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BY
MIKKEL PORSBORG ANDERSEN

DISSERTATION SUBMITTED 2018

AALBORG UNIVERSITY
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PhD supervisor: Prof. Christian Torp-Pedersen, MD, DMSc
Department of Health Science and Technology
Aalborg University, Denmark
Unit of Epidemiology and Biostatistics
Aalborg University Hospital Denmark

Assistant PhD supervisors: Associate Prof. Henrik Bøggild, MD, Ph.D.
Department of Health Science and Technology
Aalborg University, Denmark
Unit of Epidemiology and Biostatistics
Aalborg University Hospital Denmark

Associate Prof. Henrik Vardinghus-Nielsen, MA, Ph.D.
Department of Health Science and Technology
Aalborg University, Denmark

Associate Prof. Theis Lange, MSc, Ph.D.
Department of Public Health, Faculty of Health
and Medical Sciences,
University of Copenhagen, Copenhagen, Denmark
Center for Statistical Science, Peking University, Beijing, China

PhD committee: Professor Sine Agergaard
Aalborg University

Associate Professor Gabriele Berg-Beckhoff
University of Southern Denmark

Assistant Professor Sonja Alsemgeest Swanson
Erasmus Medical Center, Rotterdam and
Harvard School of Public Health, Boston

PhD Series: Faculty of Medicine, Aalborg University

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aauf@forlag.aau.dk
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CURRICULUM VITAE

Mikkel Porsborg Andersen, MSc.PH, BSc

Educations:

2014 – Ph.d. Student, Privatist
2011 – 2014 MSc. Public Health, University of Southern Denmark
2008 – 2011 BSc. Sport Science, Aalborg University

Employments:

2017 – 2017 Datamanager, Unit of Epidemiology and Biostatistics, Aalborg University Hospital
2015 – 2017 Research Assistant, Faculty of Medicine, Department of Science and Technology, Public Health and Epidemiology Group, Aalborg University
2014 – 2015 Academic employee, Faculty of Medicine, Department of Science and Technology Public Health and Epidemiology Group, Aalborg University
2010 Test Manager DGI Nord - Project 3A

Courses:

2017 Causal Inference, Erasmus MC University Medical Center
2016 Causal Inference and Mediation Analysis, Erasmus MC University Medical Center
2016 Mixed Models with Biomedical and Engineering Applications, Aalborg University
2016 Biostatistics for Clinicians and Diagnostic Research, Erasmus MC University Medical Center
2016 Health Scientific Searching and Publishing, Aalborg University
2016 Project Management and Interpersonal Skills, Aalborg University
2016 Writing and Reviewing Scientific Papers, Aalborg University
2015 Multivariate Data Analysis, Aalborg University
2015 Logistic regression and Survival analysis, Erasmus MC University Medical Center
2015 Data analysis and experimental design with R, University of Barcelona
2014 European Educational Programme in Epidemiology, Florence Italy
2014 Epidemiology and Register based Research, Aalborg University
2014 Basic course for university teachers, Aalborg University
2014 How to use and interpret large datasets from emerging –omics based technologies, The Doctoral School in medicine, Biomedical Science and Technology, Aalborg University Hospital

Teaching experience

2017 Guest Lecturer, Epidemiology and Register based Research, Aalborg University

2016 Guest Lecturer, Epidemiology and Register based Research, Aalborg University

Supervisor

2017 Bachelor and Master of Science students in Sports Science, Aalborg University

2016 Bachelor students in Sports Science, Aalborg University

Grants

2015 Received 400.000 kr. approximately 53.760 € from the Danish Health Foundation towards conducting my Ph.D.-project (Grant number 15-B-0115)

Press

The results from the publication "Association between Physical Fitness and Academic Achievement in a Cohort of Danish School Pupils" was brought in more than 60 national newspapers and I was interviewed live on Danish radio and television.

Peer Reviewed Publications

Kragholm K, **Andersen MP**, Mortensen RN, Bech LF, Polcwiartek C, Rohde C, Torp-Pedersen C, Videbech P, Nielsen J. Exposure to Selective Serotonin Reuptake Inhibitors In Utero and Early Elementary School Outcomes. Acta Psychatr Scand. 2018 Feb 2018 DOI: 10.1111/acps.12867 (Accepted).

Sessa M, Mascolo A, Mortensen RN, **Andersen MP**, Rosano GMC, Capuano A, Rossi F, Gislason G, Enghusen-Poulsen, Torp-Pedersen C. Relationship between heart failure, Concurrent chronic obstructive pulmonary disease and beta-blocker use: A Danish cohort study. Eur J Heart Fail. 2017 Nov 20. DOI: 10.1002/ejhf.1045 (Epub ahead of print).

Andersen MP, Starkopf L, Sessa M, Mortensen RN, Vardinghus-Nielsen H, Bøggild H, Lange T, Torp-Pedersen C. The indirect and direct pathways between physical fitness and academic achievement on commencement in post-compulsory education in a historical cohort of Danish school youth. BMC Public Health. 2017 Sep 11;17(1):699.

Andersen MP, Mortensen RN, Vardinghus-Nielsen H, Franch J, Torp-Pedersen C, Bøggild H. Association Between Physical Fitness and Academic Achievement in a Cohort of Danish School Pupils. J Sch Health. 2016 Sep;86(9):686–95

Sessa M, Mascolo A, **Andersen MP**, Rosano G, Rossi F, Capuano A, Torp-Pedersen C. Effect of Chronic Kidney Diseases on Mortality among Digoxin Users Treated for Non-Valvular Atrial Fibrillation: A Nationwide Register-Based Retrospective Cohort Study. PLoS ONE. 2016;11(7):e0160337.

Letter to the Editor

Kragholm K, **Andersen MP**, Torp-Pedersen C. Multiple factors related to better outcome in out-of-hospital cardiac arrest—is mediation analysis the solution?. Journal of Emergency and Critical Care Medicine. 2017 Aug;1(17)

ENGLISH SUMMARY

In many countries policy makers have aspired on reforms that can promote the population's education levels as education is essential for economic growth and human development. Researchers have through the past decade established associations between pupils' physical fitness and academic achievements. However, potential mechanisms through which pupils' physical fitness relate to their scholastic abilities has not been fully understood.

By linking objectively measured physical fitness defined as VO2max (mL·kg-1·min-1) from a baseline sample of 1164 pupils to their scholastics abilities obtained from the Danish nationwide administrative registries, the objective of this Ph.D. dissertation was to achieve a deeper insight into mechanisms and relations through which pupils' physical fitness may influence scholastic abilities. This was initiated through three studies that identify pathways that form the interrelation between pupils' physical fitness, scholastic abilities, and their family background.

Study 1: investigated an association between pupils' physical fitness and academic achievements as well as evaluated the influence of family socioeconomic status.

Study 2: investigated pathways from pupils' physical fitness to their commencement of post-compulsory education while pupils' academic achievements were treated as a mediator.

Study 3: investigated pathways from family socioeconomic status on pupils' academic achievements while pupils' physical fitness was treated as a mediator.

Pupils' physical fitness was found to be positively associated with their academic achievements for both sexes. The association was for the humanistic subjects for girls 0.08 grade/VO2max (95% Cl: 0.05; 0.11) and 0.06 grade/VO2max (95% Cl: 0.03; 0.08) for boys. For the science subjects the association was for girls 0.09 grade/VO2max (95% Cl: 0.05; 0.13) and for boys 0.06 grade/VO2max (95% Cl: 0.03; 0.09). The association for all mandatory subjects was for girls 0.09 grade/VO2max (95% Cl: 0.06; 0.11) and for boys 0.06 grade/VO2max (95% Cl: 0.03; 0.08). Even though family socioeconomic status influenced the association no effect differences among socioeconomic status groups were established indicating that the association was independent of socioeconomic status.

Pupils' physical fitness was found to be positively related to their commencement in post-compulsory education with a total effect OR of 1.87 (95% CI: 1.30; 2.73). Splitting the total effect, the direct pathway showed a OR of 1.36 (95% CI: 0.93; 1.98) and a OR of 1.37 (95% CI: 1.20; 1.57) for the indirect pathway operating

through pupils' academic achievements with proportions mediated of 51% (95% CI: 27%; 122%).

Pupils' physical fitness was found to mediate the relation between family socioeconomic status groups and pupils' academic achievements. When family socioeconomic status was based on family education the estimates showed decrease or increase in grade point average of the total effects that the natural indirect effects are accountable for. The indirect effect estimates of changes in grades was -0.13 (95% CI: -0.26; -0.01), 0.07 (95% CI: 0.00; 0.14) and 0.24 (95% CI: 0.14; 0.34) for pupils from family socioeconomic status group one, three and four, respectively, compared to pupils from family socioeconomic status group two for all comparisons. The proportion mediated through pupils' physical fitness correspond to 18% (95% CI: 1%; 57%), 6% (95% CI: 0%; 13%) and 12% (95% CI: 7%; 18%) for the same comparisons of family socioeconomic status groups. When family socioeconomic status was based on family income the estimates show the decrease or increase in grade point average of the total effects that can be assigned to the natural indirect effects. The indirect effect estimates of changes in grades -0.07 (95% CI: -0.16; 0.02), 0.22 (95% CI: 0.13; 0.32) and 0.26 (95% CI: 0.15; 0.37) for pupils from family socioeconomic status group one, three and four, respectively, compared to pupils from family socioeconomic status group two for all comparisons. The mediated proportions through pupils' physical fitness correspond to 12% (95% CI: -6%; 41%), 30% (95% CI: 16%; 54%) and 20% (95% CI: 12%; 32%) for the same comparisons of family socioeconomic status groups.

Throughout, this dissertation pupils' physical fitness was consistently established as a relevant factor in relation to the pupils' scholastic abilities by providing evidence of different pathways through which pupils' physical fitness was positively related to scholastic abilities. All three studies positively linked pupils physical fitness to their academic achievements and further showed that the physical fitness positively influenced commencement in post-compulsory education with the establishing of pupils academic achievements as a mediating mechanism on the relation. Not unexpected, the family socioeconomic status of the pupils was shown to influence the connection between physical fitness and academic achievements. However, pupils' physical fitness was shown to both influences their academic achievements independently of the family socioeconomic status as well as the physical fitness acted as a mediating mechanism on the pathway between family socioeconomic status and academic achievements.

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DANISH SUMMARY/DANSK RESUME

Uddannelse er afgørende for en nations økonomiske vækst og borgeres menneskelige udvikling. I mange lande har politikere derfor igennem historien fokuseret på initiativer til forbedring af befolkningens uddannelse og uddannelsesniveau.

Forskning har gennem det sidste årti etableret forståelse af sammenhænge mellem elevers kondition og boglige præstationer – imidlertid er de potentielle mekanismer, hvorigennem elevers kondition påvirker deres boglige evner endnu ikke fuldt ud forstået.

Ved at samkøre objektivt målte konditionsniveauer defineret som VO2max ($mL \cdot kg^{-1} \cdot min^{-1}$) fra en kohorte af 1164 elever med deres skolemæssige færdigheder samt baggrundsoplysninger indhentet gennem danske administrative registre, var formålet med denne ph.d.-afhandling at opnå en dybere indsigt i de mekanismer og relationer, hvorved elevernes fysiske kondition kan influere deres boglige evner. Dette blev undersøgt ved at identificere sammenhænge der danner forholdene mellem elevernes kondition, boglige evner og deres familiemæssige baggrund.

Studie 1: undersøgte sammenhængen mellem elevernes kondition og deres akademiske præstationer samt indflydelsen af familiens socioøkonomiske status.

Studie 2: undersøgte, hvorledes elevers kondition kan påvirke påbegyndelsen af en ungdomsuddannelse, mens elevernes karakterer fra folkeskolen behandles som et medierende led.

Studie 3: undersøgte, hvorledes familiens socioøkonomiske status kan påvirke elevernes karakterer fra folkeskolen, når elevernes kondition bliver behandlet som et medierende led.

For begge køn viste det sig, at elevernes kondition havde en positiv effekt på deres karakterer. Effekterne var for de humanistiske fag 0,08 karakter/VO2max (95% CI: 0,05; 0,11) for piger og 0,06 karakter/VO2max (95% CI: 0,03; 0,08) for drengene. For de naturvidenskabelige fag var effekten 0,09 karakter/VO2max (95% CI: 0,05; 0,13) for piger og for drenge 0,06 karakter/VO2max (95% CI: 0,03; 0,09). Effekten for alle obligatoriske fag var for piger 0,09 karakter/VO2max (95% CI: 0,06; 0,11) og for drengene 0,06 karakter/VO2max (95% CI: 0,03; 0,08). Selvom familiens socioøkonomisk status påvirkede associationen, blev der ikke fundet effektforskelle mellem de socioøkonomiske grupper, hvilket indikerer at associationen er uafhængig af socioøkonomisk status.

Elevernes kondition viste sig også at være positivt relateret til påbegyndelsen af en ungdomsuddannelse. Den samlede effekt OR var på 1,87 (95% CI: 1,30; 2,73) efter justering for køn, alder, etnicitet og familiens socioøkonomisk status. Når den samlede effekt splittes i en direkte og indirekte vej blev der fundet en OR 1,36 (95% CI: 0,93; 1,98) for den direkte vej og en OR 1,37 (95% CI: 1,20; 1,57) for den indirekte vej, der virker gennem elevernes akademiske resultater med proportioner medieret 51 % (95% CI: 27%; 122%).

Elevernes fysiske kondition viste sig også som det medierende led i sammenhængen mellem familiernes socioøkonomiske status grupper og elevernes akademiske resultater. Blev familiens socioøkonomiske status baseret på familiens uddannelse, viste de indirekte effektestimater en karakterændring på -0,13 (95% CI: -0,26; -0,01), 0,07 (95% CI: 0,00; 0,14) og 0,24 (95% CI: 0,14; 0,34) for elever fra henholdsvis familier i socioøkonomisk gruppe 1, 3 og 4, når der sammenlignes med gruppe 2. Andelen medieret igennem elevernes kondition var på 18% (95% CI: 1%; 57%), 6% (95% CI: 0%; 13%) og 12% (95% CI: 7%; 18%) i henhold til førnævnte sammenligninger. Blev familiens socioøkonomiske status baseret på familiens indkomst, viste de indirekte effektestimater en karakterændring på -0,07 (95% CI: -0,16; 0,02), 0,22 (95% CI: 0,13; 0,32) og 0,26 (95% CI: 0,15; 0,37) for elever fra henholdsvis familier i socioøkonomisk gruppe 1, 3 og 4, når der sammenlignes med gruppe 2. Andelen medieret gennem elevernes kondition var på 12% (95% CI: -6%; 41%), 30% (95% CI: 16%; 54%) og 20% (95% CI: 12%; 32%) i henhold til førnævnte sammenligninger.

I denne afhandling blev elevernes fysiske kondition konsekvent etableret som en relevant faktor i forhold til elevernes boglige evner ved at præsentere beviser for forskellige retninger, hvorpå elevernes kondition havde indflydelse på deres boglige evner. Gennem hele afhandlingen blev elevernes kondition positivt relateret til deres afgangskarakterer i folkeskolen og viste endvidere at elevernes kondition positivt påvirker påbegyndelsen af en ungdomsuddannelse hvor elevernes afgangskarakterer blev etableret som en medierende mekanisme i sammenhængen. Yderligere blev elevernes socioøkonomiske status etableret som en faktor der påvirker relationen mellem elevernes kondition og deres boglige evner. Imidlertid viste elevernes kondition både at påvirke deres boglige evner uafhængigt af familiens socioøkonomiske status såvel som elevernes kondition fungerede som en medierende mekanisme mellem familiens socioøkonomiske status og akademiske præstationer.

THIS PHD DISSERTATION IS BASED ON THE FOLLOWING THREE ARTICLES

The Dissertation is based on the following three articles. In the text, these will be referenced as Study 1, Study 2, and Study 3. The full-length articles are available in Appendix.

Study 1.

Andersen MP, Mortensen RN, Vardinghus-Nielsen H, Franch J, Torp-Pedersen C, Bøggild H. Association Between Physical Fitness and Academic Achievement in a Cohort of Danish School Pupils. J Sch Health. 2016 Sep;86(9):686–95. (Published)

Study 2.

Andersen MP, Starkopf L, Sessa M, Mortensen RN, Vardinghus-Nielsen H, Bøggild H, Lange T, Torp-Pedersen C. The indirect and direct pathways between physical fitness and academic achievement on commencement in post-compulsory education in a historical cohort of Danish school youth. BMC Public Health. 2017 Sep 11;17(1):699. (Published)

Study 3.

Andersen MP, Valeri L, Starkopf L, Mortensen RN, Sessa M, Kragholm K, Vardinghus-Nielsen H, Bøggild H, Lange T, Torp-Pedersen C. The mediated effect of pupils' physical fitness on the relation between family socioeconomic status and academic achievements in a Danish school cohort. (To be submitted)

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This Ph.D.-dissertation is based on three epidemiological studies which I conducted during my employment at the Department of Health Science and Technology, Aalborg University and at the Unit of Epidemiology and Biostatistics, Aalborg University Hospital. I have through my employments and Ph.D.-time in a whole, met and collaborated with a lot of intelligent and clever people from different research areas and work backgrounds, as well as I, have had the unique opportunity to be involved in all aspects of conducting register-based research. This has without a doubt positively impacted my personal development and learning process and thereby also influenced the genesis of this Ph.D.-dissertation, for this, I will always be you all thankful.

"Tell me and I forget, teach me and I may remember, involve me and I learn."
Benjamin Franklin.

I will indeed like to thank my main supervisor Christian Torp-Pedersen without you this Ph.D. would never have been a possibility, your way of seeing opportunities instead of limitations are priceless. Also thank you so much for involving me in all processes regarding register-based research I have learned more than I could ever have imagined before starting the Ph.D.-time it has indeed been a privilege having you as my supervisor and mentor. I look forward to collaborating with you on projects in the future, your mentorship and guidance is outstanding and extremely appreciated.

I would also like to express my gratitude to others supervisors. Henrik Bøggild thank you very much for all the many talks and discussions throughout the Ph.D.-time these have definitely made me reflect on a whole new level and increased the quality of the work. Henrik Vardinghus-Nielsen, with whom, I have been so fortunate to have as a mentor ever since I met him during my bachelor of sports science. I truly appreciate all the help and guidance you have given me over the years and thank you very much for all the support and for introducing me to Christian. Theis Lange, I am very grateful for the excellent guidance you have given me through the progress of my Ph.D., especially in relation to the aspects involving causal inference and mediation analysis without your guidance, I would not have had the same involvement and understanding of the aspects.

I would like to send a very special thanks to both Liis Starkopf and Linda Valeri, with whom, I have had the privilege to collaborate and discuss the different aspects of mediation analysis on multiple occasions. I highly appreciate all our conversations which have definitely helped me gain a deeper understanding of the aspects of mediation analysis.

Also, I would like to send a special thanks to Rikke Nørmark Mortensen I highly appreciate all the help you have given me throughout the Ph.D.-time, even though you have been extremely busy with your own work, you have always found time to both discuss research topics and help me with SAS and R programming problems. I am really grateful that you were part of the research environment it has been an absolute privilege collaborating which I hope we will continue in the future. Also a special thanks need to be sent to Maurizio Sessa I have been so fortunate to share offices with you for most of my Ph.d.-time which have been both fun and productive I can indeed say my Ph.D.-time would not have been the same without you, it has been an honor to collaborate with you and I am looking forward to continuing this in the future. I would also like to send a special thanks to Jesper Franch for the many conversations and for the help in relation to my employment at the Department of Health Science and Technology, Aalborg University. A special thanks also need to be sent to Kristian Kragholm it has been a pleasure to start collaborating with you as you have a lot of great perspective on different research topics which have engaged us in many interesting and enlightening talks both at the office and when we have been biking.

I would like to express my gratitude to the Health Foundation for their financial support without this support it is doubtful that the Ph.D. would have been conducted in the same time frame. I would also like to thank and acknowledge the Department of Education and the Department of Health and Culture at the Danish Municipality of Aalborg for providing access to the pupils' health examinations especially to their following employee Morten Ubbesen, Jannie Claudius Jakobsen, Carina Schmidt Levisen, which have all been extremely helpful in relation to my achieving the data.

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of giving me a lot of "let's say" good advice. Anyway thanks for all the support and understanding for me having to work and thereby neglecting a lot of social activities. I would especially like to thank my mom and dad for all the help and support they have given me over the years without you two, this Ph.D. would never have been a possibility. I also want to send a big thank to my girlfriend Lena for her understanding during my Ph.D.-time we have not spent that much time together even so you having always been supporting me which I will always be you grateful for. Last but not least, I would like to thank everyone, who made this time in my life as memorable as what has been the case. I will always look back at this great learning experience as a special time in my life which I am thankful, that you were a part of.

Mikkel Porsborg Andersen
February 2018

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proportion mediated in analyses of the overall study participants involving 1079 pupils.

ABBREVIATIONS

DGI	The Danish Gymnastic and Sports Association
VO_2max	Relative maximal oxygen consumption ($mL \cdot kg^{-1} \cdot min^{-1}$)
ISCED	The International Standard Classification of Education
OECD	The Organization for Economic Co-operation and Development
Approx.	Approximately
€	Euro
i.e.	That is
ANOVA	Analysis of Variance
Q-Q plots	Quantile-Quantile Plot
OR	Odds Ratio
CI	Confidence Intervals
GPA	Grade Point Average
Etc.	Et cetera

CHAPTER 1. INTRODUCTION

Education is essential for economic growth and human development [1-3] as well as it is connected to improve work skills, health status and both lower crime rates [4] and lower mortality [5, 6]. Throughout the last decade, policymakers have in different countries aspired initiatives and been constructing reforms that can increase the level of knowledge and facilitate education attendance in the attempt to meet the contemporary societal work requirements [1, 7, 8]. In England, the length of pupils' mandatory education has been extended [5] other countries have decrease the amount of time used for daily physical activities in the schools in order to use more time for core academics [9-12]. In contrast, the Danish policymakers implemented in 2014 a new School legislation with longer school days where physical activity is prioritized in an attempt to increase pupils health status, and preserve motivation towards core academic disciplines [8]. Even though policymakers' have a willingness to try new strategies to promote scholastic abilities, the scientific society has still not fully understood whether pupil physical activity may influence scholastic abilities even though research on the topic has been conducted for more than half a century the results are still inconclusive [13, 14].

It is however, a well-known fact that increased physical activity or exercise can increase the physical fitness status as an individual's physical fitness level is determined by the duration, intensity and frequency of all daily exercises and activities performed [15-17]. Physical fitness is defined as health-related elements involving a person's body composition, muscular- endurance, strength, flexibility and cardiorespiratory endurance [17-19]. These elements can be improved or maintained through bodily movement that produces energy expenditure by the skeletal muscles defined as physical activity, or even better through exercise activities that are planned, structured and repeated, leaving physical fitness level as the product achieved [15, 17]. Physical fitness is, in general, a solid indicator of a person's physical health status, and the possession of a good fitness yields multiple health benefits. [15, 16, 20-25]. Research has likewise through the last part of the decade established associations between physical fitness and academic achievements [10, 14, 18, 20, 26-36].

The reasoning for this association is that increments in physical fitness have been shown to positively influence several neurological properties [37-44] that in turn may lead to better executive function, memory and learning abilities [37, 38, 40, 41, 44-50]. These neurological properties and executive functions are intrinsically related to both academic achievements and scholastic abilities [30, 51-54]. Identifying potential mechanisms through which pupils' physical fitness may affect their scholastic abilities is of great importance as this may lead to improved societal education and health. The previous studies which have investigated relations between physical fitness and academic achievements have used singular measures of

academic achievements reflecting the relation between physical fitness and academic achievements within specific subjects [10, 14, 18, 20, 26-36]. This approach cannot evaluate if pupils' physical fitness could influence their overall scholastic abilities as it only includes few specific academic subjects. However, assessing multiple academic achievements to represent pupils' scholastic abilities is missing in the literature. Pupils' academic achievements represent the best indicator of their scholastic abilities which may affect their selection or deselection of a post-compulsory education. Nevertheless, as pupils' physical fitness could affect academic achievements it might also be related to attendance in post-compulsory education this aspect has meanwhile received little to no attention in the literature.

Despite the relation between physical fitness and academic achievements, family socioeconomic status has shown to influence both pupils' physical fitness and scholastic abilities [55-60] thereby identifying family socioeconomic status as an important factor that can affect the relation between physical fitness and academic achievements as well as pupils' commencement in post-compulsory education. However, previous studies that examine the association between physical fitness and academic achievements used vague and limited proxy measures to define the family socioeconomic status as this was based on self-reported education levels of one of the parents or the pupils' eligibility to achieve a free or prize reduced lunch program in the school [10, 18, 20, 26, 27, 29, 30, 32]. The use of this limited information's to define the family socioeconomic status could potentially lead to disputable conclusions drawn in the previous studies as it might be possible that the studies are not assessing family socioeconomic status but other factors that relate to the proxy measures. Studies that use more precise measures to define the family socioeconomic status of the pupils' are therefore needed to gain a further understanding of the impact of family socioeconomic status in the relation to pupils' physical fitness and their scholastic abilities.

Both the family setting and the school environment where pupils spend most of their daily hours are crucial arenas that can introduce pupils to healthy and good habits. Mapping potential factors or pathways that can lead to improved health and scholastic abilities would provide school administrators and policymakers with new evidence into potential mechanisms that may lead to improved health and scholastic abilities in elementary school pupils.

1.1. AIMS OF THE DISSERTATION

The overall objective of this PhD dissertation is to achieve a deeper insight into the mechanisms through which pupils' physical fitness may influence their academic achievements and commencement in post-compulsory education, by examining different pathways that form the interrelation between pupils' physical fitness, academic achievements, commencement in post-compulsory education and their family background. This will be investigated through three studies all based on data from Danish nationwide registries and from elementary school pupils health examinations conducted in the Danish municipality of Aalborg. These data contain more detailed information's regarding pupils' scholastic abilities and family background as what has previously been used. This gives the possibility of providing a more detailed insight into the mechanisms and relations between pupils' physical fitness and scholastic abilities as well as displaying new aspects of pupils' physical fitness in relation to their academic achievements, commencement in post-compulsory education and family background.

1. The aims of the first study (study 1) were to examine the association between pupils' physical fitness and academic achievements as well as evaluate the influence of family socioeconomic status on this association.

2. The aims of the second study (study 2) were to investigate the direct and indirect pathways between physical fitness and academic achievements on pupils' commencement in post-compulsory education treating the pupils' academic achievements as an intermediate mechanism.

3. The aims of the third study (study 3) were to investigate the direct and indirect pathways between family socioeconomic status and academic achievements treating the pupils' physical fitness as a mediator in this relation.

CHAPTER 2. METHOD

2.1. ETHICS

Approval to conduct the studies which this dissertation is based on was granted by the Danish Data Protection Agency (Journal number: 2014-41-2842). All data for the studies were pseudomized and made available within Statistics Denmark research environment where the data was likewise stored. Register-based studies that are pseudomized and conducted for the sole purpose of statistics and scientific research do not require ethical approval or informed consent in Denmark [61].

2.2. SETTING

The Danish municipality of Aalborg, the Danish Gymnastic and Sports Association (DGI), North Jutland and Aalborg University invited in 2008 all the municipality's 37 public elementary schools with the 9th grade level to partake in health examinations of the schools 6th-grade pupils [62]. A total of 1544 out of 1638 possible 6th-grade pupils participated in the examinations. The participating pupils were in 2010 re-invited to repeat the health examinations in the 8th grade. In all, 1164 pupils in the 8th grade repeated the health examination. All participating pupils performed a watt-max cycle ergometer test on a Monark 874E to obtain their physical fitness. Based on the individual pupil's body size, trained instructors evaluated the starting workload at either 50 or 75 watts and increased the workload by 25 watts every three minutes until the pupils' exhaustion level was reached. The pupil had to cycle at a constant pedal rate of 50 revolutions per minute and when the pupil was unable to carry on the pedal rate, this indicated that their fatigue threshold had been reached. The information obtained through the cycle ergometer test were used to calculate the maximum power output, by using the following formula for watt-max= $W1+(W2 \cdot T1/180)$. W1 denote the watt workload in the last three minutes accomplished section by the pupil, W2 denote the increment in watts from the last fully completed section to the last attempted section, T1 denote the seconds at the last three minutes attempted section and the 180 is the total number of seconds in a three minutes section. The results obtained through the watt-max tests were used in the calculation of the individual physical fitness level of the pupils measured as relative maximal oxygen consumption ($mL \cdot kg^{-1} \cdot min^{-1}$; VO_2max). This measurement of cardiorespiratory endurance yields a continuous value, and it is acknowledged as a strong indicator of the direct measured VO_2max [63, 64].

The 1164 pupils who participated in the health examination in 2010 will be the baseline population for this dissertation, but with minor exclusions due to missing information's on covariates in the studies which will be presented for each individual study in the section entitled "Study design".

2.3. DATA SOURCES

All the different data sources were connected through the personal 10 digits civil registration number that is given to all citizens in Denmark upon immigration or at birth [65]. The following Danish nationwide administrative registries were used to obtain background information on the 1164 pupils who participated in the health examination in 2010 and their parents or guardians. The parents or guardians of the individual pupils were identified through the Danish Civil Registration System [66]. This register was also used to assess information on the pupils' age, sex, and ethnicity as well as parents' cohabitations status. Information on pupils contacts with hospitals was retrieved from the Danish National Patient Register [67]. Pupil's tests scores, grade level at compulsory education graduation and deselection or commencement in post-compulsory education was retrieved from the Student Register and Academic Achievement Register [68]. Education and income status of pupil's parents was obtained through the Population Educational Register and the Income Register, respectively [68, 69]. The classification and categorization of the different information obtained will be presented in the following sections.

2.4. AGE GROUPS

Pupils were divided into the following three age groups, 13, 14 and 15 based on the pupils' age in 2010 the same month as the pupils participated in the health examination. This variable was used in a sensitivity analysis in study 1 and as a covariate in study 2 and 3.

2.5. ETHNICITY

Throughout this dissertation pupils' ethnicity was classified into two groups either being ethnic Danes or immigrant and descendant. The classification is based on Statistic Denmark's definitions which classify an ethnic Dane as a person originating from Denmark that has a parent born in Denmark and holds a Danish citizenship [70]. Immigrants are classified as a person not born in Denmark nor have parents born in Denmark and none of the parents had a Danish citizenship [70]. A descendant classifies as a person originating from Denmark with no parents born in Denmark or holding a Danish citizenship [70].

2.6. COHABITATION STATUS

Cohabitation status was assessed through the Danish Civil Registration System [66] by evaluating if the individual pupils' biological parents were registered as living together in 2010. This information was used to classify the pupils' into two categories, either pupil's biological parents living together or not living together this covariate were only included in study 3.

2.7. OVERALL HEALTH

Pupils' overall health was obtained from the Danish National Patient Register [67] and assessed through the occurrence of all types of hospital contacts for the individual pupil, 365 days prior to their health examination in 2010. Based on these information's pupils' were divided into two categories either no hospital contact or hospital contact this covariate was evaluated in study 2 and revealed no logical reason for inclusions in the studies.

2.8. ACADEMIC ACHIEVEMENTS

In Denmark, all public elementary schools arrange mandatory exams for all enrolled pupils at the end of the 9th grade. The mandatory exams mark the end of compulsory education in 9th grade and are designed by the Danish Ministry of Education [71]. The individual exam assessments are based on the Danish 7-point grading scale that awards the following numeric grades 12, 10, 7, 4, 02, 00 and -3 which are equivalent to the letters A, B, C, D, E, Fx and F in the European Credit Transfer and Accumulation System (ECTS) grading scale, respectively [72]. In this dissertation, each of the individual exam scores achieved by the pupils was averaged in order to represent academic achievements. However, the pupils' academic achievements were operationalized somewhat different between the individual studies due to the study designs.

In study 1 the exams were divided into three individual variables in order to represent the pupils' academic achievements. Variable one represents the humanistic subjects including reading, spelling, writing, structured, and oral Danish as well as oral English. Variable two represents the science subjects including science, oral and written mathematics. Variable three represent the mandatory exams included all previously mentioned and a project exam. Each pupil must have accomplished all exams within the individual variable before they can be included in the analyses. Therefore, minor differences of participating pupils occurred between variables.

In study 2 and 3 only variable three was used to represent the pupils' academic achievements. However, with the exclusion of the project exam due to the fact that pupils have the legal right to decide if the exam assessment from the project exam should be registered in the Academic Achievement Register [71] which could minimize the objectivity of this exam. In study 2 only, an additional replacement of pupils' exam scores could occur due to the fact that Danish pupils have the option of extending their compulsory education with an additional year in the 10th grade to improve academic achievements and equip them towards a post-compulsory education [71]. Pupils who choose the additional year can repeat the mandatory exams from the 9th grade level or with increased severity and perform the exams at the 10th-grade level. Nevertheless, in both circumstances, it is ways in which pupils may improve their exams results from the 9th grade. In the cases where the exams

are equivalent to the ones performed in the 9th grade and the individual pupil achieved a better exam result this was used instead. The numeric exams scores from the nine mandatory exams achieved in either the 9th or 10th grade were averaged as a grade point average which represents pupil's academic achievements.

2.9. POST-COMPULSORY EDUCATION

The pupils' attendances in post-compulsory education were derived from the Student Register [68, 73]. This was evaluated by following the pupils' after their accomplishment at either the 9th grade or 10th grade of compulsory education until September 30, 2014. Based on these information pupils' were divided into two categories as either having commenced or deselected a post-compulsory education. Post-compulsory education or youth education are in Denmark classified as all upper secondary and vocational education and training programs [74]. These education levels classifies as level 3 in the International Standard Classification of Education (ISCED) [75] which is the next education level after finishing compulsory education in 9th or 10th grade. This variable represented the outcome of study 2 which is the only study including this variable.

2.10. SOCIOECONOMIC STATUS

Throughout this dissertation the family socioeconomic status of the pupils was represented through two individual proxy-measurements based on highest achieved education level or equivalized income of the parents.

Parents' highest achieved education levels were obtained in 2010 for both parents of the individual pupil and if these differed the highest was selected to represent family education. The family education levels were categorized into four groups based on the categories from the ISCED classification [75]. The first group includes ISCED levels 0-2 and refers to early childhood, primary and lower secondary educations and containing a time span between 8-11 years. The second group includes ISCED level 3 and refers to general upper secondary education and vocational upper secondary education containing an additional time span of 2-5 years. The third group includes ISCED levels 5-6 and refers to short-cycle tertiary, medium-length tertiary and bachelors-level educations or equivalent containing an additional time span between 2-4 years. The fourth group includes ISCED levels 7-8 referring to second-cycle, masters-level or the equivalent and PhD-level containing an additional time span between 1-7 years. No education level in Denmark is classified as ISCED level 4, therefore, is this classification not used [75]. The four groups of parents' highest achieved education represent four levels of socioeconomic status based on education. In study 1 and 2, the first level of socioeconomic status was selected as the reference group whereas in study 3 the second level of socioeconomic status was selected as the reference group in the statistical analyses as this education level is the most commonly achieved in Denmark [76].

The equivalized income is a measurement provided by statistic Denmark to ensure comparability of families of different sizes [77] as well as it is possible to account for age composition within the family [78, 79]. The equivalized income measurement is based on a modified scale from the Organization for Economic Co-operation and Development (OECD) which is an approach that redistributes the income equally between all family members giving each an identically equivalized income [78, 79]. Differences in equivalized income between pupil's parents meant that they did not share household and in such situations, the highest household income was selected to represent the family income of the pupil.

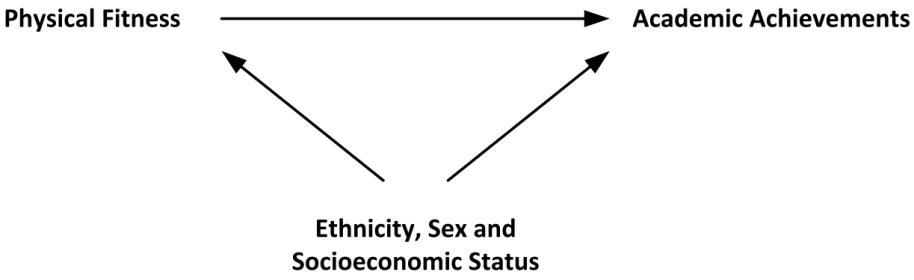
In study 1 and 2 income levels of the individual pupils' were obtained in 2010 and divided into quartiles to represent four levels of family socioeconomic status based on income assigning the lowest quartile of family socioeconomic status as the reference group. In contrast, equivalized income was in study 3 assessed over a three year period from 2008 to 2010 as an average equivalized income to achieve a more robust estimate of income to represent family socioeconomic status. The family average equivalized income was categorized into four groups based on the Danish population equivalized income distribution accounting for the parents' age composition [79]. The first group includes an equivalized income below 165,925 Danish kroner (Approx. € 22,292). Second group includes equivalized income between 165,926 to 225,250 Danish kroner (Approx. € 22,292-30,263). Third group includes equivalized income between 225,251 to 284,350 Danish kroner (Approx. € 30,264-38,203). The fourth group includes equivalized income above 284,350 Danish kroner (Approx. € 38,203). The second equivalized income group was used as the reference group in the statistical analyses for consistency to the reference group for family education in study 3.

2.11. STUDY DESIGN

To disentangle the interrelation between pupils' physical fitness, academic achievements, commencement in post-compulsory education and their family background three individual study designs based on the aforementioned data were constructed to obtain an insight into the relations and mechanisms through which pupils' physical fitness may influence scholastic abilities. These designs will be presented in causal diagrams describing the individual studies hypothesis and displaying each included covariate in the studies followed by a description of the excluded pupils in each of the studies.

2.11.1. STUDY 1

Figure 1 – Study 1 hypothesis expressed in a causal diagram

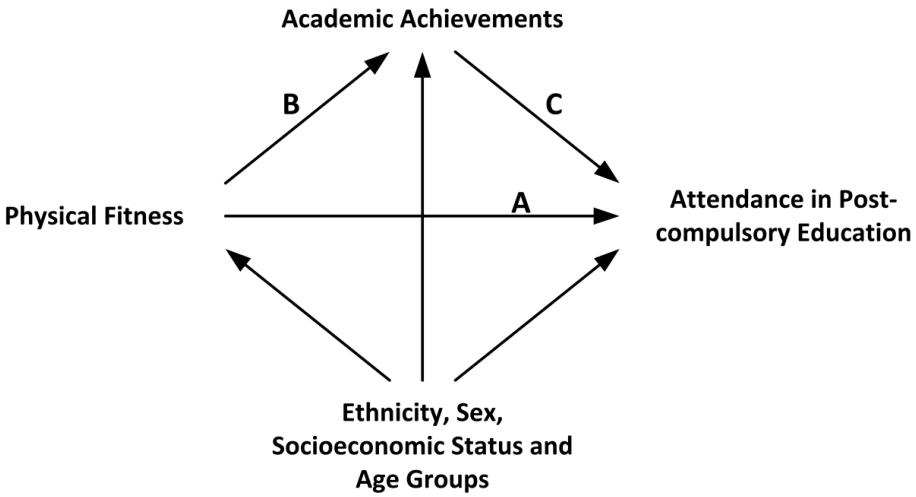


The path between physical fitness and academic achievements is the association of interest where physical fitness is the exposure and academic achievements is the outcome. Ethnicity, sex, and socioeconomic status are a set of confounding variables that will be controlled for in the statistical models (Figure 1).

In this study 45 of the 1164 pupils were excluded due to the following exclusions criteria: 2 pupils had their registration numbers incorrectly registered in the health examination data; 9 pupils were it was impossible to obtain data on both parents from Danish nationwide administrative registries; 4 pupils where there was no information available on either of the pupil's parents in the education or income registries; 30 pupils for whom it was not possible to assess information on test scores from the Academic Achievement Register. A total of 1119 pupils were eligible for inclusion in this study of which 542 were girls and 577 were boys.

2.11.2. STUDY 2

Figure 2 – Study 2 mediation hypothesis expressed in a causal diagram

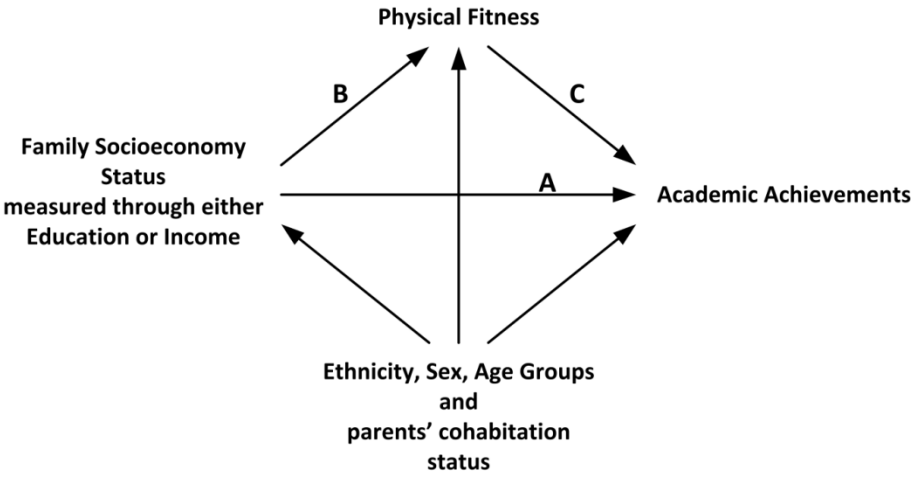


The pathways of interest are between pupils' physical fitness and their attendance in post-compulsory education while their academic achievements from compulsory education are treated as a mediator. The arrow A represents the natural direct pathway and the arrows from B to C represent the natural indirect pathway (Figure 2). Physical fitness is defined as the exposure and the outcome is defined as attendance in post-compulsory education while pupils' academic achievements are specified as the mediator. Ethnicity, sex, socioeconomic status and age groups are a set of confounding variables that will be controlled for in the statistical models to eliminate any backdoor paths by these variables due to exposure and outcome confounding, exposure and mediator confounding or mediator and outcome confounding.

In this study, 80 of the 1164 pupils were excluded due to the following exclusions criteria: 3 pupils whose civil registration number was incorrectly registered; 10 pupils where it was impossible to link to either of the parents; 4 pupils were no information was available on either of the pupil's parents in the education or income registries; 23 pupils for whom it was impossible to link to the Academic Achievement Register; 40 pupils for whom there were missing data in the mandatory exams. A total of 1084 pupils were eligible for inclusion in this study of which 530 were girls and 554 were boys with no missing data.

2.11.3. STUDY 3

Figure 3 – Study 3 mediation hypothesis expressed in a causal diagram



The pathways of interest are between family socioeconomic status and pupils' academic achievements while pupils' physical fitness is treated as a mediator. The arrow A represents the natural direct pathway and the arrows from B to C represent the natural indirect pathway (Figure 3). Family socioeconomic status is defined as the exposure and pupils' academic achievements as the outcome while pupils' physical fitness is specified as the mediator. Ethnicity, sex, age groups and parents' cohabitation status are a set of confounding variables that will be controlled for in the statistical models to eliminate any backdoor paths by these variables due to exposure and outcome confounding or exposure and mediator confounding or mediator outcome confounding.

In this study 85 of the 1164 pupils were excluded due to the following exclusions criteria: 3 pupils whose civil registration number was incorrectly registered; for 10 pupils, it was impossible to link to either of the parents; 5 pupils were no information was available on either of the pupil's parents in the education or income registries; 28 pupils for whom it was impossible to link to the Academic Achievement Register; 39 pupils for whom there were missing data in the mandatory exams. A total of 1079 pupils were eligible for inclusion in this study of which 527 were girls and 552 were boys with no missing data.

2.12. STATISTICS

In this section, the statistics applied in the different studies will be presented separately for each individual study as these differ due to the difference in study designs described above. However, before describing the statistics used in study 2 and 3 an introduction to the mediation analyses tools employed will be presented. Throughout all statistical analysis, a level of P-value< 0.05 was used to assess statistical significance.

2.12.1. STUDY 1

Demographic differences and between sexes were assessed using chi-squared tests, t-tests, and analysis of variance (ANOVA). Paired t-test was likewise used to test differences between the two academic achievements variables humanistic subjects and science subjects in both sexes. Because previous studies has found differences in both physical fitness and academic achievements between sexes [10, 80-83] all three main analyses that investigate the association between physical fitness and academic achievements were stratified by sex and adjusted for ethnicity, parental household income, and highest education level achieved, the latter used as measurements of family socioeconomic status. Additionally, all three main analyses were stratified by the two measurements of family socioeconomic status to assess interactions. The associations in all main analyses and sensitivity analyses were assessed using linear regressions, where linearity and normal distribution assumptions were assessed using residual and Q-Q plots.

The sensitivity analyses performed include four different types of scenarios to investigate if missing data on the pupils' project exam could affect the associations as it was observed that this exam was accountable for the majority of the missing data in the third variable that represents their academic achievements. The four scenarios in the sensitivity analyses assign extreme exams scores to the pupils who had missing exams scores for the project exam. The first scenario based the academic achievements on the nine available exams. The second scenario assigns pupils the lowest possible exams score (i.e. -3) and it base the grade point average on ten available exams. The third scenario assigns pupils the highest possible exams score (i.e. 12) and it base the grade point average on ten available exams. The fourth scenario excludes the project exam and calculates the grade point average based on the nine mandatory exams. This analysis therefore only includes the nine exams for all pupils.

Data management was conducted using the version 9.4 of SAS (SAS Institute Inc., Cary, North Carolina USA) and the statistical analyses were conducted using version 3.0.2 of R statistical software package (Development R-core team) [84].

2.13. MEDIATION ANALYSIS

The objective of study 2 and 3 was to extend the knowledge obtained from study 1 regarding a connection between pupils' physical fitness and academic achievements by achieving thoroughly insight into the pathways through which pupils' physical fitness may influence their academic achievements and commencement in post-compulsory education.

Mediation analysis allows the researcher to disentangle these different pathways as it provides evidence of the interrelations between different variables especially whether one variable might serves as an intermediate variable on a causal pathway between an exposure and outcome of interest. For instance in study 2 and 3 where pupils, academic achievements and physical fitness respectively serve as an intermediate variable on the two pathways of which expressed in the causal diagrams (Figure 2 and 3). This section will give an introduction to the mediation analysis approach used in this dissertation. The approach is based on counterfactuals as defined within the causal inference framework.

Counterfactuals can, in general, be thought of all potential actions that could have been conducted in a specific setting. In reality, only one of the potential actions are done and the corresponding counterfactual variables are thus the only observed defining all other potential actions as contrary to the fact or counterfactual to what actually occurred. The outcomes that would occur under each of the potential actions can be considered as counterfactual outcomes [85]. For instance, Y_1 and Y_0 are two potential counterfactuals were Y_1 denotes what would have occurred if a subject had been exposed and Y_0 denotes what would have occurred if a subject had been unexposed [85]. This reasoning will be used in the following to display and explain the different effect estimates that arise from the mediation approach applied worth noting is that the approach imputes all possible counterfactuals for each subject in the study (86, 87).

The total effect represents the change in an outcome that would be observed if all subjects were changed from Y_1 to Y_0 formulated for instance as $E[Y_1 - Y_0|c]$ were c denote a set of covariates controlled for in the models [85]. The total effect can be separated into the natural direct and natural indirect effects. The direct effect can be formulated as $E[Y_{1M0} - Y_{0M0}|c]$ were M_0 denotes the mediator which is fixed to the level it would naturally take for each subject when unexposed [85]. In the absence of interaction between the exposure and mediator, the direct effect will coincide with the controlled direct effect which can be formulated as $E[Y_{1m} - Y_{0m}|c]$ were m denotes the mediator which is fixed to a specific level for all subjects. The natural indirect effect can be formulated as $E[Y_{1M1} - Y_{1M0}|c]$ were M_1 again denotes the mediator that would be observed for each subject when exposed and M_0 denotes the mediator that would have been observed for each subject when unexposed [85]. The indirect effect thereby assesses the effect of changing the mediator assuming that all

subjects were exposed. The proportion mediated is a ratio between the indirect effect and total effect: indirect effect/total effect [85].

In the following two sections this mediation framework will be explained specifically in relation to the individual studies including how the estimation was done in practice.

2.13.1. STUDY 2

Demographic differences and between sexes were assessed using chi-squared tests, t-tests as well as Fischer's exact test.

Mediation analyses were applied to investigate the pathways between pupils' physical fitness on their post-compulsory education commencement while treating their academic achievements as an intermediate mechanism. For this study, the mediation analysis separates the total effect of pupils' physical fitness on their post-compulsory education commencement into a natural direct and indirect effect. The natural direct effect disables the pathway that operates through pupils' academic achievements (i.e., the mediator) and thereby assessing the pathway illustrated by arrow A in figure 2. The natural indirect effect assesses the pathway that operates through pupils' academic achievements illustrated by arrow B and C by disabling the pathway A in figure 2.

The estimation approach used is the so-called natural effect models including an imputation procedure for the nested counterfactuals [86, 87] based on logistic regressions which leads to odds ratio (OR) estimates of the total, natural direct, and natural indirect effects. The ratio between natural indirect and total effect reveals the proportion mediated by pupils' academic achievements. Investigation of pupils' overall health revealed no logical argument to include the variable in any of the analyses, results and discussion related to this can be found in paper 2 of the appendix. All mediation analyses were controlled for age, ethnicity, sex, and socioeconomic status. Investigation of potential interactions between sex and either physical fitness or academic achievements were conducted, but none was observed. Bootstrapping was applied to calculate 95% confidence intervals (CI) for the total, natural direct, and indirect effects using 1000 bootstrap samples and 10,000 bootstrap samples were used to calculate 95% CI for the proportion mediated.

Data management was conducted using the version 9.4 of SAS (SAS Institute Inc., Cary, North Carolina USA). All statistical analyses were performed using the version 3.2.4 of the statistical software package R (Development R-core team) [84] in particular version 0.6.0 of the medflex package was used for the mediation analyses.

2.13.2. STUDY 3

Demographic differences, as well as comparisons of differences in physical fitness and academic achievements between ethnicity and gender, were assessed using t-tests, ANOVA, chi-squared tests or Fischer's exact test.

Mediation analyses were applied to examine the pathways between family socioeconomic status and pupils' academic achievements while treating the pupils' physical fitness as a mediator. For this study, the mediation analysis separates the total effect of family socioeconomic status on pupils' academic achievements into a natural direct and indirect effect. The natural direct effect disables the pathway that operates through pupils' physical fitness and thereby assessing the pathway illustrated by arrow A in figure 3. The natural indirect effect assesses the pathway that operates through pupils' physical fitness (i.e., the mediator) illustrated by arrow B and C by disabling the pathway A in figure 3.

The estimation approach again used the so-called natural effect models including an imputation procedure for the nested counterfactuals [86, 87], but based on linear regressions to estimate the total, natural direct, and natural indirect effects as the study outcome is continuous. The ratio between natural indirect effect and total effect reveals the proportion mediated by pupils' physical fitness. All mediation analyses were controlled for age, ethnicity, sex, and cohabitation status. All models include main effects and no interactions terms. Attentions were placed on investigating interactions between socioeconomic status and either physical fitness or sex but none was observed. All models were assessed for goodness of fit using residual and Q-Q plots. Bootstrapping was applied to calculate 95% CI for the total, natural direct, indirect effects and the proportion mediated applying 10,000 bootstrap samples.

Data management was conducted using SAS software version 9.4 (SAS Institute Inc., Cary, North Carolina USA). All statistical analyses were performed using R statistical software package, version 3.3.2, (Development R-core team) [84] in particular the 0.6.0 version of the medflex package was used for the mediation analyses.

CHAPTER 3. RESULTS

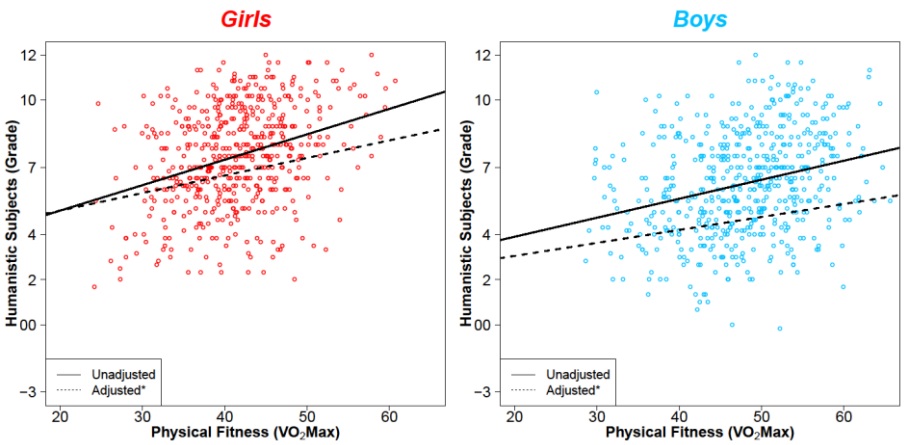
This chapter of the dissertation will present the main findings from the three articles. All demographic and bivariate analyses from the studies will not be presented. However, these are available in the three papers provided in the appendix.

3.1. STUDY 1

3.1.1. MAIN FINDINGS

All effect sizes presented in the following indicate the increase in academic achievements (i.e. grade point average) when pupils' physical fitness increases with 1 $mL \cdot kg^{-1} \cdot min^{-1}$ (VO_2max) showed by the regression coefficient (i.e. grade/VO_2max). For the analyses of pupils' physical fitness on academic achievements from humanistic subjects presented in figure 4 an effect sizes for girls of 0.08 grade/VO_2max (95% Cl: 0.05; 0.11) and 0.06 grade/VO_2max (95% Cl: 0.03; 0.08) for boys was observed when the regression analysis were adjusted for ethnicity and family socioeconomic status.

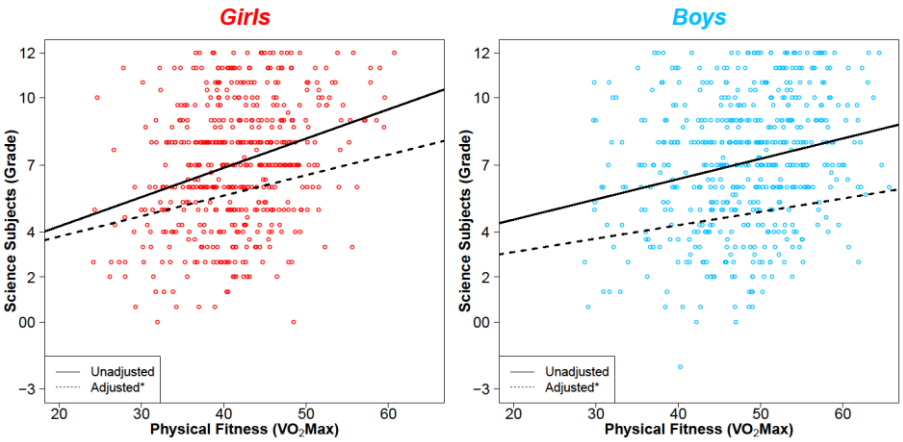
Figure 4 – Display unadjusted and adjusted associations between physical fitness and academic achievements from humanistic subjects stratified by sex and based on linear regressions. Adjustment* include family socioeconomic status and ethnicity. The regression analyses involve 536 girls or 561 boys.



For the analysis of pupils' physical fitness on science subjects presented in figure 5 an effect sizes for girls of 0.09 grade/VO_2max (95% Cl: 0.05; 0.13) and 0.06

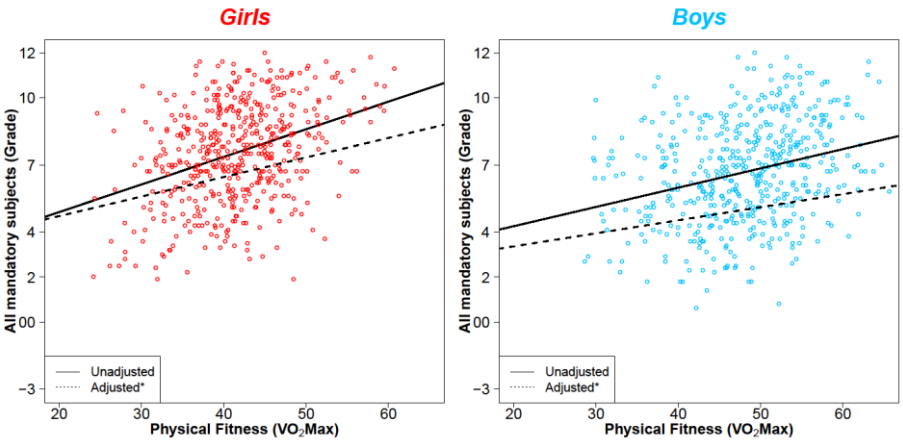
grade/VO_2max (95% Cl: 0.03; 0.09) for boys was observed when the regression analysis were adjusted for ethnicity and family socioeconomic status.

Figure 5 – Display unadjusted and adjusted associations between physical fitness and academic achievement from science subjects stratified by sex and based on linear regressions. Adjustment* include family socioeconomic status and ethnicity. The regression analyses involve 529 girls or 558 boys.



For the analysis of pupils' physical fitness on all mandatory exams subjects presented in figure 6 an effect sizes for girls of 0.09 grade/VO_2max (95% Cl: 0.06; 0.11) and 0.06 grade/VO_2max (95% Cl: 0.03; 0.08) for boys was observed when the regression analysis were adjusted for ethnicity and family socioeconomic status.

Figure 6 – Display unadjusted and adjusted associations between physical fitness and academic achievement from all mandatory subjects stratified by sex and based on linear regressions. Adjustment* include family socioeconomic status and ethnicity. The regression analyses involve 500 girls or 512 boys.



All three analyses were tested for interactions and stratified by family socioeconomic status groups based on parental equivalized income and education level which displayed no effect differences for either of the two measurements showing that the effect of pupils' physical fitness on academic achievements was independent of family socioeconomic status. The four sensitivity analyses that were performed to investigate if missing exam data for the project exam would alter the results presented in figure 6 the first three scenarios revealed that this was not the case as the analyses showed almost identical results these results are available in the first paper of the appendix. However, the fourth scenario still showed positive associations between pupils' physical fitness and their academic achievements, but with a minimal decrease in effect size for both sexes compared to the original analyses an additionally analysis with the inclusion of age as a covariate had no impact on this result. The results from the sensitivity analyses are presented in table 1.

Table 1 – Sensitivity analyses excluding the project exam from all mandatory subjects evaluating the effect of pupils' individual decision to register the exam score from the project exam as well as an additional analysis including age as a covariate. The analyses are based on linear regressions stratified by sex and adjusted for family socioeconomic status and ethnicity involving 527 girls or 552 boys.

	Girls (N = 527)		Boys (N = 552)	
	Grade/VO_2max (95% CI)		Grade/VO_2max (95% CI)	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Linear Regression models				
Mandatory subjects (9)	0.12 (0.09;0.15)**	0.08 (0.05;0.11)**	0.09 (0.05;0.11)**	0.05 (0.03;0.08)**
Mandatory subjects (9)+		0.08 (0.05;0.11)**		0.05 (0.03;0.08)**

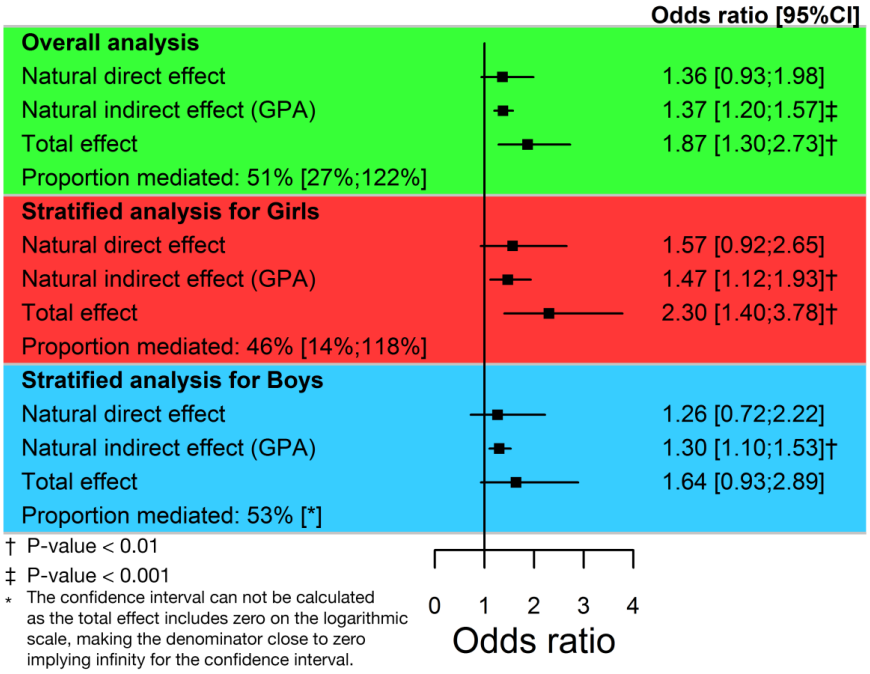
*Adjusted for socioeconomic status and ethnicity
+Adjusted ages groups
**P-value < 0.0001

3.2. STUDY 2

3.2.1. MAIN FINDINGS

All effects from the mediation analyses are presented in figure 7. The total effect displays the odds of pupils' commencement in post-compulsory education if their physical fitness were improved by 10 units of VO2max. The natural direct effects display the odds of pupils' commencement in post-compulsory education if their physical fitness were improved by 10 units of VO2max without changing the pupils' academic achievements. The natural indirect effects display the odds of pupils' commencement in post-compulsory education if their academic achievements are changes from the value it had before improving their physical fitness by 10 units of VO2max to the value it has at the improved level of physical fitness without actually changing the pupils' physical fitness.

Figure 7 – Results from the mediation analyses controlled for sex, age, ethnicity, and family socioeconomic status. The results display total, natural direct, natural indirect effects and the proportion mediated in analyses of overall study participants and stratified by sex involving 530 girls or 554 boys.



The total effect part of the mediation analyses showed an OR of 1.87 (95% Cl: 1.30; 2.37), separating this effect into natural direct effects and natural indirect effects.

The natural direct effects showed an OR of 1.36 (95% Cl: 0.93; 1.98), the width of the CI prevents the possibility of excluding the existence of other pathways not involving pupils' academic achievements. The natural indirect effects showed an OR of 1.37 (95% Cl: 1.20; 1.57), demonstrating strong evidence towards pupils' academic achievements being an intermediated variable between their physical fitness and commencement of post-compulsory education. The ratio between natural indirect effect and total effect indicated a substantial mediation by showing the proportion mediated was 51% (95% Cl: 27%; 122%) as the CI exceed 100% it is possible that the indirect pathway may be the only existing pathway.

Although interaction analysis revealed no effect differences for academic achievements or physical fitness by sexes stratified analyses were conducted due to observed difference by sex in both physical fitness and academic achievements from the bivariate analyses. Stratifying previous mediation analysis by sex showed total effects OR estimates for girls of 2.30 (95%CI: 1.40; 3.78) and for boys 1.64 (95%CI: 0.93; 2.89), by separating these total effect into natural direct effects and natural indirect effects. The natural direct effect showed OR estimates for girls of 1.57 (95%CI: 0.92; 2.65) and for boys 1.26 (95%CI: 0.72; 2.22). The natural indirect effect showed OR estimates of 1.47 (95%CI: 1.12; 1.93) and 1.30 (95%CI: 1.10; 1.53), for girls and boys, respectively. The proportion mediated was for girls 46% (95%CI: 14%; 118%) and 53% for boys. The CI for boys' was not possible to calculate as the total effect was not significant implying that when calculating the proportion mediated one is essentially dividing by a zero, which is not mathematically well-defined. In conclusion, the stratified analysis revealed similar result as when girls and boys formed the population together but with loss of statistical power related to the reduced sample size also showed by the increased width of CI's in the stratified analyses. However, it was chosen to present the analyses both with and without stratification by sex as the impact of sex differences have not been fully understood in the literature.

3.3. STUDY 3

3.3.1. MAIN FINDINGS

All effects from the mediation analyses are presented in figure 8 and 9. The total effects displayed the pupils' change in grades (i.e. academic achievements) when their family socioeconomic status is changed from the socioeconomic reference group 2 to one of the three other socioeconomic status groups for all the pupils. The natural direct effects displayed the pupils' change in grades (i.e. academic achievements) when their family socioeconomic status is changed from socioeconomic status reference group 2 to one of the three other socioeconomic status groups for all the pupils, without changing their physical fitness from the value it has at socioeconomic status reference group 2. The natural indirect effects displayed the pupils' change in grades (i.e. academic achievements) when their physical fitness is changed from the value it has at family socioeconomic status reference group 2 to the value it takes at one of the three other socioeconomic status groups for all the pupils, while actually maintaining their family socioeconomic status at the reference group 2.

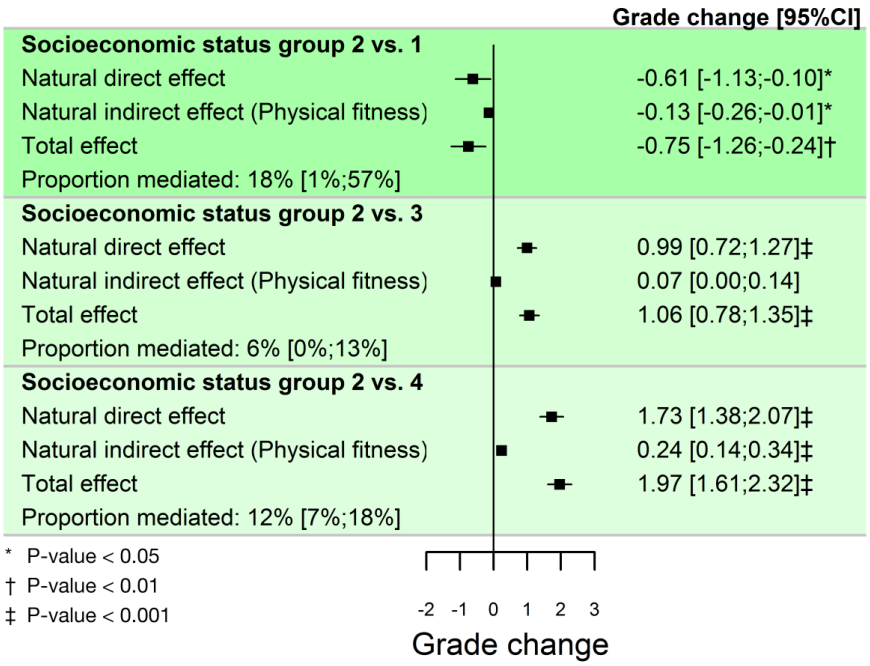
For this study, the family socioeconomic status was based on either family education or income. The results of the following mediation analyses are therefore presented individually in two sections entitled: family socioeconomic status based on family education and family socioeconomic status based on family income.

Family socioeconomic status based on family education

All effects from the mediation analysis where family socioeconomic status is based on family education are displayed in figure 8. The total effect part of the mediation analyses displayed better academic achievements for pupils when the family socioeconomic status groups were improved by demonstrating that pupils from family socioeconomic status groups 1, 3 and 4 had grade point average differences of -0.75 (95% CI: -1.26; -0.24), 1.06 (95% CI: 0.78; 1.35) and 1.97 (95% CI: 1.61; 2.32) compared to counterparts from the reference group 2 of socioeconomic status, respectively. The natural direct effects parts of the divided total effects displayed that pupils from family socioeconomic status groups 1, 3 and 4 had grade point average differences of -0.61 (95% CI: -1.13 -0.10), 0.99 (95% CI: 0.72; 1.27) and 1.73 (95% CI: 1.38; 2.07) compared to counterparts from the reference group 2 of socioeconomic status, respectively. Hereby showing evidence of other pathways not passing through pupils' physical fitness must exist. Nevertheless, the natural indirect effects parts of the divided total effects displayed that pupils from family socioeconomic status groups 1, 3 and 4 had grade point average differences of 0.13 (95% CI: -0.26; -0.01), 0.07 (95% CI: 0.00; 0.14) and 0.24 (95% CI: 0.14; 0.34) compared to counterparts from the reference group 2 of socioeconomic status, respectively. Thus, the evidence is established for a mediated effect by pupils'

physical fitness on the pathway between family socioeconomic status and pupils' academic achievements. The proportion mediated through pupils' physical fitness displayed magnitudes of 18% (95% CI: 1%; 57%), 6% (95% CI: 0%; 13%) and 12% (95% CI: 7%; 18%) for pupils from family socioeconomic status groups 1, 3 and 4 compared to counterparts from the reference group 2 of socioeconomic status, respectively.

Figure 8 – Results from the mediation analyses of socioeconomic status groups based on education and controlled for sex, age, ethnicity, and parents' cohabitation status. The results display total, natural direct, natural indirect effects and the proportion mediated in analyses of study participants involving 1079 pupils.

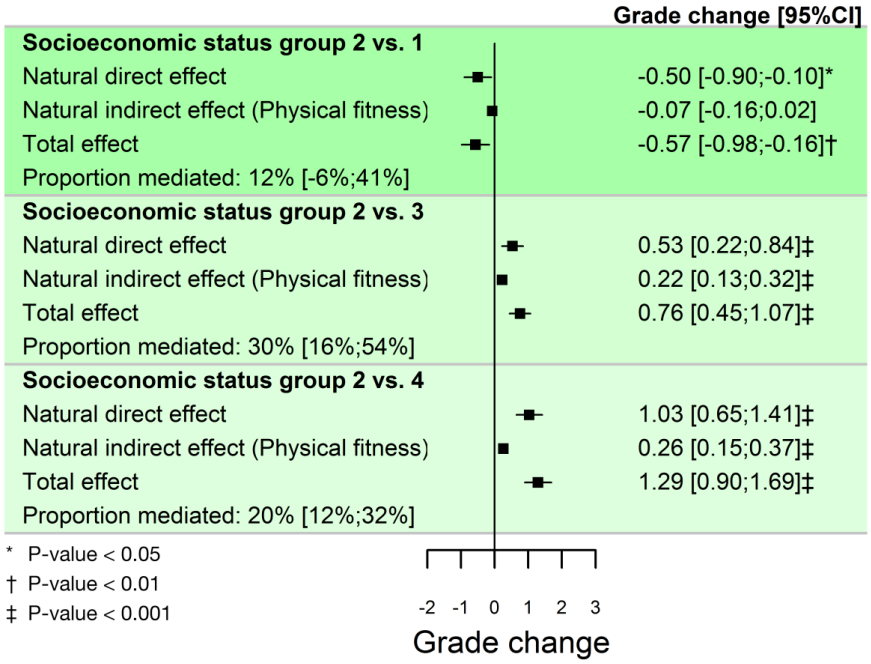


Family socioeconomic status based on family income

Figure 9 display all effects from the mediation analysis when family socioeconomic status is based on family income. The total effects display better academic achievements for pupils when the family socioeconomic status groups were improved by demonstrating that pupils from family socioeconomic status groups 1, 3 and 4 had differences in grade point average of -0.57 (95% CI: -0.98; -0.16), 0.76 (95% CI: 0.45; 1.07) and 1.29 (95% CI: 0.90; 1.69) compared to reference counterparts in socioeconomic group 2, respectively. Dividing the total effects the

natural direct effects part showed that pupils from family socioeconomic status groups 1, 3 and 4 had differences in grade point average of -0.50 (95% CI: -0.90; -0.10), 0.53 (95% CI: 0.22; 0.84) and 1.03 (95% CI: 0.65; 1.41) compared to reference counterparts in socioeconomic group 2, respectively. Hereby showing evidence of other pathways not passing through pupils' physical fitness must exist. Nevertheless, the natural indirect effects parts of the divided total effects displayed that pupils from family socioeconomic status groups 1, 3 and 4 had differences in grade point average of -0.07 (95% CI: -0.16; 0.02), 0.22 (95% CI: 0.13; 0.32) and 0.26 (95% CI: 0.15; 0.37) compared to reference counterparts in socioeconomic group 2, respectively. Thus, the evidence is established for a mediated effect by pupils' physical fitness on the pathway between family socioeconomic status and pupils' academic achievements. The proportion mediated through pupils' physical fitness displayed magnitudes of 12% (95% CI: -6%; 41%), 30% (95% CI: 16%; 54%) and 20% (95% CI: 12%; 32%) for pupils from family socioeconomic status groups 1, 3 and 4 compared to reference counterparts in socioeconomic group 2, respectively.

Figure 9 – Results from the mediation analyses of socioeconomic status groups based on income and controlled for sex, age, ethnicity, and parents' cohabitation status. The results display total, natural direct, natural indirect effects and the proportion mediated in analyses of study participants involving 1079 pupils.



Even though interaction analyses revealed no effect differences between socioeconomic status and either sex or physical fitness stratified analyses by sex was performed due to the same reason as in study 2. However, as in study 2, the stratified analyses performed in this study also revealed similar results as when girls and boys formed the population together, but with loss of statistical power related to the reduced sample size also indicated by the CI's in the stratified analyses. These analyses are available in the appendix specifically in the supplementary material of the third paper.

CHAPTER 4. DISCUSSION

The overall objective of this Ph.D. dissertation was to provide insight into mechanisms and relations through which pupils' physical fitness may influence scholastic abilities. This chapter will discuss the main findings and considerations made across the various studies followed by limitations of the dissertation.

4.1. MAIN FINDINGS

The overall findings of this dissertation establish pupils' physical fitness as a relevant mechanism in relation to their scholastic abilities. Independently of the analyses performed in the different studies pupils' physical fitness consistently showed to influence scholastic abilities supporting the growing body of evidence indicating a connection between physical fitness and academic achievements [10, 14, 18, 20, 26-36]. The plausible explanation for these findings is that concurrent with improvements in pupils' physical fitness levels several neurological functions and structures are improved [37-44, 88] which also positively affects executive functions, memory and learning abilities [37, 38, 40, 41, 44-50]. These neurological improvements or executive functions are intrinsically related to scholastic abilities [30, 51-54]. Even though, a recently published study was unable to establish executive function as a mediator on the pathway between physical fitness and academic achievement [89] the opposite was observed in a study by van der NIet et al. were executive function mediated the pathway [90]. Nevertheless, these divergent results emphasize the need for more pathway analyses to understand the mechanisms involved in the relation between pupils physical fitness and scholastic abilities as this potentially could lead to the possibility of understanding the causal relations in the future.

The bulk of evidence still supports the aforementioned explanation suggesting that pupils' physical fitness affects neurological structures that in turn promote academic achievements which have also been suggested as the possible causal link in the literature [14, 33, 44]. Study 2 of this dissertation extended the current knowledge by establishing a positive effect of pupils' physical fitness on their commencement of a post-compulsory education demonstrating that increased physical fitness among pupils enhanced the likelihood of their commencement in a post-compulsory education. Nevertheless, a substantial part of the effect was mediated by the pupils' academic achievements from compulsory education. The study contributes to the literature by illuminating that the causal pathway of the connection might go from pupils' physical fitness through their academic achievements to commencement in post-compulsory education thereby extending the potential causal pathway to pupils' commencement in post-compulsory education.

Both study 1 and 2 confirmed prior findings of a relation between pupils' physical fitness and their academic achievements [10, 14, 18, 20, 26-36] while controlling for the family socioeconomic status of the pupils. In relation to this, study 3 established that family socioeconomic status of the pupils affected their academic achievements and demonstrated that part of this effect was mediated through pupils' physical fitness. Thus extending the insight of the potential causal pathway by displaying that pupils' physical fitness might be a pathway through which family socioeconomic status influence pupils' academic achievements. The explanation for the connection might be that family aspects that endorse pupils' academic achievements are linked to the family socioeconomic status like engaging in healthy activities that lead to increased physical fitness in pupils or other mechanisms not involving pupils' physical fitness which was also established in the study by providing evidence of other pathways not passing through pupils' physical fitness. These mechanisms could, for instance, be parents' involvement or abilities to support their offspring in their daily activities which are likely related to the family socioeconomic status [55, 91]. In study 2 it was likewise not possible to exclude the possibility of other intermediate mechanisms that could exist between pupils' physical fitness and commencement in post-compulsory education.

Previous studies have suggested that pupils' motivation and self-esteem could be potential mechanisms that influence both pupils participation in physical activity and academics and thereby improving their performance in both activities [20, 27, 92-94]. However, increments in pupils' physical activity or exercise determents their physical fitness level [15, 17] and other studies have shown that improvements of these factors lead to enhanced self-esteem and motivation in pupils [91, 92, 95] which suggest that these factors might be intermediate variables. It is also possible that parents' abilities, support or involvement leads to enhanced self-esteem or motivation in their offspring's which again could be related to the family socioeconomic status. Thus, it could be argued that these might be partially controlled for through family socioeconomic status should these mechanisms not be intermediate variables. Nevertheless these mechanisms were not possible to examine in this dissertation, but definitely emphasize the need for further pathways analyses to get a deeper insight and understanding into the intermediate mechanisms that form the interrelation between pupils' physical fitness, academic achievements, commencement in post-compulsory education and their family background. The dissertation contributes to the literature by giving an overview of the interrelations and provides evidence towards pupils' physical fitness being a relevant mechanism in relation to academic achievements and pupils' commencement in post-compulsory education.

The dissertation was based on high-quality data including objectively measured physical fitness of the pupils' and detailed information's obtained from the Danish nationwide administrative registries. The registries are normally used in the Danish society for administrative purposes such as healthcare registration, legal rights, tax-

payments, etc. which ensured a high registration quality [65, 66]. The use of these data sources increases the accuracy and quality of the information's used in the studies and findings obtained. Based on the finding of this dissertation it seems questionable if the reduction of time for physical activity in the daily school setting is a beneficial strategy, especially if the pupils or parents do not believe in the necessity of the pupil to compensate for the reduced time for physical activity in their spare time. The finding suggests that both school and family should facilitate activities that can improve pupil's physical fitness as this might affect their scholastic abilities. However, in any circumstances improvements in physical fitness would promote health as indicated by others [15, 16, 20-21].

4.2. ACADEMIC ACHIEVEMENTS

The pupils' academic achievements were in this dissertation assessed through a series of mandatory exams in different subjects which should represent the best indicator of pupils' scholastic abilities at the end of compulsory education. This was in contrast to the use of a certain measurement of pupils' academic achievements which have been the preferred approach in the literature [10, 14, 18, 20, 26-36]. The use of all mandatory exams at the completion of compulsory education provides a more precise measurement to represent the pupils' academic achievements as it incorporates the possibility that some pupils may perform better or worse in specific subjects which is a limitation in the previous studies as this is not possible to account for with the use of a single exam in a specific academic subject.

Additionally by reflecting pupils' academic achievements through all mandatory exams gives a more precise indication of the pupils' scholastic abilities at the completion of compulsory education. These mandatory exams have itself a great advantage as the exams are graded through external censors ensuring that no personal relations can influence the pupils' exams scores [71] which increase the objectivity of pupils' academic achievement measurements used in this dissertation. However, as it was observed that pupils have the legal right to decide if the exam assessment from the project exam should be registered in the Academic Achievement Register [71]. The additional sensitivity analysis was performed to investigate if this legal right could introduce systematic errors in the measurement of the pupils' academic achievements. The sensitivity analysis did not change the evidence of a positive connection between pupils' physical fitness and academic achievements, but it reduced the effect slightly indicating that the suspicion regarding the systematic error was accurate.

This strongly indicates that the best measurement of pupils' academic achievements to represent their scholastic abilities are all mandatory exams excluding the project exam establishing the estimates from the sensitivity analysis as the most accurate to show the relation between pupils' physical fitness and academic achievements in study 1. The measurement also represents the most objective indicator of pupils'

scholastic abilities at the end of the 9th grade of compulsory education and emphasizes this as the measurement of choice to represents the pupils' scholastic abilities. This measurement was also applied in study 3 and partly in study 2 as the exams scores for the 10th grade of compulsory education was incorporated as well to get an even more precise measurement of scholastic abilities on pupils who attended the 10th grade of compulsory education. The used of a whole series of mandatory exams provided evidence of a relation between pupils' physical fitness and their scholastic abilities at the end of compulsory education and thereby extending current knowledge regarding the relation between pupils' physical fitness and academic achievements.

4.3. FAMILY SOCIOECONOMIC STATUS

This dissertation assessed two measurements to indicate the family socioeconomic status which were in contrast to previous studies were socioeconomic status was included in the investigation of the relation between pupils' physical fitness and academic achievements as these used a single proxy-measurement of socioeconomic status either education or income [10, 18, 20, 26, 27, 29, 30, 32]. However, as it has been indicated by Galobardes et. al [96] if studies wish to control for socioeconomic status more than a single measurement should be incorporated to avoid bias estimates. Even though, education and income might be highly correlated they can explain different causal mechanisms [97, 98] therefore by controlling for both eliminates a possible backdoor path caused by lack of adjustment for one of these variables. This approach was applied in both study 1 and 2, but it is possible that this could have affected the precision of the estimates due to the possibility of "unnecessary adjustment" in the regression models [99]. However, as the main objective with the adjustment were to eliminate any potential confounding caused by the proxy-measurements the adjustment for both are emphasized as the most sensible approach especially in relation to study 2, as the method used in that study build on assumptions of no-unmeasured confounding [85].

In opposed to studies 1 and 2, study 3 used family socioeconomic status based on either family income or education as the exposure to investigate the impact on pupils' academic achievements across the different socioeconomic status groups. It has been stated by Galobardes et. al [96] that when researchers are interested in assessing socioeconomic status as the exposure it is not crucial which indicator of socioeconomic status is used when the aim is to assess differences across socioeconomic groups as long as the life course stages are considered in the choice of indicators. In relation to this, it was chosen to classify income differently compared to study 1 and 2 where the classifications were based on income quartiles of the specific population of the studies. Study 3 however used four groups based on the Danish population equivalized income distribution accounting for the parents' age composition which thereby both include the life course stages of the families and increase the generalizability to the Danish population. The reason for using two

indicators of socioeconomic status was to test the robustness of the overall results as independently of which measurement was used it should depict the same tendencies for the different socioeconomic status groups especially in a homogenous country as Denmark were income and education are intrinsically related. Even so, it is still possible to observe differences in estimates across the different socioeconomic groups between the two measures [96]. The study did show minor variations in the estimates but the same overall tendencies across the different socioeconomic status groups were shown independently of which proxy measurements were used suggesting that both measurements indicate family socioeconomic status in a similar manner.

Previous studies that included socioeconomic status have used vague and limited information's to indicate family socioeconomic status as these only included self-reported education status of the parents or the pupils eligibility for a free/price reduced lunch program in school as indicators for the family socioeconomic status [10, 18, 20, 26, 27, 29, 30, 32]. In contrast, this dissertation used both exact education level and income level of the individual families obtained from the Danish administrative registries. The study thereby provides a deeper insight into the impact of using exact education or income levels in the family as proxy-measurements of socioeconomic status and established family socioeconomic status as a relevant mechanism when examining the relations between pupil's physical fitness, academic achievements, and post-compulsory education commencement.

4.4. LIMITATION

This dissertation was based on observational data reducing the possibility of inferring causal conclusions by nature. However, if the adjusted variables in the individual studies were sufficient to eliminate any backdoor paths and successful conditional exchangeability was establish between the investigated groups then it is possible that some of the results may indicate causal relations, but no test is available or possible to conduct in investigating if this would be the case [100]. It is possible that there could be unmeasured confounding not sufficiently controlled for in the models indicating unblocked backdoor paths eliminating the possibility of causal conclusions. Also, the mediation approach applied includes assumptions of no unmeasured confounding [85, 86, 101], but as indicated this assumption is difficult to establish in observational studies. Study 2 and 3 are based on an assumption of a causal path between pupils physical fitness and academic achievement, however, such has not been established even though study 1 established an association between pupils physical fitness and academic achievement as associations are not causations. Thus it is possible that the causal pathway may not exist in reality and thereby disrupting the assumption made.

An additional limitation in the dissertation is related to the number of included pupils in the studies even though the sample was fairly large the classification of the

pupils' into different categories could affect the statistical power of the individual studies. Especially, in relation to obtaining the counterfactuals in the mediation analyses as the procedure generates the counterfactuals based on the true values observed in each counterfactual group. However, the statistical power concerns are also reflected in the width of the CI's in the individual studies.

CHAPTER 5. CONCLUSION

In conclusion, pupils' physical fitness was consistently established as a relevant mechanism in relation to their scholastic abilities by providing evidence of different pathways through which pupils' physical fitness was positively related to scholastic abilities.

Pupils physical fitness was positively linked to their academic achievements and further showed that the physical fitness positively influenced commencement in post-compulsory education with the establishing of pupils academic achievements as a mediating mechanism on the relation. Not unexpected, the family socioeconomic status of the pupils influenced the connection between physical fitness and academic achievements. However, pupils' physical fitness was shown to both influences their academic achievements independently of the family socioeconomic status as well as the physical fitness acted as a mediating mechanism on the pathway between family socioeconomic status and academic achievements. Therefore both the socioeconomic status of the pupils and their physical fitness are concluded as relevant mechanisms that may influence their academic achievements and commencement in post-compulsory education.

Even though this dissertation provides evidence of possible mechanisms through which pupils' physical fitness may lead to improved scholastic abilities more research are needed to fully understand the mechanisms of action that forms the relation before definitive causal conclusions can be drawn.

CHAPTER 6. PERSPECTIVE AND FURTHER RESEARCH

6.1. PERSPECTIVE

Even though this dissertation did not establish causal explanations for the relation between pupils' physical fitness and their scholastic abilities it provided new insights into different pathways through which pupils' physical fitness may positively relate to their scholastic abilities. The dissertation thereby indicates pupils' physical fitness as a relevant factor in relation to scholastic abilities. In the light of these insights, parents and school administrators should be recommended towards not neglecting pupils' daily physical activities that can improve their physical fitness as this might play an important role in relation to the pupils' scholastic abilities. Even if later research would show that increments in the pupil's fitness levels do not increase their scholastic abilities improvements in physical fitness will in all circumstances promote physical health [24, 25].

Since pupils spend most of their waking hours in schools these environments should focus on both core academics and daily activities that facilitate healthy and good habits like being physically active. Danish policy makers and school administrations should focus on how to increase the knowledge and abilities of teachers towards enabling them in how to motivate and facilitate pupils' engagement in daily physical activities especially as the Danish school legislation from 2014 prioritize daily physical activity to maintain motivation and support core academic disciplines [71]. However, if teachers do not have the necessary tools or abilities to motivate the pupils it is highly unlikely that the daily physical activities in the school setting will become a habit among the pupils. Pupils that have been positively introduced to participation in physical activities in the earlier years of life are more prone to adopt this as a habit promoting an active lifestyle [7, 94, 102], which potentially could prevent obesity and other lifestyle-related diseases due to inactivity (24, 25).

6.2. FURTHER RESEARCH

In relation to further research within the area, the insights obtained through this dissertation can help guide researchers in design and construction of both experimental and observational studies aimed at getting a deeper understanding in the relation between pupils' physical fitness and their scholastic abilities as it has shown whether one partway were more plausible than another. As stated in the conclusion more research is needed to fully understand a possible causal relation between pupils' physical fitness and their scholastic abilities.

In this relation, it would be novel for this research area if studies would examine how longitudinal changes in pupils' physical fitness would affect their scholastic abilities as well as examining the concurrent neurological changes that can occur due to changes in pupil's physical fitness levels. Ideally, large well designed randomized trials with long-term follow-up and detailed information on pupil's physical fitness, neural development and scholastic abilities could potentially reveal this insight. If such trials are not available an additional approach could be to emulate or mimic the unavailable trials through the use of modern epidemiological methods within the causal inference framework [103, 104] based on observational data that also includes long-term follow-up and detailed information's on pupil's physical fitness, neural development, and scholastic abilities should such data be available.

Understanding the causality by mapping the potential mechanisms of actions through which pupils' physical fitness leads to scholastic abilities are of great importance. This could enable policymakers and school administrators with evidence to implement the most effective interventions to promote pupils scholastic abilities and health, which in turn may promote health and help reduce social inequality. The earlier years of life are an important phase in establishing healthy habits and behaviors, for instance, pupils who have an active lifestyle are more prone to carry the lifestyle through adolescent and into adulthood [92, 102].

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APPENDICES

Study 1.

Association Between Physical Fitness and Academic Achievement in a Cohort of Danish School Pupils.

Study 2.

The indirect and direct pathways between physical fitness and academic achievement on commencement in post-compulsory education in a historical cohort of Danish school youth. BMC Public Health.

Study 3.

The mediated effect of pupils' physical fitness on the relation between family socioeconomic status and academic achievements in a Danish school cohort.

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