later in life, and the relation of these with academic achievement, it seems essential to determine the beneficial effects of PA interventions on children’s and adolescents’ cognition and academic performance. In this systematic review and meta-analysis, we state that curricular exercise is the most effective PA intervention to improve children’s and adolescents’ academic achievement and classroom behaviors. Moreover, we provide evidence supporting the key role of curricular exercise in the cognitive development of these population groups. Our results are consistent enough to recommend education and public health policymakers to translate these findings to schools. Furthermore, they can be confident that these interventions are free of risks and beneficial for children’s and adolescents’ school behavior and academic achievement. Qualified professionals are essential for translating these findings into practice because they could properly design PE or integrated PA lessons to maximize their effect in children’s cognition and academic achievement. Further research is needed to strongly support which type of exercise intervention is the most appropriate for each schooltime and which is the most efficient way to implement them. Moreover, further studies are needed to elucidate how enriched PA programs could affect children’s academic achievement or on-task behaviors.

**CONCLUSIONS**

Our data reveal that if schools appropriately implement PA interventions, they can significantly improve academic achievement of children in a range that varies from 0.14 to 0.28 SD, depending on the curricular area. Moreover, these interventions could improve classroom behavior by 0.77 SD. Thus, it means that contrary to what is sometimes thought by parents and teachers, the implementation of these PA interventions in school hours does not mean a waste of time but rather is an effective strategy to improve academic performance and behaviors.

Children’s and adolescents’ healthy habits tend to persist through life. In this sense, this study should be jointly considered with previous research aimed to support that the schools are an ideal setting for promoting healthy behaviors. Among these, the promotion of PA is an effective tool for improving children’s physical and mental health and also enhancing academic achievement.

**ABBREVIATIONS**

CG: control group  
CI: confidence interval  
EPHPP: Effective Public Health Practice Project  
ES: effect size  
IG: intervention group  
PA: physical activity  
PE: physical education  
RCT: randomized controlled trial
38. Mahar MT, Murphy SK, Rowe DA, Golden J, Shields AT, Raedeke TD. Effects of a classroom-based program on physical activity...


4. **Manuscript 4:** Association between pre-pregnancy overweight and obesity and children’s neurocognitive development: a systematic review and meta-analysis of observational studies.
Association between pre-pregnancy overweight and obesity and children’s neurocognitive development: a systematic review and meta-analysis of observational studies

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Original article

Abstract

Background: Obesity and overweight during pregnancy have been negatively associated with fetal and offspring neurodevelopment. The aim of this systematic review and meta-analysis was to assess the effect of the relationship between pre-pregnancy overweight and obesity with children’s neurocognitive development.

Methods: We systematically searched MEDLINE, EMBASE, the Cochrane Library and the Web of Science databases from their inception through February 2017 for follow-up studies comparing the relationship between pre-pregnancy weight status and children’s cognition. The Mantel-Haenszel fixed-effects method was used to calculate pooled effect size (ES) values and their corresponding 95% confidence intervals (CIs) comparing children’s neurocognitive development between pre-pregnancy normal weight, as reference, with overweight and obesity categories.

Results: Fifteen articles were included in the systematic review, and nine of them in the meta-analysis. The pooled ES values for overweight and obese mothers were −0.02 (95% CI: −0.05 to 0.02) and −0.06 (95% CI: −0.09 to −0.03), respectively. The pooled ES for the relationship between pre-gestational excess weight (overweight and obesity) and children’s neurocognitive development was −0.04 (95% CI: −0.06 to −0.02).

Conclusions: Pre-pregnancy obesity might have negative consequences on the neurocognitive development of offspring.

Key words: Pregnancy, obesity, children, cognition, cognitive function, neurocognitive development
Key Messages

- This systematic review identified 15 articles that investigated the relationship between pre-pregnancy weight status and children’s neurocognitive development.
- This meta-analysis showed that pre-pregnancy obesity, but not overweight, was negatively related with children’s neurocognitive development.
- Future studies are needed to better define the mechanisms underlying the associations between pre-pregnancy obesity and children’s neurocognitive development.

Introduction

Overweight and obesity prevalence have greatly increased in recent years, becoming one of the most important public health problems in most countries. Worldwide, the proportion of adults with excess weight has been estimated at approximately 37% for men and 38% for women. Around 60% of women at reproductive age from the USA and Australia are classified as overweight or obese. Specifically, in 2011–12, the prevalence of obesity among women of reproductive age in the USA was 31.8%, half of whom classified as obesity class I, and the other half as obesity classes II and III. This prevalence has not stopped growing since the 1970s (less than 10%). In adults, overweight and obesity have been associated with several cardiometabolic diseases, cancer and reproductive disorders, among others.

Maternal overweight and obesity could result in negative outcomes for both mother and fetus, and could also influence fertility, as well as the duration and outcomes of pregnancy. During pregnancy, overweight mothers are at risk of gestational diabetes, thromboembolism, preterm delivery, caesarean section and preeclampsia; the fetus also has an increased risk of death, congenital anomalies and macrosomia. Furthermore, obesity during pregnancy could affect the mother’s and child’s health later in life. Women could be at increased risk of heart disease, diabetes and hypertension, and children could be at increased risk of developing future obesity and heart disease. Strategies to combat excess weight, such as physical activity interventions, have shown some effectiveness in mitigating this negative influence.

Obesity and overweight during pregnancy have been negatively associated with fetal and offspring neurodevelopment. Maternal obesity produces an inflammatory uterine environment that could negatively influence brain development during gestation and, as a consequence might result in neurodevelopmental impairment in offspring.

The physiological mechanisms behind these long-term negative consequences in offspring are unclear. The fetal programming hypothesis suggests that the exposure of the fetus to an adverse intrauterine environment would be sufficient to produce permanent programming changes in tissue function and, as a result, long-term adverse effects on offspring neurodevelopment. Other factors might also influence this relationship, such as pregravid obesity which has been associated with a high risk of vitamin D deficiency that could have a direct impact on the nutritional status of the neonate. Moreover, some psychological conditions such as personality characteristics, increased stress levels or stress sensitivity in obese mothers also have been proposed as possible mediators of this association.

Three previous systematic reviews have examined the role of pre-pregnancy weight status in children’s neurodevelopment. All of them reported a negative relationship between pre-pregnancy excess weight, especially obesity, and children’s neurodevelopment, and stated that children from pre-pregnancy overweight/obese women could be at increased risk of some disorders in childhood and adolescence, such as attention deficit hyperactivity disorder, eating and psychotic disorders or motor development disorders. These systematic reviews are valuable in understanding the evidence regarding the effects of pre-pregnancy weight status on children’s cognitive skills, but they did not quantify these effects. Because of the steadily rising of women’s obesity prevalence worldwide, it seems necessary to ascertain the effect of this problem on children’s cognitive development. The aim of our systematic review and meta-analysis was to assess the effect of pre-pregnancy overweight and obesity on children’s neurocognitive development.

Methods

This meta-analysis has been registered in PROSPERO (Registration Number: CRD42016042101), and was guided by the MOOSE (Meta-analysis of Observational Studies in Epidemiology) Statement and the Cochrane Collaboration Handbook.

Search strategy

A literature search was performed in MEDLINE (via PubMed), EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic
Reviews and Web of Science databases from their inception through February 2017. The search strategy combined the following relevant terms: ‘pregnancy’, ‘maternal’, ‘gestational’, ‘weight status’, ‘obesity’, ‘adiposity’, ‘weight gain’, ‘body mass index’, ‘cognition’, ‘neurodevelopment’, ‘intellectual’, ‘intelligence’, ‘cognitive function’ and ‘academic’ (Table S1, available as Supplementary data at IJE online, for MEDLINE database search strategy). The references lists of the retrieved articles were also reviewed for any additional relevant studies. The systematic review was independently performed by two reviewers (C.A.B. and I.C.R.) and disagreements were resolved by consensus meetings. The overall percentage of agreement was calculated to evaluate inter-rater agreement for inclusion of eligible articles.

Selection criteria
Studies concerning the relationship between pre-pregnancy weight status and children’s cognition were included. Inclusion criteria were as follows: (i) participants: pregnant women and their offspring; (ii) study design: follow-up studies; (iii) exposure: calculated pre-pregnancy weight status; and (iv) outcome: children’s cognition assessed by standardized test scores or curricular-based grades related to specific subject areas. Studies were excluded when they were not written in English or Spanish, and also when they included pregnant women younger than 15 years. Studies were likewise excluded when the target population was specifically: (i) mothers with intellectual disabilities; (ii) children not born at full term; and (iii) children with mental disorders that could limit generalizability [attention-deficit/hyperactivity disorder (ADHD), conduct or neuropsychiatric disorders including schizophrenia, or any detected delay in communication, adaptive, cognition or socio-emotional domains].

Data extraction
Two researchers (C.A.B. and I.C.R.) independently collected the following data from original studies: (i) country; (ii) mothers’ age at birth; (iii) weight status criteria used for the classification of the mothers’ body mass index (BMI); (iv) cohort year of birth; (v) age of the children at evaluation; (vi) number of children in each cohort; and (vii) tool and/or scale used for the children’s neurocognitive development assessment and domains evaluated. Also, estimates regarding the association between pre-pregnancy weight status and children’s neurocognitive development were extracted as originally reported by the studies. Disagreements in data collection were resolved by discussion. The overall percentage of agreement was calculated to evaluate inter-rater agreement for inclusion in the data extraction process. Corresponding authors of studies were contacted to obtain missing data.

Quality assessment
After concealment of information about authors, affiliations, date and source of each manuscript, two investigators (C.A.B. and I.C.R.) independently assessed its methodological quality. A standardized checklist for reporting observational longitudinal research was used. This checklist includes two categories of criteria: (i) aspects that could influence effect estimates (such as the description of the validity and reliability of the measurement methods); and (ii) descriptive and contextual issues (such as the definition of the study population, eligibility criteria and method used for data collection). The rating list consists of 33 criteria, and each criterion was assessed as ‘yes’ (=1), ‘no’ (=0) or ‘not applicable’ (=?); thus, the quality score for each study ranged from 0 to 33. Disagreements were resolved by consensus with a third investigator (V.M.V.).

Data synthesis and statistical analysis
Effect size (ES) was the principal outcome; this statistic provides a measure of change in the outcome variable in terms of standard deviation units. A standardized mean difference score was calculated for each pre-pregnancy weight status category as an estimate of ES. When studies provided a linear regression β coefficient, it was used to calculate a standardized mean difference score. When studies provided odds ratio (OR) estimates, the ES was calculated using the natural log OR. A pooled estimate for each weight status category based on the World Health Organization (WHO) weight status classification was calculated when the studies presented estimates for BMI values. Other weight status criteria, such as the Centers for Disease Control and Prevention (CDC) criteria, were considered similar to those of WHO; thus, their estimates for the relationship between excess weight categories and children’s neurocognitive development were jointly considered with those from WHO when we calculated the pooled ES estimates.

Some concerns regarding repeated measurements in the same sample should be considered in this meta-analysis as follows.

i. When a study included two cohorts, their data were analysed as independent samples;
ii. When cognitive development was measured within the same cohort using different tests, a main pooled estimate considering the values for all the tests was
performed (if a test provided a total score value, this was the only one considered for the pooled estimate);

iii. When in the same cohort, the association estimates were calculated more than once with the same test, in order to avoid over-representation bias, only the latter estimate was considered for the meta-analysis. However, the effect sizes are shown in tables summarizing the original study results in order to provide information regarding whether the effect differed depending on the age of the children;

iv. When several estimates were reported within the same study, the most adjusted model was used for the pooled ES estimate.

v. Finally, only studies reporting separate data for pre-pregnancy overweight and obesity were included in the meta-analysis.

The Mantel-Haenszel fixed-effects method was used to compute pooled ES estimates and their respective 95% confidence intervals (95% CIs), which were used to examine the effect of overweight and obesity categories on children’s cognition, using normal weight as the reference category. Additionally, a pooled ES of excess weight (overweight and obesity) was conducted and compared with normal weight (reference category). Since general intelligence/full-scales scores are considered a representative construct of all mental performance, we also calculated a pooled general intelligence/composite cognitive scores ES estimate. The heterogeneity of the results across studies was evaluated using the I² statistical parameter. I² values of <25%, 25–50% and >50% usually correspond to small, medium and large heterogeneity, respectively; the corresponding P-values were also considered.

Sensitivity analysis was conducted by removing studies one by one in order to assess the robustness of the summary estimates, and to detect whether any particular study accounted for a large proportion of heterogeneity. Random-effects meta-regression was used to evaluate whether effect estimates differed according to children’s age, since this could be considered a source of heterogeneity. For this meta-regression analysis, each included study was individually considered, in order to reflect the reported measurements at different ages.

Finally, publication bias was evaluated using Egger’s regression asymmetry test for assessment of ‘small studies effects’. Statistical analyses were performed using StataSE software, version 14 (StataCorp).

Study quality

Studies met 57.58% to 84.84% of the quality criteria, as assessed by the Quality of Reporting of Observational Longitudinal Research instrument (Table S3, available as Supplementary data at IJE online). Only one study provided data as means obtained in a cognition test (Table 3). The remaining 13 articles showed estimates of β coefficients from multiple logistic regression models using normal weight as reference (Tables 4 and 5).

The data extracted from the included studies were adjusted for several family and child covariates (Table S2, available as Supplementary data at IJE online). All except five articles provided data by weight status categories. Within these articles, the estimates of the relationship between children’s neurocognitive development and mothers’ weight status were reported in a continuous scale, or as an excess weight category that combined overweight and obese individuals. Only one cohort found a small but negative association between maternal pre-pregnancy obesity and offspring general intelligence (OR = 0.84; 95% CI = 0.73 to 0.98).

Results

The search retrieved a total of 3823 articles. Of these, 836 were removed as duplicates and 2987 were screened based on the title and abstract. Finally, 15 articles met the inclusion criteria (Figure 1). The mean inter-rater agreement for inclusion of eligible articles was 85%.

Table 1 summarizes the main characteristics of the included studies. The included samples ranged from 215 to 11 025, belonging to 13 cohorts born between 1959 and 2012. Five cohorts were from the USA, two each from The Netherlands, the UK, Spain and Greece; and one each from Denmark and Poland. The mothers’ age at birth ranged from 15 to over 40 years, and children’s neurocognitive development was assessed when they were aged between 6 months and 14 years. Three studies provided data at two follow-up times. All studies but two used the WHO criteria for establishing mothers’ pre-pregnancy weight status. Studies used several different scales for measuring cognition-related aspects, such as general intelligence/total scores, language-related skills, performance and simultaneous processing and executive functions-related measurements (spatial visualization, performance, sequential processing and simultaneous processing), nonverbal skills and academic achievement. The mean inter-rater agreement for extraction data of included studies was 87%.

Tables 2 to 5 summarize the association between maternal pre-pregnancy weight status and children’s cognitive development total score as retrieved from the original articles. Among all articles, one provided data regarding the intensity of this relationship using OR estimates from logistic regression models (Table 2). Another article provided data as means obtained in a cognition test (Table 3). The remaining 13 articles showed estimates of β coefficients from multiple logistic regression models using normal weight as reference (Tables 4 and 5).

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included information regarding the reasons for refusing to participate in the study, and no studies included the justification for the number of participants. Furthermore, only one study\textsuperscript{41} discussed the qualitative or quantitative impact of potential biases. Only four studies\textsuperscript{30,34,41,42} informed about the reliability and validity of the tool used to measure neurocognitive development.

Meta-analyses

For the calculation of the pooled ES of overweight and obesity categories, only the studies providing separate data for these pre-pregnancy weight status categories were included.\textsuperscript{33–38,40–43} ES for the relationship between weight status and children’s neurocognitive development were $-0.02$ (95% CI: $-0.05$ to $0.02$) and $-0.06$ (95% CI: $-0.09$ to $-0.03$) for pre-pregnancy overweight and obesity, respectively. Heterogeneity estimates were $I^2=0.0\%$ ($P=0.98$) and $I^2=0.0\%$ ($P=0.680$) for pre-pregnancy overweight and obesity analyses, respectively (Figure 2). The pooled effect for the excess weight category was $-0.04$ (95% CI: $-0.06$ to $-0.02$). The heterogeneity estimate was $I^2=0.0\%$ ($P=0.83$).

Additionally, the pooled ES estimate for weight status and children’s general intelligence, or full-scales scores,\textsuperscript{33–35,37,38,40,43} were $-0.02$ (95% CI: $-0.06$ to $0.02$) and $-0.05$ (95% CI: $-0.10$ to $0.00$) for pre-pregnancy overweight and obesity analyses, respectively. Heterogeneity estimates were $I^2=0.0\%$ ($P=0.89$), and $I^2=0.0\%$ ($P=0.60$) for pre-pregnancy overweight and obesity analyses, respectively (Figure 3). The pooled effect for the excess weight category was $-0.03$ (95% CI: $-0.06$ to $0.00$). The heterogeneity estimate was $I^2=0.0\%$ ($P=0.85$).

Sensitivity analyses

Sensitivity analyses suggested that the pooled ES or heterogeneity were not modified either in the overweight or in the obesity analyses by removing the included cohorts one by one (Table S4, available as Supplementary data at IJE online).
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<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Receptive language skills</td>
</tr>
<tr>
<td>Polanska et al. 2015</td>
<td>Poland</td>
<td>30.5 (4.5)</td>
<td>WHO</td>
<td>2007</td>
<td>1.0 (0.1)</td>
<td>437</td>
<td>Bayley Scales of Infant Toddler Development:</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>✓ Cognitive skills</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>✓ Composite language</td>
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<td></td>
<td></td>
<td>2.0 (0.2)</td>
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</tr>
<tr>
<td>Pugh et al. 2015</td>
<td>USA</td>
<td>NA</td>
<td>WHO</td>
<td>1983–86</td>
<td>10.0</td>
<td>530</td>
<td>Stanford-Binet Intelligence Scale:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ IQ</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Wisconsin Card Sorting test:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Perseverative errors</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td>Trail making test part B:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Executive function</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Wide Range Achievement Test-Revised (WART-R) and Wechsler Individual Achievement test (WAI):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Mathemtaks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Reading</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Spelling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tanda et al. 2012</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>25.4 (0.5)</td>
<td>CDC</td>
<td>1979–94</td>
<td>6.0 (0.6)</td>
<td>3412</td>
<td>Peabody Individual Achievement Test (PIAT):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Mathemtaks</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Reading recognition</td>
</tr>
<tr>
<td>Torres-Espinola et al.</td>
<td>Spain</td>
<td>31.0 (3.8)</td>
<td>WHO</td>
<td>2007–12</td>
<td>0.5</td>
<td>215</td>
<td>Bayley Scales of Infant Development (BSID-III):</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Cognitive skills</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Receptive language</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Expressive language</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>✓ Composite language</td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
<td>1.5</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>197</td>
</tr>
</tbody>
</table>

(Continued)
The random-effects meta-regression model showed that the effect of prepregnancy overweight ($P = 0.48$) or obesity ($P = 0.32$) on children’s neurocognitive development was not related with children’s age. This model showed that children’s age was also not related with the heterogeneity observed across the studies. (Figure S1A-B, available as Supplementary data at IJE online)

**Publication bias**

Funnel plots did not display evidence of publication bias for any of the pooled subgroup analyses (overweight $P = 0.29$ and obesity $P = 0.23$) [25] (Table S5, available as Supplementary data at IJE online).

**Discussion**

The association between pre-pregnancy weight status and neurocognitive development among healthy offspring has not yet been elucidated. This meta-analysis aimed to assess the effect of pre-pregnancy mothers’ overweight and obesity on offspring’s neurocognitive development. Overall, this study showed that mothers who are obese before pregnancy, but not overweight, have a negative influence on the offspring’s neurocognitive development (ES = $-0.06$; 95% CI: $-0.09$ to $-0.03$). Furthermore, pre-pregnancy obesity could have a small negative, though not statistically significant, effect on children’s general intelligence (ES = $-0.05$; 95% CI: $-0.10$ to $0.00$).

The results of this meta-analysis are in line with previous reviews that have suggested a negative relationship between pre-pregnancy obesity and children’s neurocognitive development. Even though a mild, or even negligible, influence of pre-pregnancy obesity on children’s neurodevelopment or general intelligence, this finding should be cautiously taken into consideration due to the worldwide increasing number of women of childbearing age, and considering that gestation and childhood are critical periods in neurocognitive development. Furthermore, additional experimental research on the relationship between pre-pregnancy obesity and children’s neurodevelopment, including longer follow-up periods, is needed.

The model proposed by van der Burg et al. [45] suggests that mother’s obesity produces a chronic systemic inflammation ambience with negative consequences for fetal development. This obesity-related inflammatory process increases insulin concentrations, leptin levels and other low-grade inflammatory markers that could produce errors in brain maturation. Other physiological obesity-related changes such as oxidative stress and endothelial...
dysfunction might also negatively influence children’s brain maturity.  

Besides this hypothesis, new explanations have been suggested to clarify this relationship. The epigenetic hypothesis proposes that the fetus receives a set of information related to environmental factors from the mother, which is capable of producing changes in gene expression responsible not only for metabolic diseases but also for psychiatric disorders across the life span.

Previous research has described that these effects might be the consequence of interaction between genes and increased levels of fatty acids, glucose, leptin and inflammatory markers that might have an influence on plasticity and cognitive function. Children from obese mothers are at greater risk of developing insulin resistance and cardiometabolic diseases and also of having excess overall and central adiposity. Additionally, obesity has been associated with cognitive deficits, not only in children but also in adolescents and adults, regardless of socioeconomic factors. A bidirectionality in causal pathways has been suggested, in such a way that lower scores on tests for executive function have been related with the development of obesity across the life span.

In addition to obesity during pregnancy, pre-pregnancy obesity has been associated with neurocognitive developmental deficits such as cognitive deficits and also with autism spectrum and psychotic disorders in offspring. Our meta-analysis confirms that pre-pregnancy obesity, but not overweight, could be associated with worse neurocognitive development scores in children. Current evidence has elucidated that neural circuits and brain structure growth are continuous procedures from conception to adulthood, and therefore related to executive functions and cognition acquisition. In that way, offspring from obese mothers

### Table 2. Odds ratio (95% CI) for excess of weight (overweight/obesity) as predictor of children’s cognition (normal weight as reference category)

<table>
<thead>
<tr>
<th>Author</th>
<th>Tool for children’s cognition assessment and dimensions</th>
<th>Children’s age</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brion et al. 2010</td>
<td>Diagnostic Analysis of Nonverbal Accuracy test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ ALSPAC. Nonverbal skills</td>
<td>2.5</td>
<td>0.97 (0.83 to 1.14)</td>
</tr>
<tr>
<td></td>
<td>MacArthur Toddler and Communication Questionnaire</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ ALSPAC. Sentence length</td>
<td>2.5</td>
<td>0.88 (0.78 to 1.00)</td>
</tr>
<tr>
<td></td>
<td>✓ ALSPAC. Word production</td>
<td>2.5</td>
<td>0.95 (0.84 to 1.08)</td>
</tr>
<tr>
<td></td>
<td>Dutch Version of the Parent Report of Children’s Abilities (PARCA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ Generation R. Nonverbal skills</td>
<td>3.2</td>
<td>1.08 (0.90 to 1.30)</td>
</tr>
<tr>
<td></td>
<td>Language Development Survey</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ Generation R. Sentence length</td>
<td>3.2</td>
<td>0.88 (0.74 to 1.05)</td>
</tr>
<tr>
<td></td>
<td>✓ Generation R. Word production</td>
<td>3.2</td>
<td>0.91 (0.76 to 1.08)</td>
</tr>
<tr>
<td></td>
<td>Wechsler Intelligence Scale for Children II</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ ALSPAC. IQ</td>
<td>8</td>
<td>0.84 (0.73 to 0.98)</td>
</tr>
</tbody>
</table>

*Range or mean (SD) of children at measurement point as reported by the original studies.

### Table 3. Children’s cognition mean scores (±SD) by excess of weight category

<table>
<thead>
<tr>
<th>Author</th>
<th>Tool for children’s cognition assessment and dimensions</th>
<th>Children’s age</th>
<th>Overweight ± SD</th>
<th>Effect size</th>
<th>Obesity ± SD</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torres-Espinola et al. 2015</td>
<td>Bayley Scales of Infant Development (BSID-III):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ Composite cognitive</td>
<td>0.5</td>
<td>109.1 ± 8.0</td>
<td>0.20</td>
<td>112.8 ± 7.1</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td>✓ Expressive language</td>
<td>0.5</td>
<td>10.7 ± 2.0</td>
<td>0.36</td>
<td>11.1 ± 1.8</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>✓ Receptive language</td>
<td>0.5</td>
<td>12.2 ± 2.2</td>
<td>0.27</td>
<td>12.6 ± 2.3</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>✓ Composite language</td>
<td>0.5</td>
<td>109.0 ± 9.8</td>
<td>0.41</td>
<td>111.0 ± 8.9</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td>✓ Composite cognitive</td>
<td>1.5</td>
<td>123.4 ± 11.3</td>
<td>0.27</td>
<td>121.6 ± 9.6</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>✓ Expressive language</td>
<td>1.5</td>
<td>10.4 ± 2.0</td>
<td>−0.15</td>
<td>10.4 ± 2.1</td>
<td>−0.16</td>
</tr>
<tr>
<td></td>
<td>✓ Receptive language</td>
<td>1.5</td>
<td>11.9 ± 1.1</td>
<td>0.00</td>
<td>11.4 ± 1.3</td>
<td>−0.30</td>
</tr>
<tr>
<td></td>
<td>✓ Composite language</td>
<td>1.5</td>
<td>106.2 ± 8.2</td>
<td>−0.19</td>
<td>105.5 ± 8.8</td>
<td>−0.26</td>
</tr>
</tbody>
</table>

*Range or mean (SD) of children at measurement point in years as reported by the original studies.

*Normal weight as category of comparison.*
might be at higher risk of suffering from deficits in their brain maturation and neurocognitive development, regardless of the age at which they are evaluated.

Additional pathways that could potentially explain worse neurocognitive development in offspring from obese mothers could include some gestational complications, which are more common among obese mothers, such as congenital abnormalities, preeclampsia, gestational diabetes mellitus, iatrogenic preterm delivery or increased rates of labour induction and caesarean deliveries.\(^57\) In particular, research has related gestational diabetes and hypertension during pregnancy with delay in brain maturity and induction of neurobehavioural abnormalities in offspring, affecting intellectual function, although the causal influence remains unclear.\(^{33,35,39}\)

Previous studies\(^{31,33,45}\) have suggested that the relationship between a mother’s excess weight and neurocognitive development could be confounded by other pre- and postnatal factors such as home conditions, family income or maternal and paternal educational or intelligence levels.\(^60\) Our findings suggest that the relationship between pre-pregnancy obesity and children’s neurocognitive development scores could be independent of those confounders, as all the included studies considered family sociodemographic variables in their analyses. Conversely, we cannot ignore the possible residual confounding effect that could result from incomplete or unreliable measurements of sociodemographic variables. Furthermore, the relationships between mothers’ pre-pregnancy weight status and children’s cognitive function were softened after controlling for some covariates such as maternal age and/or education, family income or children’s age. Additional research is needed for examining how these effects could be confounded by other important mother’s (general intelligence, maternal depression, gestational diabetes or maternal glucose intolerance) and child’s (birthweight or cardiorespiratory fitness) covariates, and by more accurate socioeconomic variables measurements.

The limitations of this study are those common to meta-analyses: publication bias, selection bias, potential ecological fallacy and limited information from study reports. In particular, we should detail the following constraints that may affect the robustness of our pooled estimates.

i. Although we did not find evidence for significant publication bias in our study, it is perfectly conceivable that studies with poor results were unlikely to be published.

ii. We should consider that the meta-analyses were not conducted using the original data as provided by the studies (\(\beta\) and OR values), but by using ES estimates and their corresponding 95% CIs from the published data; thus bias cannot be ruled out.

iii. Only seven studies scored positively in at least two-thirds of the quality assessment scale items, which could threaten the internal validity of these studies. Studies should be required to include more complete information regarding sampling criteria such as the sample size rationale, number of population meeting and not meeting the eligibility criteria, reasons for refusing participation, and comparisons between those who agree to participate and those who do not. Also, more accurate information regarding the impact of bias and statistical analysis is needed.

iv. Although included studies have children’s neurocognitive development as a main outcome variable, there is not a single universally accepted scale for the measurement of this construct, and only two scales have been used in more than one study: the Wechsler Intelligence

### Table 4. Body mass index as predictor (\(\beta\) coefficients) of cognition in multiple linear regression models

<table>
<thead>
<tr>
<th>Author</th>
<th>Tool for children’s cognition assessment and dimensions</th>
<th>Children’s age (SD)^a</th>
<th>(\beta) coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basatemur et al. 2012(^{30})</td>
<td>British Ability Scale (BAS-II):</td>
<td>5.0</td>
<td>-0.08 ((P &lt; 0.0001))</td>
</tr>
<tr>
<td></td>
<td>✓ British Ability scale: g</td>
<td>7.0</td>
<td>-0.17 ((P = 0.0069))</td>
</tr>
<tr>
<td>Bliddal et al. 2014(^{31})</td>
<td>Wechsler Primary and Preschool Scales of Intelligence:</td>
<td>5.0–5.3</td>
<td>-0.27 (−0.50 to −0.03)</td>
</tr>
<tr>
<td>Polanska et al. 2015(^{39})</td>
<td>Bayley Scales of Infant Toddler Development:</td>
<td>1</td>
<td>1.6 (−1.2 to 4.5)</td>
</tr>
<tr>
<td></td>
<td>✓ Composite language</td>
<td>1</td>
<td>2.8 (−0.04 to 5.7)</td>
</tr>
<tr>
<td></td>
<td>✓ Composite cognitive</td>
<td>2</td>
<td>1.4 (−2.1 to 4.9)</td>
</tr>
<tr>
<td>Veldijk et al. 2011(^{44})</td>
<td>Kaufman Assessment Battery for Children (K-ABC):</td>
<td>7.3 (0.3)</td>
<td>-0.66 (−1.08 to −0.25)</td>
</tr>
<tr>
<td></td>
<td>✓ Sequential processing scale</td>
<td>7.3 (0.3)</td>
<td>-0.66 (−1.11 to −0.22)</td>
</tr>
<tr>
<td></td>
<td>✓ Simultaneous processing scale</td>
<td>7.3 (0.3)</td>
<td>-0.55 (−0.95 to −0.14)</td>
</tr>
<tr>
<td></td>
<td>✓ Mental processing scale</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^aRange or mean (SD) of children in years at measurement point as reported by the original studies.
Table 5. β coefficient for linear regression models using cognition variables as dependent variables (normal weight as reference category)

<table>
<thead>
<tr>
<th>Author</th>
<th>Tool for children’s cognition assessment and dimensions</th>
<th>Children’s age (SD)</th>
<th>Overweight (95% CI) Effect size</th>
<th>Obesity (95% CI) Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casas et al. 2013</td>
<td>Bayley Scales of Infant Development: INMA</td>
<td>1.2</td>
<td>−0.88 (−2.64 to 0.88) −0.02</td>
<td>−2.72 (−5.35 to −0.10) −0.05</td>
</tr>
<tr>
<td></td>
<td>Bayley Scales of Infant Development: RHEA</td>
<td>1.5</td>
<td>1.41 (−2.26 to 5.08) 0.04</td>
<td>−3.71 (−8.45 to 1.02) −0.09</td>
</tr>
<tr>
<td>Daniki et al. 2017</td>
<td>McCarthy Scales of Children’s Abilities (MCSA):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>✓ Verbal scale</td>
<td>4.3 (0.2)</td>
<td>−0.88 (−3.34 to 1.58) −0.03</td>
<td>−2.24 (−5.32 to 0.84) −0.06</td>
<td></td>
</tr>
<tr>
<td>✓ Perceptual-p scale</td>
<td>4.3 (0.2)</td>
<td>−2.90 (−5.40 to −0.40) −0.09</td>
<td>−4.60 (−7.74 to −1.47) −0.12</td>
<td></td>
</tr>
<tr>
<td>✓ Quantitative scale</td>
<td>4.3 (0.2)</td>
<td>−0.82 (−3.42 to 1.77) −0.02</td>
<td>−4.43 (−7.68 to −1.18) −0.11</td>
<td></td>
</tr>
<tr>
<td>✓ General cognitive</td>
<td>4.3 (0.2)</td>
<td>−1.84 (−4.28 to 0.60) −0.06</td>
<td>−4.03 (−7.08 to −0.97) −0.10</td>
<td></td>
</tr>
<tr>
<td>✓ Memory scale</td>
<td>4.3 (0.2)</td>
<td>−0.28 (−2.82 to 2.25) −0.01</td>
<td>−2.83 (−6.00 to 0.34) −0.07</td>
<td></td>
</tr>
<tr>
<td>✓ Executive function</td>
<td>4.3 (0.2)</td>
<td>−2.47 (−4.97 to 0.04) −0.07</td>
<td>−4.92 (−8.06 to −1.78) −0.12</td>
<td></td>
</tr>
<tr>
<td>✓ Mental development index</td>
<td>1.5–3.1</td>
<td>−0.21 (−0.88 to 0.46) −0.01</td>
<td>−0.57 (−1.63 to 0.48) −2.13 (−3.32, −0.93) −0.02^a −0.05^b</td>
<td></td>
</tr>
<tr>
<td>Hinkle et al. 2013</td>
<td>Standardized test:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>✓ Reading</td>
<td>NA</td>
<td>−0.11 (−0.19 to −0.03) −0.04</td>
<td>−0.14 (−0.27 to 0.00) −0.14 (−0.29, 0.02)^b −0.03^a −0.03^b</td>
<td></td>
</tr>
<tr>
<td>✓ Mathematics</td>
<td>NA</td>
<td>−0.06 (−0.13 to 0.02) −0.02</td>
<td>−0.06 (−0.16 to 0.04) −0.14 (−0.29, 0.01)^b −0.02^a −0.03^b</td>
<td></td>
</tr>
<tr>
<td>Huang et al. 2014</td>
<td>Wechsler Intelligence Scale for Children:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>✓ Verbal scale</td>
<td>7.1 (0.8)</td>
<td>−0.50 (−1.3 to 0.4) −0.02</td>
<td>−2.50 (−4.0 to −1.0) −0.03</td>
<td></td>
</tr>
<tr>
<td>✓ Performance scale</td>
<td>7.1 (0.8)</td>
<td>−0.20 (−1.1 to 0.8) −0.01</td>
<td>−1.00 (−2.7 to 0.7) −0.01</td>
<td></td>
</tr>
<tr>
<td>✓ Full-scale IQ</td>
<td>7.1 (0.8)</td>
<td>−0.30 (−1.10 to 0.50) −0.01</td>
<td>−2.00 (−3.50 to −0.50) −0.03</td>
<td></td>
</tr>
<tr>
<td>Neggers et al. 2003</td>
<td>Differential Ability Scales (DAS):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>✓ IQ</td>
<td>5.3 (0.3)</td>
<td>−1.10 (SE: 2.00) −0.04</td>
<td>−4.70 (SE: 1.40) −0.20</td>
<td></td>
</tr>
<tr>
<td>✓ Nonverbal score</td>
<td>5.3 (0.3)</td>
<td>−0.47 (SE: 2.6) −0.01</td>
<td>−5.6 (SE: 1.8) −0.19</td>
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<td>−2.45 (−3.53 to −1.36) −0.23</td>
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SE, standard error.
^aObesity class I.
^bObesity class II and III.
^cRange or mean (SD) of children at measurement point in years as reported by the original studies.
^dNormal weight as category for comparison.
Figure 2. Pooled estimated effect size for children’s neurodevelopment. a) This cohort represents the pooled effect size estimation for REAH sample of children’s scores obtained on Bayley Scales of Infant Development (BSID) and McCarthy Scales of Children’s Abilities (MCSA), extracted from Casas et al 2013 and Daraki et al 2017, respectively. b) This cohort represents the pooled effect size estimation for Pugh et al sample of children’s scores obtained on Stanford-Binet Intelligence Scale and Wide Range Achievement Test-Revised (WART-R) and Wechsler Individual Achievement test (WAIT), extracted from Pugh et al 2015 and Pugh et al 2016, respectively. CI: Confidence Interval.

Figure 3. Pooled estimated effect size for children’s general intelligence/composite cognitive scores. CI: Confidence Interval.
Scale (in two studies) and the Bayley Scales of Infant Development (in three studies). Moreover, when limiting the analysis to general intelligence or composite scores, ES were similar.

v. Though meta-regression analyses did not find any statistically significant differences across children’s age at evaluation, due to the reduced number of studies included in the meta-regression analysis, this finding should be taken cautiously.

vi. Because most studies lack rationale for the sample size estimates, the prevalence of excess weight in the samples could influence our pooled ES estimates. However, subgroup analyses including only studies from the USA, where the obesity prevalence is one of the highest in the world, showed similar pooled ES to when all studies were included: −0.02 (95% CI: −0.10 to 0.07) for overweight and −0.06 (95% CI: −0.12 to −0.01) for obesity. Therefore, we thought that the inclusion of cohorts from North America and Europe could actually be considered as an external validity indicator for our findings. Additionally, sensitivity analyses reinforced the results of this study, showing no ES changes when removing studies one by one.

Our meta-analysis provides supporting evidence that pre-pregnancy obesity may have negative consequences on offspring’s neurocognitive development. Therefore, in order to mitigate the risk of future health cognition problems in childhood, it may be advisable to implement interventions aimed at preventing overweight and obesity in all women of childbearing age, and particularly those who are planning a pregnancy. Further research is needed to elucidate the specific cognition functions more negatively affected by this relationship and to determine the effects of some variables that could act as moderators or mediators in this relationship.

Supplementary Data
Supplementary data are available at IJE online.

Funding
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Conflict of interest: None declared.

References


47. O’Reilly JR, Reynolds RM. The risk of maternal obesity to the long-term health of the offspring. *Clin Endocrinol* 2013;78:9–16


5. **Manuscript 5**: Pregnancy leisure physical activity and children’s neurodevelopment: systematic review and meta-analysis.
Pregnancy leisure physical activity and children’s neurodevelopment: systematic review and meta-analysis.

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Short title: Pregnancy PA and children’s cognition.
Objective: The aim of this systematic review and meta-analysis was to assess the effect of leisure physical activity during pregnancy on children’s neurocognitive development.


Selection criteria: Follow-up studies concerning the relationship between leisure physical activity during pregnancy and children’s cognition were included. Study selection and data extraction were performed in duplicate after removing identifying information.

Data collection and Analysis: Effect size (ES) and their corresponding 95% confidence intervals (CIs) were calculated for all primary outcomes (general intelligence and language-related skills). The DerSimonian and Laird method was used to compute pooled ES estimates for each primary outcome.

Main results: Six studies met the inclusion criteria (11388 children aged from one to 10). Pooled ES estimates for the relationship between physical activity during leisure time and children’s neurocognitive development were 0.16 (95% CI: 0.08 to 0.25) for general intelligence and 0.07 (95% CI: 0.02 to 0.13) for language-related skills.
Conclusion: Our data show that children from mothers who have performed some physical activity during leisure time scored better on general intelligence through only slightly better on language-related skills than their peers.

Key words: pregnancy, physical activity, cognition, children, learning

INTRODUCTION

There is a growing interest in the effect of prenatal environment on children’s development and its consequences later in life. Previous research has revealed that some unhealthy behaviours during pregnancy such as sedentary habits could negatively affect fetuses’ and children’s development. Although the latest recommendations of the American College of Obstetrics and Gynaecology (ACOG) for pregnant women without complications indicated that they should accumulate at least 30 minutes of moderate-intensity physical activity on most days of the week, the fact is that the world prevalence of inactivity among women is 33.9%. 

Research has shown that physical activity during pregnancy could have a positive effect on neonatal and maternal outcomes, such as gestational age, Apgar score, gestational diabetes, maternal weight gain and type of delivery. Furthermore, physical activity has been related with less incidence and better management of postpartum depression and mood, as well as with better scores in offspring’s cognition variables, academic achievement and classroom behaviours.

Previous studies have reported that physical exercise programs during pregnancy are associated with children’s higher scores in orientation, state regulation, academic achievement and cognition. Different pathways behind this relationship have been
proposed including improvements in the intrauterine environment, better circulation and higher placental volumes, and a decreasing risk of gestational depression, a disorder that is known to negatively affect psychological development in early infancy.\textsuperscript{13–15}

As the worldwide prevalence of pregnant women who do not meet the ACOG’s physical activity recommendations is steadily rising\textsuperscript{1}, it seems necessary to estimate the effect of mothers’ sedentary behaviours on children’s cognitive development. Thus, this systematic review and meta-analysis aimed to assess the effect of leisure physical activity during pregnancy on children’s neurocognitive development.

METHODS

This meta-analysis has been registered in PROSPERO (Registration Number: CRD42016042101), and was guided by the MOOSE (Meta-analysis of Observational Studies in Epidemiology) Statement\textsuperscript{16} and the Cochrane Collaboration Handbook.\textsuperscript{17}

A literature search was performed in MEDLINE (via PubMed), EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science and ClinicalTrials.gov databases from their inception to February 22, 2017. The search strategy combined the following relevant terms: ‘pregnancy’, ‘maternal’, ‘gestational’, ‘physical activity’, ‘physical education’, ‘exercise’, ‘fitness’, ‘sport’, ‘leisure time’, ‘cognition’, ‘psycho*’, ‘neuro*’, ‘cognition’, ‘intelligence’, ‘memory’, ‘attention’, and ‘academic’. The references’ list from the retrieved articles, and previous systematic reviews and meta-analysis were also reviewed for any additional relevant study. The systematic review was independently performed by two reviewers (CAB and ICR) and disagreements were resolved by consensus. Study records were managed using the Mendeley reference manager.
Study selection

Studies concerning the relationship between leisure physical activity during pregnancy and children’s cognition were included. Inclusion criteria were specified as follows: (i) participants: pregnant women and their offspring; (ii) study design: follow-up studies; (iii) exposure: leisure physical activity (understood as one that includes sports and exercise during free time) performed during pregnancy; and (iv) outcome: children’s cognition assessed by standardised test scores or curricular-based grades related to specific subject areas. Only studies written in English or Spanish were included.

Studies were excluded when the target population was: (i) children with any disorder that could limit the generalisation of data such as attention-deficit/hyperactivity disorder (ADHA), neuropsychiatric disorder including schizophrenia, or any detected delay in communication, adaptive, cognition or socio-emotional domains; and (ii) children not born at full term.

Data extraction

Two researchers (CAB and ICR) independently collected the following data from selected studies: (1) country, (2) mothers’ age at birth, (3) number of mothers/children in each cohort, (4) age of children at evaluation, (5) definition of leisure physical activity during pregnancy, and (6) tool and/or scale used for the children’s neurodevelopment assessment and cognitive/academic domains measured (Table 1). Disagreements in data collection were resolved by discussion.

Studies were classified into three groups according to the measured outcomes: i) general intelligence; ii) language-related skills; and iii) other measurements.
Quality assessment

After concealment of information about authors, affiliations, date and source of each manuscript; two investigators (CAB and ICR) independently assessed its methodological quality. A standardised checklist for reporting of observational longitudinal research proposed by Tooth et al\(^{18}\) was used. This checklist includes two categories of criteria: i) aspects that could influence effect estimates, and ii) descriptive and contextual issues. The rating list consists of 33 criteria and each of them was assessed as ‘yes’ (= 1), ‘no’ (= 0) or ‘not applicable’ (= ?); thus the quality score for each study ranged from 0 to 33. Disagreements were resolved by consensus with a third investigator (VMV).

Data synthesis and statistical analysis

Effect size (ES) was the principal statistical outcome, which provides a measure of change in the outcome variable in terms of standard deviation units. A standardised mean difference score was calculated for each pregnancy leisure physical activity as an estimate of ES\(^{19}\). When studies provided a linear regression $\beta$ coefficient, it was used to calculate a standardised mean difference score\(^{19,20}\).

Some concerns should be noted: i) in cohorts in which the association estimates were calculated more than once during the follow-up period, only the latter estimate was considered for the meta-analysis; ii) when estimates for physical activity during leisure time and general activity were reported, only the former were considered; and iii) when the paper reported data for more than one statistical model, the most adjusted one (controlling for a greater number of covariates) was considered for ES calculation.

The DerSimonian and Laird method\(^{21}\) was used to compute pooled ES estimates and their respective 95% confidence intervals (95% CIs), which were used to examine the
effect of leisure physical activity during pregnancy on children’s general intelligence and language-related skills, using no leisure physical activity during pregnancy as the reference category. The heterogeneity of the results across studies was evaluated using the $I^2$ statistic. Depending on $I^2$ values, heterogeneity might be considered as: not important (0% to 40%), moderate (30% to 60%), substantial (50% to 90%) and considerable (75% to 100%); moreover, the corresponding p-values were also taken into account.\textsuperscript{17}

A sensitivity analysis was conducted by removing studies one by one in order to assess the robustness of the summary estimates, and to detect whether any particular study accounted for a large proportion of heterogeneity.

Random-effects meta-regression was used to evaluate whether effect estimates differed according to children’s age, since this could be considered a source of heterogeneity.

Finally, publication bias was evaluated using Egger’s regression asymmetry test for assessment of ‘small studies effects’.\textsuperscript{22} The trim-and-fill computation was used to assess the effect of publication bias on the interpretation of results.\textsuperscript{23} Statistical analyses were performed using StataSE software, version 14 (StataCorp).

**RESULTS**

The search retrieved a total of 3398 articles. Of these, 905 were removed as duplicates, and 2493 were screened based on the title and abstract. Finally, six studies met the inclusion criteria\textsuperscript{24–29} (Figure 1).

Table 1 summarises the main characteristics of the included studies. The total sample included 11388 children (5784 in sedentary groups). Two cohorts were from the United States\textsuperscript{24,25}, and one from each from the following countries: Brazil\textsuperscript{26}, Poland\textsuperscript{29}, Spain\textsuperscript{27}.
and the United Kingdom. The mothers’ age at birth ranged from 20 to over 35 years, and children’s neurocognitive development was assessed when they were aged between one and 10 years. Two studies provided data for two follow-ups.

Criteria for considering pregnant women as physically active varied across studies: three required 60, 90 and 150 min per week of leisure physical activity, respectively, two of them at 55% of maximal aerobic capacity. Two defined being active as any physical activity during leisure time, and one of them categorized mothers’ physical activity based on METs. The last one required at least 3 METs or 2.5 h per week to be considered active.

A variety of tools were used to evaluate children’s cognitive function, which included measurements for: i) general intelligence (i.e.: general intelligence, IQ mental scores and cognitive composite score), ii) language related skills (i.e.: oral skill language, language grades, vocabulary scores, verbal IQ and language composite scores), and iii) other measurements such as mathematics, average of mathematics and language, and grade point average.

**Study quality**

As assessed by the Quality of Reporting of Observational Longitudinal Research instrument, studies met 51.51% to 66.66% of the quality criteria (Table S1). Only one study included information regarding differences between participants and non-participants, and another about the reliability of measurements methods. Furthermore, no study discussed the qualitative or quantitative impact of potential biases and missing data not accounted for in analyses. All of them lacked information regarding non-consenters and missingness.
Meta-analyses

Pooled ES for the relationship between leisure physical activity during pregnancy and children’s neurocognitive development was: 0.16 (95% CI: 0.08 to 0.25) for general intelligence and 0.07 (95% CI: 0.02 to 0.13) for language-related skills. Heterogeneity estimates were $I^2 = 26.6\%$ (p = 0.252) and $I^2 = 59.6\%$ (p = 0.042), respectively (Figure 2).

Sensitivity analyses

Sensitivity analyses suggested that, removing the included cohorts one by one, did not modify the pooled ES for general intelligence or for language-related skills, or heterogeneity estimates.

Random-effects meta-regression model

The random-effects meta-regression model showed that the effect of leisure physical activity during pregnancy on children’s neurocognitive development (general intelligence and language-related skills) was not related with children’s age. This model showed that children’s age was also not related with the heterogeneity observed across the studies (Figure S1A-B).

Publication bias

Funnel plots did not display evidence of publication bias for the pooled general intelligence ES estimate (p = 0.428). Conversely, there was evidence of publication bias for the language-related skills estimate (p = 0.043). Additionally, trim-and-fill computation showed that two studies were needed to remove publication bias (p = 0.834) (Figure S2).
DISCUSSION

Previous experimental research has demonstrated that exercise during pregnancy not only does not adversely affect the fetus’ neurodevelopment, but also enhances the neuroelectric response of the neonatal brain. This meta-analysis aimed to assess the effect of leisure physical activity during pregnancy on offspring’s neurocognitive development. Our study shows that children from mothers who have performed some leisure physical activity during pregnancy scored better on general intelligence though only slightly better on language-related skills than their peers.

Leisure time physical activity includes sports and exercise during free time, while general physical activity could also include occupational and household activities. Therefore, the total amount of physical activity that mothers could exert during a whole day should be evaluated in order to accurately consider the effect of the mother’s daily physical activity on children’s cognition. The latest physical activity recommendations encourage pregnant women without complications to accumulate, before, during and after pregnancy, at least 20-30 minutes per day of moderate-intensity exercise all, or almost all, days of the week. The included studies did not clearly define the amount of physical activity needed to be considered active during pregnancy; nevertheless, our findings are in concordance with studies that have associated the practice of any physical activity during pregnancy with better neonatal and maternal outcomes. The dose-response and characteristics of exercise during pregnancy that result in more benefit on neonatal and maternal health parameters still remain unanswered.

In line with previous experimental findings, our meta-analysis confirms that leisure physical activity could have a positive effect on children’s neurodevelopment. Several hypotheses have tried to explain the relationship between physical activity and
children’s cognition. The intrauterine environment hypothesis proposes that physical activity could modify the environment in which the fetus has grown,\textsuperscript{31} playing a critical role in children’s physical and mental development.\textsuperscript{32} Additionally, this hypothesis suggests that the placenta plays an essential role in the supply of oxygen to the fetus and the increase of blood circulation seems to be crucial for the fetus’ neurologic development,\textsuperscript{33} and the BDNF transferred from mother to child could result in improved cognitive functioning.\textsuperscript{34}

The epigenetic hypothesis proposes that the fetus receives from the mother a set of information related to environmental factors that, in turn, could modulate gene expression, and that might be responsible for different disorders across the life span.\textsuperscript{35} Some aspects such as gestational diabetes, hypertension or elevated insulin levels could influence child development through these epigenetic modifications. Physical activity might help control or mitigate these gestational disorders in such a way that children from active mothers could be at lower risk of developing some non-communicable diseases.\textsuperscript{36}

Finally, it has been described that maternal behaviours could affect children’s development. In this sense, positive effects of physical activity on mothers’ mood, anxiety and depression symptoms have been reported. Conversely, sedentary behaviour may increase the risk of depression and anxiety disorders during pregnancy, and mothers’ depression has been associated with worse children’s behaviours and psychological development.\textsuperscript{15,37}

Some limitations that might limit the robustness of our estimates should be acknowledged: i) the finding of significant publication bias for the language-related skills analyses could limit the generalization of our results in this area; ii) children’s
cognitive performance was measured with a variety of tools from which only two outcomes could be pooled (language-related skills and general intelligence); thus, more research is needed to elucidate the effect of physical activity during pregnancy on other cognition dimensions; and iii), the criteria for quantifying physical exercise during pregnancy varied across the included studies; thus, more precisely defined criteria are needed to determine which physical activity characteristics enhance children’s cognition.

CONCLUSION

This meta-analysis provides consistent evidence supporting that physical activity during leisure time in pregnancy has a positive effect on offspring’s neurocognitive development. Therefore, benefits of physical activity during pregnancy could be extended from mothers to their offspring. Although the evidence is limited, health caregivers should encourage healthy pregnant women to be active during this life period; our result also alerts about the necessity of providing opportunities for physical activity to pregnant women. Finally, further research is needed to elucidate the effect on other cognition domains such as core executive functions and metacognition; also it is essential to determine the influence of some covariates such as diet, sedentary time or total amount of daily physical activity that might act as moderators or mediators in this relationship.

Acknowledges: no applicable

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Authors’ contribution: VMV and CAB designed the study. VMV was the Principal Investigator and Guarantor. ICR, CAB, and VMV were the main coordinators of the study. CAB, JAMH and MGM conducted the study. MGM, MSL and ICR provided statistical and epidemiological support. VMV wrote the article with the support of MSL, ICR and CAB. All of the authors revised and approved the final version of the manuscript.

Ethical approval: no applicable

Disclosure of interest: the authors declare no conflicts of interest.

REFERENCES


11. Labonte-Lemoyne E, Curnier D, Ellemberg D. Exercise during pregnancy


393  **Figure legends:**

394  **Figure 1.** Literature search PRISMA consort diagram

395  **Figure 2.** Pooled estimated effect size for academic achievement/ ES: Effect Size; CI Confidence Interval. a) Effect size estimate for boys subgroup. b) Effect size estimate for girls subgroup.
Table 1. Characteristics of included studies.

<table>
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<th>Study</th>
<th>Country</th>
<th>Mother’s age*</th>
<th>Children’s age**</th>
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<th>n PA group</th>
<th>Leisure PA classification</th>
<th>Cognition measurement (Tool and cognitive/academic domain)</th>
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</thead>
</table>
| Clapp et al 1996     | United States | 31±1          | 5                | 20                | 20         | 20 min x 3d/w; at 55% of maximal capacity | Wechsler Preschool and Primary Scale for Intelligence (WPPI)  
✓ General intelligence  
Peabody Picture Vocabulary test/Expressive One Word Picture/Clinical Evaluation of Language Fundamentals  
✓ Oral skill language |
| Clapp et al 1998     | United States | 31±1          | 1                | 52                | 52         | 30 min x 3d/w; at 55% of maximal capacity | Bayley Scale of Infant Development  
✓ Mental score |
| Domingues et al 2014 | Brazil    | 20-35         | 4                | 3594              | 553        | At least 150min/w         | Wechsler Preschool and Primary Scale for Intelligence  
✓ IQ |
| Esteban-Cornejo et al 2015 | Spain | NA            | 10.18±3.31       | 1098              | 770        | Any leisure PA            | Grades reported  
✓ Math  
✓ Language  
✓ Average of both  
✓ Grade point average |

Abbreviations: NA: Not available; PA: Physical activity; G: Group.
**Table 1.** Characteristics of included studies.

* Mothers’ age at birth; ** age of children at evaluation

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<tr>
<th>Study</th>
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<td>&gt;3 MET and &gt;2.5 h/w</td>
<td>Cognitive composite score</td>
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Abbreviations: NA: Not available; PA: Physical activity; G: Group.
* Mothers’ age at birth; ** age of children at evaluation.
Records identified through database searching (n=3398)
- MEDLINE: 974
- EMBASE: 1249
- COCHRANE DATABASES: 137
- WOS: 836
- ClinicalTrials.gov: 202

Duplicate records removed (n=905)

Irrelevant records excluded based on title and abstract review (n=2480)

Records excluded (n=7)
- n= 1 Randomized controlled trial
- n= 1 protocol
- n= 4 did not provided data for cognition variables
- n=1 provided data for mother’s physical activity and cognition

Records screened (n=2493)

Full text articles assessed for eligibility (n=13)

Studies included in quantitative synthesis (meta-analysis) (n=6)

General intelligence n=4

Language-related skills n=5
6. **Manuscript 6**: Cardiorespiratory fitness as a mediator of the relationship between birth weight and cognition in schoolchildren: a mediation analysis.
# Cardiorespiratory fitness as a mediator of the relationship between birth weight and cognition in schoolchildren: a mediation analysis

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| Complete List of Authors: | Alvarez-Bueno, Celia  
Cavero-Redondo, Ivan  
Díez-Fernández, Ana; Universidad de Castilla-La Mancha, Nursing  
Pardo-Guijarro, Maria Jesus  
Sánchez-López, Mairena; Universidad de Castilla-La Mancha  
Martinez-Vizcaíno, Vicente |
| Keywords: | Birth weight, Cardiovascular, Epidemiology, Exercise, Neurodevelopment, Physical Activity |
| Free Text Keywords: | fitness, birth weight, cognitive function |
Cardiorespiratory fitness as a mediator of the relationship between birth weight and cognition in schoolchildren: a mediation analysis.

Fitness, birth weight and cognition.

Álvarez-Bueno, Celia; Cavero-Redondo, Iván; Díez-Fernández, Ana; Pardo-Guijarro, María Jesús; Sánchez-López, Mairena; and Martínez-Vizcaino, Vicente.

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Telephone number: 969 179100 (Ext: 4683)

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CAB is supported by a grant from the Spanish Ministry of Education, Culture and Sport (FPU13/03137). ICR is supported by a grant from the University of Castilla-La Mancha (FPU13/01582).

**Conflicts of interest:** None
ABSTRACT

Background

The aims of this study were to examine differences in cognition parameters by birth weight categories; and to analyze whether the relationships between birth weight and cognitive functions are mediated by cardio respiratory fitness (CRF) in schoolchildren.

Methods

A cross-sectional study using a sample of 664 schoolchildren from the MOVI-KIDS study. Variables: i) cognitive function was measured by the Battery of General and Differential Aptitudes (BADyG); ii) birth weight, reported by parents; and iii) CRF, (20-m shuttle run test). ANCOVA models were estimated to explore differences in cognitive function levels across birth weight and CRF categories. Hayes’s PROCESS macro was used for the simple mediation analysis.

Results

CRF acts as a full mediator of the relationship between birth weight with the verbal and numerical factors, and general intelligence; and as a partial mediator when logical reasoning and the spatial factor were the dependent variables.

Conclusions

Our data suggest that, in schoolchildren, the influence of birth weight on cognitive function is mediated by CRF. This finding highlights that, to improve children’s cognition, it is important to diminish the prevalence of low birth weight, and also to promote physical activity at early ages.
INTRODUCTION

Low birth weight (LBW) infants are at increased risk of short stature, metabolic disorders, and neonatal morbidity and mortality (1). Research has shown that these newborns are also at increased risk for a wide range of neurosensory impairments and emotional problems, and poorer general health than those with a normal birth weight (2). These negative effects, which have been observed during the perinatal state, are tracked from infancy to adulthood (3).

In terms of cognition dimensions, LBW has been related to a decrease in general intelligence levels and, consequently, poorer school performance, learning difficulties and behavioral problems (4). Furthermore, LBW impairs executive functions such as flexibility, planning, working verbal, visuospatial memory and inhibition (5), which are closely related to academic and behavioral problems. Whereas research has suggested that structural brain alterations might be behind these cognitive impairments in LBW infants (6), compensatory brain mechanisms to cope with these functional deficits in these children have been described (7).

A relationship between birth weight and physical fitness parameters has been described (8), in such a way that LBW children are at risk of lower aerobic and neuromuscular fitness (9), though differences become less apparent as children get older (10). Conversely, higher levels of physical fitness have been related to better cognitive function and academic achievement in children (11). Although the mediator effect of fitness on the relationship between birth weight and academic performance as measured by a mean of marks has been previously described in preadolescents (12), the dimensions of cognition influenced by both birth weight and cardiorespiratory fitness
(CRF) remain unclear, and also which relationships between birth weight and cognition dimensions in schoolchildren are mediated by CRF.

Thus, the aim of this study was twofold: i) to examine differences in cognitive parameters by birth weight categories controlling for potential confounders or mediators; and ii) to analyze whether the relationships between birth weight and cognitive functions are mediated by CRF in schoolchildren.

MATERIAL AND METHODS

Study Design and Population

This was a cross-sectional analysis of baseline data (collected September–November 2013) from a cross-over randomized cluster trial (NCT01971840) aimed at assessing the effectiveness of a multidimensional physical activity intervention (MOVI-KIDS) for preventing obesity, improving fitness and reducing cardiovascular risk in schoolchildren attending the last year of preschool and the first grade of primary school (aged 4-7 years) (13). The MOVI-KIDS study included 1604 schoolchildren from 21 schools (19 public and 2 private) from Cuenca and Ciudad Real provinces, Castilla-La Mancha region, Spain. For the analyses of this study we only included the primary school children (n=664), since cognition scale has not been validated for preschool children.

The Clinical Research Ethics Committee of the “Virgen de la Luz” Hospital in Cuenca approved the study protocol. After obtaining the approval of the director and school committee of each school, we sent a letter to the parents of all children inviting them to a meeting in which the study objectives were outlined and a written consent for their children's participation was requested. Then, we held informative talks class by class, in which the schoolchildren were asked to participate in the study.
Anthropometric measurements

Measurement procedures have been extensively described elsewhere (13). To minimize inter-observer variability, the variables were measured in each school in standardized conditions by trained researchers.

Weight and height were measured twice with the child barefoot and in light clothing. Weight was measured with a scale (Seca® 861, Vogel and Halke, Hamburg, Germany), and height was measured using a wall stadiometer (Seca® 222, Vogel and Halke, Hamburg, Germany) with the child upright and the sagittal midline touching the backboard. The mean of the two measurements of weight and height was used to calculate body mass index (BMI [kg/m²]).

Birth weight was obtained by a self-administered questionnaire completed by the children’s parents.

Cognitive function variables

Cognitive function was measured using the Battery of General and Differential Aptitudes (BADyG) scales, validated for Spanish children aged 6–8 years (14). This scale provides information for the following domains:

- Logical reasoning, which measures verbal intelligence and mental flexibility based on capacities of inductive reasoning (the process of using a rational, systematic series of steps based on procedures and previously given statements to arrive at a conclusion).

- Verbal factor, which measures the capacity of verbal reasoning and comprehension. Designed to provide a measure of overall verbal intellectual abilities.
- Numerical factor, which measures the velocity and security of children in easy mental calculation.

- Spatial factor, which measures the ability of less automatized reasoning, searching for changes in figures that maintain their size, distance, shape and relative positions.

- General intelligence, which summarizes positive correlations among different cognitive tasks, assuming that an individual's performance in cognitive tasks are related to each other. It is calculated as the sum of two verbal tests, two numerical tests and two spatial tests.

**Cardiorespiratory fitness (CRF)**

CRF was assessed using the 20-m shuttle run test (15). Participants were required to run between two lines 20 meters apart while keeping pace with audio signals emitted from a pre-recorded compact disc. The initial speed was 8.5 km/h, which was increased by 0.5 km/h every minute considering that 1 min equals one stage. Participants were encouraged to keep running as long as they can during the test. We recorded the last half stage that each child completed as an indicator of his/her CRF. Estimations of submaximal oxygen consumption ($VO_{2max}$) were obtained using Leger’s formula 

$$(31.025 + (3.238 \times \text{velocity}) - (3.248 \times \text{age}) + (0.1536 \times \text{age} \times \text{velocity})).$$

**Parental socioeconomic status (SES)**

Data for parental socioeconomic status (SES) were gathered by using self-reported occupation and education questions completed by either the father or the mother. According to the scale proposed by the Spanish Society of Epidemiology (16), paternal and maternal education were separately considered as: i) primary education
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(functionally illiterate, without any studies or uncompleted primary education), ii) middle education (primary education or high school/secondary education) and iii) university education (university degree or PhD). Additionally, parental occupation was classified into five categories: i) freelance with no staff, ii) supervisor/manager or freelance with less than 10 employees, iii) supervisor/manager or freelance with 10 employees or more, iv) non-qualified staff and unskilled worker, and v) household chores, unemployed and others. An index of family SES was calculated from these items considering the highest parents’ education and parental occupation classifying SES as: lower, lower middle, middle, upper middle, and upper.

**Statistical analysis**

The distribution of continuous variables was checked for normality using both graphical (normal probability plot) and statistical (the Kolmogorov–Smirnov test) procedures. Descriptive data is presented as mean and standard deviation (SD). Sex differences in quantitative variables were tested using the Student T-test. Partial correlation coefficients were estimated to examine the relationship between birth weight, BMI and CRF controlling for age in months, by sex.

After categorizing birth weight as low (<2.500 gr) and normal (>2.500 gr), according to the World Health Organization (WHO) (17), analysis of covariance (ANCOVA) models was estimated to test mean differences in cognition variables among birth weight and CRF categories (poor: first quartile, medium: second and third quartiles, and good: fourth quartile) controlling for age in months, sex, SES and BMI (model 1); and with further adjustment for CRF or birth weight depending on the fixed factor (model 2).

Mediation analysis models were conducted to examine whether the association between birth weight and cognitive parameters was mediated by CRF using the PROCESS
macro for SPSS (18). The goal of these models was to investigate: the total (c) and the
direct effects (a, b, c’), as indicated by the unstandardized regression coefficient
between the independent and the dependent variables in each model; and the indirect
effect, obtained from the product of coefficients (a*b), and indicating the change in
cognition variables for every unit change in birth weight that was mediated by the
proposed mediator. Age in months, sex, SES and BMI were added as covariates in these
models.

This macro used bootstrapping methods as recommended by Preacher and Hayes (19)
for testing mediation hypotheses, using a resampling procedure of 10000 bootstrap
samples. Point estimates and corresponding 95% confidence intervals were estimated
for the indirect effect. Additionally, we estimated mediation models using multiple
regression procedures according to the steps outlined by Sobel (20), calculating the
percentage of mediation as a ratio of indirect to total effect and dividing the indirect
effect by its standard error in order to test if this indirect effect was significantly
different from zero.

All statistical analyses were performed using the IBM SPSS 22 Statistic software; the
criterion for statistical significance was set at p<0.05.

RESULTS

Of the 1604 participants included in the MOVI-KIDS study, 664 schoolchildren (343
girls, 51.65%) from the first grade (6-7 years) who had valid data were included in this
study. Children who accepted to participate did not differ in age or sex from those who
did not. Characteristics of the study sample are shown in Table 1. Additional
information regarding blood pressure values, and anthropometric and physical fitness
characteristics are described in Supplemental Table S1 (online).
All variables were considered with normal distribution as examined by Kolmogorov-Smirnov test and graphical methods. Partial correlation coefficients between birth weight, CRF and cognition variables, controlling for age, are shown in Table 2. Birth weight was positively associated to logical reasoning, the spatial factor and general intelligence (p<0.05). Cardiorespiratory fitness was positively associated with all cognition variables (Range of values from 0.18 to 0.27; p<0.001).

Table 3 presents the mean differences in cognition variables by birth weight categories, controlling for age, sex, SES and BMI in model 1. Overall, as compared with LBW, children with normal birth weight scored better in all cognition variables, although only differences in logical reasoning, the spatial factor and general intelligence were statistically significant (p<0.05). When CRF was included as a covariate (model 2), differences in the mean cognitive parameters by birth weight categories were mitigated, remaining statistical significance only for the spatial factor dimension (p=0.038).

The mean differences in cognition dimensions by CRF categories are shown in Table 4. In model 1, in which age, sex, SES and BMI were included as covariates, children in the higher CRF categories scored better in all cognition variables (p<0.01), except for the spatial factor, in which differences across CRF categories were not found (p=0.095). When birth weight was included as a covariate (model 2), differences remained similar in all variables.

Mediation analysis diagrams are depicted in Figure 1. Overall, CRF mediated the relationship between birth weight and all cognition variables. In the first regression step (path a), birth weight was positively related with CRF (p<0.001). In the second step (path c), the regression coefficient of birth weight on the dependent variable (logical reasoning, the verbal factor, the numerical factor, the spatial factor or general intelligence)
intelligence) was also significant (p<0.05). In the last regression model, the potential mediator was positively related to the dependent variable (path b) (p<0.05), but when both birth weight and CRF were included in the model (path c'), the regression coefficient decreased significantly. Finally, the indirect effect was significant in all models, in such a way that CRF proved to be a full mediator of the relationship between birth weight and the verbal factor (percentage mediated [%Med]=35.5; p=0.008), the numerical factor (%Med=31.7; p=0.009) and general intelligence (%Med=28.6; p=0.006). Likewise, CRF proved to be a partial mediator in logical reasoning (%Med=29.4, p=0.005) and the spatial factor (%Med=16.2, p=0.029).

DISCUSSION

To our knowledge, this is the first study examining, in primary schoolchildren, the influence of CRF in the relationship between birth weight and cognitive function using mediation analysis procedures. Our data show that, after controlling for potential confounders, as compared to LBW, normal birth weight children scored higher in all cognition variables, except for verbal and numerical factors. Furthermore, children with higher aerobic capacity have better cognitive functions than their LBW peers, except for spatial factor. Lastly, CRF fully mediates the relationship between birth weight and the verbal factor, the numerical factor and general intelligence; and partially the relationship with logical reasoning and the spatial factor.

As compared with normal weight children, LBW negatively influences the development of the brain from in utero to the second decade of life (21). These negative effects may be expressed through worst cognitive function and academic achievement scores (22). Our results support previous findings, and reveal that the effect of LBW on cognition could be significantly mitigated by aerobic capacity. This is important because it
provides evidence that improving CRF might be a useful strategy to prevent the negative effects of LBW.

Neuroimaging methods have identified the potential mechanisms involved in childhood aerobic fitness, and brain structure and function. Specifically, children with lower levels of aerobic fitness have a poorer integrity of cognitive control processes (23). Conversely, better aerobic fitness levels result in changes in some cerebral regions that are needed to start a cascade of processes for inhibition, control or attention that, finally, lead to an improvement in cognitive functions related with enhanced cerebral activity (23) and academic achievement (24). Children with higher fitness also performed better in behavioral measures of reaction time and response accuracy (25). Our data support these findings, since children in the higher CRF categories scored higher in all cognition dimensions, even after controlling for birth weight and other confounders.

There is a lack of studies testing whether aerobic fitness mediates the relationship between cognition dimensions (general intelligence, logic reasoning, the verbal factor, the numerical factor and the spatial factor); the only similar one has tested the mediation effect of aerobic capacity between birth weight and academic achievement in preadolescents (12). Our study, using a frequently used battery including the main dimensions of cognition, confirms that CRF mediates the relationship between birth weight and cognition in 6-7 years old children, supporting that improvements in CRF could benefit the cognitive functions that underlie the academic performance since early in life.

Overall, our data suggest that the potentially deleterious effect of LBW on brain structures and function could be partially or totally avoided through physical activity interventions aimed at increasing aerobic fitness. Since physical activity behaviors are
acquired at early ages, parents and schools should provide children with opportunities to be active, particularly those with LBW.

Limitations

Some limitations of this study should be stated; i) the cross-sectional design prevents us from making causal inferences; however, it is possible to argue that the temporal ambiguity that threatens this type of cross-sectional study, as in our case, could be minimized because it seems clear that birth weight precedes cognition levels at 6-7 years of age. Regardless, prospective studies should be implemented to clearly establish the temporality of these relationships. ii) The CRF measurement did not use the gold standard measure, but a 20-m shuttle run test that has been proven to be a useful field test to estimate aerobic capacity was used. iii) We did not take into account other health-related physical fitness components, which could lead to a better understanding of the benefits of physical fitness on academic achievement; future studies using structural equation procedures or multiple mediator models might be useful to clarify more specifically the potential mediator role of different health-related fitness dimensions. iv) Children weighting more than 4000 g at birth were included in this study; a sensitivity mediation analysis removing children who were macrosomic at birth showed similar results. v) Finally, birth weight, cognitive function and CRF relationships could be potentially confounded by some sociodemographic variables such as age, current BMI or SES; we have included them as covariates in the models in order to control for them.

Conclusions

Our data suggest that CRF mediates the association between birth weight and cognitive function in schoolchildren, and therefore, improving CRF levels in LBW children might mitigate or avoid the deleterious effect of LBW on children’s general intelligence, logic
reasoning, verbal factor, numerical factor and spatial factor. Additionally, these results 
alert for the importance of implementing interventions aimed at improving and 
maintaining schoolchildren’s health-related physical fitness. Finally, children with both 
LBW and low fitness levels, detected by screening programs in clinical or school 
settings, should be a target subgroup in which long-life physical activity interventions 
are a priority.
FINANCIAL SUPPORT

This study was funded by the Ministry of Economy and Competitiveness – Carlos III Health Institute and FEDER funds (FIS PI12/02400 and FIS PI12/00761). Additional funding was obtained from the Research Network on Preventative Activities and Health Promotion (Ref. – RD12/0005/0009).

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Conflicts of interest: None.
REFERENCES


Figure caption/legend

**Figure 1.** Mediation models testing whether the relationship between birth weight and cognition variables was mediated by cardiorespiratory fitness (CRF), controlling for age (months), sex, socioeconomic status and body mass index. Abbreviations: IE (95%CI), Indirect Effect (95% Confidence Interval); %Med, percentage mediated by proposed mediator. Symbols: *p<0.05; **p<0.001.
ACKNOWLEDGE

We would like to thank all schools, families and pupils for their enthusiastic participation in the study.

In addition to the authors, the following are included in the MOVI-KIDS Study Group:
Table 1. Characteristics of the study sample.

<table>
<thead>
<tr>
<th></th>
<th>Total (n=664)</th>
<th>Boys (n=321)</th>
<th>Girls (n=343)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>75.19 (3.45)</td>
<td>75.12 (3.57)</td>
<td>75.22 (3.36)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>118.64 (5.20)</td>
<td>119.25 (5.19)</td>
<td>118.09 (5.10)</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>22.95 (5.00)</td>
<td>23.33 (5.22)</td>
<td>22.61 (4.76)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>16.19 (2.68)</td>
<td>16.28 (2.77)</td>
<td>16.10 (2.61)</td>
</tr>
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<td>Birth weight (g)</td>
<td>3279.69 (508.88)</td>
<td>3319.87 (544.74)</td>
<td>3243.72 (472.43)</td>
</tr>
<tr>
<td>Low birth weight (%)</td>
<td>7.3</td>
<td>6.5</td>
<td>7.9</td>
</tr>
<tr>
<td>Normal birth weight (%)</td>
<td>92.7</td>
<td>93.5</td>
<td>92.1</td>
</tr>
<tr>
<td>CRF (ml/kg/min)</td>
<td>49.85 (2.87)</td>
<td>50.44 (3.30)</td>
<td>49.30 (2.29)</td>
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<tr>
<td>Q1 (%)</td>
<td>31.7</td>
<td>30.1</td>
<td>33.2</td>
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<tr>
<td>Q2-3 (%)</td>
<td>42.3</td>
<td>35.8</td>
<td>48.2</td>
</tr>
<tr>
<td>Q4 (%)</td>
<td>25.9</td>
<td>34.1</td>
<td>18.6</td>
</tr>
<tr>
<td>Cognition variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logic Reasoning</td>
<td>27.26 (8.75)</td>
<td>27.15 (8.89)</td>
<td>27.22 (8.56)</td>
</tr>
<tr>
<td>Verbal Factor</td>
<td>21.70 (5.78)</td>
<td>21.42 (5.89)</td>
<td>21.95 (5.66)</td>
</tr>
<tr>
<td>Numerical Factor</td>
<td>17.24 (8.16)</td>
<td>17.81 (8.69)</td>
<td>16.64 (7.68)</td>
</tr>
<tr>
<td>Spatial Factor</td>
<td>15.78 (6.56)</td>
<td>15.69 (6.63)</td>
<td>15.76 (6.45)</td>
</tr>
<tr>
<td>General Intelligence</td>
<td>54.92 (16.82)</td>
<td>55.08 (17.62)</td>
<td>54.60 (16.07)</td>
</tr>
<tr>
<td>Socioeconomic status</td>
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<td></td>
</tr>
<tr>
<td>Low (%)</td>
<td>2.9</td>
<td>2.2</td>
<td>3.7</td>
</tr>
<tr>
<td>Low-medium (%)</td>
<td>28.0</td>
<td>30.9</td>
<td>24.7</td>
</tr>
<tr>
<td>Medium (%)</td>
<td>43.7</td>
<td>40.4</td>
<td>47.0</td>
</tr>
<tr>
<td>Medium-high (%)</td>
<td>20.1</td>
<td>22.2</td>
<td>18.3</td>
</tr>
<tr>
<td>High (%)</td>
<td>5.3</td>
<td>4.4</td>
<td>6.3</td>
</tr>
</tbody>
</table>

BMI, Body mass index; CRF, Cardiorespiratory fitness; Q, quartile.

Data presented as mean (SD).

CRF indicates vo2 max values obtained with Leger’s formula. Boldface type indicates statistical significance p<0.05.
Table 2. Pearson correlation coefficients (r) between cognition with anthropometric and CRF parameters, controlling for age (in months) and sex.

<table>
<thead>
<tr>
<th>Logic Reasoning</th>
<th>Verbal Factor</th>
<th>Numerical Factor</th>
<th>Spatial Factor</th>
<th>General Intelligence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>Total</td>
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<td>0.08</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>0.09</td>
<td>0.04</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>0.14*</td>
<td>0.11</td>
<td>0.06</td>
</tr>
<tr>
<td>CRF</td>
<td>Total</td>
<td>0.27**</td>
<td>0.21**</td>
<td>0.23**</td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>0.26**</td>
<td>0.23**</td>
<td>0.23**</td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>0.24**</td>
<td>0.19**</td>
<td>0.13*</td>
</tr>
</tbody>
</table>

CRF, cardiorespiratory fitness.

*p<0.05; **p<0.001.
Table 3. Mean differences (SD) in cognition dimensions by birth weight categories.

<table>
<thead>
<tr>
<th></th>
<th>Low birth weight</th>
<th>Normal birth weight</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logic Reasoning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>24.5 (8.6)</td>
<td>27.7 (8.8)</td>
<td>0.036</td>
</tr>
<tr>
<td>Model 2</td>
<td>25.5 (9.2)</td>
<td>27.8 (8.8)</td>
<td>0.135</td>
</tr>
<tr>
<td>Verbal Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>20.4 (5.5)</td>
<td>22.0 (6.6)</td>
<td>0.084</td>
</tr>
<tr>
<td>Model 2</td>
<td>21.4 (5.5)</td>
<td>22.1 (4.4)</td>
<td>0.434</td>
</tr>
<tr>
<td>Numerical Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>15.3 (8.0)</td>
<td>17.5 (8.8)</td>
<td>0.119</td>
</tr>
<tr>
<td>Model 2</td>
<td>16.7 (8.6)</td>
<td>17.5 (8.8)</td>
<td>0.519</td>
</tr>
<tr>
<td>Spatial Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>13.3 (6.8)</td>
<td>16.1 (6.6)</td>
<td>0.011</td>
</tr>
<tr>
<td>Model 2</td>
<td>13.7 (6.8)</td>
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<tr>
<td>General Intelligence</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>49.7 (17.3)</td>
<td>55.7 (15.4)</td>
<td>0.038</td>
</tr>
<tr>
<td>Model 2</td>
<td>52.6 (17.3)</td>
<td>55.9 (15.4)</td>
<td>0.261</td>
</tr>
</tbody>
</table>

Model 1: Age (months), sex, socioeconomic status and body mass index.
Model 2: Model 1 + Cardiorespiratory fitness.
Boldface type indicates statistical significance p<0.05.
**Table 4.** Mean differences (SD) in cognition variables by cardiorespiratory fitness categories.

<table>
<thead>
<tr>
<th></th>
<th>Poor</th>
<th>Medium</th>
<th>Good</th>
<th>p-value</th>
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<tr>
<td>Logic Reasoning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>26.2 (8.6)</td>
<td>27.0 (9.8)</td>
<td>30.5 (8.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2</td>
<td>26.4 (8.6)(^{M&gt;G})</td>
<td>27.0 (8.4)(^{G})</td>
<td>30.3 (8.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Verbal Factor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>21.1 (4.9)</td>
<td>21.9 (5.6)</td>
<td>23.6 (5.4)</td>
<td>0.001</td>
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<tr>
<td>Model 2</td>
<td>21.2 (4.9)(^{M})</td>
<td>21.9 (5.6)</td>
<td>23.5 (5.4)</td>
<td>0.002</td>
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<td>Numerical Factor</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>16.4 (7.3)(^{M})</td>
<td>16.9 (8.4)</td>
<td>19.8 (7.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Model 2</td>
<td>16.5 (7.3)(^{M})</td>
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<td>19.7 (7.6)</td>
<td>0.002</td>
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<tr>
<td>Spatial Factor</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Model 1</td>
<td>15.7 (6.1)(^{M&gt;G})</td>
<td>15.4 (7.0)(^{G})</td>
<td>17.1 (6.5)</td>
<td>0.059</td>
</tr>
<tr>
<td>Model 2</td>
<td>15.9 (6.1)(^{M&gt;G})</td>
<td>13.4 (5.6)(^{G})</td>
<td>17.0 (6.5)</td>
<td>0.095</td>
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<tr>
<td>Model 1</td>
<td>53.4 (15.9)(^{M})</td>
<td>54.3 (15.4)</td>
<td>60.8 (16.4)</td>
<td>&lt;0.001</td>
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<tr>
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<td>53.7 (15.9)(^{M})</td>
<td>54.3 (15.4)</td>
<td>60.4 (16.4)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

M-G, medium-good; G, good; M, medium.

Model 1: Age (months), sex, socioeconomic status and body mass index.

Model 2: Model 1+ Birth weight.

Boldface type indicates statistical significance p<0.05.

Pairwise mean comparisons using the Bonferroni post hoc test were statistically significant except for superscript letters (M-G, Medium-Good; M, Medium; P<0.05).
Figure 1. Mediation models testing whether the relationship between birth weight and cognition variables was mediated by cardiorespiratory fitness (CRF), controlling for age (months), sex, socioeconomic status and body mass index/Abbreviations: IE (95% CI), Indirect Effect (95% Confidence Interval); %Med, percentage mediated by proposed mediator. Symbols: *p<0.05; **p<0.001.

134x119mm (600 x 600 DPI)
**Supplemental Table S1.** Additional descriptive characteristics of the study sample.

<table>
<thead>
<tr>
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<th>Total (n=664)</th>
<th>Boys (n=321)</th>
<th>Girls (n=343)</th>
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</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>103.12 (10.40)</td>
<td>103.77 (10.69)</td>
<td>102.49 (9.94)</td>
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<tr>
<td>DBP (mmHg)</td>
<td>62.36 (8.79)</td>
<td>61.04 (8.44)</td>
<td>63.36 (8.94)</td>
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<tr>
<td>Waist circumference (cm)</td>
<td>56.95 (6.56)</td>
<td>57.43 (6.62)</td>
<td>56.50 (6.48)</td>
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<tr>
<td>Tricipital skinfold thickness (mm)</td>
<td>12.21 (4.92)</td>
<td>11.42 (5.13)</td>
<td>12.92 (4.58)</td>
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<tr>
<td>Fat mass (%)</td>
<td>20.20 (6.25)</td>
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<td>FMI (Kg/m$^2$)</td>
<td>3.43 (1.76)</td>
<td>3.35 (1.74)</td>
<td>3.50 (1.78)</td>
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</table>

**Fitness measurements**

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<tbody>
<tr>
<td>Standing-long jump test (cm)</td>
<td>96.79 (19.78)</td>
<td>101.33 (10.57)</td>
<td>56.50 (6.48)</td>
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<tr>
<td>Flexibility (cm)</td>
<td>21.18 (5.11)</td>
<td>26.23 (5.43)</td>
<td>92.72 (17.96)</td>
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<tr>
<td>Velocity (s)</td>
<td>16.37 (1.86)</td>
<td>16.09 (1.96)</td>
<td>28.02 (4.62)</td>
</tr>
</tbody>
</table>

SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; FMI: Fat Mass/Height$^2$
8. ABSTRACTS
ABSTRACTS

Abstract manuscript 1:

Introduction: Schools provide a relevant context for improving children’s and adolescents’ physical and mental health by increasing physical activity during school hours and/or beyond. The interest in the relationship between physical activity programmes and cognition during development has recently increased, with evidence suggesting a positive association. We present a protocol of systematic reviews and metaanalysis of intervention studies that, by determining the effects of chronic physical exercise on children’s and adolescents’ cognitive and metacognitive functions, cognitive life skills, academic behaviours and achievement, aims to ensure procedural objectivity and transparency, and maximise the extraction of relevant information to inform policy development.

Methods: This protocol is guided by Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) and by the Cochrane Collaboration Handbook. Databases to be utilised for a thorough selection of the pertinent literature are MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Web of Science, PsycINFO and ERIC. Selection is proposed to encompass an international and a national publication level, with inclusion of experimental studies written in English or in Spanish, respectively. Also, relevant references included in the selected studies will be considered suitable for review as supplemental sources. We present an integrated approach to the methodological quality assessment of the selected studies, including the Jadad Scale for the assessment of the quality of randomised controlled trials and the Quality Assessment Tool for Quantitative Studies for pre–post studies and non-randomised controlled trials. The pre–
post interventions mean differences will be the primary indicator of the intervention outcome. Statistical analysis: A subgroup analysis is proposed based on cognitive functions and their neural correlates, metacognitive functions and cognitive life skills, academic achievement areas and academic behaviours.

_Trial registration number:_ PROSPERO CRD42015029913
Abstract manuscript 2:

Objective: The objective was two-fold: i) to assess the effect of physical activity (PA) interventions on children’s and adolescents’ cognition and metacognition; and ii) to determine the characteristics of individuals and PA programs that enhance the development of cognitive and metacognitive functions.

Method: We systematically searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science and PsycINFO databases from their inception to October 16, 2016. Intervention studies aimed at examining the exercise-cognition interaction at a developmental age were included in this systematic review and metaanalysis.

Random-effects models were used to calculate pooled effect size (ES) values and their corresponding 95% confidence intervals (CIs). Subgroup analyses were conducted to examine the effect of participants’ and PA programs’ characteristics.

Results: Thirty-six studies were included in this systematic review and meta-analysis. Pooled ES estimations were: i) non-executive cognitive functions 0.23 (95% CI: 0.09 to 0.37); ii) core executive functions 0.20 (95% CI: 0.10 to 0.30), including working memory (0.14 [95% CI: 0.00 to 0.32]), selective attention-inhibition (0.26 [95% CI: 0.10 to 0.41]) and cognitive flexibility (0.11 [95% CI: -0.10 to 0.32]); and iii) metacognition 0.23 (95% CI: 0.13 to 0.32), including higher-level executive functions (0.19 [95% CI: 0.06 to 0.31]) and cognitive life skills (0.30 [95% CI: 0.15 to 0.45])
Abstract manuscript 3:

Context: Previous systematic reviews have examined the effects of physical activity interventions on children’s and adolescents’ cognition and academic achievement. But it remains unclear the effect of physical activity on different areas of academic achievement and classroom behaviours, and how different characteristics of physical activity interventions could modify the effect.

Objectives: The objective was two-fold: i) to assess the effect of physical activity interventions on academic achievement and classroom behaviours in childhood; and ii) to determine the characteristics of individuals and physical activity programs that enhance academic performance.

Data sources: Studies identified form the data base inception to October 16, 2016.

Study selection: Intervention studies aimed at examining the effect of exercise on academic achievement and classroom behaviours at developmental age.

Data extraction: Two independent researchers conducted data extraction. Random-effects models were used to calculate pooled effect size (ES) for all primary outcomes (language and mathematics related skills, reading, composite score and time in on-task behaviour). Positive values represent a direct relationship between physical activity programs and academic achievement scores or time in on-task behaviours.

Results: A total of 26 studies (10205 children, aged from 4-to-13) were included. Pooled ES (95% CI) estimates were: i) 0.16 (-0.06, 0.37) for language-related skills; ii) 0.21 (0.09, 0.33) for mathematics-related skills; iii) 0.13 (0.02, 0.24) for reading; iv) 0.26 (0.07, 0.45) for composite scores; and v) 0.77 (95% CI: 0.22, 1.32) for time in on-task behaviours.
Limitations: limitations included the variety of tools used to measure academic achievement and the limited number of studies that reported the effect of after-school physical activity interventions.

Conclusion: Physical activity, especially physical education, improves classroom behaviours and benefits several aspects of academic achievement, especially mathematics-related skills, reading and composite scores in youth.
Abstract manuscript 4:

*Background:* Obesity and overweight during pregnancy have been negatively associated with foetal and offspring neurodevelopment. The aim of this systematic review and meta-analysis was to assess the effect of the relationship between pre-pregnancy overweight and obesity with children’s neurocognitive development.

*Methods:* We systematically searched MEDLINE, EMBASE, the Cochrane Library, and the Web of Science databases from their inception through February 2017 for follow-up studies comparing the relationship between pre-pregnancy weight status and children’s cognition. The Mantel-Haenszel fixed effects method was used to calculate pooled effect size (ES) values and their corresponding 95% confidence intervals (CIs) comparing children’s neurocognitive development between pre-pregnancy normal weight as reference with overweight and obesity categories.

*Results:* Fifteen articles were included in the systematic review, and nine of them in the meta-analysis. The pooled ES values for overweight and obese mothers were -0.02 (95% CI: -0.05 to 0.02) and -0.06 (95% CI: -0.09 to -0.03), respectively. The pooled ES for the relationship between pre-gestational excess weight (overweight and obesity) and children’s neurocognitive development was -0.04 (95% CI: -0.06 to -0.02).

*Conclusions:* Pre-pregnancy obesity might have negative consequences on the neurocognitive development of offspring.

*Keywords:* pregnancy, obesity, children, cognition, cognitive function, neurocognitive development.
Abstract manuscript 6:

Objective: The aim of this systematic review and meta-analysis was to assess the effect of leisure physical activity during pregnancy on children’s neurocognitive development.


Selection criteria: Follow-up studies concerning the relationship between leisure physical activity during pregnancy and children’s cognition were included. Study selection and data extraction were performed in duplicate after removing identifying information.

Data collection and Analysis: Effect size (ES) and their corresponding 95% confidence intervals (CIs) were calculated for all primary outcomes (general intelligence and language-related skills). The DerSimonian and Laird method was used to compute pooled ES estimates for each primary outcome.

Main results: Six studies met the inclusion criteria (11388 children aged from one to 10). Pooled ES estimates for the relationship between physical activity during leisure time and children’s neurocognitive development were 0.16 (95% CI: 0.08 to 0.25) for general intelligence and 0.07 (95% CI: 0.02 to 0.13) for language-related skills.

Conclusion: Our data show that children from mothers who have performed some physical activity during leisure time scored better on general intelligence through only slightly better on language-related skills than their peers.
Abstract manuscript 5:

Objective: The aims of this study were to examine differences in cognition parameters by birth weight categories; and to analyze whether the relationships between birth weight and cognitive functions are mediated by cardio respiratory fitness (CRF) in schoolchildren.

Design and methods: A cross-sectional study using a sample of 664 schoolchildren from the MOVI-Kids study. Variables: i) cognitive function was measured by the Battery of General and Differential Aptitudes (BADyG); ii) birth weight, reported by parents; and iii) CRF, (20-m shuttle run test). ANCOVA models were estimated to explore differences in cognitive function levels across birth weight and CRF categories. Hayes’s PROCESS macro was used for the simple mediation analysis.

Results: CRF acts as a full mediator of the relationship between birth weight with the verbal and numerical factors, and general intelligence; and as a partial mediator when logical reasoning and the spatial factor were the dependent variables.

Conclusions: Our data suggest that, in schoolchildren, the influence of birth weight on cognitive function is mediated by CRF. This finding highlights that, to improve children’s cognition, it is important to diminish the prevalence of low birth weight, and also to promote physical activity at early ages.
9. CONCLUSIONS
CONCLUSIONS

The main conclusions of this thesis related to the aims are:

Conclusions on the aim 1: To provide a novel protocol designed to review interventional studies addressing the chronic exercise–cognition interaction in children and adolescents for obtaining relevant information for policymakers and decision makers particularly in, but not limited to, the education sector. (Manuscript 1)

- It is provided a clear and structured procedure for maximizing the extraction of relevant information and providing summarized information on the importance of the effects of physical activity programs on children’s cognition, metacognition and academic achievement.

Conclusions on the aim 2: To assess the effect of PA interventions on children’s and adolescents’ cognition, distinguishing between core executive functions and metacognition. (Manuscript 2)

- Physical activity programs benefit multiple facets of non-executive, executive and metacognitive functions and skills in children and adolescents.
- The domains of cognition most sensitive to exercise were working memory, inhibition, higher-level executive functions and cognitive life skills.

Conclusions on the aim 3: To determine which individual and PA program characteristics are most favourable to aid the development of cognitive and metacognitive functions. (Manuscript 2)

- Participants’ age seems to uniquely act as an amplifier of the size of intervention effects in non-executive functions.
- Curricular physical education and programs aimed at increasing the amount of exercise seem to be the most effective for improving children’s working
memory and higher-level executive functions. While, enriched PA programs seem to particularly improve inhibitory efficiency.

**Conclusions on the aim 4:** To assess the effect of physical activity interventions on children’s and adolescents’ academic achievement and classroom behaviours. (Manuscript 3)

- Physical activity programs significantly benefit multiple facets of academic achievement: mathematics-related skills, reading and composite scores. Additionally, it shows that classroom behaviours are improved after physical activity interventions.

**Conclusions on the aim 5:** To determine the individual and physical activity programs’ characteristics that are most favourable to aid the development of academic performance (Manuscript 3)

- No individual characteristics seem to have influence on the effectiveness of physical activity programs.
- Curricular physical education lessons seem to be the most appropriate framework to improve children’s academic achievement, although integrating physical activity in classroom lessons also benefited mathematics-related skills.

**Conclusions on the aim 6:** To assess the effect of pre-pregnancy overweight and obesity on children’s neurocognitive development. (Manuscript 4)

- Mothers who are obese prior to pregnancy, but not overweight, have a negative influence on the offspring’s neurocognitive development. Furthermore, pre-pregnancy obesity could have a small negative effect on children’s general intelligence.
Conclusions on the aim 7: To assess the effect of leisure physical activity during pregnancy on children’s neurocognitive development (Manuscript 5).

- Children from mothers who have performed some leisure physical activity during pregnancy scored better on general intelligence though only slightly better on language-related skills than their peers.

Conclusions on the aim 8: To examine differences in cognition parameters by birth weight categories controlling for potential confounders or mediators (Manuscript 6)

- After controlling for potential confounders, as compared to low birth weight, normal birth weight children scored higher in all cognition variables. Furthermore, children with higher aerobic capacity have better cognition functions than their lower birth weight peers.

Conclusions on the aim 9: To analyze whether the relationships between birth weight and cognitive functions are mediated by CRF in schoolchildren (Manuscript 6).

- Cardiorespiratory fitness fully mediates the relationship between birth weight and the verbal factor, the numerical factor and general intelligence; and partially the relationship with logical reasoning and the spatial factor.
10. CONCLUSIONES
CONCLUSIONES

Las principales conclusiones de esta tesis doctoral relacionadas con los objetivos, son:

Conclusiones al objetivo 1: Proporcionar una metodología novedosa para revisar los estudios de intervención en relación al efecto de las intervenciones de ejercicio crónico en la cognición de niños y adolescentes, diseñada con la finalidad de obtener información relevante para los encargados de formular y tomar decisiones políticas a este respecto, particularmente en el sector de la educación. (Manuscrito 1)

- Se proporciona un procedimiento claro y estructurado para maximizar la extracción y presentación resumida de información sobre la importancia de los efectos de los programas de actividad física en la cognición, la metacognición y el rendimiento académico de los niños.

Conclusiones al objetivo 2: Evaluar el efecto de las intervenciones de actividad física en la cognición de niños y adolescentes, distinguiendo entre funciones ejecutivas centrales y metacognición. (Manuscrito 2)

- Los programas de actividad física benefician múltiples facetas de las funciones no ejecutivas, funciones ejecutivas centrales y metacognición en niños y adolescentes.

- Los dominios cognitivos más sensibles a la actividad física son: la memoria de trabajo, la inhibición, las funciones ejecutivas de alto nivel y las habilidades cognitivas de la vida.

Conclusiones al objetivo 3: Determinar qué características individuales y de los programas de actividad física son las más favorables para ayudar al desarrollo de funciones cognitivas y metacognitivas. (Manuscrito 2)
- La edad de los participantes parece estar relacionada únicamente con las funciones no ejecutivas, aumentando el efecto de los programas de actividad física.
- La educación física curricular y los programas destinados a aumentar la cantidad de actividad física diaria parecen ser los más efectivos para mejorar la memoria de trabajo y las funciones ejecutivas de más alto nivel de los niños. Además, los programas de actividad física enriquecidos parecen mejorar especialmente la inhibición.

**Conclusiones al objetivo 4:** Evaluar el efecto de las intervenciones de actividad física sobre el rendimiento académico y los comportamientos en el aula de los niños y adolescentes. (Manuscrito 3)

- Los programas de actividad física benefician de manera significativa múltiples facetas del rendimiento académico: habilidades relacionadas con las matemáticas, lectura y notas totales; así como los comportamientos en el aula.

**Conclusiones al objetivo 5** Determinar las características individuales y de los programas de actividad física que son más favorables para el desarrollo del rendimiento académico. (Manuscrito 3)

- Ninguna característica individual parece influir en la efectividad de los programas de actividad física.
- Las lecciones de educación física curricular parecen ser las más apropiadas para mejorar el rendimiento académico de los niños. Además, la integración de la actividad física en el aula también beneficia las habilidades relacionadas con las matemáticas.
**Conclusiones al objetivo 6:** Evaluar el efecto del sobrepeso y la obesidad pre-gestacional en el desarrollo neurocognitivo de los niños. (Manuscrito 4)

- La obesidad materna pre-gestacional, pero no el sobrepeso, tiene una influencia negativa en el desarrollo neurocognitivo de los descendientes. Además, la obesidad pre-gestacional puede tener un efecto negativo pequeño sobre en la inteligencia general de los niños.

**Conclusiones al objetivo 9:** Evaluar el efecto de la actividad física desarrollada en el tiempo libre durante el embarazo en el desarrollo neurocognitivo de los niños. (Manuscrito 5).

- Los niños de madres que han realizado alguna actividad física en el tiempo libre durante el embarazo obtuvieron mejores calificaciones en inteligencia general, aunque sólo un poco mejor en habilidades relacionadas con el lenguaje que los niños de madres que no realizaron actividad física en el tiempo libre durante el embarazo.

**Conclusiones al objetivo 7:** Examinar las diferencias por categorías de peso al nacer en distintos parámetros cognitivos, controlando por potenciales factores de confusión o mediadores. (Manuscrito 6)

- Los niños con peso normal al nacer obtienen mejores puntuaciones en todas las variables cognitivas en comparación con los niños de bajo peso al nacer, controlando por posibles factores de confusión. Además, los niños con mayor capacidad aeróbica tienen mejores funciones cognitivas que los de bajo peso al nacer.
Conclusiones al objetivo 8: Analizar si las relaciones entre el peso al nacer y las funciones cognitivas están mediadas por capacidad cardiorrespiratoria en los escolares. (Manuscrito 6).

- La capacidad cardiorrespiratoria es un mediador total en la relación entre el peso al nacer y el factor verbal, el factor numérico y la inteligencia general. Además, es un mediador parcial en la relación entre el peso al nacer con el razonamiento lógico y el factor espacial.
11. REFERENCES
REFERENCES


31. Caterina Pesce et al 2016. Coupling our plough of thoughtful moving to the star of
children’s right to play: from neuroscience to multisectoral promotion. Physical Activity and Educational Achievement Insights from Exercise Neuroscience. Edited by Romain Meeusen, Sabine Schaefer, Phillip Tomporowski, Richard Bailey


Kinetics.


70. U.S. National Association for Sports and Physical Education guideline.


123. Physical activity and exercise during pregnancy and the postpartum period.


12. APPENDIX
APPENDIX

Appendix 1. PROSPERO register. The association between physical activity and academic performance of schoolchildren: a protocol for a systematic review.
PROSPERO International prospective register of systematic reviews

Review title and timescale

1. Review title
   Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
   The association between physical activity and academic performance of schoolchildren: a protocol for a systematic review

2. Original language title
   For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. Anticipated or actual start date
   Give the date when the systematic review commenced, or is expected to commence.
   02/11/2015

4. Anticipated completion date
   Give the date by which the review is expected to be completed.
   31/08/2016

5. Stage of review at time of this submission
   Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.
   The review has not yet started  ✗

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<tr>
<td>Piloting of the study selection process</td>
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<td>No</td>
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<tr>
<td>Formal screening of search results against eligibility criteria</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Data extraction</td>
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<td>Risk of bias (quality) assessment</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Data analysis</td>
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</table>

Provide any other relevant information about the stage of the review here.

Review team details

6. Named contact
   The named contact acts as the guarantor for the accuracy of the information presented in the register record.
   Miss Alvarez-Bueno

7. Named contact email
   Enter the electronic mail address of the named contact.
   Celia.Alvarezbueno@uclm.es

8. Named contact address
   Enter the full postal address for the named contact.
   Calle Santa Teresa Jomet, s/n; Cuenca. CP 16071

9. Named contact phone number
   Enter the telephone number for the named contact, including international dialing code.
   969179100 (Ex:4659)

10. Organisational affiliation of the review
    Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
Review team members and their organisational affiliations
Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

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<td>Celia</td>
<td>Álvarez-Bueno</td>
<td>Universidad de Castilla-La Mancha</td>
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<tr>
<td>Mrs</td>
<td>Mairena</td>
<td>Sánchez-López</td>
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<td>Mrs</td>
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<td>Gutiarró-Pardo</td>
<td>Universidad de Castilla-La Mancha</td>
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<tr>
<td>Mr</td>
<td>Iván</td>
<td>Cavero-Redondo</td>
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<tr>
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<td>Martínez-Vizcaíno</td>
<td>Universidad de Castilla-La Mancha</td>
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Funding sources/sponsors
Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
None

Conflicts of interest
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.
Are there any actual or potential conflicts of interest?
None known

Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

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Review methods

Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
The purpose of this systematic review is to determinate the relationship between physical activity and children’s academic performance based on data of experimental studies.

Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
The search will be conducted in MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane database of systematic reviews, and Web of Science databases from their inception. The following search term will be used: physical activity, physical education, exercise, cognition, academic, academic achievement, intelligence, children, preschool, preschooler, young children, and trial. No electronic limitation on language or publication status will be added.

URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.
I give permission for this file to be made publicly available
Yes

Condition or domain being studied
Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Children’s academic performance

19 Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.

Children involved in experimental studies on physical activity programs. Studies including children with physical or mental disorders that could impede participation in physical activity program will be excluded.

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed.

We will include studies reporting any type of physical activity program, except acute physical activity programs. We will exclude studies evaluating physical activity programs combined with other intervention such as nutritional interventions.

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).

We will include those studies comparing physical activity programs with control group, different types of physical activity programs, and studies developing physical activity programs without control group.

22 Types of study to be included
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.

Experimental studies

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

24 Primary outcome(s)
Give the most important outcomes.

Academic performance measured by total subject/areas or standardized test

Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.

Improvement on specific areas/skills pre-post intervention

Give information on timing and effect measures, as appropriate.

26 Data extraction (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.

The Jadad Scale will be used to assess the methodological quality of studies. Any disagreement in the assessment of risk of bias will be discuss to reach consensus.

28 Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.

Researchers will create tables to summarize the included studies and show their key characteristics and any important question related to the aim of this review. Reviewers will determine whether a meta-analysis is possible, when data have been extracted. If it is possible to carry out a meta-analysis, STATA 13 software will be used to combine data
with 95% CIs. Fixed-effect model will be used if there is no evidence of heterogeneity, otherwise random-effect model will be used.

29 Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.
If it is possible, a subgroup analyses will be performed based on cognitive skills or academic achievement areas measured (non-verbal ability, spatial ability, abstract reasoning, mathematics, language,...), or on test used to measure them (Cognitive Assessment System (CAS), Color-Word Stroop test, General Intelligence Test (GfT), Canadian Achievement Test, curriculum based marks, etc.).

Review general information

30 Type and method of review
Select the type of review and the review method from the drop down list.
Intervention, Systematic review

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Spain

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Completed and published
39  Any additional information
    Provide any further information the review team consider relevant to the registration of the review.

40  Details of final report/publication(s)
    This field should be left empty until details of the completed review are available.
    Give the full citation for the final report or publication of the systematic review.
    Give the URL where available.
Appendix 2. PROSPERO register. Association between pre-pregnancy BMI and children’s neurocognitive development
**Review title and timescale**

1. **Review title**
   Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
   - Association between pre-pregnancy BMI and children’s neurocognitive development

2. **Original language title**
   For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3. **Anticipated or actual start date**
   Give the date when the systematic review commenced, or is expected to commence.
   - 06/06/2016

4. **Anticipated completion date**
   Give the date by which the review is expected to be completed.
   - 05/09/2016

5. **Stage of review at time of this submission**
   Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.
   - The review has not yet started

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<thead>
<tr>
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<tr>
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<tr>
<td>Piloting of the study selection process</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Formal screening of search results against eligibility criteria</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Data extraction</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Risk of bias (quality) assessment</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Data analysis</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Provide any other relevant information about the stage of the review here.

**Review team details**

6. **Named contact**
   The named contact acts as the guarantor for the accuracy of the information presented in the register record.
   - Dr Alvarez-Bueno

7. **Named contact email**
   Enter the electronic mail address of the named contact.
   - Celia.Alvarezbueno@uclm.es

8. **Named contact address**
   Enter the full postal address for the named contact.
   - Calle Santa Teresa Jornet, s/n; Cuenca. CP 16071

9. **Named contact phone number**
   Enter the telephone number for the named contact, including international dialing code.
   - 969179100 (Ex:4659)

10. **Organisational affiliation of the review**
    Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
    - Universidad de Castilla-La Mancha. Centro de Estudios Sociosanitarios. Cuenca
    - Website address:

11. **Review team members and their organisational affiliations**
    Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.
    | Title | First name | Last name | Affiliation |
    |-------|------------|-----------|-------------|
    | Dr    | Celia      | Alvarez-Bueno |

12. **Funding sources/sponsors**
    Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
    - None

13. **Conflicts of interest**
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Are there any actual or potential conflicts of interest?

None known

Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

<table>
<thead>
<tr>
<th>Title</th>
<th>First name</th>
<th>Last name</th>
<th>Organisation details</th>
</tr>
</thead>
</table>

Review methods

15 Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
The aim of this systematic review is to assess the effect of the relationship between the pre-pregnancy weight status and the children’s neurocognitive development.

16 Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
MEDLINE (via PubMed), EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, and Web of Science. Including studies written in Spanish and English

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available
Yes

18 Condition or domain being studied
Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.
The relationship between mother’s weight status and offspring’s neurocognitive development

19 Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.
Mothers

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
None

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).
Neurocognitive scores of children from underweight, overweight and obese pre-gestational mothers will be compared against neurocognitive scores of children from normoweight mothers

22 Types of study to be included
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
Longitudinal studies

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

24 Primary outcome(s)
Give the most important outcomes.
Children’s neurocognitive development
Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
None
Give information on timing and effect measures, as appropriate.

26 Data extraction (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.
A standardized checklist of predefined criteria based on CONSORT statements of reporting requirements for non-randomized interventions will be used. The checklist includes criteria in two categories: i) aspects that could influence effects estimates, and ii) descriptive and contextual issues.

28 Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.

Effect size will be observed as primary outcome, this provides a measure of change in standard deviation units. A standardized mean difference score will be calculated for each woman's pre-pregnancy weight status category to determine effect size

29 Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.
Subgroup analyses will performed comparing normoweight with each weight status category: underweight, overweight and obesity in order to observe which had the highest effect size and to control the heterogeneity in each weight status category

Review general information

30 Type and method of review
Select the type of review and the review method from the drop down list.
Meta-analysis, Systematic review

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English
Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Spain

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences. Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Completed but not published

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.
Appendix 3. PROSPERO register. Effects of physical activity during pregnancy on children’s cognition: systematic review and meta-analysis.
PROSPERO International prospective register of systematic reviews

Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Effects of physical activity during pregnancy on children’s cognition: systematic review and meta-analysis

2 Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.

3 Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
13/02/2017

4 Anticipated completion date
Give the date by which the review is expected to be completed.
31/07/2017

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.
The review has not yet started ✗

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<td>No</td>
</tr>
<tr>
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Provide any other relevant information about the stage of the review here.

Review team details

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Mrs Alvarez-Bueno

7 Named contact email
Enter the electronic mail address of the named contact.
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9 Named contact phone number
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969179100 (Ex:4659)

10 Organisational affiliation of the review
Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
Universidad de Castilla-La Mancha. Helath and Social Research Center. Cuenca
11 Review team members and their organisational affiliations

Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

<table>
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<tr>
<th>Title</th>
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<tbody>
<tr>
<td>Mrs</td>
<td>Celia</td>
<td>Alvarez-Bueno</td>
<td></td>
</tr>
<tr>
<td>Mr</td>
<td>Iván</td>
<td>Cavero-Redondo</td>
<td></td>
</tr>
<tr>
<td>Dr</td>
<td>Mairena</td>
<td>Sánchez-López</td>
<td></td>
</tr>
<tr>
<td>Miss</td>
<td>Miriam</td>
<td>Garrido-Miguel</td>
<td></td>
</tr>
<tr>
<td>Mr</td>
<td>José Alberto</td>
<td>Martínez-Hortelano</td>
<td></td>
</tr>
<tr>
<td>Professor</td>
<td>Vicente</td>
<td>Martínez-Vizcaíno</td>
<td></td>
</tr>
</tbody>
</table>

12 Funding sources/sponsors

Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.

None

13 Conflicts of interest

List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.

Are there any actual or potential conflicts of interest?

None known

14 Collaborators

Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

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<th>Last name</th>
<th>Organisation details</th>
</tr>
</thead>
</table>

Review methods

15 Review question(s)

State the question(s) to be addressed / review objectives. Please complete a separate box for each question.

The aim of this study is to determine the effect of physical activity during pregnancy on children’s cognition

16 Searches

Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.


17 URL to search strategy

If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available

Yes

18 Condition or domain being studied

Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.

Physical activity during pregnancy and its relationship with offspring’s cognition
19  Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.
Participants will be pregnant women and their offspring, including any follow-up studies.

20  Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed.
Any physical activity condition during pregnancy will be considered. Children's cognition could be assessed at any age and throughout standardized test or curricular-based marks.

21  Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).
Cognition of children whose mothers performed physical activity during pregnancy will be compared with children's cognition whose mothers were sedentary during pregnancy.

22  Types of study to be included
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
Prospective or retrospective observational studies relating physical activity during pregnancy and children's cognition.

23  Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.

24  Primary outcome(s)
Give the most important outcomes.
Mean differences between children’s cognition score whose mothers were physical active during pregnancy and children's cognition scores whose mothers were sedentary during pregnancy.

Give information on timing and effect measures, as appropriate.

25  Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
No secondary outcomes will be considered.

Give information on timing and effect measures, as appropriate.

26  Data extraction (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.

27  Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.
A standardized checklist for reporting of observational longitudinal research will be used (Quality of reporting of observational longitudinal research). This checklist includes two categories of criteria: i) aspects that could influence effect estimates, and ii) descriptive and contextual issues. The rating list consists of 33 criteria and each criterion will be assessed as ‘yes’ (= 1), ‘no’ (= 0) or not applicable (=?); thus the quality score for each study ranged from 0 to 33.

28  Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where appropriate a brief outline of analytic approach should be given.
Effect size will be observed as primary outcome, this provides a measure of change in standard deviation units. A standardized mean difference score will be calculated for each woman's physical activity during pregnancy category to determine effect size. If it is possible to carry out a meta-analysis, STATA 14 software will be used to combine the pooled effect size with 95% CIs.

29  Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. ‘None planned’ is a valid response if no subgroup analyses are planned.
Subgroup analysis and meta-regression models will be performed based on participants' characteristics and physical activity types. Furthermore, the design and the risk of bias will be considered for additional subgroup analysis.

**Review general information**

30 Type and method of review
Select the type of review and the review method from the drop down list.
Meta-analysis, Systematic review

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English
Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Spain

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Completed but not published

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.
40 Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.
Appendix 4. Supplementary material manuscript 2: The effect of physical activity interventions on children’s cognition and metacognition: a systematic review and meta-analysis.
**Table S1. Characteristics of the included studies.**

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>N (CG/EG1/EG2)</th>
<th>Age (SD)</th>
<th>CG/EG1/EG2</th>
<th>Place in the school plan</th>
<th>Task characteristics</th>
<th>Intervention design</th>
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</thead>
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<tr>
<td>Adsiz et al 2012</td>
<td>Turkey</td>
<td>60 (30/30)</td>
<td>11-12</td>
<td>CG: no extra PA EG: sport activities 3d/w</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>Engaging PA: volleyball and gymnastics</td>
</tr>
<tr>
<td>Ardoy et al 2014</td>
<td>Spain</td>
<td>67 (18/24/23)</td>
<td>13 (0.82)</td>
<td>CG: 55min 2d/w (usual PE) EG1: 55 min 4d/w EG2: 55 min 4d/w</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>CG: fitness and health, games and sports, motor skills, corporeal expression and activities in the natural environment EG1: as CG, but doubled the number of sessions EG2: as EG1, but performed at a higher intensity Fitness activity. 80 extra min for motor skills training, and education on snack and water consumption</td>
</tr>
<tr>
<td>Castelli et al 2011</td>
<td>US</td>
<td>59 (0/59)</td>
<td>8.79</td>
<td>EG: 40 min 5d/w</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td></td>
</tr>
<tr>
<td>Chang et al 2013</td>
<td>Taiwan</td>
<td>26 (13/13)</td>
<td>7.1 (0.33)</td>
<td>EG1: 35 min 2d/w EG2: 35 min 2d/w</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>EG1: soccer exercise low intensity EG2: soccer exercise moderate intensity EG1: passive stretching, aerobic exercise, running, group games EG2: pranayama, sithilikarna vyayama, asanas 60 min of usual PE and 120 min of skill-based and tennis-specific training</td>
</tr>
<tr>
<td>Chaya et al 2012</td>
<td>India</td>
<td>180 (90/90)</td>
<td>7.8 (0.9)</td>
<td>EG1: 45 min 6d/w PE EG2: 45 min 6d/w yoga</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
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<tr>
<td>Crova et al 2014</td>
<td>Italy</td>
<td>70 (33/37)</td>
<td>9.6 (0.5)</td>
<td>EG: 60 min 1d/w (usual PE) EG: 180 min 1d/w</td>
<td>Curricular PE</td>
<td>Enhanced and enriched PA</td>
<td></td>
</tr>
<tr>
<td>Davis et al 2007</td>
<td>US</td>
<td>94 (29/33/32)</td>
<td>9.2 (0.84)</td>
<td>CG sedentary activities EG1: 20 min 5d/w EG2: 40 min 5d/w</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>EG1: low-dose exercise: 20 min of jump rope, running games, modified soccer or basketball, and static and dynamic stretching + 20 min sedentary activities. EG2: high-dose exercise: 40 min of jump rope, running games, modified soccer and basketball</td>
</tr>
<tr>
<td>Davis et al 2011</td>
<td>US</td>
<td>171 (60/55/56)</td>
<td>9.3 (1.0)</td>
<td>CG sedentary activities EG1: 20 min 5d/w EG2: 40 min 5d/w</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>EG1: low-dose exercise: running games, jump rope, modified soccer and basketball EG2: high-dose exercise: running games, jump rope, modified soccer and basketball</td>
</tr>
<tr>
<td>de Greeff et al 2016</td>
<td>The Netherlands</td>
<td>499 (250/249)</td>
<td>8.1 (0.7)</td>
<td>CG: usual PE EG: 20-30 min 3d/w</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Moderate to vigorous intensity PE on solving mathematical problems (10-15) and on language (10-15)</td>
</tr>
<tr>
<td>Fisher et al 2011</td>
<td>UK</td>
<td>64 (30/34)</td>
<td>6.2 (0.3)</td>
<td>EG: 60 min 1d/w (usual PE) EG: 120 min 1d/w</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>Maximization of PA time within PE sessions, by minimising instruction time and waiting time during equipment changes</td>
</tr>
<tr>
<td>Fredericks et al 2006</td>
<td>South Africa</td>
<td>53 (13/13/14/13)</td>
<td>5.5-6.5</td>
<td>CG: usual PE EG1: free-play EG2: educational toys. EG3: 20 min 7d/w</td>
<td>Extracurricular PA</td>
<td>Enhanced and enriched PA</td>
<td>EG1: free play EG2: educational toys EG3: Warm-up activities, flip-flops, beanie back-roll, side-to-side tips, quarter-turn roll, ball throw and tap, accentuation hoop and animal-walk exit</td>
</tr>
</tbody>
</table>

CG: Control Group; EG: Experimental Group; SD: Standard deviation; PA: Physical Activity; PE: Physical Education; d/w: days per week; min: minutes
<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>N</th>
<th>Age</th>
<th>CG/EG1/EG2</th>
<th>Place in the school plan</th>
<th>Task characteristics</th>
<th>Intervention characteristics</th>
<th>Length (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallotta et al 2015</td>
<td>Italy</td>
<td>156</td>
<td>8-11</td>
<td>CG: no treatment</td>
<td>Curricular PE</td>
<td>EG1: enhanced PA</td>
<td>EG1: traditional, PA: health, fitness, sensory-motor, social and communicative development (endurance, strength, flexibility, circuit training)</td>
<td>20</td>
</tr>
<tr>
<td>Goudas et al 2016</td>
<td>Greece</td>
<td>73</td>
<td>12.32</td>
<td>CG: usual PE</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>Warm-up (8-10min); training program (45 min); cool-down (5-7 min)</td>
<td>36</td>
</tr>
<tr>
<td>Koutsandreou et al 2016</td>
<td>Germany</td>
<td>71</td>
<td>9.35</td>
<td>CG: usual PE</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>Goal setting, group learning, reflection on action and written worksheets</td>
<td>4</td>
</tr>
<tr>
<td>Krafft et al 2014</td>
<td>US</td>
<td>43</td>
<td>9.7 (0.8)-</td>
<td>CG: usual PE</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>CG: sedentary activities</td>
<td>32</td>
</tr>
<tr>
<td>Lakes et al 2004</td>
<td>US</td>
<td>193</td>
<td>Grade 5</td>
<td>CG: 45 min 4d/w (usual PE)</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>EG: aerobic exercise such as tag and jump rope</td>
<td>26</td>
</tr>
<tr>
<td>Lakes et al 2013</td>
<td>US</td>
<td>81</td>
<td>12.2-12.3</td>
<td>CG: 40-45 min 5d/w (usual PE)</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>Martial arts: blocks, kicks, punches, martial arts movement, broad-breaking techniques, complete body-stretching techniques and deep-breathing relaxation techniques</td>
<td>36</td>
</tr>
<tr>
<td>Manjunath et al 2001</td>
<td>India</td>
<td>20</td>
<td>10-13</td>
<td>CG1: yoga asanas, pranayama, kriyas, meditation, bhajans and relaxation techniques</td>
<td>After-school PA</td>
<td>Enriched PA</td>
<td>EG1: yoga: asanas, pranayama, kriyas, meditation, bhajans and relaxation techniques</td>
<td>4</td>
</tr>
<tr>
<td>Manjunath et al 2004</td>
<td>India</td>
<td>90</td>
<td>13.1(2.3)-</td>
<td>CG: routine activities</td>
<td>After-school PA</td>
<td>EG1: Enhanced PA</td>
<td>EG2: physical training: sitting exercises, jogging, bending - forward, backward and side ways</td>
<td>1.5</td>
</tr>
</tbody>
</table>

CG: Control Group; EG: Experimental Group; SD: Standard deviation; PA: Physical Activity; PE: Physical Education; d/w: days per week; min: minutes
Table S1. Characteristics of included studies. (continue)

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>N (CG/EG1/EG2)</th>
<th>Age</th>
<th>CG/EG1/EG2</th>
<th>Place in the school plan</th>
<th>Task characteristics</th>
<th>Intervention characteristics</th>
<th>Length (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mavilidi et al 2015 60</td>
<td>Australia</td>
<td>111 (26/31/31/23)</td>
<td>4.94 (0.56)</td>
<td>CG1: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>CG1: academic: verbal repetition of words</td>
<td>4</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CG2: gesturing (not considered)</td>
<td></td>
<td></td>
<td>CG2: academic and gestures: mimic gestures for practice words</td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG1: 15 min 2d/w</td>
<td></td>
<td></td>
<td>EG1: aerobic and cognitively engaging: physical exercise enacted the actions indicated by the words</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>EG2: 15 min 2d/w</td>
<td></td>
<td></td>
<td>EG2: aerobic: running, walking around the class</td>
<td></td>
</tr>
<tr>
<td>Pesce et al 2013 61</td>
<td>Italy</td>
<td>250 (96/71/83)</td>
<td>6.8 (1.5)-7.1 (1.3)</td>
<td>CG: 60 min 1d/w (usual PE)</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>CG: generalist-led PE</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG1: 60 min 1d/w</td>
<td></td>
<td></td>
<td>EG1: specialist-led PE</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG2: 60 min 1d/w</td>
<td></td>
<td></td>
<td>EG2: cognitively enriched, specialist-led PE</td>
<td></td>
</tr>
<tr>
<td>Pesce et al 2016 a 62</td>
<td>Italy</td>
<td>460 (230/230)</td>
<td>5-10</td>
<td>CG: 60 min 1d/w (usual PE)</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>EG: fitness, coordination, cognition and life skills training embedded in PA games</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG: 60 min 2d/w</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pesce et al 2016 b 10</td>
<td>Italy</td>
<td>90 (45/45)</td>
<td>14.5 (0.5)</td>
<td>CG: usual PE (60 min 2d/w)</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>Life skills teaching: oral presentation of life skill, application in sport games and multi-sport PA followed by group-based reflection on action</td>
<td>36</td>
</tr>
<tr>
<td>Reed et al 2010 63</td>
<td>US</td>
<td>155 (75/80)</td>
<td>4.42-9.45</td>
<td>CG: no classroom-based PA</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>Integrated PA (running, hopping, walking…) into core lessons</td>
<td>16</td>
</tr>
<tr>
<td>Reed et al 2013 64</td>
<td>US</td>
<td>470 (305/165)</td>
<td>11.1 (1.9)-10.2 (2.3)</td>
<td>EG: 45 min 1d/w Elementary school</td>
<td>Curricular PE</td>
<td>Elementary: Enhanced PA</td>
<td>Elementary (EG and CG): developmental curriculum based on motor skills</td>
<td>34</td>
</tr>
<tr>
<td>Schmidt et al 2015 65</td>
<td>Switzerland</td>
<td>181 (55/69/57)</td>
<td>11.35 (0.6)</td>
<td>EG: 45 min 5d/w Middle school</td>
<td>Curricular PE</td>
<td>Middle: Enhanced PA</td>
<td>Middle (EG and CG): Multi activity sports themed curriculum</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CG: 50 min 5d/w (usual PE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spitzer et al 2013 66</td>
<td>Germany</td>
<td>44 (20/24)</td>
<td>12.5-13</td>
<td>CG: no extra PA</td>
<td>Curricular PE</td>
<td>Enhanced and enriched PA</td>
<td>CG: low cognitive engagement and low physical exertion</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG: 30 min 3d/w</td>
<td></td>
<td></td>
<td>EG1: team games, high cognitive engagement and high physical exertion (football or basketball)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG: 45 min 2d/w</td>
<td></td>
<td></td>
<td>EG2: aerobic exercise, low cognitive engagement and high physical exertion (run, circuits of 200 m)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EG: 45 min 2d/w</td>
<td></td>
<td></td>
<td>Basketball, soccer, hockey, handball and dancing lessons</td>
<td>16</td>
</tr>
</tbody>
</table>

CG: Control Group; EG: Experimental Group; SD: Standard deviation; PA: Physical Activity; PE: Physical Education; d/w: days per week; min: minutes.
<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>N</th>
<th>Age</th>
<th>CG/EG1/EG2</th>
<th>Place in the school plan</th>
<th>Task characteristics</th>
<th>Intervention characteristics</th>
<th>Length (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subramanian et al 2015</td>
<td>India</td>
<td>343</td>
<td>14</td>
<td>120 min 6d/w</td>
<td>Curricular PE</td>
<td>Enhanced PA</td>
<td>CG: supervised but unstructured PA: gymnasium, music, drawing, football, gardening, skipping, basketball… EG: structured PA: vigorous intensity PA, muscle strengthening and stretching, and bone strengthening exercises</td>
<td>24</td>
</tr>
<tr>
<td>Tarp et al 2016</td>
<td>Denmark</td>
<td>632</td>
<td>12.7</td>
<td>60 min 5d/w</td>
<td>Integrated PA</td>
<td>Enhanced PA</td>
<td>PA + promotion of daily PA: PA in subjects, PA homework, and active transport + weekly: schedules PA during recess</td>
<td>20</td>
</tr>
<tr>
<td>Telles et al 2013</td>
<td>India</td>
<td>98</td>
<td>10.5</td>
<td>45 min 5d/w</td>
<td>Curricular PE</td>
<td>Enriched PA</td>
<td>EG1: PE program (jogging in place, bending sideways, spinal twisting relay races or games) EG2: Yoga (pranayama, sitlikarka vyayama, asanas) Running games, circuit training (sit-ups, push-ups, rope skipping), cognitive effort (modified soccer games, tag games)</td>
<td>12</td>
</tr>
<tr>
<td>Van der Niet 2016</td>
<td>Netherlan ds</td>
<td>105</td>
<td>8.8</td>
<td>30 min 2d/w</td>
<td>Extracurricular PA</td>
<td>Enhanced and enriched PA</td>
<td></td>
<td>22</td>
</tr>
<tr>
<td>Wilson et al 2016</td>
<td>Australia</td>
<td>116</td>
<td>11.2</td>
<td>10 min 5d/w</td>
<td>Extracurricular PA</td>
<td>Enhanced PA</td>
<td>Tag/chasing games or invasion-type games</td>
<td>4</td>
</tr>
<tr>
<td>Zervas et al 1991</td>
<td>Greece</td>
<td>17</td>
<td>13.1</td>
<td>60 min 2-3d/w</td>
<td>After-school PA</td>
<td>Enhanced PA</td>
<td>15 min warm-up (stretching and free exercise) and 60 min interval or continuous running</td>
<td>25</td>
</tr>
</tbody>
</table>

CG: Control Group; EG: Experimental Group; SD: Standard deviation; PA: Physical Activity; PE: Physical Education; d/w: days per week; min: minutes.
Table S2. Cognitive tasks and functions measured in the included studies. The distinction between core and higher-level executive functions is made based on Diamond’s (2013) classification, and extended to encompass the intersecting and partially overlapping construct of cognitive life skills (Danish et al., 2004).

<table>
<thead>
<tr>
<th>Author</th>
<th>Non-executive Cognitive Functions</th>
<th>Core Executive Functions</th>
<th>Metacognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adsiz et al 2012</td>
<td>NA</td>
<td>The Bourdon Attention test:</td>
<td>NA</td>
</tr>
<tr>
<td>Ardoy et al 2014</td>
<td>Spanish Overall and Factorial Intelligence Test (IGF-M):</td>
<td>✓ Selective attention</td>
<td>Spanish Overall and Factorial Intelligence Test (IGF-M):</td>
</tr>
<tr>
<td></td>
<td>✓ Non-verbal ability</td>
<td>✓ Trail Making test:</td>
<td>✓ Reasoning (Abstract Reasoning):</td>
</tr>
<tr>
<td></td>
<td>✓ Spatial ability</td>
<td>✓ Cognitive flexibility</td>
<td>✓ Reasoning (Verbal Reasoning):</td>
</tr>
<tr>
<td>Castelli et al 2011</td>
<td>NA</td>
<td>Stroop Color-Word test:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td></td>
</tr>
<tr>
<td>Chang et al 2013</td>
<td>NA</td>
<td>Eriksen flanker task:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td></td>
</tr>
<tr>
<td>Chaya et al 2012</td>
<td>Malin’s Intelligence Scale for Indian Children (MISIC):</td>
<td>✓ Working memory (Analogies):</td>
<td>Malin’s Intelligence Scale for Indian Children (MISIC):</td>
</tr>
<tr>
<td></td>
<td>✓ Working memory (Coding)</td>
<td>✓ Working memory (Object assembly):</td>
<td>✓ Problem solving (Object assembly):</td>
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<tr>
<td>Crova et al 2014</td>
<td>NA</td>
<td>Random number generation (RNG):</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Working memory</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ Simultaneous</td>
<td>✓ Selective attention</td>
<td>✓ Planning</td>
</tr>
<tr>
<td></td>
<td>✓ Successive</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ Simultaneous</td>
<td>Cognitive Assessment System (CAS):</td>
<td>✓ Planning</td>
</tr>
<tr>
<td></td>
<td>✓ Successive</td>
<td>✓ Selective attention</td>
<td></td>
</tr>
<tr>
<td>deGreeff et al 2016</td>
<td>NA</td>
<td>Digit span backward:</td>
<td>NA</td>
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<td></td>
<td></td>
<td>✓ Working memory</td>
<td></td>
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<td></td>
<td></td>
<td>Visual span backward:</td>
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<tr>
<td></td>
<td></td>
<td>✓ Working memory</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Golden Stroop:</td>
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<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
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<td></td>
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<td>Wisconsin card sorting test</td>
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<td></td>
<td></td>
<td>✓ Cognitive flexibility</td>
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<td>✓ Simultaneous</td>
<td>✓ Working memory</td>
<td>✓ Planning</td>
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<td>✓ Successive</td>
<td>Cognitive Assessment System (CAS):</td>
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<td>✓ Selective attention</td>
<td>Attention network test (ANT):</td>
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<td>Fredericks et al 2006</td>
<td>The aptitude test for school beginners</td>
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<td>The aptitude test for school beginners:</td>
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<td>✓ Reasoning</td>
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<td>✓ Gestalt</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>✓ Spatial</td>
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</tbody>
</table>

NA: not available
Table S2. Cognitive tasks and functions measured in the included studies. The distinction between core and higher-level executive functions is made based on Diamond’s (2013) classification, and extended to encompass the intersecting and partially overlapping construct of cognitive life skills (Danish et al., 2004).

(continue)

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<thead>
<tr>
<th>Author</th>
<th>Non-executive Cognitive Functions</th>
<th>Core Executive Functions</th>
<th>Metacognition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallotta et al 2015 53</td>
<td>NA</td>
<td>D2-R test of attention:</td>
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<td></td>
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<td>Ghahramadi et al 2016 54</td>
<td>NA</td>
<td>Continue Performance Test (CPT)</td>
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<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td></td>
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<tr>
<td>Goudas et al 2006</td>
<td>NA</td>
<td>NA</td>
<td>Knowledge test</td>
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<td></td>
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<td>✓ Goal setting</td>
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<td></td>
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<td></td>
<td>Goudas’ self-beliefs test:</td>
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<td>✓ Positive thinking</td>
</tr>
<tr>
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<td></td>
<td>✓ Goal setting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>✓ Problem solving</td>
</tr>
<tr>
<td>Hillman et al 2014 6</td>
<td>NA</td>
<td>Flanker task:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
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</tr>
<tr>
<td>Kamijo et al 2011 55</td>
<td>NA</td>
<td>Sternberg Task:</td>
<td>NA</td>
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<tr>
<td>Koutsandreou et al 2016 96</td>
<td>NA</td>
<td>Letter digit span:</td>
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<td></td>
<td></td>
<td>✓ Working memory</td>
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</tr>
<tr>
<td>Krafft et al 2014 57</td>
<td>NA</td>
<td>Antisaccade:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td></td>
</tr>
<tr>
<td>Lakes et al 2004 59</td>
<td>NA</td>
<td>Wechsler Intelligence Scale for Children:</td>
<td>Response to Challenge Scale:</td>
</tr>
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<td>Lakes et al 2013 50</td>
<td>NA</td>
<td>Hearts and flowers test:</td>
<td>✓ Self-regulation</td>
</tr>
<tr>
<td>Manjunath et al 2001 58</td>
<td>NA</td>
<td>Inhibition</td>
<td>NA</td>
</tr>
<tr>
<td>Manjunath et al 2004 59</td>
<td>NA</td>
<td>Verbal and spatial test:</td>
<td>Tower of London test:</td>
</tr>
<tr>
<td>Manjunath et al 2013 50</td>
<td>NA</td>
<td>Memory performance:</td>
<td>✓ Planning</td>
</tr>
<tr>
<td>Pesce et al 2013 61</td>
<td>NA</td>
<td>Selective attention:</td>
<td>✓ Planning</td>
</tr>
<tr>
<td>Pesce et al 2016 a 62</td>
<td>NA</td>
<td>Random Generation number (RNG):</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>✓ Working memory</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CAS attention subscale:</td>
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<tr>
<td></td>
<td></td>
<td>✓ Selective attention:</td>
<td></td>
</tr>
<tr>
<td>Pesce et al 2016 b 18</td>
<td>Behavioural application:</td>
<td>Random generation number (RNG):</td>
<td>GOAL knowledge questionnaire:</td>
</tr>
<tr>
<td></td>
<td>✓ Decision making</td>
<td>✓ Working memory</td>
<td>✓ Goal setting</td>
</tr>
<tr>
<td></td>
<td></td>
<td>✓ Inhibition</td>
<td>Self-efficacy questionnaire:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>✓ Self-regulation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>✓ Problem solving</td>
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</table>

NA: Not available
Table S2. Cognitive tasks and functions measured in the included studies. The distinction between core and higher-level executive functions is made based on Diamond’s (2013) classification, and extended to encompass the intersecting and partially overlapping construct of cognitive life skills (Danish et al., 2004).

<table>
<thead>
<tr>
<th>Author</th>
<th>Non-executive Cognitive Functions</th>
<th>Core Executive Functions</th>
<th>Metacognition</th>
</tr>
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<tr>
<td>Reed et al</td>
<td>NA</td>
<td>NA</td>
<td>The Standard Progressive Matrices: Fluid intelligence</td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td></td>
<td>The Standard Progressive Matrices: Fluid intelligence</td>
</tr>
<tr>
<td>Reed et al</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Schmidt et al</td>
<td>NA</td>
<td>Non-spatial n-back task:</td>
<td>NA</td>
</tr>
<tr>
<td>2015</td>
<td>9</td>
<td>Working memory</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhibition</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Additional block of Flanker task:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive flexibility</td>
<td>NA</td>
</tr>
<tr>
<td>Spitzer et al</td>
<td>NA</td>
<td>D2 test attention:</td>
<td>NA</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td>Selective attention-Inhibition</td>
<td>NA</td>
</tr>
<tr>
<td>Subramanian et al</td>
<td>NA</td>
<td>Two target letter cancellation test (LCT):</td>
<td>NA</td>
</tr>
<tr>
<td>2015</td>
<td>9</td>
<td>Inhibition</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ruff figural fluency test (perseveration):</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive flexibility</td>
<td>NA</td>
</tr>
<tr>
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<td></td>
<td>Cognitive flexibility</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trail Making test:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive flexibility</td>
<td>NA</td>
</tr>
<tr>
<td>Tarp et al</td>
<td>NA</td>
<td>Flanker task:</td>
<td>NA</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td>Inhibition</td>
<td>NA</td>
</tr>
<tr>
<td>Telles et al</td>
<td>NA</td>
<td>Stroop Color-Word test:</td>
<td>NA</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td>Inhibition</td>
<td>NA</td>
</tr>
<tr>
<td>Van der Niet</td>
<td>NA</td>
<td>Visual Memory span test:</td>
<td>Tower of London: Planning</td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td>Working memory</td>
<td>NA</td>
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<td></td>
<td>Digital span test:</td>
<td>NA</td>
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<td></td>
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<td>Working memory</td>
<td>NA</td>
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<td></td>
<td></td>
<td>Golden Stroop test:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhibition</td>
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<tr>
<td></td>
<td></td>
<td>Trail Making test:</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cognitive flexibility</td>
<td>NA</td>
</tr>
<tr>
<td>Wilson et al</td>
<td>NA</td>
<td>Five minutes psychomotor vigilance task:</td>
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<td>9</td>
<td>Sustained attention</td>
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<td>Zervas et al</td>
<td>NA</td>
<td>Cognitrone test:</td>
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<td>1991</td>
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NA: not available
### Table S3A. Quality assessment of RCTs following the Jadad scale.

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<th>Dropouts</th>
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<td>-</td>
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<tr>
<td>Crova et al 2014</td>
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<td>0</td>
<td>3</td>
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<tr>
<td>Davis et al 2007</td>
<td>1</td>
<td>-</td>
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<td>3</td>
</tr>
<tr>
<td>Davis et al 2011</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>de Greff et al 2016</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Fisher et al 2013</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
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<tr>
<td>Fredericks et al 2006</td>
<td>1</td>
<td>-</td>
<td>0</td>
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<tr>
<td>Gallotta et al 2015</td>
<td>1</td>
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<td>0</td>
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<td>Ghahramani et al 2016</td>
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<td>-</td>
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<td>Goudas et al 2006</td>
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<td>-</td>
<td>0</td>
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<td>Hillman et al 2014</td>
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<td>Kami et al 2014</td>
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<tr>
<td>Koutsandreou et al 2016</td>
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<td>Krafft et al 2014</td>
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<td>Lakes et al 2004</td>
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<td>Lakes et al 2013</td>
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<td>Manjunath et al 2001</td>
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<td>Movilidi et al 2015</td>
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<td>Pesce et al 2013</td>
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<td>1</td>
<td>0</td>
<td>3</td>
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<td>Schmidt et al 2015</td>
<td>1</td>
<td>-</td>
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<td>3</td>
</tr>
<tr>
<td>Subramanian et al 2015</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Tarp et al 2016</td>
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</tr>
<tr>
<td>Telles et al 2013</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
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<tr>
<td>Van der Niet et al 2016</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>3</td>
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<tr>
<td>Wilson et al 2016</td>
<td>1</td>
<td>1</td>
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<td>3</td>
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<tr>
<td>Zervas et al 1991</td>
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### Table S3B. Quality assessment of non-RCTs following the EPHPP tool for quantitative studies.

<table>
<thead>
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<th>Study</th>
<th>Selection bias</th>
<th>Study design</th>
<th>Confounders</th>
<th>Blinding</th>
<th>Data collection</th>
<th>Withdrawals/drop-outs</th>
<th>Total</th>
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<tbody>
<tr>
<td>Adsiz et al 2012</td>
<td>Moderate</td>
<td>Strong</td>
<td>Weak</td>
<td>Moderate</td>
<td>Weak</td>
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<td>Castelli et al 2011</td>
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<td>Weak</td>
<td>Moderate</td>
<td>Strong</td>
<td>Weak</td>
<td>Weak</td>
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<tr>
<td>Manjunath et al 2004</td>
<td>Moderate</td>
<td>Strong</td>
<td>Weak</td>
<td>Moderate</td>
<td>Weak</td>
<td>Strong</td>
<td>Weak</td>
</tr>
<tr>
<td>Reed et al 2013</td>
<td>Moderate</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
<td>Strong</td>
<td>Weak</td>
<td>Moderate</td>
</tr>
<tr>
<td>Spitzer et al 2013</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Weak</td>
<td>Moderate</td>
<td>Weak</td>
<td>Weak</td>
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Table S4. Subgroup analyses based on the place in the school time and task characteristics of the interventions.

<table>
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<th>Subgroup analyses</th>
<th>Based on place in the school plan characteristics</th>
<th>Based on task characteristics</th>
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<tr>
<td></td>
<td>N° of studies</td>
<td>ES* (95%CI)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education ^a</td>
<td>9</td>
<td>0.42 (0.14, 0.70)</td>
</tr>
<tr>
<td>Integrated or extracurricular PA ^a</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>After-school PA ^d</td>
<td>8</td>
<td>0.12 (-0.03, 0.27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WORKING MEMORY</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education ^a</td>
<td>6</td>
<td>0.06 (-0.12, 0.24)</td>
</tr>
<tr>
<td>Integrated or extracurricular PA ^a</td>
<td>4</td>
<td>0.23 (-0.08, 0.54)</td>
</tr>
<tr>
<td>After-school PA ^d</td>
<td>3</td>
<td>0.26 (-0.06, 0.58)</td>
</tr>
<tr>
<td>SELECTIVE ATTENTION-INHIBITION</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education ^a</td>
<td>14</td>
<td>0.41 (0.15, 0.67)</td>
</tr>
<tr>
<td>Integrated or extracurricular PA ^a</td>
<td>3</td>
<td>0.07 (-0.15, 0.30)</td>
</tr>
<tr>
<td>After-school PA ^d</td>
<td>7</td>
<td>0.07 (-0.15, 0.28)</td>
</tr>
<tr>
<td>COGNITIVE FLEXIBILITY</td>
<td></td>
<td></td>
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<tr>
<td>Curricular physical education ^a</td>
<td>3</td>
<td>-0.01 (-0.44, 0.22)</td>
</tr>
<tr>
<td>Integrated or extracurricular PA ^a</td>
<td>1</td>
<td>0.14 (-0.04, 0.31)</td>
</tr>
<tr>
<td>After-school PA ^d</td>
<td>1</td>
<td>0.31 (0.05, 0.58)</td>
</tr>
<tr>
<td>HIGHER-LEVEL EXECUTIVE FUNCTIONS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education ^a</td>
<td>8</td>
<td>0.25 (0.06, 0.43)</td>
</tr>
<tr>
<td>Integrated or extracurricular PA ^a</td>
<td>1</td>
<td>-0.07 (-0.46, 0.33)</td>
</tr>
<tr>
<td>After-school PA ^d</td>
<td>4</td>
<td>0.14 (-0.07, 0.35)</td>
</tr>
<tr>
<td>COGNITIVE LIFE SKILLS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education ^a</td>
<td>8</td>
<td>0.30 (0.15, 0.45)</td>
</tr>
<tr>
<td>Integrated or extracurricular PA ^a</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>After-school PA ^d</td>
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<td>-</td>
</tr>
</tbody>
</table>

ES: Effect Size; CI: Confidence Interval; PA: Physical Activity

*a Positive ES values indicate higher score in outcomes in favour of intervention group.

*b Curricular physical education refers to activities in classes of physical education

*c Integrated or extracurricular PA refers to exercise programs such as active breaks, teaching subjects as maths with physically active tasks, active recess or lunch time PA

*d After-school PA refers to exercise programs that take place out of school time, in or out school setting.

*e Enhanced PA refers to exercise programs aim at increase the amount of time devoted to PA

*f Enriched PA refers to exercise programs that deliberately increase in non-physical—coordinative and/or cognitive—demands of the PA tasks
Table S5. Subgroup analysis considering the effect of physical activity on accuracy and time for preforming the test

<table>
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<th>Selective attention- Inhibition</th>
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<th>Total</th>
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<tbody>
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<td></td>
<td>ES 95%  CI</td>
<td>ES 95%  CI</td>
<td>ES 95%  CI</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.15 -0.01, 0.32  58.6</td>
<td>0.14 -0.03, 0.31</td>
<td>0.15 0.01, 0.29  54.9</td>
</tr>
<tr>
<td>Time</td>
<td>-0.29 -0.53, -0.05 -</td>
<td>-0.14 -0.54, 0.26</td>
<td>-0.25 -0.45, -0.04  0.0</td>
</tr>
<tr>
<td>Accuracy/time</td>
<td>Accuracy 0.44 0.06, 0.81 86.2</td>
<td>Accuracy 0.08 -0.23, 0.39</td>
<td>0.29 0.04, 0.54 83.4</td>
</tr>
<tr>
<td></td>
<td>Time -0.03 -0.25, 0.19 67.4</td>
<td>Time -0.09 -0.31, 0.12</td>
<td>51.5 0.05 -0.20, 0.11 61.8</td>
</tr>
</tbody>
</table>

ES: effect size; CI: interval confidence. Positive values indicate higher scores in outcomes in favour of intervention group.
Table S6. Meta-regression of the Cognition parameters and children age mean and length of intervention of included studies

<table>
<thead>
<tr>
<th></th>
<th>Children age mean</th>
<th></th>
<th></th>
<th>Length of intervention</th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td>$I^2$</td>
<td>$\beta$ (95% CI)</td>
<td>$p$</td>
<td>$I^2$</td>
<td>$\beta$ (95% CI)</td>
</tr>
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<td>Non-executive cognitive functions</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>61.04</td>
<td>0.08 (0.00, 0.15)</td>
<td><strong>0.036</strong></td>
<td>68.33</td>
<td>0.01 (-0.02, 0.05)</td>
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<td>Core executive function</td>
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<td>-0.01 (-0.02, -0.01)</td>
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<td>0.209</td>
<td>77.05</td>
<td>0.01 (-0.01, 0.04)</td>
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<td>69.73</td>
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<td></td>
<td></td>
<td></td>
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<td>HIGHER-LEVEL EXECUTIVE FUNCTIONS</td>
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<td>0.01 (-0.01, 0.02)</td>
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<td>0.243</td>
<td>0.00</td>
<td>0.00 (-0.01, 0.02)</td>
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</table>

CI: Confidence Interval.

Note: Positive ES values indicate higher score in outcomes in favour of intervention group.
Table S7. Sensitivity analysis

Table S7A. Sensitivity analysis for non-executive cognitive functions

<table>
<thead>
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<th>Non-Executive Cognitive Function</th>
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<th>Upper limit</th>
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<th>F</th>
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<td>Ardoy et al 2014 (EG1)</td>
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<td>0.09</td>
<td>0.38</td>
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<td>Davis et al 2007 (EG1)</td>
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ES: Effect Size; EG: Experimental Group; CG: Control Group.

Table S7B. Sensitivity analysis for core executive functions

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ES: Effect Size; EG: Experimental Group; CG: Control Group.
Table S7. Sensitivity analysis

Cognitive flexibility

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ES: Effect Size; EG: Experimental Group; CG: Control Group.

Table S7C. Sensitivity analysis for metacognition

Higher level executive functions

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ES: Effect Size; EG: Experimental Group; CG: Control Group.

Cognitive life skills

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ES: Effect Size; EG: Experimental Group; CG: Control Group.

Note: Positive ES values indicate higher score in outcomes in favour of intervention group.
Figure S1. Flow chart

Records identified through database searching (n=4582)
- MEDLINE: 1034
- EMBASE: 931
- COCHRANE DATABASES: 597
- WOS: 1275
- PsycINFO: 745

Records identified through complementary searching (n=4)

Duplicate records removed (n=777)

Irrelevant records excluded based on title and abstract review (n=3728)

Records screened (n=3809)

Records excluded (n=45)
- n=7 did not include cognition measurements
- n=6 included adults
- n=7 cross-sectional
- n=17 academic performance outcomes
- N=6 acute physical exercise studies
- n=2 included children with developmental delay

Full text articles assessed for eligibility (n=81)

Studies included in qualitative synthesis (n=36)

Studies included in quantitative synthesis (meta-analysis) (n=24)

Non-executive cognitive functions
- N=5

Core executive functions
- n=23
- N=10 working memory
- N=17 selective attention-inhibition
- N=4 cognitive flexibility

Metacognition
- n=10
- N=6 Higher-level executive functions
- N=4 cognitive life skills
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Figure S2. Publication bias
Appendix 5. Supplementary material manuscript 3: Academic achievement and physical activity: a meta-analysis.
### Table 1. Quality assessment of studies included.

#### Table 1A. Quality assessment of RCTs following the Jadad Scale.

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<td>0</td>
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<td>3</td>
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<td>Reed et al 2010</td>
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<td>1</td>
<td>-</td>
<td>1</td>
<td>3</td>
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<tr>
<td>Resaland et al 2016</td>
<td>1</td>
<td>-</td>
<td>0</td>
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<td>1</td>
<td>3</td>
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<td>Riley et al 2016</td>
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<td>0</td>
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<tr>
<td>Tarp et al 2016</td>
<td>1</td>
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<td>0</td>
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<td>3</td>
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<td>1</td>
<td>0</td>
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<td>Wilson et al 2016</td>
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<td>1</td>
<td>0</td>
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<td>1</td>
<td>3</td>
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</table>

#### Table 1B. Quality assessment of non-RCTs following the EPHPP tool for quantitative studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection bias</th>
<th>Study design</th>
<th>Confounders</th>
<th>Blinding</th>
<th>Data collection</th>
<th>Withdrawals and drop-outs</th>
<th>Total</th>
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<tr>
<td>Ericsson et al 2012</td>
<td>Strong</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
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<td>Weak</td>
</tr>
<tr>
<td>Gao et al 2012</td>
<td>Strong</td>
<td>Weak</td>
<td>Weak</td>
<td>Moderate</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
</tr>
<tr>
<td>Goh et al 2016</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
<td>Moderate</td>
<td>Weak</td>
<td>Weak</td>
<td>Weak</td>
</tr>
<tr>
<td>Käll et al 2013</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
<td>Moderate</td>
<td>Weak</td>
<td>Weak</td>
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<td>Mahar et al 2006</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
<td>Moderate</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td>Mullender-Wijnsma et al 2015</td>
<td>Strong</td>
<td>Moderate</td>
<td>Strong</td>
<td>Moderate</td>
<td>Strong</td>
<td>Weak</td>
<td>Moderate</td>
</tr>
<tr>
<td>Spitzer et al 2015</td>
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<td>Weak</td>
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<td>Weak</td>
<td>Weak</td>
<td>Weak</td>
</tr>
<tr>
<td>Vazou et al 2016</td>
<td>Strong</td>
<td>Strong</td>
<td>Strong</td>
<td>Moderate</td>
<td>Weak</td>
<td>Weak</td>
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Table 2. Subgroup analyses based on the school time that the physical intervention takes place

<table>
<thead>
<tr>
<th>Subgroups analyses</th>
<th>Nº of studies</th>
<th>Effect size (95% CI)</th>
<th>( I^2 )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Academic achievement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LANGUAGE-RELATED SKILLS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education</td>
<td>6</td>
<td>0.15 (-0.11, 0.41)</td>
<td>74.5</td>
<td>0.001</td>
</tr>
<tr>
<td>After-school PA</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Integrated or extracurricular PA</td>
<td>1</td>
<td>0.24 (0.03, 0.45)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>MATHEMATICS-RELATED SKILLS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education</td>
<td>7</td>
<td>0.16 (0.00, 0.32)</td>
<td>45.4</td>
<td>0.089</td>
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<tr>
<td>After-school PA</td>
<td>2</td>
<td>0.06 (-0.22, 0.35)</td>
<td>0.0</td>
<td>0.972</td>
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<tr>
<td>Integrated or extracurricular PA</td>
<td>7</td>
<td>0.29 (0.07, 0.51)</td>
<td>74.2</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>READING</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education</td>
<td>4</td>
<td>0.21 (0.05, 0.37)</td>
<td>36.2</td>
<td>0.195</td>
</tr>
<tr>
<td>After-school PA</td>
<td>2</td>
<td>-0.03 (-0.31, 0.25)</td>
<td>0.0</td>
<td>0.835</td>
</tr>
<tr>
<td>Integrated or extracurricular PA</td>
<td>4</td>
<td>0.08 (-0.14, 0.29)</td>
<td>29.4</td>
<td>0.236</td>
</tr>
<tr>
<td><strong>COMPOSITE SCORES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curricular physical education</td>
<td>6</td>
<td>0.30 (0.03, 0.56)</td>
<td>75.6</td>
<td>0.001</td>
</tr>
<tr>
<td>After-school PA</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Integrated or extracurricular PA</td>
<td>2</td>
<td>0.22 (-0.15, 0.59)</td>
<td>85.0</td>
<td>0.010</td>
</tr>
</tbody>
</table>

CI: Confidence interval; PA: Physical activity
Table 3. Sensitivity analysis, performed by excluding the studies one by one from the pooled effect size estimates.

### Language-related skills

<table>
<thead>
<tr>
<th>Reference</th>
<th>Effect size (95%CI)</th>
<th>$i^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ardoy et al 2014 (IG1)</td>
<td>0.16 (-0.07, 0.39)</td>
<td>76.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Ardoy et al 2014 (IG2)</td>
<td>0.10 (-0.10, 0.29)</td>
<td>66.6</td>
<td>0.010</td>
</tr>
<tr>
<td>Mullender-Wijnsma et al 2016</td>
<td>0.15 (-0.11, 0.41)</td>
<td>74.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 1, IG1)</td>
<td>0.13 (-0.12, 0.36)</td>
<td>72.7</td>
<td>0.003</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 1, IG2)</td>
<td>0.18 (-0.07, 0.42)</td>
<td>76.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 2, IG1)</td>
<td>0.18 (-0.09, 0.45)</td>
<td>76.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 2, IG2)</td>
<td>0.22 (0.08, 0.37)</td>
<td>30.9</td>
<td>0.203</td>
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</tbody>
</table>

### Mathematics-related skills

<table>
<thead>
<tr>
<th>Reference</th>
<th>Effect size (95%CI)</th>
<th>$i^2$</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Ardoy et al 2014 (IG1)</td>
<td>0.10 (-0.10, 0.29)</td>
<td>66.6</td>
<td>0.006</td>
</tr>
<tr>
<td>Ardoy et al 2014 (IG2)</td>
<td>0.16 (-0.07, 0.39)</td>
<td>76.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Davis et al 2011 (IG1)</td>
<td>0.22 (0.09, 0.34)</td>
<td>60.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Davis et al 2011 (IG2)</td>
<td>0.21 (0.09, 0.34)</td>
<td>60.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Gao et al 2012 (Cohort 1)</td>
<td>0.16 (0.06, 0.27)</td>
<td>43.7</td>
<td>0.036</td>
</tr>
<tr>
<td>Gao et al 2012 (Cohort 2)</td>
<td>0.18 (0.07, 0.30)</td>
<td>54.1</td>
<td>0.006</td>
</tr>
<tr>
<td>Lakes et al 2004</td>
<td>0.20 (0.07, 0.32)</td>
<td>58.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Mullender-Wijnsma et al 2016</td>
<td>0.21 (0.08, 0.34)</td>
<td>60.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Resaland et al 2016</td>
<td>0.21 (0.09, 0.33)</td>
<td>60.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Riley et al 2016</td>
<td>0.23 (0.10, 0.35)</td>
<td>57.9</td>
<td>0.003</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 1, IG1)</td>
<td>0.23 (0.10, 0.35)</td>
<td>58.1</td>
<td>0.002</td>
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<tr>
<td>Sallis et al 1999 (Cohort 1, IG2)</td>
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<td>Sallis et al 1999 (Cohort 2, IG1)</td>
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<td>0.001</td>
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<tr>
<td>Sallis et al 1999 (Cohort 2, IG2)</td>
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<td>58.7</td>
<td>0.002</td>
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<td>Tarp et al 2016</td>
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<td>55.5</td>
<td>0.005</td>
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<td>Vazou et al 2016</td>
<td>0.19 (0.07, 0.31)</td>
<td>56.8</td>
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### Reading

<table>
<thead>
<tr>
<th>Reference</th>
<th>Effect size (95%CI)</th>
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<th>p</th>
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<tr>
<td>Davis et al 2011 (IG1)</td>
<td>0.14 (0.02, 0.26)</td>
<td>31.2</td>
<td>0.168</td>
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<tr>
<td>Davis et al 2011 (IG2)</td>
<td>0.15 (0.03, 0.26)</td>
<td>28.2</td>
<td>0.194</td>
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<td>Gao et al 2012 (Cohort 1)</td>
<td>0.11 (0.00, 0.22)</td>
<td>21.3</td>
<td>0.253</td>
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<tr>
<td>Gao et al 2012 (Cohort 2)</td>
<td>0.15 (0.04, 0.26)</td>
<td>24.2</td>
<td>0.229</td>
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<tr>
<td>Mullender-Wijnsma et al 2016</td>
<td>0.16 (0.03, 0.28)</td>
<td>24.7</td>
<td>0.224</td>
</tr>
<tr>
<td>Resaland et al 2016</td>
<td>0.14 (0.02, 0.25)</td>
<td>31.1</td>
<td>0.169</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 1, IG1)</td>
<td>0.12 (-0.01, 0.25)</td>
<td>31.8</td>
<td>0.164</td>
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<tr>
<td>Sallis et al 1999 (Cohort 1, IG2)</td>
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<td>0.452</td>
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### Composite scores

<table>
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<td>Ahamed et al 2006</td>
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<td>75.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Ardoy et al 2014 (IG1)</td>
<td>0.26 (0.06, 0.47)</td>
<td>79.0</td>
<td>0.000</td>
</tr>
<tr>
<td>Ardoy et al 2014 (IG2)</td>
<td>0.18 (0.04, 0.31)</td>
<td>53.6</td>
<td>0.044</td>
</tr>
<tr>
<td>Resaland et al 2016</td>
<td>0.31 (0.08, 0.54)</td>
<td>73.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Sallis et al 1999 (Cohort 1, IG1)</td>
<td>0.28 (0.08, 0.51)</td>
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<td>Sallis et al 1999 (Cohort 1, IG2)</td>
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<td>0.32 (0.11, 0.53)</td>
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</table>

CI: Confidence Interval; IG: Intervention Group.
Table 4. Meta-regression of the academic achievement areas and children’s mean age and length of intervention of included studies

<table>
<thead>
<tr>
<th>Academic achievement</th>
<th>Children’s mean age</th>
<th>Length of intervention</th>
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<td>$\beta$ (95%CI)</td>
<td>$I^2$</td>
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<td>LANGUAGE-RELATED SKILLS</td>
<td>0.09 (-0.12, 0.30)</td>
<td>76.11</td>
</tr>
<tr>
<td>MATHEMATICS-RELATED SKILLS</td>
<td>0.02 (-0.09, 0.13)</td>
<td>59.71</td>
</tr>
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<td>0.07 (-0.11, 0.27)</td>
<td>24.48</td>
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<tr>
<td>COMPOSITE SCORE</td>
<td>0.18 (-0.08, 0.45)</td>
<td>76.16</td>
</tr>
</tbody>
</table>

CI: Confidence Interval

Figura 1. Assessment of potential publication bias by Egger’s test.
Appendix 6. Supplementary material manuscript 3: Association between pre-pregnancy overweight and obesity and children’s neurocognitive development: a systematic review and meta-analysis of observational studies.
**Table S1.** Search strategy for MEDLINE database.

<table>
<thead>
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<th>‘pregnancy’</th>
<th>AND</th>
<th>‘Weight status’</th>
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<th>‘cognition’</th>
<th>OR</th>
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</thead>
<tbody>
<tr>
<td>OR</td>
<td></td>
<td>‘obesity’</td>
<td>OR</td>
<td>‘neurodevelopment’</td>
<td>OR</td>
</tr>
<tr>
<td>‘maternal’</td>
<td>OR</td>
<td>‘adiposity’</td>
<td>OR</td>
<td>‘intellectual’</td>
<td>OR</td>
</tr>
<tr>
<td>OR</td>
<td></td>
<td>‘weight gain’</td>
<td>OR</td>
<td>‘intelligence’</td>
<td>OR</td>
</tr>
<tr>
<td>‘gestational’</td>
<td></td>
<td>‘body mass index’</td>
<td></td>
<td>‘cognitive function’</td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>‘academic’</td>
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</tr>
<tr>
<td>Author</td>
<td>Maternal, paternal and familiar covariates</td>
<td>Child’s covariates</td>
<td>Other covariates</td>
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</tr>
<tr>
<td>-------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basatemur et al. 2012 [30]</td>
<td>Maternal age&lt;br&gt;Maternal highest academic qualification&lt;br&gt;Father’s highest academic qualification&lt;br&gt;Family socioeconomic class&lt;br&gt;Organization for Economic Cooperation and Development equivalized family income&lt;br&gt;Current maternal smoking status&lt;br&gt;Maternal diabetes during pregnancy</td>
<td>Children’s gender&lt;br&gt;Children’s birth&lt;br&gt;Children’s ethnicity&lt;br&gt;Children’s BMI at 5 and 7 years</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bliddal et al. 2014 [31]</td>
<td>Maternal IQ&lt;br&gt;Maternal marital status&lt;br&gt;Maternal and parenteral Education level&lt;br&gt;Postnatal parenteral smoking in the home&lt;br&gt;Duration of exclusive breastfeeding&lt;br&gt;Maternal age&lt;br&gt;Parity&lt;br&gt;Maternal prenatal smoking</td>
<td>Age child at the age of testing&lt;br&gt;Birth weight (grams)&lt;br&gt;Gestational age (days)&lt;br&gt;Children’s sex</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brion et al. 2010 [32]</td>
<td>Maternal education&lt;br&gt;Paternal education&lt;br&gt;Family income&lt;br&gt;Social class&lt;br&gt;Maternal smoking</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Casas et al. 2013 [33]</td>
<td>Maternal education&lt;br&gt;Paternal education&lt;br&gt;Maternal country of birth&lt;br&gt;Maternal and paternal social class&lt;br&gt;Maternal age&lt;br&gt;Breastfeeding duration&lt;br&gt;Maternal smoking&lt;br&gt;Maternal employment status during pregnancy&lt;br&gt;Maternal smoking status after birth&lt;br&gt;Parity</td>
<td>Child gender and region&lt;br&gt;Nursery attendance&lt;br&gt;Main childminder&lt;br&gt;Paternal BMI</td>
<td>NA</td>
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</tr>
<tr>
<td>Danki et al. 2017 [34]</td>
<td>Maternal age&lt;br&gt;Maternal origin&lt;br&gt;Maternal education level&lt;br&gt;Parity&lt;br&gt;Maternal smoking during pregnancy&lt;br&gt;Paternal BMI</td>
<td>Child sex</td>
<td>Examiner Quality of assessment</td>
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<td></td>
</tr>
<tr>
<td>Hinkle et al. 2012 [35]</td>
<td>Maternal age&lt;br&gt;Race-ethnicity&lt;br&gt;Marital status&lt;br&gt;Parity&lt;br&gt;Smoking during pregnancy&lt;br&gt;Household poverty status</td>
<td>Schooling&lt;br&gt;Child sex</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hinkle et al. 2013 [36]</td>
<td>Race-ethnicity&lt;br&gt;Parity&lt;br&gt;Poverty&lt;br&gt;Smoking during pregnancy</td>
<td>Child’s sex, Child’s age at final assessment&lt;br&gt;Schooling&lt;br&gt;Child weight status</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huang et al. 2014 [37]</td>
<td>Maternal age&lt;br&gt;Maternal education&lt;br&gt;Maternal race&lt;br&gt;Marital status&lt;br&gt;Socioeconomic status&lt;br&gt;Parity&lt;br&gt;Smoking during pregnancy&lt;br&gt;Home environment&lt;br&gt;Zinc supplementation status&lt;br&gt;Weight gain during pregnancy&lt;br&gt;Mother’s age&lt;br&gt;Smoking&lt;br&gt;Alcohol use</td>
<td>NA</td>
<td>Hospital</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neggers et al. 2003 [38]</td>
<td>Mother’s PPVT score&lt;br&gt;Home environment&lt;br&gt;Smoking during pregnancy&lt;br&gt;Mother’s age</td>
<td>Child care status&lt;br&gt;Birth weight</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IQ: Intelligence quotient; BMI: Body Mass Index; NA. Not Available
<table>
<thead>
<tr>
<th>Author</th>
<th>Maternal, paternal and familiar covariates</th>
<th>Child’s covariates</th>
<th>Other covariates</th>
</tr>
</thead>
</table>
| Polanska et al. 2015 [39]     | Parenteral age  
Parenteral education  
Marital status                  | Child gender  
Cognitive development  
Child day care attendance      | Examiner                      |
| Pugh et al. 2015 [40]         | Maternal race  
Parity  
Employment  
Family income  
Maternal intelligence  
Home environment  
Maternal prenatal depression  
Maternal prenatal substance use | Age  
Child sex                      | NA                             |
| Pugh et al. 2016 [41]         | Maternal race  
Parity  
Employment  
Family income  
Maternal intelligence  
Home environment  
Maternal prenatal depression  
Maternal prenatal substance use | Age  
Child sex                      | NA                             |
| Tanda et al. 2012 [42]        | Maternal weight gain below IOM recommendation                                  | Child’s PPVT age in months at cognitive test  
Year of cognitive testing       | NA                             |
| Torres-Espinola et al. 2015   | Maternal age  
Maternal education  
Placental weight  
Weight gain during pregnancy   | Unadjusted                        | Unadjusted          |
| Veldwijk et al. 2017 [44]     | Unadjusted                                                        | Unadjusted                        | Unadjusted          |

PPVT: Peabody Picture Vocabulary Test; NA: Not Available
Table S3. Study quality assessed by Quality of reporting of observational longitudinal research tool.

| Reference                  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | Total score |
|----------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Bliddal et al 2014 [31]   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 20|
| Brion et al 2010 [32]     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 20|
| Casas et al 2013 [33]     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 22|
| Daraki et al 2017 [34]    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 24|
| Hinkle et al 2012 [35]    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 20|
| Hinkle et al 2013 [36]    |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 23|
| Huang et al 2014 [37]     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 25|
| Neggers et al 2003 [38]   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 19|
| Polanska et al 2015 [39]  |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 20|
| Pugh et al 2015 [40]      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 21|
| Pugh et al 2016 [41]      |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 28|
| Tanda et al 2013 [42]     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 25|
Table S3. Study quality assessed by Quality of reporting of observational longitudinal research tool.

| Reference                  | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | Total score |
| Torres-Espinosa et al 2015 |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 21 |
| Veldwijk et al 2011        |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   | 21 |
Table S4. Sensitivity analysis of potential bias due to including each study in the review according to weight status categories.

<table>
<thead>
<tr>
<th>Weight Status</th>
<th>Study</th>
<th>Effect size (CI)</th>
<th>I²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight</td>
<td>Casas et al. 2013 [33]</td>
<td>-0.02 (-0.05, 0.02)</td>
<td>0.0</td>
<td>0.951</td>
</tr>
<tr>
<td></td>
<td>Daraki et al. 2014 [34] (a)</td>
<td>-0.02 (-0.05, 0.02)</td>
<td>0.0</td>
<td>0.954</td>
</tr>
<tr>
<td></td>
<td>Hinkle et al. 2012 [35]</td>
<td>-0.02 (-0.06, 0.02)</td>
<td>0.0</td>
<td>0.956</td>
</tr>
<tr>
<td></td>
<td>Huang et al. 2014 [37]</td>
<td>-0.02 (-0.06, 0.02)</td>
<td>0.0</td>
<td>0.956</td>
</tr>
<tr>
<td></td>
<td>Neggers et al. 2003 [38]</td>
<td>-0.02 (-0.05, 0.02)</td>
<td>0.0</td>
<td>0.952</td>
</tr>
<tr>
<td></td>
<td>Pugh et al. 2015 [40,42] (b)</td>
<td>-0.01 (-0.05, 0.02)</td>
<td>0.0</td>
<td>0.999</td>
</tr>
<tr>
<td></td>
<td>Tanda et al. 2013 [43]</td>
<td>-0.02 (-0.05, 0.02)</td>
<td>0.0</td>
<td>0.952</td>
</tr>
<tr>
<td></td>
<td>Torres-Espinola et al. 2015 [44]</td>
<td>-0.02 (-0.05, 0.02)</td>
<td>0.0</td>
<td>0.963</td>
</tr>
<tr>
<td>Obesity</td>
<td>Casas et al. 2013 [33]</td>
<td>-0.06 (-0.09, -0.03)</td>
<td>0.0</td>
<td>0.713</td>
</tr>
<tr>
<td></td>
<td>Daraki et al. 2014 [34] (a)</td>
<td>-0.06 (-0.09, -0.03)</td>
<td>0.0</td>
<td>0.595</td>
</tr>
<tr>
<td></td>
<td>Hinkle et al. 2012 [35]</td>
<td>-0.07 (-0.10, -0.03)</td>
<td>0.0</td>
<td>0.688</td>
</tr>
<tr>
<td></td>
<td>Huang et al. 2014 [37]</td>
<td>-0.06 (-0.09, -0.03)</td>
<td>0.0</td>
<td>0.615</td>
</tr>
<tr>
<td></td>
<td>Neggers et al. 2003 [38]</td>
<td>-0.06 (-0.09, -0.03)</td>
<td>0.0</td>
<td>0.755</td>
</tr>
<tr>
<td></td>
<td>Pugh et al. 2015 [40,42] (b)</td>
<td>-0.05 (-0.08, -0.02)</td>
<td>0.0</td>
<td>0.855</td>
</tr>
<tr>
<td></td>
<td>Tanda et al. 2013 [43]</td>
<td>-0.06 (-0.09, -0.03)</td>
<td>0.0</td>
<td>0.566</td>
</tr>
<tr>
<td></td>
<td>Torres-Espinola et al. 2015 [44]</td>
<td>-0.06 (-0.10, -0.01)</td>
<td>0.0</td>
<td>0.567</td>
</tr>
</tbody>
</table>

CI: Confidence Interval;

(a) Daraki et al 2017 including REAH sample from Casas et al 2013
(b) Pugh et al 2016 including sample from Pugh et al 2015

Table S5. Assessment of potential publication bias.

<table>
<thead>
<tr>
<th></th>
<th>Slope</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight</td>
<td>0.00</td>
<td>-0.04</td>
<td>0.04</td>
<td>0.936</td>
</tr>
<tr>
<td>Obesity</td>
<td>-0.03</td>
<td>-0.09</td>
<td>0.01</td>
<td>0.136</td>
</tr>
</tbody>
</table>
13. OTHER SCIENTIFIC CONTRIBUTIONS
OTHER SCIENTIFIC CONTRIBUTIONS

Research Fellowship

Spanish Ministry of Education, Culture and Sport (FPU13/03137), 2014-2018. Pre-Ph.D Research fellowship. Senior Mentor: Dr. Vicente Martínez-Vizcaíno

Spanish Ministry of Education, Culture and Sport, MSc Research fellowship, 2012-2013. Senior Mentor: Dr. Vicente Martínez-Vizcaíno

Research stays

“Foro Italico” University of Rome, Rome, Italy. 2016 June 15th to September 15th. Senior Mentor: Dr. Caterina Pesce

Department of Kinesiology, University of Georgia, Athens, Georgia, USA. 2017 May 24th to August 24th. Senior Mentor: Dr. Phillip D. Tomporowski.

Awards

Best research work: Results of a supervised exercise program. I Session of Research in Primary Care of Castilla-La Mancha. 06/21/2013.

Ex AEQUO Award: Physical activity and health of schoolchildren. Spanish Association of Medicine and Health School and University. 10/18/2015.

1º ACCESIC to the second best research work in primary care at the IV Research Session in Primary Care of Castilla-La Mancha: Glycosylated hemoglobin versus plasma glucose as a predictor of risk of arterial stiffness by propensity score. 04/23/2016.
Peer-Reviewed Publications

Published


Cavero-Redondo I, Martínez-Vizcaíno V, Álvarez-Bueno C, Recio-Rodriguez JI, Gómez-Marcos MA, García-Ortiz L. *Relationship between glycaemic levels and*


Under review


**Convention/Conference**


program (MOVI-KIDS study) on preventing obesity in preschoolers. 24th European Congress on Obesity 2017, Porto, Portugal.


Determinantes y consecuencias de los patrones de actividad física durante el embarazo en gestantes de Toledo. Simposio Internacional de Cuidados de Salud Basados en Evidencia y V Congreso de Investigación en Enfermería Iberoamericano de países de lengua oficial portuguesa 2016, Coimbra, Portugal.


NM A Palencia, MS Martínez, MMG Herraiz, SA Arribas, AG García, CA Bueno. *La actividad física vigorosa se relaciona con menor adiposidad y con una condición física saludable en niños de 9-10 años*. Symposium EXERNET “Investigación en ejercicio físico y salud, presente y futuro en España” 2014, Granada, Spain

González García, A; Lucas de la Cruz, L; Cañete García-Prieto, J; Arias Palencia, NM; Pozuelo Carrascosa, D; Álvarez Bueno, C. *Rebote adiposo en escolares de Cuenca y Ciudad Real*. II Jornadas de Investigación en Atención Primaria de Castilla-La Mancha 2014, Ciudad Real, España.

Lucas de la Cruz, L; González García, A; Pozuelo Carrascosa, D; Arias Palencia NM; Álvarez Bueno, C; Guijarro Herráiz, MM. *Tiempo de sueño y adiposidad en escolares de 4 a 6 años*. II Jornadas de Investigación en Atención Primaria de Castilla-La Mancha 2014, Ciudad Real, España.

García Cebrián, L; Pato Mochales, D; Cavero Redondo, I; Álvarez Bueno, C; Notario Pacheco, B; Fernández Cuesta, A. *Beneficios del ejercicio físico en niños y jóvenes con asma inducido por el ejercicio: revisión sistemática*. II Jornadas de Investigación en Atención Primaria de Castilla-La Mancha 2014, Ciudad Real, España.
Effectiveness of brief interventions in primary health care settings to decrease alcohol consumption by adult non-dependent drinkers: a systematic review of systematic reviews

Celia Álvarez-Bueno a, Beatriz Rodríguez-Martín a, Luis García-Ortiz b,c, Manuel Ángel Gómez-Marcos b,c, Vicente Martínez-Vizcaíno a,d,⁎

a Social and Health Care Research Center, University of Castilla-La Mancha, Cuenca Spain
b Primary Care Research Unit, the Almedilla Health Center, Castilla and León Health Service-SACYL, Salamanca Spain
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d Facultad de Ciencias de la Salud, Universidad Autónoma de Chile, Chile

Abstract

Objective. To evaluate the effectiveness of brief interventions in the primary health care setting to decrease alcohol consumption in non-alcoholic adult drinkers.

Method. Systematic review of systematic reviews and meta-analyses of randomized clinical trials published in English and Spanish and indexed in EMBASE, MEDLINE (PubMed), Web of Science, Scopus, and The Cochrane Library, from their inception to January 2014. The quality of the studies was evaluated with the AMSTAR instrument.

Results. Seven studies, published from 1999 to 2011, were included in the review (six meta-analyses, one systematic review). These studies were heterogeneous in terms of design, type and length of interventions analyzed, participants, responsible professionals, and results. Five studies reported a moderate decrease in alcohol consumption and four showed a decrease in the number of participants who consumed alcohol above the established risk level.

Conclusion. Brief interventions have a moderate effect on reducing alcohol consumption among excessive drinkers or people who consume excessive amounts of alcohol and as a consequence these interventions increased the number of people drinking alcohol below established limits of risk. Brief interventions with multiple contacts or follow-up sessions are the most effective.

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Introduction

Alcohol consumption is a widespread, culturally accepted practice in most Western countries; according to World Health Organization data (WHO, 2014), worldwide consumption in 2010 was equal to 6.2 L of pure alcohol consumed per person aged 15 years or older. Alcohol abuse is related to at least 60 different health conditions (Room et al., 2005), and 5.9% of global deaths are attributable to alcohol consumption (WHO, 2014). As a result, there is a major concern about the economic consequences; in addition, both techniques have demonstrated positive results in a benefits–cost analysis (Fleming et al., 2000). Evidence exists that these techniques are effective when applied in primary care settings (Fernández et al., 2003), and that training family practitioners in these techniques is effective (Anderson et al., 2004).

Meta-analyses and systematic reviews have also examined the effectiveness of brief interventions conducted in primary care settings to decrease alcohol consumption, but the heterogeneity of these interventions and the conclusions of studies about their effectiveness in terms of sex, unit of expression and size of effect make it difficult for health professionals to apply these strategies. Therefore, the objective of the present study is to summarize and critically evaluate the evidence provided in meta-analyses and systematic reviews which have analyzed the effectiveness of brief interventions conducted in primary care settings to reduce alcohol consumption among non-alcoholic adult drinkers.

Early detection (Fiellin et al., 2000) and brief counseling (Rodríguez-Martos, 2002) have been shown to be effective techniques which reduce alcohol consumption and mitigate the related individual and social consequences; in addition, both techniques have demonstrated positive results in a benefits–cost analysis (Fleming et al., 2000). Evidence exists that these techniques are effective when applied in primary care settings (Fernández et al., 2003), and that training family practitioners in these techniques is effective (Anderson et al., 2004).
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c Medicine Department, University of Salamanca, REDAPP, IB5AL, Salamanca Spain
d Facultad de Ciencias de la Salud, Universidad Autónoma de Chile, Chile

ARTICLE INFO

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Keywords:
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Patient education
Prevention
Primary health care
Review

ABSTRACT

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http://dx.doi.org/10.1016/j.ypmed.2014.12.010
0039-6109/© 2014 Published by Elsevier Inc.
Effectiveness of physical activity interventions on preventing gestational diabetes mellitus and excessive maternal weight gain: a meta-analysis


Background It is commonly accepted that pregnancy-related physiological changes (circulatory, respiratory, and locomotor) negatively influence the daily physical activity of pregnant women.

Objectives The aim of this study is to conduct a meta-analysis of randomised controlled trials (RCTs) for assessing the effectiveness of physical exercise interventions during pregnancy to prevent gestational diabetes mellitus and excessive maternal weight gain.

Search strategy Keywords were used to conduct a computerised search in six databases: Cochrane Library Plus, Science Direct, EMBASE, PubMed, Web of Science, and ClinicalTrials.gov.

Selection criteria Healthy pregnant women who were sedentary or had low levels of physical activity were selected for RCTs that included an exercise programme.

Data collection and analysis Two independent reviewers extracted data and assessed the quality of the included studies. Of 4225 articles retrieved, 13 RCTs (2873 pregnant women) met the inclusion criteria. Pooled relative risk (RR) or weighted mean differences (WMDs) (depending on the outcome measure) were calculated using a random-effects model.

Main results Overall, physical exercise programmes during pregnancy decreased the risk of gestational diabetes mellitus (RR = 0.69; P = 0.009), particularly when the exercise programme was performed throughout pregnancy (RR = 0.64; P = 0.038). Furthermore, decreases were also observed in maternal weight (WMD = −1.14 kg; 95% CI −1.50 to −0.78; P < 0.001). No serious adverse effects were reported.

Conclusion Structured moderate physical exercise programmes during pregnancy decrease the risk of gestational diabetes mellitus and diminish maternal weight gain, and seem to be safe for the mother and the neonate; however, further studies are needed to establish recommendations.

Keywords Exercise, gestational diabetes mellitus, maternal weight gain, physical activity, pregnancy.

Tweetable abstract Exercise programmes decreased the risk of gestational diabetes mellitus and excessive weight gain.

Linked article This article is commented on by L Poston. To view this mini commentary visit http://dx.doi.org/10.1111/1471-0528.13446.

Introduction Gestational diabetes mellitus (GDM) is one of most frequent complications of pregnancy. It has been associated with serious disorders such as pre-eclampsia, hypertension, preterm birth, and a higher frequency of induced and caesarean deliveries. Also, it has been related to a higher risk for perinatal morbidity, impaired glucose tolerance, and type-II diabetes after pregnancy. Finally, the offspring are at an increased risk of becoming overweight or obese, and of developing type-I or -II diabetes later in life. Meanwhile, pregnancy for most women is associated with greater weight gain than recommended. It is known that excessive maternal weight gain (MWG) is a risk factor for hypertension, GDM, pre-eclampsia, caesarean delivery, macrosomia, stillbirth, and perinatal complications. Moreover, it is also independently associated with postpartum weight retention and higher body mass index in...
Protocolo de un ensayo aleatorizado de clusters para evaluar la efectividad del programa MOVI-2 en la prevención del sobrepeso en escolares

Vicente Martínez-Vizcaíno\textsuperscript{a,*}, Mairena Sánchez-López\textsuperscript{a,b}, Fernando Salcedo-Aguilar\textsuperscript{c}, Blanca Notario-Pacheco\textsuperscript{a}, Montserrat Solera-Martínez\textsuperscript{a}, Pablo Moya-Martínez\textsuperscript{a}, Pablo Franquelo-Morales\textsuperscript{d}, Sara López-Martínez\textsuperscript{e} y Fernando Rodríguez-Artalejo\textsuperscript{f}, en nombre del grupo MOVI-2\textsuperscript{b}

\textsuperscript{a}Centro de Estudios Socio-Sanitarios, Universidad de Castilla-La Mancha, Cuenca, España
\textsuperscript{b}Facultad de Educación, Universidad de Castilla-La Mancha, Ciudad Real, España
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\textsuperscript{d}Servicio de Urgencias, Hospital Virgen de la Luz, Cuenca, España
\textsuperscript{e}Laboratorio de Andalucía Clínica, Hospital Virgen de la Luz, Cuenca, España
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RESUMEN

\textbf{Introducción y objetivos:} Se ha demostrado que el programa MOVI de actividad física recreativa durante los días lectivos reduce la adiposidad y mejora el perfil lipídico en escolares. Sin embargo, puede que la mayor actividad física durante la semana se compensara con mayor sedentarismo en el fin de semana, de forma que MOVI no alcanzaría toda su efectividad potencial. Por ello diseñamos el programa MOVI-2, que también incluye actividad física durante el fin de semana. Se comunican la justificación y los métodos de un ensayo sobre la efectividad de MOVI-2 en la prevención del sobrepeso y la reducción del riesgo cardiovascular en 1,200 escolares de cuarto y quinto curso de primaria en Cuenca.

\textbf{Métodos:} Se asigna aleatoriamente a 10 colegios al programa MOVI-2 y 10 colegios al grupo de control. MOVI-2 consiste en actividad física recreativa en horario extracurricular, con dos sesiones de 90 min en días lectivos y una sesión de 150 min los sábados, durante cada semana de un curso académico. Se espera que el grupo control mantenga la actividad física habitual. Las variables principales, que se miden en cada niño al inicio y final de MOVI-2, son: peso y talla, perímetro de cintura, pliegue cutáneo tricipital, porcentaje de grasa corporal, presión arterial, perfil lipídico y resistencia a la insulina. Las variables secundarias son: actividad física realizada, condición física, calidad de vida y del sueño, rendimiento académico, disfrute con la actividad física y autoconcepto físico.

\textbf{Conclusiones:} Este estudio informará de si MOVI-2 supera algunas limitaciones potenciales de las intervenciones de actividad física en escolares (número Clinicaltrials.gov, NCT01277224).

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Protocol of a Randomized Cluster Trial to Assess the Effectiveness of the MOVI-2 Program on Overweight Prevention in Schoolchildren

\textbf{ABSTRACT}

\textbf{Introduction and objectives:} The MOVI physical activity program has been shown to reduce adiposity and to improve serum lipid profiles in schoolchildren. However, MOVI may not have achieved its maximum potential effectiveness, as increased physical activity on weekdays may have been offset by more sedentary behavior at weekends. We therefore developed the MOVI-2 program, which includes physical activity at weekends as well. This paper reports the rationale and methods of a trial to assess the effectiveness of MOVI-2 in preventing overweight and reducing cardiovascular risk in 1,200 4th- and 5th-grade primary schoolchildren in Cuenca, Spain.

\textbf{Methods:} Ten schools were randomly assigned to MOVI-2 and 10 schools to the control group. MOVI-2 consisted of recreational physical activity in after-school time, including two 90-min sessions on weekdays and one 150-min session on Saturdays, during each week of an academic year. The control group was expected to follow their usual patterns of physical activity. The primary end points, which were assessed at the start and the end of the MOVI-2 program, were weight and height, waist circumference, skinfold thickness, body fat percentage, blood pressure, lipid profile, and insulin resistance. Secondary end points were physical activity, fitness, health-related quality of life, sleep quality, academic performance, enjoyment with physical activity, and physical self-concept.

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\textsuperscript{b} Al final del artículo se relacionan los participantes del grupo MOVI-2.

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Effects of exercise during pregnancy on mode of delivery: a meta-analysis

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Key words
Exercise, physical activity, type of delivery, pregnancy outcome, pregnancy

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Conflict of interest
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

Abstract
Objective. We conducted a systematic review and meta-analysis to examine the influence of physical exercise interventions on the mode of delivery. Design. Review and meta-analysis of randomized controlled trials. Setting. Health centers, hospitals and local area obstetric practices from Spain, Norway, USA and Brazil, from where pregnant women were selected. Population. Healthy pregnant women with low to moderate levels of physical activity. Methods. Key words were used to conduct a computerized search for articles on the topic in six databases, Cochrane Library Plus, Science Direct, EMBASE, PubMed, Web of Science and ClinicalTrials.gov. Ten randomized controlled trials were identified and included in the meta-analysis. Main outcome measures. Mode of delivery (normal, instrumental vaginal, or cesarean delivery) and physical activity. Results. Relative risk reductions and their 95% confidence interval were calculated for each study, and the heterogeneity of the studies was estimated using Cochran’s Q statistic. The evidence suggests that physical exercise during pregnancy may increase the likelihood of normal delivery (relative risk = 1.12, 95% confidence interval 1.01–1.24; p = 0.041), in particular when exercise takes place during the second and third trimesters (relative risk = 1.14, 95% confidence interval 1.01–1.32; p = 0.048), even reducing the risk of cesarean delivery (relative risk = 0.66, 95% confidence interval 0.46–0.96; p = 0.028). Conclusions. Regular exercise during pregnancy appears to modestly increase the chance for normal delivery among healthy pregnant women. This applies to women with low to moderate levels of physical activity, but studies are needed to understand better the effect of physical exercise of moderate to vigorous intensity in the different trimesters.

Abbreviations: PA, physical activity; RCT, randomized controlled trial; RR, relative risk.

Introduction
Historically, pregnant women have often been encouraged to reduce physical activity (PA) and even stop working during pregnancy because it was assumed that PA reduced placental circulation and, as a consequence, increased the risk of problems such as miscarriages.

Key Message
The influence of physical exercise in pregnancy is a controversial issue. This review suggests that regular physical exercise during pregnancy slightly increases the probability of normal deliveries, and therefore could be recommended for healthy pregnant women.
Risk of extrapyramidal side effects comparing continuous vs. bolus intravenous metoclopramide administration: a systematic review and meta-analysis of randomised controlled trials

Iván Cavero-Redondo, Celia Álvarez-Bueno, Diana P Pozuelo-Carrascosa, Ana Díez-Fernández and Blanca Notario-Pacheco

Aims and objectives. To provide evidence about whether intravenous metoclopramide continuous infusion is associated with fewer extrapyramidal side effects than bolus infusion.

Background. Many studies have described the effects produced by the administration of metoclopramide, as a continuous intravenous infusion or intravenous bolus directly, but there is a lack of consensus about the best administration of this drug to minimise extrapyramidal side effects.

Design. A meta-analysis was conducted.

Methods. The search data base was conducted in: Cochrane Library, PubMed, Web of Knowledge and Scopus, to collect randomised controlled trials examining the association between extrapyramidal side effects and intravenous metoclopramide continuous or bolus infusion. Meta-analyses were conducted for the eligible randomised controlled trials by Comprehensive Meta-Analysis. Risk difference and 95% CIs were calculated with the Cochran’s Q-statistic, and heterogeneity was assessed with the I² test.

Results. Eleven randomised controlled trials were included. Meta-analysis showed that continuous intravenous infusion of metoclopramide produced less extrapyramidal side effects (8%; 95% CI, 5–11%; p < 0.001; I² = 65%). These improvements were particularly strong in studies scored ≥3 in the Jadad scale (12%; 95% CI, 3–24%; I² = 0%), in emergency patients (12%; 95% CI, 2–25%; I² = 0%), in patients who used concomitant drugs (9%; 95% CI, 5–12%; I² = 80%) and when observation (8%; 95% CI, 5–14%; I² = 69%) or analogue scale (7%; 95% CI, 1–13%; I² = 64%) were used to quantify the number of extrapyramidal reactions in patients.

Conclusions. Compared with bolus administration, continuous intravenous infusion of metoclopramide reduces the appearance of extrapyramidal side effects.

Relevance to clinical practice. Continuous infusion is an effective intervention to reduce in patients discomfort caused by the extrapyramidal side effects of metoclopramide.

What does this paper contribute to the wider global clinical community?
- Intravenous continuous infusion of metoclopramide is a significant effective intervention
- The continuous intravenous infusion of metoclopramide may reduce the discomfort caused by extrapyramidal side effects to patients
- Clinicians do not have to spend more time than the required to alleviate these unwanted effects of metoclopramide

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Prevalencia de delgadez, sobrepeso y obesidad en escolares españoles de 4-6 años en 2013; situación en el contexto europeo

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Resumen

*Introducción y objetivos:* tanto el exceso de peso como la delgadez se relacionan con diversos problemas de salud que pueden continuar hasta la edad adulta. Los objetivos de este estudio fueron estimar la prevalencia de delgadez, sobrepeso y obesidad en escolares de 4-6 años de las provincias de Cuenca y Ciudad Real (España), mediante criterios del Grupo Internacional de Trabajo sobre Obesidad y de la Organización Mundial de la Salud, y comparar estas cifras con otros estudios europeos.

*Métodos:* estudio observacional-transversal que incluyó a 1.585 escolares realizados en septiembre de 2013. Las mediciones de peso y talla fueron realizadas por enfermeras entrenadas y mediante procedimientos estándarizados. El estatus ponderal se definió según los criterios del Grupo Internacional de Trabajo sobre Obesidad y la Organización Mundial de la Salud.

*Resultados:* según criterios del Grupo Internacional de Trabajo sobre Obesidad, la prevalencia de delgadez, sobrepeso y obesidad fue del 20.51%, 11.84% y 8.58%, respectivamente; y del 3.97%, 13.92% y 10.79% cuando se utilizaron los criterios de la Organización Mundial de la Salud. No se encontraron diferencias estadísticamente significativas por sexo ni provincia para ninguna categoría de estatus ponderal. Para ambos criterios, la prevalencia de delgadez fue menor a medida que aumentaba la edad, mientras que la prevalencia de sobrepeso/obesidad fue mayor.

*Conclusiones:* la prevalencia de exceso de peso podría haber tocado techo en España, aunque continúa siendo un importante problema de salud pública. El aumento de la prevalencia de bajo peso debería ocupar un lugar relevante en las intervenciones de salud pública.

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The Accuracy of Diagnostic Methods for Diabetic Retinopathy: A Systematic Review and Meta-Analysis

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Abstract

Objective

The objective of this study was to evaluate the accuracy of the recommended glycemic measures for diagnosing diabetic retinopathy.

Methods

We systematically searched MEDLINE, EMBASE, the Cochrane Library, and the Web of Science databases from inception to July 2015 for observational studies comparing the diagnostic accuracy of glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), and 2-hour plasma glucose (2h-PG). Random effects models for the diagnostic odds ratio (dOR) value computed by Moses’ constant for a linear model and 95% CIs were used to calculate the accuracy of the test. Hierarchical summary receiver operating characteristic curves (HSROC) were used to summarize the overall test performance.

Results

Eleven published studies were included in the meta-analysis. The pooled dOR values for the diagnosis of retinopathy were 16.32 (95% CI 13.86–19.22) for HbA1c and 4.87 (95% CI 4.39–5.40) for FPG. The area under the HSROC was 0.837 (95% CI 0.781–0.892) for HbA1c and 0.735 (95% CI 0.657–0.813) for FPG. The 95% confidence region for the point that summarizes the overall test performance of the included studies occurs where the cutoffs ranged from 6.1% (43.2 mmol/mol) to 7.8% (61.7 mmol/mol) for HbA1c and from 7.8 to 9.3 mmol/L for FPG. In the four studies that provided information regarding 2h-PG, the pooled accuracy estimates for HbA1c were similar to those of 2h-PG; the overall performance for HbA1c was superior to that for FPG.
Reliability and validity of the Spanish version of the Children’s Sleep Habits Questionnaire (CSHQ-SP) in school-age children


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Accepted for publication 2 May 2016

Abstract

Background Sleep disorders in schoolchildren are a common problem worldwide, and when are not adequately diagnosed and treated, their negative impact on daytime functioning may be significant. The aim of this study was to evaluate the psychometric properties of the Spanish version of the Children’s Sleep Habits Questionnaire (CSHQ).

Methods Participants were 286 school-aged children from a community-based sample, aged 4 to 7 years. The sleep behaviour was evaluated using the CSHQ and actigraphy (ActiSleep monitor). The CSHQ was adapted to the Spanish language. The internal consistency of the questionnaire and the test–retest reliability between scores at baseline and three-weeks-later were estimated. Associations between CSHQ items and accelerometer sleep quality indicators were used as indicators of concurrent validity.

Results Cronbach’s alpha coefficients for the subscales ranged from 0.60 to 0.81, and 0.81 for the full scale; the intraclass correlation coefficients ranged from 0.56 to 0.81. A moderate correlation was observed in sleep latency and awakenings measurements using both parents’ reported sleep habits (CSHQ-SP) and sleep quality indicators (ActiSleep).

Conclusions The CSHQ-SP has demonstrated adequate psychometric properties, and it serves as a useful instrument for clinical and research setting.

Introduction

Sleep disorders in schoolchildren are a common problem that has received increased attention in recent years (Owens et al. 2005) and have been related to several physical, cognitive, behavioural and emotional problems, and overall, to decreasing levels of quality of life (Astill et al. 2012).

It has been suggested that sleep disorders could be underdiagnosed in clinical practice (Meltzer et al. 2010) because a high proportion of paediatricians do not regularly screen infants and toddlers for sleep problems (Owens 2001) and also because most parents do not report significant sleep disturbances to their paediatricians (Stein et al. 2001).

Recent studies, including children from birth to 36 months, using parent questionnaires and interviews, have reported sleep difficulties in 10–75% of children worldwide (Mindell et al. 2011). In Spain, sleep disorders seem to be a common problem in children (Pin Arboledas et al. 2011), although there is a lack
ABSTRACT

Introduction: Glycosylated haemoglobin level (HbA1c) is an indicator of the average blood glucose concentrations over the preceding 2–3 months and is used as a convenient and well-known biomarker in clinical practice. Currently, epidemiological evidence suggests that HbA1c level is an independent risk factor for cardiovascular events such as myocardial infarction, stroke, coronary heart disease and heart failure. This protocol aim is to conduct a systematic review and meta-analysis to determine relationships of HbA1c levels with cardiovascular outcomes and cause of death, and to analyse the range of HbA1c levels that is a predictor of cardiovascular disease and/or mortality based on data from published observational studies.

Methods and analysis: The search will be conducted using Medline, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Web of Science databases from their inception. Observational studies written in Portuguese, Spanish or English will be included. The Quality In Prognosis Studies tool will be used to assess the risk of bias for the studies included in the systematic review or meta-analysis. HRs for cardiovascular outcomes and causes of death will 95% CIs will be determined as primary outcomes. Subgroup analyses will be performed based on cardiovascular outcomes, cause of death studied, and type of population included in the studies.

Ethics and dissemination: This systematic review will synthesise evidence on the potential of using HbA1c level as a prognostic marker for cardiovascular disease outcomes and/or mortality. The results will be disseminated by publication in a peer-reviewed journal. Ethics approval will not be needed because the data used for this systematic review will be obtained from published studies and there will be no concerns about privacy.

Trial registration number: PROSPERO CRD42015032552.

INTRODUCTION

Cardiovascular disease (CVD) is a chronic disorder that develops insidiously throughout an individual’s life and usually has progressed to an advanced stage by the time symptoms occur. The percentage of all deaths due to CVD before the age of 75 years in Europe is 42% in women and 38% in men. CVD, especially coronary heart disease, is the leading cause of premature death worldwide.

In 2007, The Reynolds Risk Score for predicting CVD risk was developed, which incorporates information on glycosylated haemoglobin (HbA1c), but this score was only used in people with known diabetes. In 2010, the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines considered HbA1c level to be an appropriate index for CVD risk assessment in asymptomatic adults without a diagnosis of diabetes. Finally, the Canadian Cardiovascular Society proposed that CVD risk could be stratified by measuring levels of fasting plasma glucose, HbA1c, or both.

HbA1c level is an indicator of the average blood glucose concentrations over the preceding 2–3 months and is used as a convenient and well-known biomarker in clinical practice.
A follow-up study to assess the determinants and consequences of physical activity in pregnant women of Cuenca, Spain

Raquel Poyatos-León1, Gema Sanabria-Martínez1, Jorge Cañete García-Prieto2, Celia Álvarez-Bueno2, Diana P. Pozuelo-Carrascosa2, Iván Cavero-Redondo2, Antonio García-Hermoso3, Sagrario Gómez-Cantarino4, Miriam Garrido-Miguel2 and Vicente Martínez-Vizcaíno2,5*

Abstract

Background: In recent years, the influence of physical exercise on pregnancy outcomes has been widely debated. Despite the numerous studies addressing the relationship between maternal physical activity and pregnancy outcomes, the evidence for consistent and significant impact of regular exercise during pregnancy on fetal growth remains lacking. The aims of this study were, first, to assess the level of physical activity performed throughout the pregnancy by objective (accelerometer) and self-reported (questionnaire) measurements, and, second, to ascertain pre-pregnancy physical activity levels, to estimate the relationship between levels of physical activity and some pregnancy and neonatal outcomes.

Methods/design: This was a prospective cohort study. Participants were pregnant women (n = 194) aged 18 to 40 years who attended for three quarterly appointments for pregnancy ultrasound scans at the Virgen de la Luz Hospital in Cuenca, Spain. All participants provided written informed consents to participate in the study. Physical activity during the pregnancy follow-up was assessed by a self-reported Pregnancy Physical Activity Questionnaire and sleep log; also objectively by a GT3X accelerometer (ActiGraph). Furthermore, pregnancy symptoms inventory, nutritional behavioural assessment, socio-demographic characteristics, and anthropometry and body composition were measured.

At the end of the follow up, the following main outcomes were determined: pregnancy outcomes (incidence of gestational diabetes mellitus, pre-eclampsia, pregnancy-induced hypertension, weight gain during pregnancy, type of delivery, and neonatal outcomes (gestational age, birth weight, gender, Apgar score 1 min/5 min, type of resuscitation (I/II/III/IV), and pH of umbilical cord blood). Descriptive statistics for cross-sectional data, linear mixed regression models for absolute differences in changes baseline-final measurements were used as statistical analyses.

(Continued on next page)
RESEARCH ARTICLE

Diagnostic Accuracy Study of an Oscillometric Ankle-Brachial Index in Peripheral Arterial Disease: The Influence of Oscillometric Errors and Calcified Legs

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Abstract

Background

Peripheral arterial disease (PAD) is an indicator of widespread atherosclerosis. However, most individuals with PAD, in spite of being at high cardiovascular risk, are asymptomatic. This fact, together with the limitations of the Doppler ankle-brachial index (ABI), contributes to PAD underdiagnose. The aim of this study was to compare oscillometric ABI and Doppler ABI to diagnose peripheral arterial disease, and also to examine the influence of oscillometric errors and calcified legs on the PAD diagnoses.

Methods and Findings

We measured the ankle-brachial indexes of 90 volunteers (n = 180 legs, age 70 ± 14 years, 43% diabetics) using both oscillometer OMRON-M3 and Doppler. For concordance analyses we used the Bland and Altman method, and also estimated the intraclass correlation coefficient. Receiver Operating Characteristic Curves were used to examine the diagnostic performance of both methods. The ABI means were 1.06 ± 0.14 and 1.04 ± 0.16 (p = 0.034) measured by oscillometer and Doppler ABIs respectively, with limits of agreement of 0.20 and intraclass correlation coefficient = 0.769. Oscillometer yielded 23 “error” measurements, and also overestimated the measurements in low ankle pressures. Using Doppler as gold standard, oscillometer performance for diagnosis of PAD showed an Area Under Curve = 0.944 (sensitivity: 66.7%, specificity: 96.8%). Moreover, when considered calcified legs and oscillometric “error” readings as arteriopathy equivalents, sensitivity rose to 78.2%, maintaining specificity in 96%. The best oscillometer cut-off point was 0.96 (sensitivity: 87%, specificity: 91%, positive likelihood ratio: 9.66 and negative likelihood ratio: 0.14).
Association between physical activity, sedentary behavior, and fitness with health related quality of life in healthy children and adolescents

A protocol for a systematic review and meta-analysis

Alberto Bermejo-Cantarero, MSc, Celia Álvarez-Bueno, MPH, Vicente Martínez-Vizcaino, MD, PhD, Antonio García-Hermoso, PhD, Ana Isabel Torres-Costoso, PhD, Mairena Sánchez-López, PhD

Abstract

Background: Health related quality of life (HRQoL) is a subjective, multidimensional and changing over time construct. When HRQoL is decreased, a child is less likely to be able to develop normally and mature into a healthy adult. Physical inactivity is a priority public health problem. Evidence suggests how even moderate levels of physical activity or high fitness levels are associated with benefits for the health in children and adolescents. The aims of this systematic review are to examine the relationship between physical activity, sedentary behavior, and fitness with HRQoL, and estimate the effects of interventions that have tested the effectiveness of the increase of the physical activity, the improvement of the physical fitness or the avoidance of sedentary behaviors in HRQoL in healthy subjects aged under 18 years old.

Methods: This systematic review and meta-analysis protocol was conducted following the preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) statement. To identify relevant studies, the following electronic databases will be searched: MEDLINE, EMBASE, Cochrane Database, Web of Science, and PEDro. Reference lists of relevant studies will be examined for links to potential related articles. The methodological quality of the observational included studies will be scored using a quality assessment checklist. For the intervention studies, the risk of bias will be estimated using The Cochrane Collaboration tool for assessing risk of bias. Reviewers will determine whether a meta-analysis is possible when data have been extracted. If it is, subgroup analyses will be carried out by age and socioeconomic status, and by the different dimensions of the HRQoL. If is not possible, a descriptive analysis will be conducted.

Conclusion: To our knowledge, this systematic review and meta-analysis will be the first that synthesizes the existing results about the relationship between physical activity, sedentary behavior, physical fitness, and HRQoL, and the effect of physical activity interventions on HRQoL, in healthy subjects under 18 years old. This study will clarify this relationship and will provide evidence for decision-making. Limitations may include the quality of the selected studies and their characteristics. Only studies published in English and Spanish will be included.

Systematic review registration: PROSPERO CRD42015025823.
RESEARCH ARTICLE

Insulin and bone health in young adults: The mediator role of lean mass

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Abstract

Background
The positive relationship between lean mass (LM) and bone health is well known, but a positive association between insulin and LM has also been described. Insulin has some anabolic properties on bone through the stimulation of osteoblast differentiation, yet the role of LM as a confounder or mediator in this relationship remains uncertain.

Objective
To examine whether the association between insulin levels and bone health is mediated by LM.

Methods
A cross-sectional study was conducted at the Castilla La Mancha University (Spain) involving 466 young adults (113 young men; 19.5±2.3 years). LM and total-body bone mineral content (BMC) were measured by dual energy x-ray absorptiometry, and insulin was measured in fasting serum samples.

Results
Young adults with high total LM had higher values of total-body BMC than their peers after controlling for age and sex, this relationship persisted after adjusting for insulin levels (p<0.001). In mediation analyses, insulin levels were positively associated with total-body BMC (b = 0.05; p<0.001) and total LM acted as an intermediate variable, attenuating the association between insulin levels and total-body BMC (b = -31.98; p>0.05) as indicated by Sobel test values for indirect effect (z = 4.43; p<0.001).

Conclusions
LM plays an important role in the relationship between insulin levels and bone health, in such a way that while increases in LM have a positive influence on bone health, they are also negatively associated with insulin levels.
Abstract

Background: There is inconsistent evidence about the effect of physical activity on the prevention and treatment of depression during the postnatal period. The aim of this meta-analysis was to determine the effect of physical activity interventions during pregnancy and the postpartum period for controlling postpartum depressive symptoms.

Methods: We systematically searched Cochrane Library Plus, Science Direct, EMBASE, CINAHL, PubMed, Web of Science, and Scopus, from January 1990 to May 2016, for randomized or nonrandomized controlled trials addressing the effect of physical activity on postpartum depression. The inverse variance-weighted method was used to compute pooled estimates of effect size and respective 95% confidence intervals (95% CI) for physical activity intervention on postpartum depression. Subgroup analyses were performed comparing women with and without postpartum depressive symptoms according to specific scales measuring this construct. Meta-regression and sensitivity analysis were computed to evaluate heterogeneity.

Results: Twelve studies were included in the meta-analysis. Effect size for the relationship between physical activity interventions during pregnancy and the postpartum period on postpartum depressive symptoms was 0.41 (95% CI 0.28-0.54). Heterogeneity was $I^2 = 33.1\%$ ($P = .117$). When subgroup analyses were done, pooled effect sizes were 0.67 (95% CI 0.44-0.90) for mothers who met postpartum depressive symptoms criteria at baseline based on specific scales, and 0.29 (95% CI 0.14-0.45) for mothers who did not meet those depressive symptoms criteria at baseline.

Conclusion: Physical exercise during pregnancy and the postpartum period is a safe strategy to achieve better psychological well-being and to reduce postpartum depressive symptoms.

Keywords

intervention programs, motor activity, peripartum depression, physical exercise, postnatal depression, postpartum depression
BMJ Open

The effects of physical activity interventions on glycated haemoglobin A1c in non-diabetic populations: a protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Epidemiological evidence suggests that physical activity has a positive effect on reducing glycated haemoglobin A1c (HbA1c) levels not only in diabetics, but also in healthy subjects. Moreover, a positive association of HbA1c levels with cardiovascular disease and mortality in non-diabetic populations has recently been reported. This is a protocol for a systematic review and meta-analysis aiming to estimate the effects of physical activity on glycaemic control measured by HbA1c levels in non-diabetic populations; and to determine which type of physical activity has a greater influence on glycaemic control.

Methods and analysis The search will be conducted using MEDLINE, EMBASE, the Cochrane Library and Web of Science databases from inception to mid-2017. Randomised controlled trials, non-randomised experimental studies and controlled pre–post studies written in English, Portuguese, French or Spanish will be included. The Cochrane Collaboration’s tool and The Quality Assessment Tool for Quantitative Studies will be used to assess the risk of bias for studies included in the systematic review. Standardised pre–post intervention mean differences of HbA1c will be calculated as the primary outcome. Subgroup analyses will be performed based on the characteristics of physical activity intervention and population included in the studies.

Ethics and dissemination This systematic review will synthesise evidence on the association of physical activity and HbA1c in non-diabetic populations. This study is important from the clinical and public health point because it will estimate the effect of physical activity on the glycemic control, and it will also examine which is the type of physical activity that should be recommended for preventing type 2 diabetes and its complications. The results will be disseminated by publication in a peer-reviewed journal. Ethical approval will not be required because the data used for this systematic review will be obtained from published studies and there will be no concerns about privacy.

Trial registration number PROSPERO CRD42016050991.

Strengthen and limitations of this study

- This study presents a comprehensive methodology for analysing the effect of physical activity interventions on glycaemic control measured using HbA1c levels in general and non-diabetic populations.
- Two researchers will independently perform study selection, data extraction and quality assessment.
- The assessment of risk of bias of the selected studies and heterogeneity among studies included, with particular reference to study design and sample characteristics, is a featured point in this evidence review.
- The differences among physical activity interventions might be a source of variable quality and heterogeneity among studies, and may limit the quality of the evidence of this meta-analysis.

INTRODUCTION

Guidelines from the American Diabetes Association1 and the WHO2 propose glycated haemoglobin A1c (HbA1c) levels of >6.5% (48.0 mmol/mol) for the diagnosis of diabetes. Also, recent meta-analyses have reported an increase in all-cause mortality with HbA1c levels around 5.7% (39.0 mmol/mol) in non-diabetic subjects and around 7.5% (58.0 mmol/mol) in diabetic populations.3,4 HbA1c is a useful biochemical test for identifying people with subclinical diabetes at the onset of clinical symptoms.5 Since microvascular complications of diabetes are present in the early stages of the disease, controlling HbA1c levels should not be restricted to the diabetic population.

Substantial evidence supports the view that physical activity reduces the risk of dying prematurely owing to its positive influence on a variety of health conditions, such as cognition, cardiovascular disease, and chronic diseases.6-9 Physical activity is a possible strategy for preventing type 2 diabetes and its complications.10,11 Physical activity interventions have a greater influence on glycaemic control in non-diabetic populations when compared to other risk factors such as BMI.12 In non-diabetic populations, the effect of physical activity on glycaemic control may be more pronounced than in diabetic populations. Therefore, the effect of physical activity interventions on glycaemic control and the type of physical activity that should be recommended for non-diabetic populations are still unclear.

...
Glycated haemoglobin A1c as a risk factor of cardiovascular outcomes and all-cause mortality in diabetic and non-diabetic populations: a systematic review and meta-analysis

Iván Cavero-Redondo,1 Barbara Peleteiro,2,3 Celia Álvarez-Bueno,1 Fernando Rodríguez-Artalejo,4 Vicente Martínez-Vizcaíno1,5

ABSTRACT

Objective To examine the relationship between glycated haemoglobin A1c (HbA1c) levels and the risk of cardiovascular outcomes and all-cause mortality based on data from observational studies and to determine the optimal levels of HbA1c for preventing cardiovascular events and/or mortality in diabetic and non-diabetic populations.

Review methods We systematically searched Medline, Embase, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews and Web of Science databases, from inception to July 2016, for observational studies addressing the association of HbA1c levels with mortality and cardiovascular outcomes. Random effects models were used to compute pooled estimates of HR and respective 95% CI for all-cause mortality, cardiovascular mortality and risk of cardiovascular events, separately for people with and without diabetes.

Results Seventy-four published studies were included in the systematic review, but only 46 studies could be incorporated in the meta-analysis. In both diabetic and non-diabetic populations, there was an increase in the risk of all-cause mortality when HbA1c levels were over 6.0% and 6.0%, respectively. The highest all-cause mortality in people with diabetes was HbA1c above 9.0% (HR=1.69; 95%CI 1.09 to 2.66) and in those without diabetes was HbA1c above 6.0% (HR=1.74; 95%CI 1.38 to 2.20). However, both diabetic and non-diabetic populations with lower HbA1c levels (below 6.0%HR=1.57; 95%CI 1.14 to 2.17 and below 5.0%HR=1.19; 95%CI 1.04 to 1.36, respectively) had higher all-cause mortality. Similar pooled estimates were found when cardiovascular mortality was the outcome variable.

Conclusion HbA1c is a reliable risk factor of all-cause and cardiovascular mortality in both diabetics and non-diabetics. Our findings establish optimal HbA1c levels, for the lowest all-cause and cardiovascular mortality, ranging from 6.0% to 8.0% in people with diabetes and from 5.0% to 6.0% in those without diabetes.

INTRODUCTION

Cardiovascular diseases (CVD) are the first cause of mortality in the world, representing 31% of all global deaths. In 2012, 17.5 million people died by CVD according to WHO.1 Prevention of CVD through the control of risk factors is a priority in most developed countries.2 Glycated haemoglobin A1c (HbA1c) level is an indicator of the average blood glucose concentrations over the preceding 2 to 3 months that is recommended by the American Diabetes Association (ADA)3 and the WHO4 for the diagnosis of diabetes. This indicator has exhibited
The accuracy of an oscillometric ankle-brachial index in the diagnosis of lower limb peripheral arterial disease: A systematic review and meta-analysis

Ángel Herráiz-Adillo | Iván Cavero-Redondo | Celia Álvarez-Bueno | Vicente Martínez-Vizcaíno | Diana P. Pozuelo-Carrascosa | Blanca Notario-Pacheco

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Iván Cavero-Redondo, Universidad de Castilla-La Mancha, Health and Social Research Center, Cuenca, Spain.
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Summary
Introduction: Peripheral arterial disease (PAD) remains underdiagnosed and undertreated, partly because of limitations in the Doppler ankle-brachial index (ABI), the non-invasive gold standard.

Objective: This systematic review and meta-analysis aims to compare the diagnostic accuracy of the oscillometric ABI and the Doppler ABI, and to examine the influence of two approaches to analysis: legs vs subjects and inclusion of oscillometric errors as PAD equivalents vs exclusion.

Methods: Systematic searches in EMBASE, MEDLINE, Web of Science and the Cochrane Library databases were performed, from inception to February 2017. Random-effects models were computed with the Moses-Littenberg constant. Hierarchical summary receiver operating characteristic curves (HSROC) were used to summarise the overall test performance.

Results: Twenty studies (1263 subjects and 3695 legs) were included in the meta-analysis. The pooled diagnostic odds ratio (dOR) for the oscillometric ABI was 32.49 (95% CI: 19.6-53.8), with 65% sensitivity (95% CI: 57-74) and 96% specificity (95%CI: 93-99). In the subgroup analysis, the “per subject” group showed a better performance than the “per legs” group (dOR 36.44 vs 29.03). Similarly, an analysis considering oscillometric errors as PAD equivalents improved diagnostic performance (dOR 31.48 vs 28.29). The time needed for the oscillometric ABI was significantly shorter than that required for the Doppler ABI (5.90 vs 10.06 minutes, respectively).

Conclusions and relevance: The oscillometric ABI showed an acceptable diagnostic accuracy and feasibility, potentially making it a useful tool for PAD diagnosis. We recommend considering oscillometric errors as PAD equivalents, and a “per subject” instead of a “per leg” approach, in order to improve sensitivity. Borderline oscillometric ABI values in diabetic population should raise concern of PAD.

1 INTRODUCTION

Peripheral arterial disease (PAD) is an age-dependent manifestation of atherosclerosis, which is highly prevalent in Western countries. Uncommon before the age of 50, its rates increase to about 20% by the age of 80. Moreover, PAD has proved to be an independent risk factor for coronary artery and cerebrovascular disease, and all-cause mortality.

However, this condition remains both underdiagnosed and undertreated, with no consensus regarding on whom and when screening...
Factors affecting the validity of the oscillometric Ankle Brachial Index to detect peripheral arterial disease

Ángel HERRÁIZ-ADILLO 1, Iván CAVERO-REDONDO 2, Celia ÁLVAREZ-BUENO 2 *, Vicente MARTÍNEZ-VIZCAÍNO 2, 3, Diana P. POZUELO-CARRASCOSA 2, Blanca NOTARIO-PACHECO 2

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ABSTRACT

BACKGROUND: The use of oscillometric Ankle Brachial Index (ABI) to diagnose peripheral arterial disease (PAD) has raised concern, especially due to a lack of agreement and sensitivity. This study aimed to evaluate those factors affecting the validity of oscillometric ABI in comparison to Doppler ABI to detect PAD.

METHODS: Through univariate and multivariate linear regression, we studied those factors affecting the differences between oscillometric and Doppler ABI; through univariate and multivariate logistic regression we analyzed the false negative rate of oscillometric ABI to detect PAD.

RESULTS: We analyzed 197 consecutive subjects (394 legs) from two settings: Primary Care and Vascular Service. The means of oscillometric ABI and Doppler ABI were 1.094 (95% CI: 0.843-1.345) and 1.073 (95% CI: 0.769-1.374) (P=0.001), respectively. In men, covariates explaining the differences between oscillometric and Doppler ABI were Doppler ankle blood pressure (β=-0.610, P<0.001), ankle circumference (β=-0.176, P=0.004) and oscillometric brachial blood pressure (β=0.136, P=0.037); in women, those were weight (β=0.351, P<0.001) and Doppler ankle blood pressure (β=-0.318, P<0.001). Sensitivity and specificity of oscillometric ABI to detect PAD were 80.6% and 97.4%, respectively, and covariates explaining the rate of false negatives in PAD population were setting (Exp(β)=1.72, P=0.009) and tobacco (packs/year) (Exp(β)=1.049, P=0.002).

CONCLUSIONS: Although some factors influencing the lack of agreement between oscillometric and Doppler ABI were identified, the correction of oscillometric ABI seems impractical, since Doppler is needed, the bias is not always uniformly distributed and its clinical relevance is small. According to sensitivity, borderline oscillometric ABI in Primary Care settings and smokers suggest PAD.

(Cite this article as: Herráiz-Adillo A, Cavero-Redondo I, Álvarez-Bueno C, Martínez-Vizcaíno V, Pozuelo-Carrascosa DP, Notario-Pacheco B. Factors affecting the validity of the oscillometric Ankle Brachial Index to detect peripheral arterial disease. Int Angiol 2017;36: ____. DOI: 10.23736/S0392-9590.17.03860-3)

Key words: Ankle Brachial Index - Oscillometry - Peripheral arterial disease - Sensitivity and specificity.

Peripheral arterial disease (PAD) is a prevalent manifestation of atherosclerosis, which affects 19.8% of men and 16.8% of women in elderly population. This condition is considered a strong marker for cardiovascular risk and mortality, especially at the expense of high rates of coronary artery disease and cerebrovascular disease. However, between 20% and 30% of PAD subjects remain undiagnosed and undertreated, in part because of the limitations of the Doppler Ankle Brachial Index (ABI), the non-invasive gold standard for PAD diagnosis. Secondary prevention measures after early diagnosis may reduce morbidity and mortality in this silent cohort.

The oscillometric ABI has arisen as a useful method for PAD diagnosis, especially because of its simplicity, low cost, short learning curve and feasibility. Au-
Original breve

Relación entre los niveles de glucemia y la rigidez arterial en adultos no diabéticos

Q1 Iván Cavero-Redondo, Vicente Martínez-Vizcaíno, Celia Álvarez-Bueno, José Ignacio Recio-Rodríguez, Manuel Ángel Gómez-Marcos y Luis García-Ortiz

INFORMACIÓN DEL ARTÍCULO

Resumen

Objetivo: Examinar, en una población no diabética, si la asociación entre la rigidez arterial y los niveles glucémicos depende de la prueba utilizada como indicador glucémico, glucosa en ayunas o hemoglobina glicosilada A1c (HbA1c).

Población de pacientes y métodos: Análisis transversal de una submuestra de 220 no diabéticos del estudio EVIDENT II en el que se determinaron los parámetros relacionados con glucosa en ayunas, HbA1c y rigidez arterial (velocidad de onda de pulso, índice de aumento radial y central y presión de pulso central). Las diferencias de medias entre los parámetros relacionados con la rigidez arterial en cada tercil de HbA1c y glucosa en ayunas se determinaron mediante un análisis de covarianza.

Resultados: La media de todos los parámetros de rigidez arterial aumentaba por cada tercil de HbA1c, aunque las diferencias de medias solamente fueron estadísticamente significativas para la velocidad de la onda de pulso (p < 0,001), incluso tras ajustar por los potenciales factores de confusión (HbA1c ≤ 5,3% = 6,88 m/s; HbA1c 5,3%–5,59% = 7,06 m/s; y HbA1c 5,6% = 7,93 m/s; p = 0,004). Por el contrario, las diferencias de medias en la velocidad de onda de pulso por terciles de glucosa en ayunas no mostraron diferencias estadísticamente significativas después de ajustar por estos factores de confusión (glucosa 4,44 mmol/l ≤ 7,18 m/s; glucosa 4,44 mmol/l-4,87 mmol/l= 7,26 m/s; y glucosa ≥ 4,88 mmol/l= 7,93 m/s; p = 0,066).

Conclusiones: Los niveles de glucosa en la población no diabética se asociaron a rigidez arterial, aunque de forma más estrecha cuando esos niveles se determinaron usando HbA1c.

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Relationship between glycaemic levels and arterial stiffness in non-diabetic adults

Abstract

Objective: To examine, in a non-diabetic population, whether the association between arterial stiffness and glycaemic levels depends on the test used as a glycaemic indicator, fasting plasma glucose (FPG) or glycated haemoglobin A1c (HbA1c).

Patient population and methods: A cross-sectional analysis of a 220 non-diabetic subsample from the EVIDENT II study in which FPG, HbA1c and arterial stiffness-related parameters (pulse wave velocity, radial and central augmentation index, and central pulse pressure) were determined. Mean differences in arterial stiffness-related parameters by HbA1c and FPG tertiles were tested using analysis of covariance.

Results: All means of arterial stiffness-related parameters increased by HbA1c tertiles, although mean differences were only statistically significant in pulse wave velocity (p ≤ .001), even after controlling for

Keywords:
Glycated haemoglobin
Fasting plasma glucose
Arterial stiffness
HbA1c
Pulse wave velocity

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24th European Congress on Obesity

ECO 2017

May 17-20 2017– Porto, Portugal

Thursday, June 22, 2017

Dear Mrs. Celia Álvarez-Bueno

On behalf of the ECO 2017 Programme Organizing Committee, we are pleased to confirm that Mrs. Celia Álvarez-Bueno attended ECO 2017 Congress and was the author/co-author/presenter of the following poster:

Paper ID: T4P44
Title: "Effectiveness of the MOVI-KIDs physical activity intervention improving children’s academic achievement"

Author(s): Celia Álvarez-Bueno; Ivan Cavero-Redondo; Miriam Garrido-Miguel; Blanca Notario-Pacheco; María Martínez-Andrés; Mairena Sánchez-López

Institution: ¹Health and Social Research Center. Universidad de Castilla-La Mancha, Cuenca, Spain; ²Health and Social Research Center. Universidad de Castilla-La Mancha, Ciudad Real, Spain

If you require any further information please visit the web site at www.eco2017.easop.org

Regards,

VIAGENS ABREU, S.A.
Cont. nº 500 297 177
Praça da Trindade, 142, 4º
4000-539 PORTO
RNAVT 1702

By the Congress Secretariat

ABREU EVENTS
Praça da Trindade, 142, 4º
4000-285 Porto-Portugal
Thursday, June 22, 2017

Dear Mr. Iván Cavero-Redondo

On behalf of the ECO 2017 Programme Organizing Committee, we are pleased to confirm that Mr. Iván Cavero-Redondo attended ECO 2017 Congress and was the author/co-author/presenter of the following poster:

**Paper ID:** T4P93  
**Title:** "Physical activity intervention program (MOVI-KIDS study) on preventing obesity in preschoolers"  
**Author(s):** Iván Cavero-Redondo¹; Celia Alvarez-Bueno¹; Miriam Garrido-Miguel¹; Vicente Martínez-Vizcaíno¹; Ana Díez-Fernandez¹; Abel Ruiz de la Hermosa Fernandez-Infante²  
**Institution:** ¹Health and social research center, Universidad de Castilla-La Mancha, Cuenca, Spain; ²Health and social research center, Universidad de Castilla-La Mancha, Ciudad Real, Spain

If you require any further information please visit the web site at [www.eco2017.easo.org](http://www.eco2017.easo.org)

Regards,

**VIAGENS ABREU, S.A.**  
Cont. nº 500 297 177  
Praça da Trindade, 142, 4º  
4050-939 PORTO  
RNAYT 1702

By the Congress Secretariat

**ABREU EVENTS**  
Praça da Trindade, 142, 4º  
4000-285 Porto-Portugal
On behalf of the Scientific and Organising Committees, we hereby certify that the contribution entitled:

“The relationship between active commuting to school and cognitive performance in 4-7 years old Spanish children. The MOVI-KIDS study.”

whose authors are:

Abel Ruiz de la Hermosa Fernández Infante, Andrés Redondo Tébar, Celia Álvarez Bueno, Roberto Gulias González, María Jesús Pardo Guijarro and Mairena Sánchez López

Has been presented as an oral communication at the International Symposium Active Brains for All: Exercise, Cognition and Mental Health, held in Granada (Spain) on 12th June 2017.

Francisco B. Ortega
President of the Scientific and Organising Committees

Irene Esteban-Cornejo
Secretary of the Scientific and Organising Committees
El Comité Científico y Organizador certifica que la contribución titulada:

"Resiliencia como mediador entre la capacidad cardiorespiratoria y la calidad de vida relacionada con la salud en adultos jóvenes"

cuyo autor/es son:

Miriam Garrido Miguel, Celia Alvarez Bueno, Blanca Notario Pacheco, Isabel María Parreño Madrigal, Alberto Bermejo Cantarero, Laura Muñoz de Morales Romero y Jose Alberto Martínez Hortelano

ha sido presentada como póster en el Simposio EXERNET. Investigación en Ejercicio, Salud y Bienestar: "Exercise is Medicine" celebrado en Cádiz los días 14 y 15 de octubre de 2016.

Cádiz, a 15 de octubre de 2016

Carmen Padilla Moledo
Presidenta del Comité Organizador

David Jiménez Pavón
Presidente del Comité Organizador

José Antonio Casajús Mallén
Presidente de EXERNET

José Castro Piñero
Responsable Grupo GALENO

CTS-158
El Comité Científico y Organizador certifica que la contribución titulada:

"Asociación entre IMC pre-gestacional y desarrollo neurocognitivo en niños: una revisión sistemática y meta-análisis de estudios observacionales"

cuyo autor/es son:

Celia Alvarez Bueno, Ivan Cavero Redondo, Minerva Velasco-Abellan, Veronica Artalejo de Mora, Ana Isabel Cobo Cuenca, Noelia Martinez Espinosa y Jose Alberto Martinez Hortelano

ha sido presentada como póster en el Simposio EXERNET. Investigación en Ejercicio, Salud y Bienestar: “Exercise is Medicine” celebrado en Cádiz los días 14 y 15 de octubre de 2016.

Cádiz, a 15 de octubre de 2016

Carmen Padilla Moledo  
Presidenta del Comité  
Organizador

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José Antonio Casajús Mallén  
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CT5-158
CERTIFICADO DE COMUNICACIÓN ORAL

El Comité Científico de la XXXIV Reunión Anual de la Sociedad Española de Epidemiología (SEE) y XI Congresso da Associação Portuguesa de Epidemiologia (APE), celebrada en Sevilla los días 14 al 16 de septiembre de 2016, certifica que ha sido presentado como comunicación oral el trabajo titulado

CAPACIDAD CARDIORRESPIRATORIA Y PRESIÓN ARTERIAL EN ESCOLARES: OBESIDAD COMO MEDIADOR

cuyos autores son

DP. POZUELO CARRASCOSA, I. CAVERO REDONDO, C. ALVAREZ BUENO, M. GARRIDO MIGUEL, M. MARTINEZ ANDRES, B. RODRIGUEZ MARTIN, AJ. CERRILLO URBINA, L. RUIZ HIDALGO, MJ. GONZALEZ LOPEZ

Y para que así conste, e certificado en Sevilla, 16 de septiembre de 2016.

José María Mayoral Cortés y Soledad Márquez Calderón
Co-Presidentes del Comité Científico
Certifica-se que a Comunicação oral "Determinantes y consecuencias de los patrones de actividad física durante el embarazo en gestantes de Toledo", do(s) autor(es) Minerva Velasco Abellán, Sagrario Gomez Cantarino, Mercedes de Dios Aguado, Beatriz Gonzalez López, Mª Josefa Rodriguez Rojas e CELIA ALVAREZ BUENO, enquadrada no eixo temático "A3 - Inovação e Transferência de Conhecimento", foi apresentada por Minerva Velasco Abellán, em 07 de junho de 2016, no âmbito do Simpósio Internacional de Cuidados de Saúde Baseados na Evidência e V Congresso de Investigação em Enfermagem Iberoamericano e de Países de Língua Oficial Portuguesa, organizados pela Unidade de Investigação em Ciências da Saúde: Enfermagem (UICISA: E) da Escola Superior de Enfermagem de Coimbra, que decorreram de 06 a 08 de junho de 2016, em Coimbra, Portugal.

Coimbra, 07 de junho de 2016

[Assinatura]

Escola Superior de Enfermagem de Coimbra - Rua 5 de Outubro ou Avenida Bisaya Barreto Apartado 7001 - 3046-851 COIMBRA - NIF 600081583
Certificado nº CO02689-168/2016
CERTIFICADO DE PÓSTER ELECTRÓNICO

El Comité Científico de la XXXIV Reunión Anual de la Sociedad Española de Epidemiología (SEE) y XI Congresso da Associação Portuguesa de Epidemiologia (APE), celebrada en Sevilla los días 14 al 16 de septiembre de 2016, certifica que ha sido presentado como póster electrónico el trabajo titulado

ASOCIACIÓN ENTRE EJERCICIO FÍSICO Y RENDIMIENTO ACADÉMICO EN ESCOLARES: UN META-ANÁLISIS.

cuyos autores son


Y para que así conste, e certificado en Sevilla, 16 de septiembre de 2016.

José María Mayoral Cortés y Soledad Márquez Calderón

Co-Presidentes del Comité Científico
XI CONGRESO INTERNACIONAL DE MEDICINA Y SALUD ESCOLAR

XXX CONGRESO ESPAÑOL DE MEDICINA Y SALUD ESCOLAR Y UNIVERSITARIA

"Gestión y Promoción de la Salud integral escolar y Universitaria"

Diploma

D. Jorge Cañete García-Prieto, Dª Celia Álvarez Bueno, D. Iván Cavero Redondo, Dª Montserrat Solera Martínez y D. Abel Ruiz de la Hermosa

Por su participación científica como PONENTE
Con el estudio: "Medición de la condición física de los escolares"
En la mesa redonda "La actividad física y la salud de los escolares"

Celebrado en Cuenca, los días 16, 17 y 18 de octubre de 2015, con 20 horas.
Cuenca, 18 de octubre de 2015.

SECRETARIO

Fdo. Borja Jesús Herraiz Ahijado

Declarado de interés sociosanitario por la Consejería de Sanidad de la Junta de Comunidades de Castilla-La Mancha, con 20 horas lectivas, según O.M. de 11 de diciembre de 2001 (DOCM nº 136, de 28 de diciembre de 2001).
CONFIRMATION

Prague, 15 May 2015

Dear Dr. Iván Cavero-Redondo,

It is our pleasure to confirm that your abstract has been accepted, after peer review by the Scientific Committe and has been PRESENTED at the 22nd European Congress on Obesity, to be held in Prague, Czech Republic from 6-9 May 2015 as a POSTER PRESENTATION as follows:

Presentation title: Weight status and blood pressure (bp) in pre-school children
Presenting author: Cavero-Redondo I. (Spain)
Topic: Track 7 – Public Health and Prevention: Population trends (European comparison)
Poster session: Poster Session 1; T7:PO.008
Schedule: Thursday, May 7, 2015

Yours sincerely,

Professor Martin Fried
Scientific Committee Chair, ECO2015

Professor Gema Frühbeck
President, EASO

Handled by
Jakub Novák

JAKUB NOVÁK | Abstracts and Scientific Program Coordinator | ECO2015 Congress Secretariat
GUARANT International
E-mail: novakj@guarant.cz | www.guarant.cz
CONFIRMATION

Prague, 15 May 2015

Dear Dr. Iván Cavero-Redondo,

It is our pleasure to confirm that your abstract has been accepted, after peer review by the Scientific Committee and has been PRESENTED at the 22nd European Congress on Obesity, to be held in Prague, Czech Republic from 6-9 May 2015 as a POSTER PITCH PRESENTATION (ORALLY) as follows:

Presentation title: Fitness and fatness in Spanish pre-schoolers
Presenting author: Cavero-Redondo I. (Spain)
Topic: Track 7 – Public Health and Prevention: Population trends (European comparison)
Poster session: Poster Pitch Session 1; Session B; T7:PO.010
Schedule: Thursday, May 7, 2015; 13:15-14:45

Yours sincerely,

Professor Martin Fried
Scientific Committee Chair, ECO2015

Professor Gema Frühbeck
President, EASO

Handled by
Jakub Novák

JAKUB NOVÁK | Abstracts and Scientific Program Coordinator | ECO2015 Congress Secretariat
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CERTIFICADO DE COMUNICACIÓN ORAL

El Comité Científico del II Congreso Ibero-Americano de Epidemiología y Salud Pública, celebrado en Santiago de Compostela los días 2 al 4 de septiembre de 2015, certifica que ha sido presentado como comunicación oral el trabajo titulado

RELACIÓN ENTRE ESTATUS PONDERAL, ADIPOSIDAD Y LA PRESIÓN ARTERIAL EN NIÑOS EN EDAD PREESCOLAR

cuyos autores son


Y para que así conste, se expide el presente certificado en Santiago de Compostela a 4 de septiembre de 2015.

Alberto Ruano Ravíña
Presidente del Comité Científico

Mª Isolina Santiago Pérez
Secretaria del Comité Científico
CERTIFICADO DE COMUNICACIÓN ORAL

El Comité Científico del II Congreso Ibero-Americano de Epidemiología y Salud Pública, celebrado en Santiago de Compostela los días 2 al 4 de septiembre de 2015, certifica que ha sido presentado como comunicación oral el trabajo titulado

PREVALENCIA DE DELGADEZ Y EXCESO DE PESO EN PREESCOLARES, SEGÚN NIVEL SOCIOECONÓMICO FAMILIAR

cuyos autores son


Y para que así conste, se expide el presente certificado en Santiago de Compostela a 4 de septiembre de 2015.

Alberto Ruano Raviña
Presidente del Comité Científico

Mª Isolina Santiago Pérez
Secretaria del Comité Científico
XIX Encuentro Internacional de Investigación en Cuidados
19th International Nursing Research Conference

Certificado de comunicación oral
Certificate of oral presentation

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por la comunicación oral
presented the oral presentation

Relación entre la composición corporal y la condición física en niños en edad preescolar

Cuenca, 17-20 de noviembre de 2015

Teresa Moreno Casbas
Comité Organizador
Organising Committee
XIX Encuentro Internacional de Investigación en Cuidados
19th International Nursing Research Conference

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por la comunicación oral breve
presented the oral brief presentation

Prevalencia de delgadez, sobrepeso y obesidad en escolares españoles de 4-6 años en 2013. Situación en contexto europeo.

Cuenca, 17-20 de noviembre de 2015

Teresa Moreno Casbas
Comité Organizador
Organising Committee
Certificado de comunicación oral
Certificate of oral presentation

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Sanabria Martínez G, Poyatos León R, Cavero Redondo I, Álvarez Bueno C, Notario Pacheco B, Martínez Vizcaíno V

por la comunicación oral
presented the oral presentation

Eficacia de programas de actividad física en el embarazo para la prevención de diabetes gestacional: un meta-análisis.

Cuenca, 17-20 de noviembre de 2015

Teresa Moreno Casbas
Comité Organizador
Organising Committee
Han presentado la Comunicación Oral: SUEÑO EN ESCOLARES Y FACTORES ASOCIADOS AL RIESGO CARDIOMETABOLICO en el

II CONGRESO DE INVESTIGACIÓN EN ENFERMERÍA DE CUENCA

Organizado por la Facultad de Enfermería de la Universidad de Castilla-La Mancha y el Sindicato de Enfermería (SATSE) de Cuenca celebrado los días 26 y 27 de Noviembre de 2014, con una duración de 25 horas (1 crédito ECTS), y dirigido a profesionales titulados en ENFERMERÍA Y FISIOTERAPIA.

Para que conste a los efectos oportunos, se extiende el presente:

CERTIFICADO

En Cuenca a 27 de Noviembre de 2014

Decana de la Facultad de Enfermería

Mª Dolores Serrano Parra

Secretaria Provincial de Satse Cuenca

Mª Carmen Díaz Valentín
Diploma otorgado a

**Diana P. Pozuelo Carrascosa**

Por haber presentado un póster o comunicación en el Symposium EXERNET “Investigación en Ejercicio Físico y Salud: Presente y Futuro en España” celebrado los días 7 y 8 de noviembre de 2014 en el Instituto Mixto Universitario de Deporte y Salud, iMUDS, en Granada.

_Título del póster: “Ejercicio físico durante el embarazo: Resultados maternos y neonatales”_  
Coautores: G. Sanabria Martínez, R. Poyatos León, C. Álvarez Bueno, J. Muñoz Pinilla, L. Lucas de la Cruz

Granada a 8 de Noviembre de 2014
Diploma otorgado a

Natalia María Arias Palencia

Por haber presentado un póster o comunicación en el Symposium EXERNET “Investigación en Ejercicio Físico y Salud: Presente y Futuro en España” celebrado los días 7 y 8 de noviembre de 2014 en el Instituto Mixto Universitario de Deporte y Salud, iMUDS, en Granada.

Título del póster: “La actividad física vigorosa se relaciona con menor adiposidad y con una condición física saludable en niños de 9-10 años”
Coautores: M.S. Martínez, M.M.G. Herráiz, S.A. Arribas, A. G. García, C. A. Bueno

Granada a 8 de Noviembre de 2014

Francisco B. Ortega
Presidente del Comité Organizador

Jonatan R. Ruiz
Presidente del Comité Organizador

Manuel J. Castillo
Presidente del Comité Científico

Ángel Gutiérrez
Presidente del Comité Científico
IX JORNADAS DE PROFESORADO DE CENTROS UNIVERSITARIOS DE ENFERMERÍA

“La Investigación en Enfermería”

Don Julio Fernández Garrido, Secretario de la Conferencia Nacional de Decanos y Decanas de Enfermería, certifica que

D. Alberto González García

Ha presentado una COMUNICACIÓN TIPO POSTER en las IX Jornadas de Profesorado de Centros Universitarios de Enfermería, La investigación en Enfermería, organizadas por la Conferencia Nacional de Decanos y Decanas de Enfermería, celebradas en la EU de Enfermería y Fisioterapia de Toledo (UCLM) los días 29 y 30 de octubre de 2015.


Coautores/as: Notario Pacheco, Blanca; Solera Martínez, Montserrat; Martínez Andrés, María; Lucas de la Cruz, Lidia; Álvarez Bueno, Celia

Y para que conste a todos los efectos oportunos, se firma y sella el presente en Toledo, a 30 de octubre de 2015.

Julio Fernández Garrido
Secretario de la CNDE

Pilar Tazón Ansola
Presidenta de la CNDE
El Comité Organizador
De la II Jornada de Investigación en Atención Primaria de Castilla-La Mancha

CERTIFICA
Que la Comunicación Titulada:
"Tiempo de sueño y adiposidad en escolares de 4 a 6 años."

Autores: Lidia Lucas de la Cruz; Alberto González García; Diana Pozuelo Carrascosa; Natalia María Arias Palencia; Celia Álvarez Bueno; Marta Mª Guijarro Herráiz.

Ha sido presentada en la Jornada
Ciudad Real, a 9 de Mayo de 2014

Fdo: Francisco López de Castro
Comité Científico

Fdo: Alberto León Martín
Comité Organizador
El Comité Organizador

De la I Jornada de Investigación en Atención Primaria de Castilla-La Mancha

CERTIFICA

Que la Comunicación titulada:

"Beneficios del ejercicio físico en niños y jóvenes con Asma inducido por el ejercicio: Revisión sistemática"

Autores: García Cebrián, L; Pato Mochales, D; Cavero Redondo, I; Alvarez Bueno, C; Notario Pacheco, B; Fernández Cuesta, A.

Ciudad Real, a 21 de Junio de 2013

Fdo: Francisco López de Castro
Comité Científico

Fdo.: José María del Campo
Comité Organizador