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# Associations between physical activity and lung function in a cohort of German adolescents

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by

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## Abstract / Summary

Physical activity (PA) is one of the best-known health behaviors in the developed world, protective against diabetes and cardiovascular diseases, but also conditions such as depression and cancer. While it is generally accepted that most people would benefit from increased PA, neither current activity levels in the general population nor the relative importance of different activity domains have been well established.

While PA has been associated with improved respiratory function in different lung diseases, associations in populations with healthy lungs are less well studied. Children, adults and athletes specializing in different sports have been studied; however, results are confounded by anthropometric and sociocultural differences in populations. Furthermore neither PA nor lung health is quantified in the same way across studies, and methods of PA assessment vary in validity, replicability, and cost. Thus while it often appears that active healthy people have better lung function than inactive peers, the relationship is not clear.

PA is generally quantified as minutes per day of moderate or vigorous physical activity, i.e. activity requiring more than 3 or 6 metabolic equivalents, respectively, but occasionally also as sport participation; it can be measured either subjectively by self-report and parental report, or objectively by accelerometry, calorimetry, and/or direct observation by trained observers. Lung health may be quantified as incidence, prevalence, exacerbation or remission of different respiratory diseases; or as lung function, which at the population level is typically quantified as spirometric indices. Although spirometry is standardized, ascertainment, diagnosis, and treatment of lung diseases are often heterogeneous between populations. For all these reasons, while existing evidence proves the benefit of pulmonary rehabilitation and suggests that children with respiratory diseases are less active, there is less evidence for a relationship between PA and spirometry in healthy children or for a relationship with respiratory diagnoses, as opposed to symptoms.

In this thesis, PA and lung function were cross-sectionally determined in two large population samples, the GINIplus and the LISAplus birth cohorts. PA was measured in 1411 subjects (47% male) ages 14-17, most of whom also contributed allergy data and spirometry.

PA was measured by a combination of one-week accelerometry and activity diary: it was quantified both as minutes spent in moderate and/or vigorous activity (MVPA) and as participation in leisure sport, school sport or active transportation to school (i.e. by foot or bicycle.) Lung health was measured both by medical history (reported presence or absence of doctor-diagnosed allergic diseases, allergic symptoms, or smoking) and by spirometry. With these data we sought to answer the following questions:

1) How physically active were these adolescents? How important were different activity domains (school sport, leisure sport, transportation, school time, and all other time) in determining total moderate and vigorous activity?

2) When the effects of asthma and smoking were excluded, did physically active children of either sex have better spirometrically-assessed lung function than inactive ones?

3) Was any allergic respiratory condition (asthma, allergic rhinitis, aero-allergen sensitization, wheezing, rhinoconjunctivitis) associated with either reduced participation in sport, or decreased moderate or vigorous PA?

We observed a generally active lifestyle, with girls less active than boys. Over 2/3 of subjects participated in leisure-time sport: however, PA levels were still substantially below recommendations especially for girls. Boys and girls achieved the World Health Organization's recommended 60 minutes per day MVPA on only 27% and 17% of days, averaging 46 and 38 minutes per day: however there was large variation between individuals. Leisure sport provided 16% of total MVPA, school sport provided 5%, and transportation to school 8%. Sport participation was not associated with symptoms, female gender, or respiratory diagnoses: and while there was no association between PA and spirometry in lung-healthy children, boys with diagnosed asthma and rhinitis tended to be less active. The effect did not appear to be driven by allergic symptoms, and was only present in boys. We conclude that traditionally vulnerable adolescent populations participated fully in sport in Germany, but sport was not sufficient to ensure adequate PA especially for girls and for asthmatic boys. Observed levels of PA did not appear to benefit healthy lungs; however interventions are needed to address causation.

**Zusammenfassung**

Körperliche Aktivität gehört zu den etablierten, gesundheitsfördernden Verhaltensweisen in den Industrienationen. Regelmäßige Aktivität beugt einer Vielzahl von Krankheiten wie Diabetes und Herz-Kreislauf-Erkrankungen, sowie Depression und Krebs vor. Doch obwohl allgemein bekannt ist, dass die meisten Menschen von einer Steigerung der körperlichen Aktivität profitieren würden, sind weder die aktuellen Aktivitätslevel westlicher Populationen zufriedenstellend, noch ist der Beitrag einzelner Tagesaktivitäten in Bezug auf die Gesamtaktivität gut erforscht.

Während bei verschieden Lungenerkrankungen regelmäßige körperliche Aktivität häufig mit einer verbesserten Atemwegsfunktion assoziiert wird, ist dieser Zusammenhang bei lungengesunden Populationen weniger erforscht. Bisher haben Studien Kinder, Erwachsene und Sportler unterschiedlicher Disziplinen untersucht, doch die Ergebnisse sind nicht eindeutig, was möglicherweise auf die Studienpopulationen mit anthropometrischen und soziokulturellen Unterschieden zurückgeführt werden kann. Auch wurden in den Studien weder die Atemwegsfunktion noch die körperliche Aktivität mit gleicher Methodik erfasst, so variiert die Messung der körperlicher Aktivität in Validität, Replizierbarkeit, Genauigkeit sowie Kosten. Obwohl es häufig den Anschein erweckt, dass körperlich aktive, gesunde Menschen eine bessere Lungenfunktion aufweisen als ihre inaktive Vergleichsgruppe, ist der Zusammenhang nicht bewiesen.

Der Aktivitätslevel wird in der Regel in Minuten von moderater bis starker körperlicher Aktivität pro Tag, das heißt, Aktivität, die mehr als drei oder sechs metabolische Äquivalente benötigt, erfasst. Gelegentlich wird aber auch die Dauer einer gezielten sportlichen Aktivität oder die Teilnahme an Sportprogrammen als Maß herangezogen. Die Erfassung basiert entweder auf subjektiven Angaben durch Selbstbeobachtung oder bei Kindern durch die elterliche Beobachtung bzw. die Beobachtung durch ausgebildete Fachkräfte. Objektive Methoden stellen die Akzelerometrie und die Kalorimetrie dar. Die Lungengesundheit kann mittels Fragebogen zur Inzidenz, Prävalenz, Exazerbation oder Remission von Lungenerkrankungen beurteilt werden oder wird durch die Lungenfunktionsmessung erfasst, wobei in Kohorten dafür typischerweise die Spirometrie eingesetzt wird. Während die Spirometrie ein standardisiertes Verfahren darstellt, variieren die Erhebung, Diagnose und Behandlung von Lungenerkrankungen zwischen einzelnen Populationsstudien. Unter Berücksichtigung dieser Aspekte kann festgehalten werden, dass der der positive Einfluss von körperlicher Aktivität für die Lungenrehabilitation als belegt angesehen werden kann und vieles darauf hindeutet, dass Kinder mit Atemwegserkrankungen weniger aktiv sind. Unklar ist der Zusammenhang zwischen körperlicher Aktivität und Lungenfunktion bei lungengesunden Kindern oder bei Lungenerkrankungen mit und ohne Symptomfreiheit.

Für die vorliegende Arbeit wurden körperliche Aktivität und Lungenfunktion in zwei großen, deutschen Geburtskohorten, der GINIplus und der LISAplus Studie gemessen und mittels Querschnittsanalysen mögliche Assoziationen unter Berücksichtigung bekannter Einflussgrößen ermittelt. Die körperliche Aktivität wurde bei 1411 Probanden (47% davon

männlich) im Alter von 14-17 erfasst; von den meisten Probanden lagen auch Daten zur Spirometrie sowie allergischen Erkrankungen vor.

Die körperliche Aktivität wurde über eine Woche mittels Akzellerometrie zusammen mit einem Bewegungstagebuch erfasst und die Minuten von moderater und/oder starker körperlicher Aktivität pro Tag (MVPA) bestimmt. Durch das Tagebuch konnten spezifische sportliche Aktivitäten, wie die Teilnahme an Sportprogrammen oder Schulsport sowie der Aktivitätsgrad auf dem Schulweg - wie mit dem Fahrrad oder dem PKW gebracht - ausgewertet werden. Die Lungengesundheit wurde einerseits durch die medizinische Vorgeschichte (dokumentiertes Vorhandensein oder Nichtvorhandensein von ärztlich festgestellten allergischen Erkrankungen, allergischen Symptomen oder Rauchen) sowie durch die Lungenfunktion beurteilt. Auf der Basis dieser Daten habe ich folgende Fragen adressiert:

1) Wie körperlich aktiv waren die Jugendlichen? Welchen Beitrag leisteten unterschiedliche Aktivitätsbereiche (Schulsport, Freizeitsport, Aktivitätsgrad auf dem Schulweg) zur gemessenen moderaten bis starken Gesamtaktivität und welcher Anteil wurde während der Schul- und Freizeit geleistet?
2) Haben lungengesunde, körperlich aktive Jugendliche beiderlei Geschlechts eine bessere spirometrisch eingeschätzte Lungenfunktion als körperlich inaktive?
3) Sind allergische Erkrankungen (Asthma, allergische Rhinitis, aero-Allergen-Sensibilisierung) oder deren Symptome (Pfeifatmung, Rhinokonjunktivitis) mit einer geringeren körperlichen Aktivität oder geringeren Teilnahme an sportlichen Aktivitäten assoziiert?

Insgesamt gesehen beobachtete ich einen aktiven Lebensstil der Jugendlichen, mehr als zwei Drittel der Probanden übten während ihrer Freizeit mindestens eine Sportart aus. Trotzdem lag die Dauer der täglichen körperlichen Aktivität wesentlich unterhalb der 60-minütigenWHO-Empfehlung, nur an 27% bzw. 17% der Tage wurde diese von den Jungen bzw. Mädchen erfüllt. Die Mädchen waren weniger aktiv als die Jungen, im Mittel betrug MVPA bei Jungen 46 min/Tag und bei Mädchen 38 min/Tag, zeigte aber eine große individuelle Variabilität. Der Beitrag durch Freizeitsport zur gesamten MVPA betrug 18%, Schulsport trug 5% und der aktive Schulweg 8% bei. Mädchen übten Freizeitsport genauso häufig wie Jungen aus, ebenso war die Teilnahme bei Jugendlichen mit allergischen Erkrankungen bzw. Symptomen nicht eingeschränkt. Während sich ein Zusammenhang zwischen körperlicher Aktivität und der spirometrischen Messgrößen bei lungengesunden Jugendlichen nicht nachweisen ließ, neigten Jungen mit der Diagnose Asthma und/oder Rhinitis dazu, weniger aktiv zu sein. Diese Einschränkung schien nicht durch das Vorhandensein von allergische Symptome erklärbar zu sein und war nur bei Jungen zu beobachten.

Aus meinen Studien schließe ich, dass in Deutschland die traditionell gesundheitlich eher anfällige jugendliche Bevölkerung doch häufig Freizeitsport ausübt, aber dieser nicht ausreicht, um insbesondere bei Mädchen und asthmatischen Jungen, eine ausreichende körperliche Aktivität sicherzustellen. Trotz der hohen Variabilität der körperlichen Aktivität konnte kein

Einfluss auf spirometrische Kenngrößen bei lungengesunden Jugendlichen nachgewiesen werden. Allerdings muss der Querschnittscharakter der Studie berücksichtigt werden und Interventionsstudien wären erforderlich, um eine definitive Schlussfolgerung zu ziehen.

# 1. Introduction:

## 1.1 Background: Physical activity and respiratory function

Physical activity (PA) is perhaps the single most effective health intervention in the developed world, with known protective effects against diseases as diverse as diabetes, [1, 2] clinical depression,[3] cardiovascular diseases[4, 5] and many cancers.[6] While it is generally accepted that PA levels in the developed world are too low, [7-9] current levels are not well established and thus interventions are difficult to design, target and evaluate. Likewise, data are missing on the relative importance of different activity domains (such as sport and transportation) in determining total PA.

One proposed benefit of PA is its potential to improve respiratory function across the lifespan. [10] [11] [12] Physical activity and fitness (closely correlated) have been associated with improved respiratory outcomes during the stages of rapid lung growth,[13] [14] young adulthood,[15, 16] and aging;[12] in populations with respiratory comorbidities it is part of pulmonary rehabilitation. [17-19] Benefits of activity for healthy lungs are less studied, but lung growth is sometimes faster in active children [14] and decline is slower in physically active smokers [20] and other adults [11] [12] compared to inactive peers. However, effects are heterogeneous and often confounded by socioeconomic, ethnic and cultural differences,[21, 22] and may also be driven by respiratory comorbidities such as asthma. Clearly more research is needed to determine whether the association between PA and lung health that has been found in populations with lung comorbidity, extends to healthy lungs.

## 1.2 Methods: Measures of physical activity

Assessing behavior under field conditions is always difficult, and PA is no exception. Existing methods (self-report, parental report, observation) suffer from a number of limitations including desirability bias, recall bias, observer effects, and healthy-user bias. In the past decades accelerometry has become more common as an objective method of PA assessment under free-living (field) conditions. During the period of observation (a week is typical) subjects wear a motion-sensing device that continuously records acceleration, with more acceleration per unit time ("epoch") indicative of higher PA. Following data cleaning and verification of wear time, the device's output is categorized epoch-by-epoch to give an estimate of activity level (sedentary, light, moderate, or vigorous PA) over that epoch. These can in turn be combined with a diary to assign PA to different domains, such as work, sport and school. Following further checks to ensure that data are representative of typical routine, accelerometric data are be used to establish a snapshot of daily PA in that population.

## 1.3 Measures of respiratory function

At least two possible relationships between PA and improved lung function have been posited, with varying degrees of support and applicability to our population. One is that PA is associated with incremental improvements in lung volumes and flows as measured by spirometry. Most research into this association has focused on the use of PA in pulmonary rehabilitation, the efficacy of which has been proven. [23] While some studies have also shown effects in healthy populations [24, 25] the evidence is not as conclusive. We thus investigated the link between spirometric volumes and flows, and PA level.

The other relationship is that PA is associated with lowered incidence or severity of respiratory comorbidities, although spirometry is often normal. [26] While associations between low PA and asthma are known,[13, 27] those with rhinitis are less well studied and often confounded by asthma [28] and those with aero-allergen sensitization almost unknown. Posited explanations for the associations between low PA and allergy include activity-limiting symptoms,[29] immunomodulatory effects of PA,[13, 29] and cultural pressure for asthmatics, especially children, to avoid PA.[30, 31]

# 2. Specific aims and results

## 2.1 Specific aims

This thesis is based on the observation that PA is an essential health intervention that deserves fuller study, particularly in regard to its relationship with lung health; and that hypokinetic and allergic diseases are rising in prevalence together. We aimed to objectively quantify PA levels and domains in a cohort of German adolescents, and correlate PA measures with lung health and allergic lung disease. Specific objectives were:

*A)* Quantify physical activity in this cohort appropriately, including:
   i. Determine the relative importance of different activity domains in determining total PA;
   ii. Determine the strength of healthy-user bias in determining sport participation.

*B)* Evaluate the relationship between PA and lung health:
   i. Determine association of PA and spirometric indices, independent of effects of asthma;

*C)* Evaluate the relationship between PA and lung disease:
   i. Determine the direction and type of association of PA with measures of allergic respiratory phenotype.

This thesis combines four publications that have been published by PlosOne[32-34] and European Respiratory Journal.[35] For all four I developed the research question, performed statistical analyses, and interpreted the results. Comments and suggestions from supervisors, coauthors and reviewers were incorporated in the final versions.

## 2.2 Study population and methods

### 2.2.1 Study population

All data were drawn from the 15-year follow-ups of two German birth cohorts born between 1995 and 1999, GINIplus and LISAplus. GINIplus (German Infant Nutritional Intervention PLUS environmental and genetic influences on allergy development) was initiated to investigate allergy development after intervention with hydrolysed formulas. Further details on study design, formulas and followup are in in [36] and [37]. Of 5991 healthy, full-term newborns recruited in the regions of Munich and Wesel, 3199 were recontacted at age 15 and approached for accelerometry. LISAplus is a population-based cohort of 3097 unselected infants from the cities of Munich, Wesel, Bad Honnef and Leipzig. No intervention, nutritional or otherwise, was used in LISAplus. 1534 subjects were followed up at age 15, of which 1107 were from Munich or Wesel and thus approached for accelerometry. Details on study design are in [38].

### 2.2.2 Measures of physical activity (PA)

PA was measured using a hip-worn triaxial accelerometer (ActiGraph GT3X, Pensacola, Florida) combined with activity diary. For detailed description of accelerometer protocol, quality control, and data cleaning, see [39]. To be valid, days had at least 7-10 hours of recording that was confirmed by the diary. Valid subjects provided at least 3 valid weekdays, and one valid weekend day. Of the 1689 subjects who returned the accelerometer, 1411 (8832 days) ultimately provided valid data. Accelerations during diary-validated accelerometer wear were converted into activity levels in one-minute epochs using the algorithm from Freedson et al. [40]

In a standardized diary subjects documented times of getting up and going to bed, leisure sport, school sport, and active commuting to school during accelerometer wear. This allowed PA to be divided minute-by-minute into five non-overlapping domains. These were transportation to school, school sport, school outside sport, leisure-time sport, and other time. Leisure-time sport participation (binary yes-no) was also considered as an indicator of active lifestyle.

### 2.2.3 Measures of respiratory function

Respiratory function was quantified as presence or absence of allergic respiratory phenotype, for respiratory disease; and using spirometry, for lung health.

#### 2.2.3.1 Spirometry protocol

Spirometry was performed at the 15-year followup during the physical exam. Subjects were seated, wearing nose clips and after 15 minutes' acclimation to the indoor environment, in line with recommendations [41]. Subjects performed at least three but not more than eight trials per test to obtain optimal flow-volume curves. Quality guidelines [41] and visual inspection by physicians were applied to exclude manoeuvres incorrectly performed or with artefact (for more details see [42]. Indices measured were forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, peak expiratory flow (PEF) and mid-flow rates (forced expiratory flow in the first 25%, 50%, 75%, and between 25-75%, of FVC (FEF25, FEF50, FEF75, and FEF2575.) Z-scores based on reference values [43] were also considered where available. If subjects consented, bronchodilator response (BD) was measured and defined as in [41], namely an increase in FEV1 or FVC of at least 12% and/or 200 mL after inhalation of salbutamol.

#### 2.2.3.2 Definitions of allergic respiratory phenotype

Respiratory allergy was quantified as asthma; allergic rhinitis; atopic sensitization to aero-allergens; current wheezing; and current symptoms of rhinoconjunctivitis.

- **Asthma:** Current asthma at 15 years was defined as in [44]: yes if the child had at least two of the following: doctor diagnosis of asthma ever between age 3-15, current wheezing at 15 years of age, and asthma medication at 15 years of age.
- **Rhinitis:** Rhinitis was defined as a doctor diagnosis of either allergic rhinitis or hayfever at any time in the past year. Models of rhinitis excluded children with current asthma or asthma medication.
- **Atopic aero-allergen sensitization:** Atopic aero-allergen sensitization was defined as any sensitization to aero-allergens compared with none, defined as at least one RAST positive (IgE ≥0.35 kU/l) for the following airborne allergens: birch, mugwort, ambrosia, grass, rye, dogs, cats, dust mites *(Dermatophagoides pteronyssinus)* and indoor mold (*Cladosporium herbarum*). Models of aero-allergen sensitization excluded children with current rhinitis or asthma, or current medication for rhinitis or asthma.

### 2.2.4 Analyses

#### 2.2.4.1 PA levels and domains

The first stage of this thesis characterized PA levels and domains within the accelerometry cohort. These domains were transportation to school, school sport, school outside sport, leisure-time sport, and other time. Particular importance was paid to dedicated sporting time since it is the most common intervention suggested to increase PA, and the most common outcome in studies of self-reported PA.

The first publication [32] profiled leisure-time sport in GINIplus and LISAplus. Children who participated in leisure-time sport during accelerometry were compared to those who did not, in order to establish potential selection bias such as self-selection or differential sport access. We then calculated engagement (fraction of time in accelerometrically-monitored moderate, vigorous and moderate-to-vigorous PA (MPA, VPA, MVPA)) in different sports and considered whether team sports differed nonrandomly from individual sports. Correlates considered were as above, except that gender was now a correlate of interest.

The second publication [33] profiled PA levels in five non-overlapping domains (school sport, leisure-time sport, school, transportation, and all other time) in determining sedentary behavior, light activity, MPA, VPA and MVPA for boys and girls during all waking time. We calculated percent time in each activity level for each domain, calculated the importance of different domains in determining total MVPA and VPA, and assessed selection bias for school sport and leisure sport.

#### 2.2.4.2 Associations between PA and respiratory health (spirometry)

The third publication [35] assessed the association between PA and incremental improvements in lung volumes and flows as measured by spirometry, in the absence of known lung comorbidity (asthma or smoking.) In order to determine which part of the airway was most markedly different between active and inactive children, all lung volumes and flows (FEV1, FVC, FEV1/FVC, PEF, FEF25, FEF50, FEF75, and FEF2575) were kept separate from each other; for similar reasons, MPA and VPA were modeled separately and in addition to MVPA.

As PA measures we considered daily minutes of MPA, VPA, and MVPA, as well as sport participation was as an indicator of active lifestyle. We also considered activity regularity, as the fraction of days the subject achieved at least 30, 45 or 60 minutes MVPA; and checked for nonlinear effects by modeling quintiles of MPA, VPA and MVPA.

Spirometric indices were treated as independent variable in all models. All were corrected for known confounders of lung function such as early-life exposures, and sensitivity analyses considered spirometric Z-scores as outcome in addition to raw values.

#### 2.2.4.3 Associations between PA and respiratory disease (allergy)

The fourth publication [34] extended the previous work to the relationship between PA and allergic respiratory phenotype such as asthma and rhinitis. It is known that allergic respiratory phenotype is often associated with lower PA, but measures of both allergy and PA are poorly defined and often not adequately separated from each other. Thus existing research cannot separate the relationships with rhinitis from those with asthma or other allergic manifestation such as wheezing or atopic sensitization (here “atopy”). They also cannot assess the relative importance of different potential drivers of the relationship, such as activity-limiting symptoms (perhaps most strongly associated with VPA) or deliberate avoidance of sport by children with allergic diagnoses (perhaps most strongly associated with sport participation.) Thus we ran separate models for each measure of PA and allergy: no model contained more than one measure of allergy or PA. PA was treated as independent variable in all models. Daily minutes MPA and VPA were log-normally distributed, and sport participation was binary.

To separate the effects of asthma, rhinitis, and atopic sensitization (atopy) we divided the population into four mutually-exclusive groups. Children with asthma were one; of the remainder those with allergic rhinoconjunctivitis were another; of the remainder, those with atopy were the third group; and the fourth was lung-healthy and served as a control. Each group was compared pairwise only to controls. To assess symptoms (wheezing (asthma symptom) and nose / eye itching (rhinitis symptom)) we compared all children with the symptom, to all children without it.

## 2.3 Results:

### 2.3.1 PA levels and domains:

The first publication [32] found that boys and girls were equally likely to participate in leisure-time sport; that high BMI was weakly negatively associated with participation; and that engagement varied between sports from a low of 6% of sporting time in MVPA to a high of 74%. Boys and girls who had sport were more active than those who did not, but only on the days with sport: the increased activity on sporting days did not spill over into non-sporting days, but there was also no apparent compensation. Others have found similar effects. It is also worthwhile to note that girls and overweight children participated in sport at the same level, or almost the same, as the rest of the population; thus selection bias is not a given.

Girls averaged about 20% of sporting time in MVPA (“engagement”), and boys about 30%, but within-subject and within-sport variation was large. Boys had higher engagement in team sport, but girls had higher engagement in individual sport, an effect that was not driven by any single sport. These findings are consistent with the Köhler effect, where athletes (males are more often sampled) perform better when on a team than alone. However, our research also confirms recent findings [45] that female athletes may also adjust their performance downward to match peers. In order to minimize the harm done to female athletes, designers of interventions should consider this effect when deciding which sports to offer and how to assign team membership.

The second publication ([33]: *Physical activity levels and domains assessed by accelerometry in German adolescents from GINIplus and LISAplus*) quantified total PA and its allocation by domain. In it we found that less than half of total MVPA took place in those domains usually considered to contribute to PA, namely school sport, leisure sport, and transportation; however, school sport and leisure sport contributed disproportionately larger shares of VPA. School outside school sport was the most sedentary part of the day. MVPA allocation by domain was very similar between the sexes. Aside from the well-known conclusion that PA levels in the developed world are generally too low, we found that gender differences in sport participation are not always present; that active transportation can contribute significantly to total MVPA; and that sport is disproportionately important in its contributions to total VPA. Since sport participation was already high, interventions in this cohort may focus on reducing sedentary time in school since being sedentary is an independent risk factor for hypokinetic disorders, and on further encouraging and enabling active transportation.

### 2.3.2 Associations between PA and respiratory health:

The third publication (abstract published as[46]; paper as [35]; *Physical activity is not associated with spirometric indices in lung-healthy German youth*) found no consistent association between any spirometric index and any PA measure, although post hoc tests suggested possible weak associations between FVC and the lowest MVPA levels (either the bottom quintile compared to all the others, or the fraction of days the subject got at least 30 minutes MVPA). Sport participation was not associated with spirometry. Results were consistent across models. While in this cross-sectional design causation cannot be tested, if there is a positive relationship between accelerometrically-measured PA and spirometric indices in this cohort then it is either very small (<2 mL/min MVPA/day), mediated by asthma (excluded from the current study), or hidden by a crossover interaction.

We conclude that in this cohort, there is no tendency for active children to have larger lungs or faster flows (or for children with larger lungs or faster flows to be more active.) Previously found effects may have been due to confounding such as by disease, ceiling effects, floor effects, or publication bias: had we presented only the relationship between FVC and MVPA it would have been of borderline statistical significance. It is also possible that one-week accelerometry did not adequately capture the PA outcome of interest.

### 2.3.3 Associations between PA and respiratory disease (allergy):

The fourth publication ([34]; *Asthma and rhinitis are associated with less objectively-measured moderate and vigorous physical activity, but similar sport participation, in adolescent German boys: GINIplus and LISAplus cohorts*) found that allergic diagnoses were associated with low PA, but only in boys; and that neither symptom avoidance nor differential sport participation could explain the difference. Asthma was associated with about 30% less VPA, and both asthma and rhinitis with about 10% less MPA. Aero-allergen sensitized children did not differ in any PA measure from controls. Symptoms (wheezing and nose/eye itching) were prevalent in children with asthma and/or rhinitis, although most children with a diagnosis were receiving treatment for it. Asthmatic girls were likelier to wheeze and to be untreated than asthmatic boys. However neither symptom was associated with either PA or sport, and no diagnosis was associated with sport.

We concur with the literature that asthma has sex-specific associations with low PA, but add that this is not necessarily due to less participation in sport by these children. Rhinitis also has a small independent relationship with MPA, as has been previously shown.

## 2.4 Limitations:

Limitations of this research fall into four major groups. These are population applicability; limitations of accelerometry; cross-sectional design; and sample size.

### 2.4.1 Population applicability

This study samples the 15-year followup of two birth cohorts drawn from two study centers in Germany, coming from generally prosperous backgrounds. Followup introduced further bias, tending to oversample girls and those from highly-educated families. Children who completed accelerometry differed from the 15-year followup in many of the same ways as the followup did from the birth cohort. Furthermore both school sport and medical insurance are compulsory for most Germans, and both active transportation and sport are generally well accepted. As a result our findings do not generalize to all populations.

### 2.4.2 Limits of accelerometry

Accelerometry is a one-week snapshot of acceleration as indicator of body movement, measured in and diaried by a subject who knows he is being measured. While we made efforts to exclude atypical days (e.g. sickness, travel away from home) some observer bias is inevitable. Accelerometry is also designed mostly to measure ambulatory movements such as walking and running: it is known to undermonitor activities with low acceleration such as weight training (only 6% of time in weight training appeared to be MVPA, according to the accelerometer). Thus if strength, flexibility or complex body movements are disproportionately important to lung function, accelerometry will not capture it. However, physical fitness is fundamentally multifactorial and no single measurement can be expected to capture it.

### 2.4.3 Limits of cross-sectional design

Causation cannot be established in a cross-sectional study. It cannot be determined from our data whether boys with allergy are less active, whether preferentially inactive boys develop allergy, or whether the observed effect is due to unobserved confounding. Likewise, we cannot determine whether overweight children prefer to avoid sport or whether inactive children tend to become overweight. Even the observed null relationship with spirometry may conceivably be confounded by crossover interactions.

### 2.4.4 Sample size

Lastly, sample size is always a concern: we cannot prove any null association, only estimate how large an effect we may have missed. The decreased MPA and VPA among boys with asthma, and MPA with rhinitis, were near the detection limit for our sample, as was the estimated small relationship between MVPA and FVC (no longer significant after correction for multiple comparisons.) If replicated, these findings may be significant in a larger sample. However, they are similar in size to those found elsewhere and thus their size may be accurate.

Related to the issue of sample size is that of population applicability, detailed above. Although over 1400 children completed accelerometry, PA levels may have been consistently above or below those levels where PA is most strongly associated with spirometry. Indeed, the strongest association between PA and spirometry was that with the lowest level of MVPA, either the bottom quintile as compared to the others or the fraction of days in which at least 30 minutes MVPA was achieved. If this low level is a threshold above which benefits lessen, we may not have had sufficient power to detect it.

# 3 Conclusion and outlook

This thesis confirms the need for further increases in PA, even in a cohort where participation in sport is comparable between sexes and among children with and without different allergic respiratory diseases. Gender differences in engagement are worthy of further study, particularly the apparent discouraging effect of peers on girls in team sports, but not individual sports.

We demonstrate that traditionally inactive groups (girls, children with asthma, overweight children, and those with lower social status) can participate in sport at the same level as their peers: however, sport participation alone may not be sufficient to close the gap in total PA. Therefore we emphasize the contributions of all PA domains to total activity. Only 20% of total MVPA in this cohort was accumulated during leisure sport, and about 5% more during school sport: over half took place during "other time." Sport was disproportionately important for VPA, but still made up a minority. Encouraging children to be active at leisure, outside of organized sporting activities, has potential to add significantly to total PA. Likewise, school was the most sedentary part of the day, and some evidence suggests sedentary time as an independent risk factor for cardiometabolic dysfunction. It may therefore be worthwhile to prioritize tolerance for activity (either during class or at breaks) as a health intervention.

Our estimated null association between spirometry and accelerometric PA confirms that the PA levels of healthy people are generally not pulmonary limited, and that associations found in other populations may be due to anthropometric or sociodemographic confounding. However, it is also possible that the "snapshot" nature of accelerometry prevented it from capturing the PA variable of interest, and that other measures of PA and/or fitness should be considered independently of accelerometry.

Lastly, we confirm that even in this healthy cohort boys with asthma are less active than those without asthma, and this association cannot be explained by either symptom exacerbation or avoidance of sport. It has been suggested that active or fit children are protected against asthma development, and we encourage others with longitudinal data to explore this pathway. If it is supported by evidence, the need to increase PA in healthy children becomes particularly acute given the ongoing epidemic of allergy.

Taken together, this thesis demonstrates that physical activity is not necessarily lower in traditionally vulnerable groups within the general population. We observed comparable or higher sport participation in girls, the overweight, and those with allergic respiratory diseases; and neither overweight nor allergic symptoms was convincingly associated with inactivity. Furthermore, variations in normal spirometry did not affect PA. Thus we suggest that hypokinetic lifestyle in vulnerable groups is not a given, but can be remedied with targeted interventions.

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# 6. Publications included in thesis

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Smith, MP; von Berg, A; Berdel, D; Bauer, CP; Hoffmann, B; Koletzko, S; Nowak, D; Heinrich, J; Schulz, H. Physical activity is not associated with spirometric indices in lung-healthy German youth. European Respiratory Journal 2016;47 (4).

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PLOS | ONE

RESEARCH ARTICLE

# Sport Engagement by Accelerometry under Field Conditions in German Adolescents: Results from GINIPlus

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**Data Availability Statement:** Data are from the GINIPlus study, which includes patient-specific information. Previous work with this cohort has been published in PLOS (Physical Activity in German Adolescents Measured by Accelerometry and Activity Diary: Introducing a Comprehensive Approach for Data Management and Preliminary Results; Pfitzner et al, 2013) and the same conditions apply. Interested researches will obtain a de-identified, participant level dataset for the data pertaining the current study requiring ethical approval. Requests should be addressed to the corresponding author Holger Schulz ( schulz@helmholtz-muenchen.de).

## Abstract

### Introduction

Sporting activities differ in their ability to promote moderate-to-vigorous physical activity (MVPA). To assess adolescents' engagement in sport under field conditions we used accelerometers to measure their MVPA levels during sport. We pay special attention to differences between team and individual sport and between common sports.

### Methods

Diary data and 7-day accelerometry from 1054 Germans ages 15–17 were combined to measure physical activity. 1373 diaried episodes of more than 40 common sports were identified from 626 participants and grouped into team and individual sport. We modeled the effect of team and individual sport, and described levels of MVPA and episodes of no MVPA for all recorded sports.

### Results

German boys and girls averaged 43 (SD 21) and 37 (SD 24) minutes MVPA per day. Boys got 2.2 times as much MVPA per minute during team compared to individual sport ($p<0.0001$) but there was no significant difference for girls. Percent of time spent in MVPA during sport ranged from 6% for weight training to 74% for jogging, with individual sports averaging 10–30% and team sports 30–50%. 11% of sport episodes had no MVPA: half of episodes of cycling, 5% of jogging, and none for tennis or badminton. An episode of individual sport was 17 times more likely to have no MVPA than an episode of team sport ($p<0.0001$).

### Conclusion

Under field condition, adolescents were active for only a fraction of diaried sporting time. As measured by accelerometry, individual sport often produced no MVPA. Characteristics of

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the sport, such as team vs. individual, were more predictive of MVPA than were characteristics of the participant, such as background activity levels.

## Introduction

Physical activity (PA) is known to reduce morbidity and mortality from noncommunicable disease; however, it is generally accepted that many youth are not sufficiently active [1–3]. Since activity habits tend to persist into adulthood [4] and activity declines sharply at adolescence [5], late childhood is a critical period for assessment and targeted intervention [6].

Activity in children and adolescents is generally summarized in minutes of moderate-to-vigorous physical activity (MVPA) per day or week. A typical goal is 60 minutes of MVPA per day [3, 7, 8]. Estimates of compliance levels vary between studies [3, 5] but most studies[9] agree that further increases would be beneficial. Leisure sport is a common intervention to increase MVPA, but the amount of MVPA associated with various sports under field conditions is not completely understood.

Estimates of physical activity levels for different activities are available, which typically are based on metabolic rate assessed by double-labelled water and/or indirect calorimetry [10] and are generally understood as the gold standard of activity assessment. However, laboratory measurements are not directly applicable to field conditions. One obvious difference is that not all dedicated sporting time is spent active: depending on the environment, a large fraction of sporting time may be spent during instruction, waiting one's turn or otherwise not engaged in the activity. Estimates for the fraction of young people's leisure sport time spent active range from 13% [11] to under 50% [12] up to 77% [13]. School sport has been better studied than leisure sport, [12] with estimates typically from 20–40% of class time in MVPA, compared with 15–26% for administrative and management tasks. [14] Simply multiplying laboratory-estimated metabolic equivalents by diaried sport time is thus likely to overestimate the amount of MVPA sport participants receive, and likely contributes to the discrepancy [3] between self-reported and objectively measured activity. This large and flexible discrepancy is likely to impede research into the correlates of activity and distort its apparent effects.

In this study we combine diary data on type of sport with accelerometric measurements of physical activity, in order to calculate how much time participants spend in MVPA for a given period of sport. This fraction is a common measure in studies of sport engagement [12, 15], both within and between groups[1, 16]. Thus, our data allow us to compare the percentage of time adolescents are in MVPA for both team and individual sports under field conditions, and to assess differences in engagement between sports.

Our specific goals in this study are:

- To characterize adolescents with and without leisure sport, evaluate the strength of self-selection in determining sport participation, and compare activity on days without sport in order to specifically test the hypothesis of compensation;
- To evaluate predictors of the fraction of leisure-sport time spent in MVPA, with special attention paid to team vs. individual sport and the distinction between predictors of high MVPA and no MVPA;
- To assess the engagement of adolescents in sport under field conditions by objectively measuring the fraction of time in MVPA for various sports.

## Methods

### Study population

Measurements of physical activity (PA) by accelerometry were embedded in the 15-year follow-up of the "German Infant Nutrition Intervention Programme PLUS environmental and genetic influences on allergy development" (GINIPlus). GINIPlus is an epidemiological study, not a clinical trial, and as a result it is not registered at the ISRCTN or ClinicalTrials.gov. Participants were drawn from both nutrition-interventional and observational arms. The GINI-plus study was approved by the local Ethics Committees, the Bavarian General Medical Council (Bayerische Landesärztekammer, Munich, Germany) for the study place Munich and the Medical Council of North-Rhine-Westphalia (Ärztekammer Nordrhein, Düsseldorf, Germany) for Wesel. The approval of the Ethics Committees includes the written consent procedure. Written informed consent was obtained from the parents or the legal guardian of all participants. The cohort and recruitment of the participants has been described in detail at the study website and elsewhere, including in PLOS One [16–18]. Briefly, of 5991 newborns enrolled, 3198 participated in the 15-year followup (53%). Of these, 1890 (59%) consented to accelerometry, of whom 1247 (66%) completed successfully and returned the device. Of these, 1054 (85%) provided data of acceptable quality for inclusion, and 626 participated in sport that could be assigned as "team" or "individual" (for definitions see below).

### Accelerometry

Accelerometers (ActiGraph GT3X, Pensacola, Florida) were worn on the dominant hip for 7 days. Activity on measurement days was recorded in an activity diary using a detailed schedule, including time of going to bed, getting up from bed, time and reason of removing the monitor, and leisure-time sport activities, including type of sport. One episode of sport was defined as the time between starting and finishing an episode of dedicated sporting time. It was possible, though uncommon (6.3%), for participants to have two sporting episodes in a single day. The diary does not distinguish between warmups, practice and games. We find it plausible that among participants who passed our stringent data-quality checks, errors in recording time of starting and finishing sport are random and do not correlate with the type of sport.

At least 10 hours of activity recording (weekday) or 7 (weekend) were required for a valid day: at least 3 weekdays and one weekend day were required for valid data. Levels of PA were assigned according to Freedson's [19] uniaxial cutoffs into four categories—sedentary, lifestyle, moderate, and vigorous activity—on a minute-by-minute basis during waking hours. MVPA is the sum of moderate and vigorous activity. For detailed description of accelerometer protocol, quality control, and data cleaning, see Supporting Information (S1 File) and [16, 20].

Engagement was defined as the percentage of diaried sporting time where the accelerometer indicated that the child was in MVPA, which has been well studied for school physical education, [12] but not as well for leisure sport [11, 13] and hardly at all as a function of participant-level characteristics such as gender, age, body mass index and location (study center; urban Munich or rural Wesel). Particular attention was paid to activity on non-sporting days as an indicator of baseline activity level. Initial analyses were stratified by gender and by team status of the sporting episode, and then combined into a single model with interaction terms as needed.

### Team Sport

In line with the literature, [21] *team* was defined as all sports where participants directly interact with each other, including interaction with opponents as well as teammates. All sports observed and their status as team or individual are listed in Results.

Preliminary analyses found that leisure-sport participants often received no MVPA at all during an episode of sport, requiring this "zero MVPA" to be accounted for statistically. Further analyses found that episodes with zero MVPA appeared to be a phenomenon distinct from those with low MVPA, and that team and individual sport differed significantly in their rate of zero MVPA.

## Statistical analysis

Values were provided as mean plus/minus standard deviation unless otherwise stated; for skewed variables 5$^{th}$ and 95$^{th}$ percentiles were also provided. Comparisons between individual participants (Table 1) were based on Wilcoxon's two-tailed rank-sum test; comparisons

**Table 1. Participants by Sport Participation (Mean, SD).**

| Predictor | All participants (N = 1054)[1] | | Participants with diaried sport (N = 626) | | P for difference between those with and without diaried sport[2] | |
|---|---|---|---|---|---|---|
| | Boys | Girls | Boys | Girls | Boys | Girls |
| Male (N, %) | 475 (45) | | 263 (42) | | 0.016 | |
| Age (years) | 15.7 (0.55) | 15.7 (0.54) | 15.7 (0.55) | 15.7 (0.55) | 0.14 | 0.37 |
| Parents highly educated (%)[3] | 64 | 66 | 68 | 69 | 0.052 | 0.17 |
| From Munich (urban) | 57 | 50 | 58 | 46 | 0.64 | 0.027 |
| BMI (kg/m$^2$) | 20.7 (3.2) | 21.0 (2.9) | 20.5 (3.0) | 21.1 (2.9) | 0.40 | 0.50 |
| BMI category (%)[4] | | | | | | |
| Underweight | 9.74 | 6.25 | 9.88 | 4.70 | 0.98 | 0.048 |
| Normal | 79.0 | 85.2 | 80.2 | 85.9 | 0.45 | 0.84 |
| Overweight | 8.66 | 5.21 | 7.91 | 6.35 | 0.48 | 0.10 |
| Obese | 2.60 | 3.30 | 1.98 | 3.04 | 0.33 | 0.66 |
| Overweight + obese | 11.0 | 8.51 | 9.88 | 9.39 | 0.26 | 0.31 |
| Activity on all days (min): | | | | | | |
| Sedentary[5] | 586 (81) | 598 (69) | 584 (75) | 593 (63) | 0.39 | 0.0016 |
| Lifestyle[5] | 259 (60) | 247 (51) | 261 (56) | 253 (50) | 0.29 | <0.0001 |
| Moderate[5] | 29.6 (13) | 26.0 (15) | 32.1 (13) | 26.6 (14) | <0.0001 | 0.00077 |
| Vigorous[5] | 13.0 (11) | 10.8 (11) | 15.2 (11) | 11.5 (9.3) | <0.0001 | <0.0001 |
| MVPA[5] | 42.6 (21) | 36.8 (23) | 47.3 (20) | 38.2 (20) | <0.0001 | <0.0001 |
| Total vertical counts, thousands | 327 (117) | 296 (131) | 352 (108) | 309 (111) | <0.0001 | <0.0001 |
| % days with > 60 minutes MVPA | 25 (23) | 17 (22) | 31 (23) | 19 (21) | <0.0001 | <0.0001 |
| Activity on non-sport day [6] (min)[5] | | | | | | |
| Sedentary[5, 6] | 596 (87) | 610 (77) | 601 (87) | 610 (76) | 0.13 | 0.73 |
| Lifestyle[5, 6] | 251 (63) | 238 (55) | 248 (60) | 240 (57) | 0.26 | 0.24 |
| Moderate[5, 6] | 25.9 (13) | 23.3 (15) | 25.9 (13) | 22.5 (13) | 0.87 | 0.33 |
| Vigorous[5, 6] | 9.94 (9.9) | 7.85 (11) | 10.1 (9.6) | 6.90 (7.2) | 0.50 | 0.18 |
| MVPA[5, 6] | 35.8 (20) | 31.1 (23) | 36.0 (20) | 29.4 (18) | 0.59 | 0.23 |
| Total vertical counts, thousands | 288 (111) | 257 (128) | 287 (103) | 250 (98.2) | 0.83 | 0.89 |

1) Cohort previously described in[20]; subset described in [23]

2) Wilcoxon rank-sum test, two-sided

3) Based on maximum of mother and father; 1 if university entrance or higher, 0 otherwise.

4) Based on sex- and age-specific percentiles in[22]; expected percentages would be 10% underweight, 7% overweight, and 3% obese.

5) Activity levels as described in [24]. MVPA is moderate or vigorous.

6) 9 participants (1.4%) had sport every day and are thus excluded from these summary statistics

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between sport episodes (Tables 2 and 3) used repeated-measures regression to account for within-child correlation. For all analyses statistical significance was assumed at $p<0.05$. The fraction of sporting time spent in MVPA was modeled both as a binary "any MVPA versus none" and as a rate (minutes in MVPA / total diaried sporting time, when the episode had any MVPA). This separation was statistically necessary and also turned out to be clinically relevant.

As predictors of engagement we considered the typical factors of age, gender, socioeconomic status (parental education), BMI and BMI category, as well as urban vs. rural location and length of the sporting episode. Many of these are known to correlate with activity levels; location may predict baseline activity, total activity, and/or the specific sporting activities available.

Sociodemographic data, such as parental education and study center, were obtained from questionnaires. As a proxy for socioeconomic status, the maximum of mother's and father's education above college entrance when the child was 3 years old (binary yes-no) was modelled as a single predictor: it was kept in the model for consistency with other work with this cohort regardless of statistical significance. Height and weight were generally obtainable from physical examination (n = 964 out of a total of 1054), but when this was missing, self-reports were used. Among participants with both self-reported and objective measures, correlation between the two was very strong: 0.92 for weight and 0.95 for height. Only complete cases were analysed. In addition to its linear effect, BMI was categorized into *underweight*, *normal*, *overweight*, or *obese* according to German reference values [22] for the $10^{th}$, $90^{th}$, and $97^{th}$ percentiles of BMI for age and sex in the reference population.

Because of possible crossover interactions initial analyses were stratified by team status of the episode, and then combined in a single model with interaction terms as necessary.

## Results

### Study population

1054 individuals (45% male) participated in accelerometry, and 626 (42% male) participated in a total of 1373 diaried episodes of leisure sport. Characteristics of the study population and differences between those with diaried leisure sport and the rest of the cohort providing accelerometric data are described in Table 1.

Participants with diaried sport were more active than the cohort average, with higher levels of total vertical counts, moderate, vigorous, and MVPA; differences for MVPA were 10.5% in boys and 3.8% in girls ($p<0.0001$). However, this difference appeared to be entirely due to the presence of leisure sport itself because on days without diaried sport activity neither moderate nor vigorous activity differed significantly between groups.

Anthropometric and sociodemographic differences between those with and without sport were small and clinically nonsignificant. Furthermore, the data reflect an almost uniformly high standard of living within the cohort, as 2/3 of participants had at least one parent who had entered college. Prevalences of overweight and obesity (expected values 7% and 3%) were typical for 2001, when the reference population was established, in spite of the well-documented rise in adiposity in Germany during this time. Accelerometry completers were also 55% female, more than the rest of the GINI cohort (49%). However, within this subgroup there was little further selection bias for diaried sport. All further analyses were limited to those participants with any diaried leisure sport.

### Team versus Individual Sport Episodes

Sporting participants are described in Table 1, while sporting episodes are described in Table 2 and shown in Fig 1. Most participants had only team sport (n = 213) or only individual sport (n = 332): only13% (n = 81) had both. Preliminary analyses found that the only significant

**Table 2. Team and Individual Sport Episodes (N = 1373 episodes, 626 participants).** 213 participants had only team sport; 332 had only individual sport; 81 had both.

| | Team (N = 559 episodes) | | | Individual (N = 814 episodes) | | | Differs between team and individual sport episodes? (p) | |
|---|---|---|---|---|---|---|---|---|
| | Boys | Girls | P for sex difference | Boys | Girls | P for sex difference | Boys | Girls |
| **Number of episodes** | 331 | 228 | — | 239 | 575 | — | — | |
| **Percent time in MVPA**[1, 2] | | | <0.0001 | | | <0.0001 | <0.0001 | 0.37 |
| Mean (SD) | 47.8 (22) | 33.2 (19) | | 21.2 (27) | 31.3 (29) | | | |
| $5^{th}$, $95^{th}$ percentile | 6.2, 80 | 3.3, 67 | | 0, 83 | 0, 91 | | | |
| **Percent time in MVPA when >0**[1, 2] | | | <0.0001 | | | <0.0001 | <0.0001 | 0.34 |
| Mean (SD) | 48.3 (21) | 33.7 (19) | | 27.5 (27) | 36.6 (28) | | | |
| $5^{th}$, $95^{th}$ percentile | 6.7, 80 | 3.4, 67 | | 1.7, 88 | 2.2, 93 | | | |
| **Episode had no MVPA** N, (%)[3] | 3 (0.91) | 3 (1.32) | 0.65 | 55 (23.0) | 82 (14.3) | 0.0024 | <0.0001 | <0.0001 |
| **Episode length, minutes**[1] | | | 0.19 | | | 0.26 | 0.25 | 0.0071 |
| Mean (SD) | 107 (54) | 101 (42) | | 96.4 (105) | 85.8 (79) | | | |
| $5^{th}$, $95^{th}$ percentile | 55, 195 | 60, 180 | | 15, 375 | 20, 225 | | | |
| **% of sporting time:** | | | | | | | | |
| **Sedentary**[1, 2, 4] | | | <0.0001 | | | <0.0001 | <0.0001 | 0.11 |
| Mean (SD) | 12.3 (14) | 17.8 (15) | | 28.1 (22) | 20.3 (20) | | | |
| $5^{th}$, $95^{th}$ percentile | 0, 40 | 1.7, 49 | | 0, 73 | 0, 60 | | | |
| **Lifestyle**[1, 2, 4] | | | <0.0001 | | | 0.44 | <0.0001 | 0.95 |
| Mean (SD) | 39.9 (19) | 49.0 (18) | | 50.7 (24) | 48.4 (23) | | | |
| $5^{th}$, $95^{th}$ percentile | 13, 77 | 20, 79 | | 6.7, 87 | 5.7, 85 | | | |
| **Moderate**[1, 2, 4] | | | <0.0001 | | | 0.024 | <0.0001 | <0.0001 |
| Mean (SD) | 27.0 (13) | 21.6 (13) | | 7.79 (9.2) | 10.1 (12) | | | |
| $5^{th}$, $95^{th}$ percentile | 4.5, 59 | 2.2, 44 | | 0, 27 | 0, 33 | | | |
| **Vigorous**[1, 2, 4] | | | <0.0001 | | | 0.0038 | 0.0026 | <0.0001 |
| Mean (SD) | 20.8 (18) | 11.6 (14) | | 13.4 (25) | 21.2 (27) | | | |
| $5^{th}$, $95^{th}$ percentile | 0, 51 | 0, 39 | | 0, 80 | 0, 88 | | | |
| **Total counts /minute, thousands** | | | <0.0001 | | | 0.018 | 0.0023 | 0.0002 |
| Mean (SD) | 24.8 (10) | 18.3 (8.4) | | 17.8 (23) | 23.5 (21) | | | |
| $5^{th}$, $95^{th}$ percentile | 8.6, 42 | 5.5, 34 | | 1.5, 81 | 2.2, 70 | | | |

P-values from generalized linear model, with child as repeated measure.

1) Negative-binomial distributed

2) Log total weartime as offset

3) Binary distributed

4) Activity levels as described in [24]. Team sport defined as any requiring interaction with other participants, in line with[21]

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difference between groups was gender: boys were more likely to do team sport, while girls were more likely to do individual sport. Therefore, all statistical models and tables are either stratified or corrected for the effect of sex.

On average individual sport had shorter episodes than team, by 15% for girls (p = 0.0066) and 10% for boys (not significant). There was no significant difference in episode length by sex, though girls averaged somewhat shorter episodes than boys in both team and individual sport.

Both sexes got more MVPA in team sport than in individual, though the difference was only significant in boys. Team sport produced 2.2 times as much MVPA per unit time than individual sport in boys (48% of diaried team-sport time was spent in MVPA, vs. 21% of

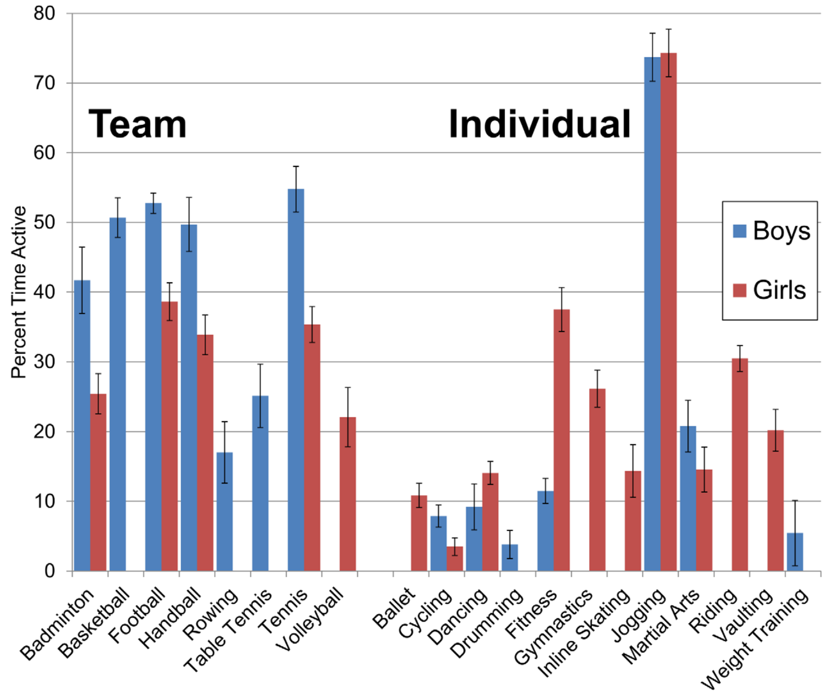


**Fig 1. Time in MVPA During Sport.** MVPA as determined in Freedson's accelerometric algorithm (Freedson et al 2005, #19). Sports shown if that sex had >10 episodes during recording. Error bars for standard error of the mean.

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individual, p<0.0001) but there was no significant difference for girls (33 vs 31%). When episodes with no MVPA were excluded, the difference between team and individual sport engagement shrank in boys to 1.76 (p<0.0001) and reversed in girls to 0.92 but remained nonsignificant. Boys in team sport got more MVPA in a given time than girls (48% vs 33%, p<0.0001) but the reverse was true in individual sport where girls were more active (31% vs 21%, p<0.0001). This remained true when episodes with no MVPA were excluded. However, both sexes got more MVPA in team sport than in individual though the difference was only significant in boys.

Individual sport had many more episodes with no MVPA: 55/239 (23%) and 82/575 (14%) of individual-sport episodes had no MVPA for boys and girls, while 3/331 (0.91%) and 3/228 (1.3%) episodes of team sport did. The difference between the rate of episodes with no MVPA in team and individual sport was highly significant (p<0.0001); so is the sex difference in the rate of zero-MVPA episodes within individual sport, though not team sport.

For both sexes, individual sport produced more variable levels of MVPA than team sport. The coefficient of variation was 1.27 for boys in individual sport, compared with 0.46 in team sport, and 0.93 for girls in individual sport compared with 0.57 in team sport. This observation was confirmed when comparing the 5$^{th}$ and 95$^{th}$ percentiles for percentage time in MVPA, which are wider for both sexes in individual sport than in team. These were 3.3% and 67% for girls in team sport, and 0% and 91% in individual sport. When sport episodes with no MVPA were excluded, the percentiles for girls in individual sport were 2.2% and 93%. Comparable results were obtained in boys.

In summary, objective assessment of sports under field conditions showed that team sport generally produced more MVPA per unit time than individual sport in both sexes, clearly in boys but less so in girls. However, the typical effect of gender was reversed in individual sport: girls got more MVPA in individual sport than boys did, and boys had more episodes with no MVPA. Individual sport was more likely than team sport to have episodes with no MVPA, and MVPA levels were more variable in individual sport even when episodes with no MVPA were excluded.

## Multivariable Predictors of Leisure Sport Engagement

Initial models of MVPA during leisure sport episodes were stratified by gender of the child and team status of the episode, but we found that within-child predictors were weak and generally homogeneous between team and individual sport and between sexes. Thus, a combined analysis for multivariable predictors of time spent in MVPA during sport episodes was performed (Table 3) in order to directly estimate the effects of gender and team sport. In the combined model, parameter estimates did not change significantly from the stratified models.

Vigorous and lifestyle activity on non-sporting days did not significantly predict sport engagement in either sex, although moderate activity did: each 10 minutes of daily moderate activity per day was associated with an average 4% increase in MVPA level during sport. (RR 1.04, p = 0.0075). No sociodemographic or anthropometric predictor was significant, except study center (RR = 0.85 for study center Munich, p = 0.0028). Leisure-sport engagement was not significantly predicted by age, BMI whether linear or categorical, parental education level (socioeconomic status), or episode length. MVPA levels in girls did not differ significantly between team and individual, but in individual sport boys had 23% lower MVPA than girls

**Table 3. Multivariable Predictors of MVPA in Sport, All Episodes.**

| Predictor | Predicts fraction of sport time in MVPA, when MVPA>0 N = 575 participants, 1183 episodes | | Predicts risk that MVPA = 0 N = 626 participants, 1373 episodes | |
|---|---|---|---|---|
| | Rate ratio % | P | Odds ratio | P |
| Intercept (baseline) | 20 | 0.033 | 0.078 | 0.40 |
| Age, years | 103 | 0.49 | 1.11 | 0.58 |
| Study center Munich | 85 | 0.0028 | 0.89 | 0.62 |
| Parental education[1] | 107 | 0.29 | 0.936 | 0.79 |
| Male | 77 | 0.0075 | 1.82 | 0.0072 |
| Episode length, 10 minutes | – | – | 0.89 | 0.0015 |
| Activity on nonsport days, 10 minutes | | – | | |
| **Moderate** [2] | 104 | 0.0075 | – | – |
| Vigorous[2] | N/A | N/A | – | – |
| Moderate*Male[2] | N/A | N/A | – | – |
| Vigorous*Male[2] | N/A | N/A | – | – |
| **Team sport**[3] | N/A | N/A | 0.0596 | <0.0001 |
| **Team[3]*Male** | 181 | <0.0001 | N/A | N/A |

1) Binary: 1 if better-educated parent entered college, 0 if not.

2) Activity levels as described in [24]. MVPA is moderate or vigorous physical activity and refers to non-sporting days only. Participants with sport every day (9, 1.4%) are missing.

3) Team sport defined as any requiring interaction with other participants, in line with [21]

N/A = P $\geq$0.05 so predictor was removed from the model.,— = not included in initial model

Predictors above the double line (age, study center, parental education, and gender; episode length when predicting zero MVPA, but not when predicting nonzero MVPA) left in model regardless of statistical significance. Nonzero MVPA modeled with negative binomial regression with log of total sporting time as offset, zeroes with logistic regression, both with child as a repeated measure.

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(rate ratio 0.77, p = 0.0075). However, boys in team sport still had significantly more MVPA than girls in team sport because male gender interacts significantly with team sport (rate ratio for male*team interaction 1.81, p<0.0001)

## Predictors of Sport Episodes with No MVPA

An episode of individual sport was 17 times as likely to have no MVPA as one of team sport (Table 3, odds ratio 0.0596 for team sport as compared with individual; p<0.0001). Other risk factors that an episode would have no MVPA were male gender (OR 1.82, p = 0.0072) and short episodes of sport (OR = 0.89 per 10 minutes, p = 0.0015). Sociodemographic predictors (age, parental education and study center) had no effect.

## Estimates of MVPA from Specific Sports

Table 4 presents average fraction of time participants spent in moderate, vigorous and MVPA for all sports in our sample that had 10 or more episodes for at least one sex, including episodes with no MVPA. The remaining sports are in Table 5. "Martial arts" in Table 4 is the combination of judo, karate, aikido and taekwondo. Sex-stratified averages are presented in Fig 1. All

**Table 4. Engagement in Sports with 10 or More Episodes for at Least One Sex.**

| Sport | Episodes (number) | | | Episode length, minutes | Percent time in | | | Counts per minute, hundreds | Sex with more MVPA per unit time |
|---|---|---|---|---|---|---|---|---|---|
| | Zero MVPA | Boys | Girls | | Moderate | Vigorous | MVPA | | |
| **Individual** | | | | | | | | | |
| Ballet | 0 | 0 | 15 | 76 | 6 | 4 | 10 | 8.84 | – |
| Cycling | 49 | 43 | 47 | 64 | 4 | 2 | 6 | 6.44 | Boys |
| Dancing | 20 | 17 | 94 | 98 | 8 | 4 | 14 | 9.94 | Girls |
| Drumming | 7 | 13 | 0 | 52 | 4 | 0 | 4 | 2.82 | – |
| Fitness | 18 | 56 | 88 | 70 | 10 | 16 | 26 | 16.9 | Girls |
| Gymnastics | 1 | 4 | 23 | 120 | 16 | 12 | 28 | 17.2 | Boys |
| Inline Skating | 9 | 6 | 35 | 78 | 12 | 2 | 12 | 9.01 | Girls |
| Jogging | 5 | 28 | 67 | 36 | 8 | 66 | 74 | 58.3 | Girls |
| Martial Arts | 4 | 13 | 15 | 84 | 10 | 6 | 18 | 12.9 | Boys |
| Riding | 5 | 1 | 123 | 100 | 8 | 22 | 30 | 27.2 | Boys (only one) |
| Vaulting | 0 | 0 | 14 | 118 | 10 | 10 | 20 | 15.3 | – |
| Weight Training | 4 | 12 | 5 | 74 | 4 | 2 | 6 | 5.80 | Boys |
| **Team** | | | | | | | | | |
| Badminton | 0 | 12 | 26 | 92 | 20 | 10 | 30 | 17.8 | Boys |
| Basketball | 1 | 41 | 10 | 102 | 24 | 26 | 50 | 26.7 | Boys |
| Football (soccer) | 1 | 152 | 53 | 100 | 26 | 22 | 50 | 24.9 | Boys |
| Handball | 1 | 26 | 35 | 100 | 24 | 16 | 40 | 21.2 | Boys |
| Rowing | 0 | 15 | 1 | 130 | 10 | 8 | 18 | 14.7 | Girls (only one) |
| Table Tennis | 2 | 19 | 10 | 124 | 18 | 4 | 22 | 14.1 | Boys |
| Tennis | 0 | 44 | 43 | 82 | 32 | 14 | 46 | 22.1 | Boys |
| Volleyball | 1 | 7 | 23 | 132 | 18 | 6 | 24 | 13.9 | Boys |

Activity levels as described in[24]. MVPA is moderate or vigorous. Moderate + vigorous may not sum to MVPA because of rounding. Team sport defined as any requiring interaction with other participants, in line with [21].

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**Table 5. Engagement in Sports with 9 or Fewer Episodes for Both Sexes.**

| Sport | Episodes, count | | | Episode length, minutes | Percent time spent in | | | Vertical-axis counts per minute, hundreds | Sex with more MVPA per unit time |
|---|---|---|---|---|---|---|---|---|---|
| | Zero MVPA (total) | Boys | Girls | | Moderate | Vigorous | MVPA | | |
| **Individual** | | | | | | | | | |
| Aikido | 0 | 2 | 1 | 74 | 10 | 8 | 16 | 12.9 | Boys |
| Archery | 4 | 6 | 2 | 112 | 2 | 0 | 2 | 4.08 | Boys |
| Boxing | 0 | 3 | 0 | 64 | 18 | 30 | 48 | 27.9 | Boys |
| Cross-Country Skiing | 0 | 1 | 0 | 52 | 46 | 6 | 52 | 22.4 | Boys |
| Golf | 0 | 2 | 0 | 176 | 24 | 18 | 42 | 21.7 | Boys |
| Hiking | 0 | 0 | 6 | 366 | 52 | 6 | 58 | 20.5 | – |
| Ice Skating | 1 | 3 | 4 | 128 | 8 | 2 | 10 | 9.64 | Boys |
| Judo | 1 | 1 | 0 | 2 | 0 | 0 | 0 | 7.19 | Boys |
| Karate | 0 | 3 | 4 | 90 | 16 | 6 | 22 | 14.1 | Boys |
| Nordic Walking | 0 | 0 | 1 | 50 | 2 | 88 | 90 | 55.6 | – |
| Shooting | 5 | 4 | 3 | 44 | 0 | 0 | 2 | 2.41 | Girls |
| Snowshoeing | 0 | 0 | 1 | 180 | 20 | 10 | 30 | 13.4 | – |
| Swimming | 0 | 0 | 1 | 74 | 4 | 0 | 4 | 3.02 | – |
| Trampoline | 1 | 4 | 2 | 54 | 4 | 40 | 46 | 65.6 | Boys |
| Walking | 1 | 3 | 9 | 96 | 24 | 8 | 32 | 15.3 | Boys |
| Yoga | 1 | 0 | 2 | 52 | 0 | 0 | 0 | 2.4 | – |
| Zumba | 0 | 0 | 4 | 52 | 26 | 10 | 36 | 20.3 | – |
| **Team** | | | | | | | | | |
| Baseball | 0 | 1 | 6 | 100 | 14 | 2 | 18 | 13.1 | Girls |
| Fencing | 0 | 0 | 4 | 158 | 6 | 6 | 10 | 8.72 | – |
| Fistball (“Faustball”) | 0 | 3 | 1 | 128 | 14 | 2 | 16 | 10.8 | Boys |
| Ice Hockey | 0 | 4 | 3 | 174 | 6 | 8 | 14 | 14.9 | Girls |
| Rugby | 0 | 0 | 3 | 120 | 14 | 18 | 32 | 17.7 | – |
| Scouting | 0 | 2 | 0 | 386 | 8 | 2 | 8 | 8.50 | Boys |

Activity levels as described in[24]. MVPA is moderate or vigorous. Moderate + vigorous may not sum to MVPA because of rounding. Team sport defined as any requiring interaction with other participants, in line with [21].

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values presented here include episodes with zero MVPA and are averaged across episodes of that sport, to better represent total time spent within that sport.

Engagement in individual sports was more variable than in team sports, making up both the largest and smallest fractions of time in MVPA in the sample. During ballet, cycling, drumming, and weight training about 4–10% of time was spent in MVPA while fitness training, gymnastics, and riding produced between 20 and 30. The highest engagement was observed in jogging, with 74% of time in MVPA. For team sport the lowest MVPA values of about 20% were observed during rowing, table tennis, and volleyball, and the highest values, ranging between 45 and 50%, were basketball, football, and tennis. Among common team sports football, basketball, handball, and tennis produced the most MVPA, while jogging, riding, gymnastics and fitness training were the most active individual sports.

We observed an interaction between team sport and sex, with boys being more engaged than girls in team sport but comparable in individual sport when including only episodes with MVPA. Furthermore,boys were less engaged when zero-MVPA episodes of sport (almost twice as prevalent in boys) were included in the average. Fig 1 indicates that this interaction was not driven by any single team or individual sport. The only team sport in which girls averaged more MVPA across all episodes than boys was rowing, and that estimate was based on a single episode for girls and is thus unreliable. The sexes were much more similar for individual sport, with girls more engaged than boys in dancing, fitness, and inline skating and with very similar engagement in weight training and jogging. Thus it appears that while boys were reliably more engaged than girls in most team sports, the sex difference in individual sport as a whole was much weaker and perhaps depends on which sports are included in the sample.

Most individual sports with 10 or more episodes for at least one sex had at least one episode with zero MVPA, even those with otherwise high MVPA such as jogging. The association of individual sport with zero MVPA did not appear to be a result of the specific individual sports in our sample, and it appeared to be distinct from low MVPA. 5/95 episodes of jogging had no MVPA (5%), 49/90 episodes of cycling (54%), 20/111 (18%) episodes of dancing, and 4/28 (14%) episodes of martial arts.

## Discussion

Accelerometric and diary data were combined to assess the engagement in common leisure sports in adolescents under field conditions and determine predictors of MVPA levels for different sports. General physical activity levels of our sample were well within the wide range reported for youth [2, 25–30] but participants with diaried leisure sport had above-average levels of activity. This was entirely due to their participation in sport, since activity on days without leisure sport was comparable between groups. This indicates that outside sporting time, physical activity behavior is similar between adolescents who do and do not participate in sport.

Engagement in leisure sport compared favorably with that in school physical education (school sport) but was still relatively low. Our previous work with this cohort [20] found that 22% of school physical education time was spent in MVPA, which is about two-thirds of what we found for leisure sport. However, engagement in leisure sport was highly variable, with no MVPA at all in many episodes, particularly in individual sport. Engagement in different sports ranged from $^{1}/_{10}$ to ¾ of total time in MVPA. This range is comparable to that reported in the literature for youth. [11] [12][13]. Taken together, these findings imply that much of the difference between accelerometric and self-reported activity levels [3, 10, 31, 32] may be explicable by the assumption that 100% of sport time is spent active.

Our study is comparable to existing literature in recording only sporting time, rather than distinguishing between warmups, practices and games, and our estimates of engagement level can thus be compared with theirs. Furthermore, we are able to compare different sports within the same sample in a way that other studies are not, since they generally either do not record the specific sport or are limited to one, such as Morales et al [13] which estimated that 77% of basketball time was spent in MVPA. While our estimate was only 2/3 that, it was still the highest among team sports. The difference may reflect individual characteristics such as age and gender (our cohort included girls, while Morales et al did not), differences in measurement methods, differential engagement in practice and games, or other factors.

Our observed higher engagement in team sport than individual may result from the well-known Köhler effect, where less-capable members of a group perform better in the group than alone [33] particularly when they are aware that their performance is limiting that of the group. Little research has examined how the effect influences more-capable group members, but we suggest that it may also help explain why girls were less engaged than boys in team sports despite being comparably engaged in individual sports. Since team sport is generally zero-sum, winning may be more motivating for males, who average relatively higher competitiveness [34, 35] and lower agreeability [36] than females. Furthermore, females may consciously lower their engagement as a result of the well-known "likability-competence trade-off" [37] [38]. Indeed, at least one study [39] found that female, but not male, runners adjusted their performance downward to match a less-capable partner—even when the partner was not only a stranger, but a computer simulation.

It is difficult to make recommendations from this finding, since sport choices are not randomized but are instead based on availability of the sport and personal preference of the participant. However, coaches and participants should be aware of the social interactions generated by peers and coaches during sport, particularly the potentially detrimental effects for females.

More generally, we draw attention to the wide range of engagement levels we observed both within and between sports. To increase both participation and engagement,we suggest increasing the sporting options available and lowering the barriers to participation. We suggest that this will increase the chances that adolescents find sports which they enjoy, find socially acceptable, and are willing to engage in at a high level.

## Study Strengths and Limitations

Our study is favorable in its large sample—626 sport participants and over 1,000 sport episodes, compared with 228 participants for [12] and 14 basketball classes for [13]—in its objective assessment of MVPA, and its documentation of specific sport type. However, study participants were recruited as followup of a birth cohort, and assessed their PA levels through accelerometry and diary, both of which are labor-intensive for the participant. Selection bias is thus likely at all stages, from initial enrollment in the cohort to availability for followup, consent to and completion of accelerometry, and a series of demanding quality checks of the data. Many of our findings, such as the null effects of age and socioeconomic status, almost certainly reflect this; and even within the GINI cohort, earlier work (data in [20]) found associations between accelerometry completion and both healthy weight and female gender. Thus the null finding between SES and physical activity needs a cautious interpretation, because of the potential for bias.

We find no strong effects on PA from any sociodemographic predictor, in spite of the known effects in other populations. However, our goal was not to capture all possible predictors of PA: numerous factors affect PA and many are population-specific and/or difficult to measure objectively. Furthermore, many do not vary much in this relatively high-SES, native-German population and thus their effects could not be estimated within it. We thus checked only those within-participant confounders that are easy to measure and most commonly cited as predictors of activity, and realize that even these effects are specific to our population.

Another limitation is that our estimates of engagement in leisure sport completely rely on the accuracy of diaried sporting time. This limitation is common to all studies of behavior that rely on self-report, and we minimized it as much as possible with a series of stringent quality checks, particularly for inconsistencies between diaried wear time and wear time determined by the NHANES algorithms, to exclude unreliable participants and to minimize inconsistencies. Hence, errors in recording time of starting and finishing sport are likely to be small. Furthermore we did not have any indications that error was associated with sport type, and thus the assumption of random errors is plausible.

This study is fundamentally cross-sectional, measuring variations within a large and homogeneous cohort over a period of about a week per participant. We were unable to estimate longer-term effects, such as seasonal variation or within-participant replicability. However, our study is among the largest of its type (n>1,000 participants) and as far as we know the only one to examine engagement in specific sports under field conditions.

## Conclusions

Objectively-assessed leisure-sport engagement varies substantially between adolescents and between sports under field conditions in Germany. Adolescents are active for only a fraction of diaried sporting time, and episodes of individual sport often appear to have no MVPA. Boys are more engaged than girls in team sport, but are slightly less engaged and much more likely to have no MVPA in an episode of individual sport. Given this gender difference, we suggest that engagement can be maximized by allowing and enabling participants to choose the sporting activities they most enjoy, bearing in mind that team sports may be more preferred by boys and individual sports by girls. We also suggest monitoring and managing social pressures between sporting participants, particularly pressures towards low engagement if these are present.

Adolescents with sport are more active than those without it, but only on days with sport. We found no evidence for activity compensation: MVPA accumulated during sport is simply added onto the daily total.

## Supporting Information

**S1 File. Technical—Accelerometry and statistics.**
(DOC)

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## Author Contributions

Conceived and designed the experiments: HS MS. Performed the experiments: HS JH DB. Analyzed the data: MS. Wrote the paper: MS HS DN JH DB.

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RESEARCH ARTICLE

# Physical Activity Levels and Domains Assessed by Accelerometry in German Adolescents from GINIplus and LISAplus

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**Data Availability Statement:** Data are from the GINIplus study and LISAplus study, which includes patient-specific information. Interested researches will obtain a de-identified, participant level dataset for the data pertaining the current study requiring ethical approval. Requests should be addressed to the corresponding author Holger Schulz (schulz@helmholtz-muenchen.de).

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## Abstract

### Background

Physical activity (PA) is a well-known and underused protective factor for numerous health outcomes, and interventions are hampered by lack of objective data. We combined accelerometers with diaries to estimate the contributions to total activity from different domains throughout the day and week in adolescents.

### Methods

Accelerometric and diary data from 1403 adolescents (45% male, mean age 15.6 ± 0.5 years) were combined to evaluate daily levels and domains of sedentary, light, and moderate-to-vigorous activity (MVPA) during a typical week. Freedson's cutoff points were applied to determine levels of activity. Total activity was broken down into school physical education (PE), school outside PE, transportation to school, sport, and other time.

### Results

About 2/3 of adolescents' time was spent sedentary, 1/3 in light activity, and about 5% in MVPA. Boys and girls averaged 46 (SD 22) and 38 (23) minutes MVPA per day. Adolescents were most active during leisure sport, spending about 30% of it in MVPA, followed by PE (about 20%) transport to school (14%) and either school class time or other time (3%). PE provided 5% of total MVPA, while leisure sport provided 16% and transportation to school 8%. School was the most sedentary part of the day with over 75% of time outside PE spent sedentary.

### Conclusions

These German adolescents were typical of Europeans in showing low levels of physical activity, with significant contributions from leisure sport, transportation and school PE.

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Leisure sport was the most active part of the day, and participation did not vary significantly by sex, study center (region of Germany) or BMI. Transportation to school was frequent and thus accounted for a significant fraction of total MVPA. This indicates that even in a population with good access to dedicated sporting activities, frequent active transportation can add significantly to total MVPA.

## Background

Physical activity (PA) is gaining increased attention as a modifiable protective factor for most of the common diseases of the developed world, including cardiovascular disease and obesity [1, 2] as well as being associated with lower all-cause mortality [3]. The World Health Organization suggests that children and adolescents should get 60 minutes moderate-to-vigorous physical activity (MVPA) per day. [4] In German adolescents, PA behaviour has so far been mainly studied by questionnaires, e.g. in the KiGGS study [5–7] and only limited information is obtained by objective measures, e.g. in HELENA [8, 9]. While it is generally agreed that school-age children are insufficiently active, little is known of activity allocation throughout the day or the relative importance of different activity domains in determining the observed high levels of sedentary behaviour and low levels of moderate or vigorous activity. [10, 11]

Past studies have often relied on self-reports, or parental reports, to measure PA levels. These generally overestimate time in sport [12–14]; assume subjects are continuously active during sport, which they typically are not; [15–17] and underestimate or do not consider PA that takes place outside of dedicated activities. For all these reasons, the reported correlation between self-reported and objectively measured PA is weak [12] so objective measurements of PA are increasingly used in field studies.

Accelerometry is one of the most popular objective methods for assessing PA outside the laboratory. Accelerometric measures correlate well with metabolic measurements in controlled studies under laboratory conditions [14], and can also assess activity during daily or weekly routine under field conditions. Subjects wear a motion sensor typically for a few days or a week; sometimes diaries are used to connect the documented motion with specific activities such as school physical education, [15] sport [16], or recess [15]. Following data validation, various algorithms are available to convert accelerometric counts epoch-by-epoch (one minute being a typical epoch length for children and adolescents) into estimates of activity level during that epoch. Based on metabolic demands, these levels are *sedentary*, *light*, *moderate* and *vigorous activity*. Health recommendations for children and healthy adults generally focus on daily or weekly minutes of MVPA.

Our goals in this study are:

- To quantify the amounts of sedentary, light, moderate, and vigorous physical activity in a large cohort of German adolescents;
- To assess the relative importance of different activity domains (school physical education (PE), school outside PE, transportation to school, and leisure sport) in determining total objectively-measured MVPA and VPA.

## Methods

### Study population / Approach of participants

This study sampled adolescents from two different German birth cohorts: GINIplus and LISAplus, born between 1995 and 1999 in Munich or Wesel. Accelerometry was done between 2011 and 2014, and subjects were 15.6 (SD 0.5) years old at the time of accelerometry. GINIplus (German Infant Study on the influence of Nutrition Intervention plus environmental and genetic influences on allergy development) is an ongoing prospective cohort, initiated to investigate the influence on allergy development of nutrition intervention during infancy, air pollution and genetics. [18–20] LISAplus (Influence of Life-style related factors on the development of the Immune System and Allergies in East and West Germany, Plus the influence of traffic emissions and genetics) is an ongoing population-based birth cohort of unselected infants, designed to assess influence of life-style factors, traffic emissions and genetics on the development of the immune system and allergies in East and West Germany. Details on study design are published elsewhere. [18, 19, 21, 22]

Accelerometry participants were recruited from the entire 15-year followup of GINIplus and LISAplus that resided in the study centers Munich and Wesel, which includes all of GINIplus but only 64% of LISAplus. For a flowchart see Fig 1; for more details on followup see [23]. Attempts were made to contact subjects at age 15 by paper mail, electronic mail, and/or telephone, and at this time consent for accelerometry was requested. If consent was given, subjects received a postcard one week before the scheduled start time of accelerometry requesting consent to send the device. Those who confirmed consent by postcard were sent the device. Almost all of these (>99%) returned the device after the scheduled week.

Of the 3199 subjects from GINIplus who were successfully recontacted at age 15, all were approached for accelerometry, 1890 (59%) gave initial consent and 1247 (66%) gave final consent, completed successfully, and returned the device. Of the 1740 subjects from LISAplus who were successfully recontacted, 1107 (64%) were from Munich or Wesel and thus approached for accelerometry. Of these 654 (59%) gave initial consent and 435 completed (66%). Of the 1682 adolescents from GINIplus and LISAplus who completed accelerometry, 1411 (83%) successfully passed data-quality checks. Of these, 1403 were enrolled in school full time. These 1403 subjects (8781 days) are profiled in the current study.

Recruitment, response, and exclusions of subjects are shown in Fig 1.

### Ethics, Consent and Permissions

Studies were conducted in Germany, in the Munich and Wesel area. The approval of the Ethics Committees includes the written consent procedure. Written informed consent was obtained from the parents or the legal guardian of all participants.

Initial recruitment of the GINI and LISA cohorts was approved by the Department of Medicine, of Ludwig Maximilians University, Munich (ethics reference number 111/94 (GINI) and 138/97 (LISA)); the Board of Physicians of West Rhine-Westphalia (reference number 9061 (GINI)) and the Medical Faculty of the University of Leipzig (reference number 560 (LISA)). The 15-year followups were approved by the respective local Ethics Committees, the Bavarian Board of Physicians (Bavarian General Medical Council reference number 10090 (GINI) and 12067 (LISA)); the Medical Council of North-Rhine-Westphalia (reference number 2102446 (LISA)); and the Board of Physicians in Saxony (reference number EK-BRO2 (LISA.)

### Accelerometry

Accelerometry protocol was the same as in [13] and [29]. Subjects who confirmed consent to accelerometry were mailed a package containing the following: two monitors including

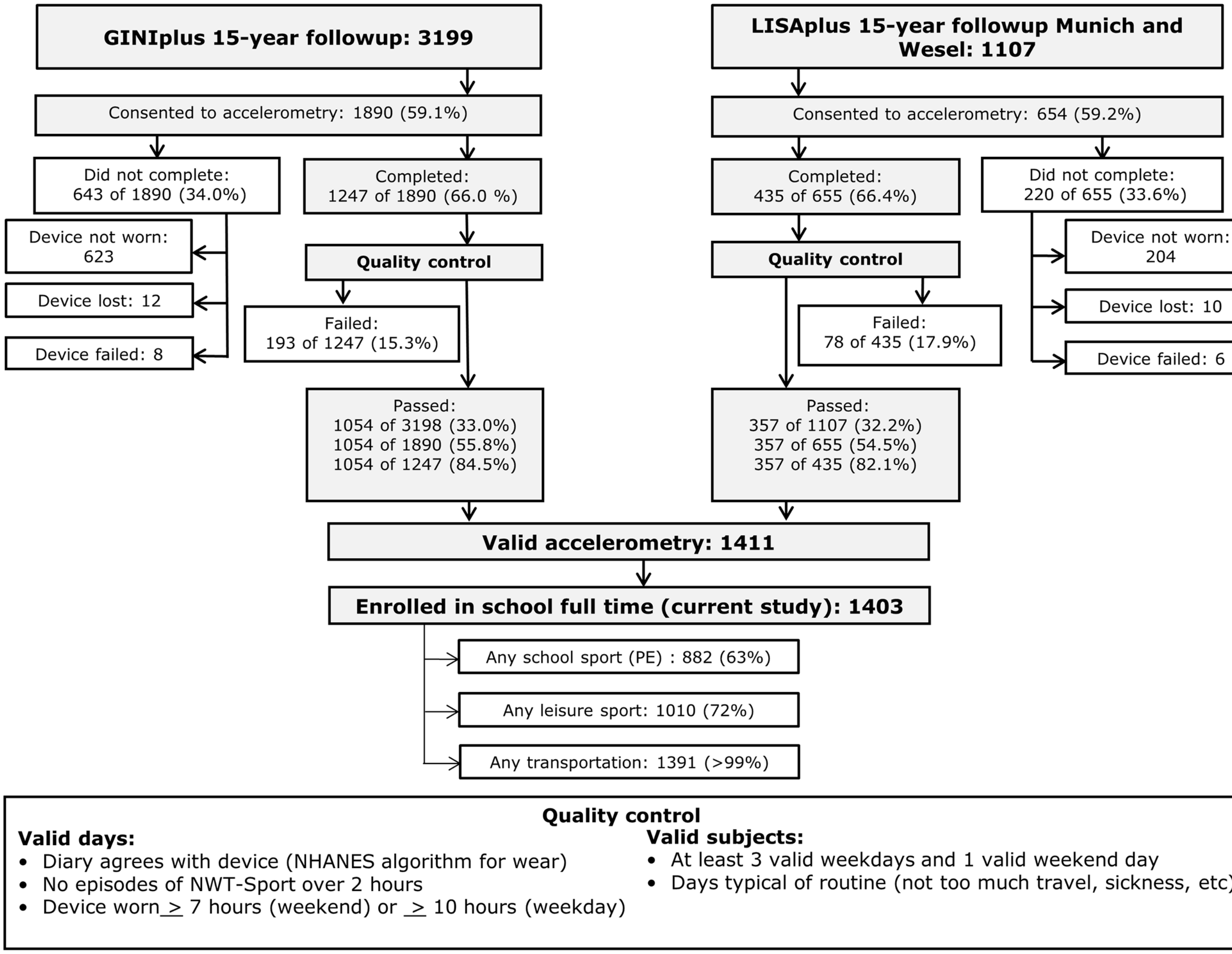


**Fig 1. Accelerometry Response Rate.** GINIplus15 and LISAPlus15 are the 15-year followups of birth cohorts GINIplus and LISAPlus. For details on GINIplus and LISAplus see von Berg et al, 2003 and 2015 [24–26]and Chen et al, 2007 [19] respectively. We give the number and percentage of subjects as a percentage of those contacted for accelerometry, those who gave their consent, and those who completed accelerometry and returned the device. Quality control failure includes inconsistency between diary and weartime criteria of Troiano et al, 2007 [27] using SAS programs published by NHANES [28](58% of excluded days); other non-wear time issues (27% of excluded days); and technical issues (7.4% of excluded days). Many days were invalid for more than one reason.

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mounting strips with identification labels for hip and foot, personalized cover letter, brief instruction sheet, and pre-printed diary with instructions for filling it in and sample of proper methods [13], and a stamped, pre-addressed envelope for returning monitors after one week of PA measurement. Almost all devices were successfully returned.

Triaxial accelerometers (ActiGraph GT3X, Pensacola, Florida) were worn on the dominant hip for 7 consecutive days, after which they were returned by mail. This device has demonstrated validity in adolescents [30, 31] and performed satisfactorily in our sample: less than 2% of accelerometers (see Fig 1) were either lost or suffered technical failure as detected by flashing light or implausibly continuous high or low counts as compared with the diary. While this device is not waterproof, the 14 technical failures include any damage due to water exposure, such as that caused by failure to remove the device during swimming or showering.

**Data Management and Quality Control.** Sampling rate was set to 30 Hz and the measured accelerations stored at 1 Hz after conversion into activity counts. Counts were summed over 60-second epochs. This was the most common length in two recent reviews: Cain et al [4], found that of 68 accelerometric studies in adolescents, 63% used an epoch length of 60 seconds, 13% used 30 seconds, 4.4% 15 seconds and 3% less than 5 seconds, and Guinhoya et al [11] found that 60-second epochs were the commonest even when including studies of children, as well as adolescents. Furthermore, it is known from sport physiology [32] that cardiovascular adaptation to a certain exercise level takes about 1 to 2 minutes before reaching a steady state. Thus the physiological benefits of very brief epochs of PA have not been ascertained, and our choice of 60 seconds represents both clinical relevance and maximal intercomparability with other studies.

Data filtering was set to default ('normal') as recommended by ActiGraph. Activity counts of all three axes (vertical, horizontal and mediolateral), the inclinometer signal, and number of steps were measured. ActiLife software was used for initialization of accelerometers (version 5.5.5, firmware 4.4.0) and for download of data. Activity counts were assigned to the four intensity levels—sedentary, light, moderate, and vigorous physical activity—using Freedson's et al (2005) commonly-used uniaxial cut-points for children [33]. PA data were checked to identify invalid days both by visual inspection and by semiautomatic methods.

**Activity Diary.** Subjects were instructed to document each of the following events as close as possible to the time they occurred: time of waking up and going to bed; time and reason for removing one or both monitors (non-wear time, NWT) such as for showering or swimming; time and method of travel to and from school, such as by walking or driving; time of starting and finishing school; time of starting and finishing school sport; and time and type of sporting activity. A note at the end of the 7$^{th}$ recording day instructed the participant to stop the measurement and immediately return monitors and diary to the study center in the provided envelope. [13]

Diary information was digitized using a 7-day template and a specific coding for events such as sickness, trips, type of sport performed, and NWT. Data entries were reviewed by a second study assistant to avoid transcription errors. Since the goal of this study was to capture a representative sample of daily PA, days were disqualified if they were judged to be not representative of typical routine as described in Pfitzner et al [13]. Diary-based reasons for exclusion of a day were: traveling for more than one day or reported common cold or headache for more than one day (excluded from the second day on). Days were excluded if the sensor was worn incorrectly or the subject reported flashing LED indicative of technical problems.

**Validation of wear time.** NWT was identified both by visual inspection of accelerometer tracings and by comparing the diary data to the results from the monitor according to the NWT algorithm of Troiano et al [27] using SAS programs published by NHANES.[34] These programs identify probable NWT as at least 60 minutes of consecutive zero counts with less than two consecutive intervals with counts less than or equal to 100. In most cases the diary agreed with the automatic programs upon wear time and NWT. In the event of large discrepancies between the NHANES criteria and the diary entry, the measuring day was excluded from analysis.

A large discrepancy was defined as being more than 45 minutes of diaried NWT when the program indicated the device was worn, or more than 150 minutes where the program indicated NWT but the diary did not. These limits are the 10$^{th}$ and 90$^{th}$ percentiles for daily discrepancy in a subset of this cohort, [13] following the recommendation [35] to specify the accepted level of uncertainty in PA data. Days with smaller discrepancies were included in the analysis, with activity domain and weartime determined from the diary entries.

Of a total 11,572 recorded days, 2740 (17.1%) were invalid. Most invalid days (1140, 58%) were the result of inconsistency between the diary and the NHANES weartime criteria, reflecting our high standard of data cleaning and suggesting a relatively accurate allocation of activity on the days that passed quality control. Other reasons included non-wear time issues (526 days, 26.7%), and technical issues (145 days, 7.4%). Many days were invalid for more than one reason. In addition, 271 days were excluded because the subject did not have at least 3 valid weekdays and one valid weekend day.

**Handling of non-wear time during sport.** When the accelerometer was removed during -time sport or school PE (in the diary as NWT-Sport or NWT-PE) it was necessary to account for the missing time in order to avoid underestimating total PA levels. NWT-Sport (or PE) was rare, occurring on only 297 / 8781 valid days (3.4%).

For periods of documented NWT- Sport longer than 30 minutes but shorter than 120 minutes, 15 minutes was subtracted before imputation in order to account for non-sport activities such as showering and changing clothes. For longer periods of NWT-Sport, e.g. during a competition, imputation would become unreliable, so any single period of NWT-Sport (either or PE) longer than 120 minutes disqualified that day from inclusion. When imputing activity, school PE and sport were kept separate; imputation was not used for any other periods of NWT. For each domain, imputation was done by dividing total moderate and vigorous PA from that domain, with total device weartime during that domain; assuming that those average levels were maintained during NWT-Sport or NWT-PE; and imputing the missing time with average levels. If the subject had any periods of that activity domain (sport or PE) where the device was worn, his own average was used; if not then sex-specific averages from the whole study population were used. Imputation increased average MVPA by about a minute per day (1.1 minutes for boys, 0.54 for girls.)

**Validation of days.** Since our goal was to measure typical activity, subjects were required to have at least one valid weekend day of recording in addition to at least three valid weekdays. This reflects the known differences in activity between weekends and weekdays and thus improves representativeness of data.

Days were required to have at least 10 hours of valid recording time to be considered valid, or as little as 7 hours if subjects were awake for less than 10 hours, as is recommended in [13] and [29]. This is not uncommon in adolescents, especially on weekends, and further reflects our desire to capture typical routine. Of 8781 days, only 116 (1.3%) had less than 10 hours recording.

## Activity domains

Every minute of accelerometer weartime fell into one of five categories (domains).

- **School physical education (PE) (882 subjects, 63%).** Time between diaried start and end of school physical education (PE), when both start and end were diaried. Since many German schools require PE, it is likely that most children who did not report any during valid accelerometric days still had it on other days.
- **School outside PE (1400 subjects, > 99%).** Time between diaried start and end of school, when subject was not in diaried school physical education (PE). The remaining 3 subjects attended school but did not wear the device during it. However, each still accumulated at least three valid weekdays (10 hours wear) and one weekend day.
- **Leisure sport (1010 subjects, 72%).** Time between diaried start and end of sport that took place outside school PE. This includes any activity the subject deliberately classifies as sport and reports in the diary, including both team sports such as football and individual sports such as jogging. Leisure sport in a subset of this cohort has been previously profiled. [29]
- **Transportation to school (1391 subjects, > 99%).** Time spent between diaried departure for school and arrival at school. The trip home from school sometimes took much longer

than the trip to school (as much as 493 minutes) implying that subjects did not go straight home. As a result only the trip to school is described.

- **Other time.** All other waking time.

Data were not collected on any activities besides sleeping, NWT, and the stated activity domains.

## Collection and Definition of Confounders

In addition to the measured confounders age, height, weight, BMI, and BMI category we also considered socioeconomic status and study center (location) as possible correlates of PA. Confounders were defined as follows:

- **Height, weight, BMI and BMI category.** Height and weight were measured objectively at a physical exam at age 15. BMI was calculated from height and weight as $kg/m^2$, and BMI category was taken from age- and sex- specific percentiles from a German reference population, [36] with $10^{th}$, $90^{th}$, and $97^{th}$ percentile defining the boundaries between underweight, normal weight, overweight, and obese.
- **Study center Munich compared with Wesel.** Subjects were drawn in roughly equal numbers from the urban region Munich, and the rural/suburban region of Wesel. These two cities may differ in the availability of active transportation, encouragement of PA, or other factors with potential to influence PA levels. Thus we checked whether study center was associated with leisure-sport and PE participation.
- **Parental education (socioeconomic status).** Socioeconomic status (SES) may be associated with PA through availability of leisure sport, neighbourhood characteristics affecting active commuting to school, cultural encouragement of PA, or other factors. High SES was defined as yes if the child's better-educated parent reported entering university or higher, and no otherwise.

Selection bias was quantified by comparing anthropometric and sociodemographic characteristics of successful accelerometry completers, with the populations from which they were recruited, in Table 1.

Group differences within the accelerometry cohort were quantified by comparing average daily activity (total time awake, accelerometric weartime, minutes in sedentary, light, moderate, vigorous, and MVPA) for the whole cohort and for the subsets that had any leisure sport and any PE. We also calculated the percentage of days each group achieved the 60 minutes MVPA recommended by the World Health Organization [4]. (Table 2).

Activity levels within each domain (total minutes, and minutes in sedentary, light, moderate, and vigorous activity) were quantified first only on days with that domain (Table 3), and then averaged over the week by domain (Table 4). Thus Table 3 shows how subjects allocated the time they spent in each activity domain, while Table 4 shows the relative importance of the five activity domains in determining total PA levels within this population.

## Statistical Methods

All analyses were performed using SAS 9.2 or 9.3 (Cary, NC.) Intergroup comparisons were performed using t-test for height and weight; Kruskal-Wallis test for global null hypothesis for categorical values (BMI category) and Wilcoxon's two-tailed rank-sum test for binary or non-normal continuous variables. P-value for significance was 0.05, but p-values in the tables are shown up to 0.10.

**Table 1. Population Characteristics/ Selection Bias within GINIplus and LISAplus.**

| | Entire cohort | | Initial consent | | Accelerometry completers | | Study population | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | GINILISA 15-year followup Munich and Wesel | | Gave initial consent to accelerometry | | Completed accelerometry, returned the device | | Passed quality control | | | |
| | Boys | Girls | Boys | Girls | Boys | Girls | Boys | Girls | Boys | Girls |
| N | 4306 | | 2544 | | 1682 | | 1403 | | ** | |
| Male, % | 51.1 | | 48.9 | | 47.4 | | 46.3 | | <0.0001 | |
| Height, cm | 177 (7.5) | 167 (6.3) | 176 (7.5) | 167 (6.2) | 177 (7.6) | 167 (6.2) | 177 (7.4) | 168 (6.2) | — | 0.01 |
| Weight, kg | 65.1 (13) | 58.7 (9.8) | 65.1 (13) | 58.8 (9.8) | 64.8 (12) | 58.8 (9.8) | 64.5 (12) | 59.0 (9.6) | — | — |
| BMI, $kg/m^2$ | 20.8 (3.4) | 21.0 (3.1) | 20.8 (3.3) | 21.0 (3.0) | 20.7 (3.2) | 20.9 (3.0) | 20.6 (3.2) | 21.0 (2.9) | — | — |
| Study center Munich, % | 59 | 59 | 63 | 60 | 64 | 58 | 65 | 58 | 0.0001 | — |
| Parents highly educated[2], % | 65 | 68 | 64 | 66 | 70 | 70 | 71 | 71 | 0.0004 | 0.06 |
| BMI category,[3]% | | | | | | | | | 0.03 | — |
| Underweight | 7.9 | 6.6 | 7.9 | 6.6 | 7.6 | 5.5 | 9.1 | 6.3 | ** | ** |
| Normal weight | 80 | 84 | 80 | 83 | 80 | 85 | 80 | 85 | ** | ** |
| Overweight | 7.9 | 6.1 | 7.9 | 6.4 | 8.7 | 5.9 | 8.6 | 5.0 | ** | ** |
| Obese | 4.1 | 3.6 | 4.0 | 3.7 | 3.3 | 3.9 | 2.7 | 3.9 | ** | ** |

Mean (SD) if not otherwise stated.

Values given as percent for binary and categorical variables, mean (median); $5^{th}$, $95^{th}$ percentiles for skewed, mean (SD) for centrally distributed.

1) P-values for selection (study population vs. entire 15-year followup) given as Wilcoxon's two-tailed rank-sum test for binary and otherwise noncentral variables, t-test for height and weight, Kruskal-Wallis for BMI category.—if p>0.10, ** if pairwise comparison inappropriate (see global null).

2) If higher-educated parent entered university

3) From age- and sex-specific $10^{th}$, $90^{th}$, and $97^{th}$ BMI cutpoints from a German reference population in (Kromeyer-Hauschild, 2001). P-value calculated for global null hypothesis (all categories equal) from Kruskal-Wallis test.

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## Results

### Population

Of the 4306 adolescents in the GINIplus and LISAplus 15-year followups (Table 1) 2544 gave initial consent to accelerometry, 1682 completed accelerometry, and 1403 (successful completers) passed quality control. Selection bias was evident in both consent to and completion of accelerometry: in particular completers were likelier to come from highly-educated families and to be female. Small differences were also apparent for study center Munich (completers tended to be urban) and for slightly greater height in girls.

### Daily Activity

PA was monitored in 1403 subjects for an average of 884 minutes (14.7 hours) per day and on average just over 6 days per subject, ranging from 4 to 7. (Table 2) Boys and girls averaged 45.5 (SD 22) and 37.6 (SD 23) minutes MVPA per day, and achieved over 60 minutes MVPA on 27% and 18% of days respectively. 1% of subjects (6 boys, 8 girls) achieved 60 minutes of MVPA every day. Subjects spent roughly 2/3 of time sedentary, 1/3 in light activity, and less than 5% in MVPA.

Adolescents with diaried leisure sport (N = 1010) or PE (N = 882) were comparable to the rest of successful accelerometry completers in both sociodemographic and anthropometric characteristics (Table 2). Averaged across all days, boys and girls with diaried leisure sport

**Table 2. Population Characteristics and Selection.**

| | Study population (N = 1403) | | | Population with diaried leisure sport (N = 1010) | | | | Population with diaried school sport (PE) (N = 882) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Boys | Girls | P for sex difference | Boys | Girls | P for sex-stratified difference[1] | | Boys | Girls | P for sex-stratified difference[1] | |
| **Male (N, %)** | 650 (46) | | ** | 455 (45) | | — | | 407 (46) | | — | |
| **Age, years** | 15.6 (0.5) | 15.6 (0.5) | — | 15.6 (0.5) | 15.6 (0.5) | — | — | 15.6 (0.5) | 15.6 (0.5) | — | — |
| **Height, cm** | 177 (7.4) | 168 (6.2) | <0.0001 | 177 (7.4) | 168 (6.2) | — | — | 177 (7.4) | 168 (6.3) | — | — |
| **Weight, kg** | 64.5 (12) | 59.0 (9.6) | <0.0001 | 64.0 (11) | 59.0 (9.4) | — | — | 64.4 (12) | 58.5 (9.3) | — | 0.09 |
| **BMI, kg/m$^2$** | 20.6 (3.2) | 21.0 (2.9) | 0.001 | 20.4 (2.9) | 21.0 (2.9) | 0.04 | — | 20.6 (3.1) | 20.8 (2.9) | — | 0.1 |
| **Study center Munich, %** | 64.9 | 57.5 | 0.005 | 66.4 | 56.4 | — | — | 62.6 | 56.6 | — | — |
| **Higher-educated parent entered university, %** | 71.1 | 71.1 | — | 75.8 | 73.2 | 0.0001 | 0.04 | 70.9 | 71.2 | — | — |
| **BMI category,[4]%** | ** | ** | ** | ** | ** | ** | ** | ** | ** | ** | ** |
| **Underweight** | 9.06 | 6.29 | ** | 9.07 | 5.26 | — | — | 9.41 | 7.43 | — | 0.1 |
| **Normal weight** | 79.7 | 84.9 | ** | 82.1 | 86.4 | — | — | 78.9 | 84.9 | — | — |
| **Overweight** | 8.59 | 4.95 | ** | 7.03 | 5.08 | — | — | 9.41 | 4.25 | — | — |
| **Obese** | 2.70 | 3.88 | ** | 1.81 | 3.27 | — | — | 2.29 | 3.40 | — | — |
| **Any diaried leisure sport (%)** | 70.0 | 73.7 | — | ** | ** | ** | ** | 74.2 | 76.4 | 0.003 | 0.03 |
| **Any school physical education PE (%)** | 62.6 | 63.1 | — | 66.4 | 65.4 | 0.003 | 0.03 | ** | ** | ** | ** |
| **Accelerometric data, min/day;** Mean (SD) | | | | | | | | | | | |
| Time from getting up to going to bed (includes accelerometer non-wear, NWT) Mean (SD) | 904 (52) | 898 (49) | 0.02 | 906 (50) | 899 (49) | | | 904 (52) | 899 (47) | | |
| **Accelerometer wear;[3, 4]** Does not include NWT Mean (SD) | 887 (54 | 881 (49) 799, 962 | 0.01 | 888 (54) | 881 (49) | — | — | 887 (53) | 882 (47) | — | — |
| **Sedentary[3]** | 583 (79) | 598 (69) | 0.0001 | 580 (74) | 594 (65) | — | 0.005 | 583 (77) | 597 (67) | — | — |
| **Light[3]** | 260 (59) | 246 (50) | <0.0001 | 261 (57) | 250 (49) | — | 0.0002 | 260 (60) | 248 (49) | — | — |
| **Moderate[3, 4]** | 31.3 (14) | 26.5 (15) | <0.0001 | 33.1 (14) | 26.8 (14) | <0.0001 | 0.00035 | 32.2 (14) | 26.9 (14) | 0.049 | 0.02 |
| **Vigorous[3, 4]** | 14.2 (12) | 11.1 (11) | ** | 15.7 (12) | 11.8 (11) | <0.0001 | <0.0001 | 14.4 (12) | 11.5 (10) | — | 0.006 |
| **MVPA[3, 4]** | 45.5 (22) | 37.6 (23) | ** | 48.8 (22) | 38.6 (20) | <0.0001 | <0.0001 | 46.5 (23) | 38.3 (22) | — | 0.007 |
| **MVPA difference from average[3, 4]** | ** | ** | ** | 3.24 | 1.01 | ** | ** | 0.94 | 0.72 | ** | ** |
| **% days with MVPA over 60 minutes[3, 4]** | 27.2 | 17.7 | <0.0001 | 31.2 | 19.0 | <0.0001 | <0.0001 | 28.6 | 19.1 | 0.10 | 0.004 |
| **MVPA over 60 minutes every day;** N, % subjects[3, 4] | 6, 0.92 | 8, 1.06 | - | 4, 0.88 | 5, 0.90 | — | — | 4, 0.98 | 6, 1.26 | — | — |

Mean (SD) unless otherwise stated.

Table 2 footer: P-values calculated using t-test for centrally distributed variables (age, height, BMI, weartime, sedentary, and light); Kruskal-Wallis for categorical (BMI category); Wilcoxon's two-tailed rank-sum for binary and skewed (all others.)—if p>0.10, ** if pairwise comparison inappropriate (see global null.) For time and activity levels spent in various activity domains (leisure sport, school PE, transportation, school) see Table 4.

1) P-value for difference from whole cohort

2) From BMI cutpoints in (Kromeyer-Hauschild, 2001).[36]

3) Freedson's uniaxial algorithm for children from (Freedson, 2005) [34]as cited in (Trost, 2010).[34, 37]

4) Data include estimated moderate and vigorous activity during nonwear time if the subject diaried they were in school PE or leisure sport.

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averaged 3.3 and 1.0 additional daily minutes of MVPA than the full population, and increased the fraction of days with over 60 minutes MVPA slightly from 27.2 to 31.2% (boys) and 17.7 to 19.0% (girls), both p <0.0001. (Table 2). Differences were smaller for PE, which was associated with 1.0 and 0.7 additional minutes MVPA per day (not significant for boys, p = 0.007 for girls) and one percentage point increase in days achieving the 60-minute recommendation (not significant for boys, p = 0.004 for girls).

## Profiles of Activity Domains

Participation in leisure-sport and PE was similar between the sexes. Adolescents with any leisure sport averaged 2.2 days with leisure sport, ranging from 1–5 days ($5^{th}$ and $95^{th}$ percentiles, Table 3). On each day with leisure sport, boys and girls dedicated an average of 111 and 95.2 minutes to it (1.9 and 1.6 hours), getting 33.3 and 22.7 minutes MVPA from it (30 and 24% of sporting time.)

Boys and girls with any PE during valid recording, both averaged 1.1 days with PE over the course of the week ($5^{th}$ and $95^{th}$ percentiles 1–2 days (Table 3)). On each day with PE, adolescents of both sexes spent about 83 minutes in PE; boys and girls got 24.0 and 13.4 minutes MVPA from it (28.5 and 16.3% of time). Lastly, on days with any transportation to school boys and girls spent 33.1 and 35.5 minutes in it, for a total of 4.8 minutes MVPA, or 14% of transportation time in MVPA.

**Table 3. Profiles of Activity Domains.** Domains profiled only on days when the subject reported the activity.

| | School outside PE | | PE[1] (physical education) | | Transport to school | | Leisure sport[1] | | All other waking time[1] | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Boys | Girls | Boys | Girls | Boys | Girls | Boys | Girls | Boys | Girls |
| **Number of subjects with any (N (% of total)** | 649 (>99) | 751 (>99) | 407 (63) | 475 (63) | 642 (99) | 749 (99) | 455 (70) | 555 (74) | 650 (100) | 753 (100) |
| **Number of days with that domain, among subjects with any** | 4.20 (0.92) | 4.20 (0.94) | 1.14 (0.40) | 1.11 (0.33) | 4.17 (0.95) | 4.19 (0.95) | 2.18 (1.3) | 2.23 (1.3) | 6.25 (0.86) | 6.27 (0.88) |
| $5^{th}$, $95^{th}$ percentile | 3, 5 | 2, 5 | 1, 2 | 1, 2 | 2, 5 | 2, 5 | 1, 5 | 1, 5 | 5, 7 | 5, 7 |
| **Total time** (min/day; mean (SD))(min / day; mean (SD) | 333 (50) | 336 (52) | 84.1 (20) | 82.2 (23) | 33.1 (18) | 35.5 (18) | 111 (75) | 95.2 (53) | 609 (79) | 600 (73) |
| **Sedentary** | 241 (46) | 266 (47) | 19.2 (19) | 22.2 (16) | 15.5 (13) | 18.2 (13) | 23.3 (42) | 20.9 (23) | 403 (75) | 399 (68) |
| **Light** | 79.9 (32) | 60.5 (25) | 36.5 (19) | 43.7 (19) | 12.8 (5.9) | 12.5 (5.6) | 43.9 (45) | 44.0 (31) | 183 (50) | 180 (43) |
| **Moderate**[1] | 9.82 (6.6) | 7.40 (5.8) | 14.8 (8.9) | 9.07 (6.6) | 3.31 (2.9) | 3.54 (3.2) | 18.9 (14) | 12.2 (14) | 16.1 (9.8) | 14.9 (11) |
| **Vigorous**[1] | 2.28 (3.4) | 1.32 (3.2) | 9.27 (9.6) | 4.34 (5.9) | 1.47 (2.6) | 1.28 (2.5) | 14.4 (14) | 10.5 (11) | 6.85 (7.0) | 5.86 (7.9) |
| **MVPA**[1] | 12.1 (8.9) | 8.72 (8.4) | 24.0 (15) | 13.4 (9.9) | 4.78 (4.4) | 4.82 (4.6) | 33.3 (24) | 22.7 (19) | 23.0 (15) | 20.7 (17) |
| **Activity during that domain: percent of timeof time** | | | | | | | | | | |
| **Sedentary** | 72.4 | 79.2 | 22.8 | 27.0 | 46.8 | 51.3 | 21.0 | 22.0 | 66.2 | 66.5 |
| **Light** | 24.0 | 18.0 | 43.4 | 53.2 | 38.7 | 35.2 | 39.6 | 46.2 | 30.1 | 30.0 |
| **Moderate** | 2.95 | 2.20 | 17.6 | 11.0 | 10.0 | 10.0 | 17.0 | 12.8 | 2.64 | 2.48 |
| **Vigorous** | 0.68 | 0.39 | 11.0 | 5.28 | 4.44 | 3.61 | 13.0 | 11.0 | 1.12 | 0.98 |
| **MVPA** | 3.63 | 2.60 | 28.5 | 16.3 | 14.4 | 13.6 | 30.0 | 23.8 | 3.78 | 3.45 |

See methods for domain descriptions and definitions.

1)Data include estimated moderate, vigorous and MVPA during diaried nonwear time due to school physical education (PE) or leisure sport when the device was not worn such as swimming (see methods). Sedentary and light activity are not imputed. Calculated with Freedson's uniaxial algorithm for children from (Freedson, 2005) [33]as cited in (Trost, 2010).[33, 37].

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The fraction of time spent in MVPA was comparable and low between school outside PE and other time, being 3.6 and 3.8% (boys) or 2.6 and 3.5% (girls). However, subjects were significantly more sedentary in school than outside it, spending 72 and 80% of school outside PE in sedentary behaviour compared with 66 and 67% of other time.

## Allocation of Total MVPA by Domain

This cohort dedicated almost an hour per day to domains that are expected to contribute significantly to MVPA: on an average day 9 minutes were spent in PE, 26 minutes in leisure sport, and 23 minutes in transportation to school (Table 4.) These domains made up only 31% of total MVPA, for an average of 12.7 minutes per day. Boys and girls averaged 17 and 16% of total MVPA from leisure sport, 7.3 and 8.7% from transport to school and 6.3 and 4.5% for PE, while school outside PE provided 19 and 16%. Finally, boys and girls accumulated 51 and 55% of total MVPA during other time.

While sporting activities made up only a small fraction of total MVPA, they contributed more significantly to vigorous PA (VPA.) The combination of PE and leisure sport accounted for only 21.7% of total MVPA, but 31.2% of VPA. (Table 4.)

Contributions of the five activity domains to total moderate, vigorous, and MVPA are profiled in Fig 2.

# Discussion

This is among the largest accelerometric studies of adolescents and, we believe, the first focusing on Germans specifically. In it we found the accelerometric PA levels of this cohort of

**Table 4. Activity Allocation by Domain, All Days.**

| | **School outside PE** | | **PE[1] (physical education) (physical education)** | | **Transport to school** | | **Leisure sport[1]** | | **Other time[1]** | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Boys** | **Girls** | **Boys** | **Girls** | **Boys** | **Girls** | **Boys** | **Girls** | **Boys** | **Girls** |
| **Number of days (Mean** number of days each subject had that domain, including those with none) | 6.24 | 6.27 | 0.71 | 0.70 | 4.11 | 4.16 | 1.52 | 1.64 | 6.24 | 6.27 |
| 5th, 95th percentiles | 5, 7 | 5, 7 | 0, 2 | 0, 2 | 2, 5 | 2, 5 | 0, 4 | 0, 5 | 5, 7 | 5, 7 |
| Daily minutes within that domain **(Mean)** | | | | | | | | | | |
| **Total** | 224 | 225 | 9.23 | 9.01 | 21.9 | 23.7 | 27.3 | 25.7 | 609 | 600 |
| Sedentary | 163 | 179 | 2.15 | 2.43 | 10.3 | 12.2 | 5.41 | 5.60 | 403 | 399 |
| Light activity | 53.8 | 40.6 | 4.00 | 4.74 | 8.52 | 8.30 | 10.7 | 11.6 | 183 | 180 |
| Moderate activity | 6.60 | 4.90 | 1.61 | 1.00 | 2.18 | 2.34 | 4.81 | 3.39 | 16.1 | 14.9 |
| Vigorous activity | 1.53 | 0.89 | 1.02 | 0.49 | 0.97 | 0.85 | 3.86 | 3.03 | 6.85 | 5.86 |
| MVPA | 8.13 | 5.79 | 2.62 | 1.48 | 3.14 | 3.19 | 8.67 | 6.43 | 23.0 | 20.7 |
| **Percent of total MVPA** (Mean) | 19.2 3.65, 42.6 | 16.2 | 6.30 | 4.49 | 7.28 | 8.67 | 16.7 | 16.0 | 50.5 | 54.6 |
| (5th, 95th percentiles) | 3.65, 42.6 | 2.73, 37.9 | 0, 19.2 | 0, 15.3 | 0.41, 20.7 | 0.47, 22.8 | 0, 54.9 | 0, 52.6 | 20.8, 82.7 | 23.7, 83.8 |
| **Percent of total vigorous PA (Mean)** | 12.0 | 7.34 | 9.36 | 6.35 | 5.93 | 6.28 | 22.4 | 24.4 | 50.3 | 55.6 |
| (5th, 95th percentiles) | 0, 44.4 | 0, 32.1 | 0, 41.7 | 0, 27.5 | 0, 24.7 | 0, 27.1 | 0, 76.2 | 0, 79.4 | 10.8, 0.95 | 10.3, 100 |

Values include all subjects and all days, both with and without that activity domain.

Includes estimated moderate, vigorous and MVPA during diaried nonwear time due to school physical education (PE) or leisure sport when the device was not worn such as swimming (see Methods) Sedentary and light activity are not imputed. Activity levels calculated using Freedson's uniaxial algorithm for children (Freedson, 2005) [33]as cited in (Trost, 2010).[37]. All analyses are averaged first by subject, then by day, in order to weight all subjects equally.

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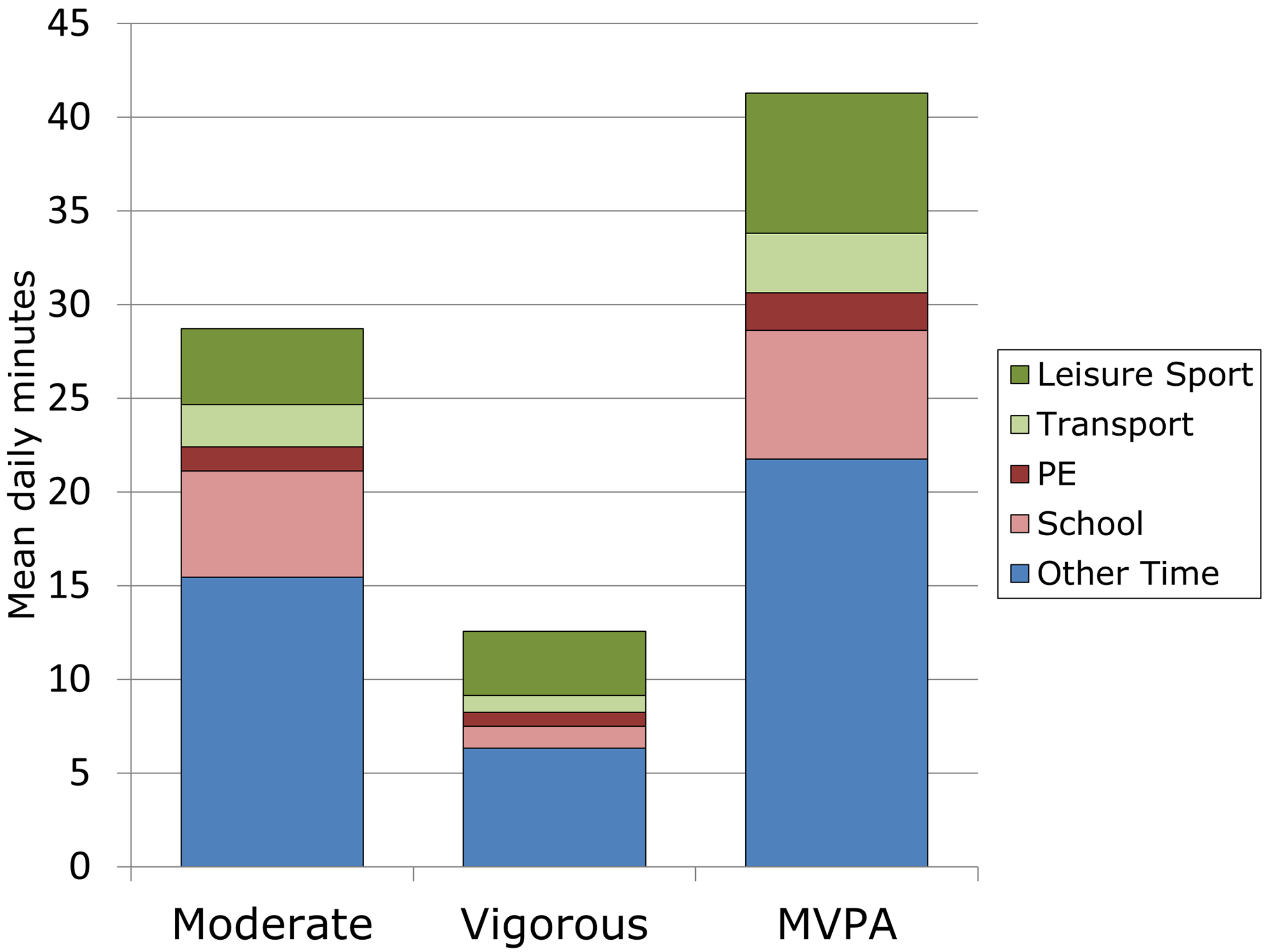


**Fig 2. Daily Activity in German Adolescents.** PE is any time between diaried start and end of school physical education (PE.) School is any time between diaried start and end of school, outside PE. Leisure Sport is any time outside of PE when the subject diaries sport. Transport is time between leaving home and arriving at school. Only the trip to school is described. Other is all other waking time when the monitor was worn. Estimates for PE and Leisure Sport include estimated moderate and vigorous activity during this period if the diary shows the device was not worn due to sport such as swimming. Calculations are based on data applying Freedson's vertical-axis algorithm for children from Freedson et al, 2005 [33] as cited in [37]. MVPA is moderate + vigorous physical activity.

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German adolescents were below WHO recommendations [38]and comparable to, or even less than, estimates for either other European adolescents [9, 11] or younger American children. [39] [40] Boys were more active than girls, but were equally likely to participate in each activity domain that we considered. Adolescents got the recommended 60 minutes of MVPA on about a quarter of days, and almost no one achieved 60 minutes every day. Objective measurements also allowed us to precisely estimate sedentary time and light activity: the majority of time was spent sedentary, with most of the remainder in light activity and about 5% in MVPA.

Access to dedicated sporting time is high in this cohort, with most subjects choosing to participate in leisure sport as well as often having school sport (PE.) Adolescents of our cohort spent 15 and 30% of sporting time in MVPA, with less in PE than in leisure sport. This is less than others have found for leisure sport [16, 17, 41] but within the typical pre-intervention range observed for PE [42] particularly in older adolescents.

Subjects devoted comparatively little time to the domains that we had expected would contribute significantly to MVPA. The average day in our sample contained 9 minutes of PE, 26 minutes of sport, and 23 minutes of transportation to school. These domains accounted for only 31% of total MVPA, or 12.7 minutes per day ((2.0, 7.5 and 3.2 minutes, respectively).

Although little of the time spent in transportation to school was spent in MVPA, it was still frequent and long enough to make up a significant contribution to total MVPA. This underlines the potentially significant contribution of transportation to activity in adolescents, as has been found elsewhere. [43] Estimates of its contribution would be higher still if we had been able to include the trip home, since young Europeans often bicycle or walk to school. [43] Since almost all subjects devoted time to transportation anyway, MVPA levels could be significantly increased by exchanging driving for active transport such as walking or bicycling.

However, being physically active is not the only reason to participate in sport. In addition to hedonic pleasure, social interaction, and strength building, sport may provide significantly more vigorous PA than activities of daily living such as transportation. In our cohort, relative contributions to daily VPA from sport activities (leisure sport and PE) were larger (32%) than contributions from transportation (6%). Thus even if children receive large amounts of MVPA from non-sport domains such as transportation, leisure sport has many other benefits which should be appreciated.

## Study Strengths and Limitations

This large study (N>1,000) was done in Germany as part of the 15-year followup of two birth cohorts. We consider our study to be population-based, but for several reasons not perfectly representative of either Germany or Europe. Firstly, we included only newborns of German-speaking parents from two arbitrarily selected regions (see selection criteria for GINIplus and LISAplus.)[22] Secondly, while the primary response during recruitment was equally distributed across all social strata, the later dropout rate was higher for low-SES children, and consent for accelerometry was further dependent on SES: however, we find only weak evidence for selection for leisure sport participation within the cohort, and none for PE. Thus this study samples a relatively privileged, prosperous subset of the German population, likely even more selected than other populations where access to active transport or sport may be limited. Thus our estimates of the contributions of activity domains are likely to be population-specific.

Accelerometry is considered to be an objective form of PA assessment, and it is among the most objective under field conditions. However, the use of self-report (diary) data has almost certainly introduced some error into our PA estimates; and while we attempt to minimize this error as far as possible through scrupulous data cleaning, some almost certainly remains. A major concern of PA measurement is related to compliance of study participants, particularly in respect to keeping an adequate diary of device wear. [44] [45] This was the single biggest reason for a day to be invalid in our study, accounting for nearly 10% (1140/11,523) of recorded days: other reasons, such as technical issues, were comparatively minor. Ultimately 84% of subjects who completed accelerometry provided valid data, comparable to or slightly better than other large studies done in Europe [9] and Canada. [45] This dropout certainly introduced selection bias, which is most clearly visible in Table 1: accelerometry completers were likelier to be female and come from well-educated and urban families and thus may be more compliant; they may also be healthier and /or more health- and sport-conscious than the general population, and we may overestimate both participation and engagement in sporting activities even within the GINIplus and LISAplus cohorts.

Likewise, in order to reduce completion bias as much as possible we kept the diary relatively simple rather than breaking down the domains further, although this cost some precision. We were not able to estimate activity that took place outside of school, PE, transport to school, and leisure sport although this domain ("other time") made up a large fraction of both total time and MVPA, including the trip home from school on every school day. Because many subjects did not go straight home, we were only able to profile the trip to school; and because subjects did not always diary the mode of transport to school we were not able to distinguish active transportation (walking, cycling) from passive transportation such as public transit or car. Lastly, our use of diary data to assign activity to the different domains has almost certainly introduced some error. We attribute 50% of MVPA to"other time," but it is possible that some sporting activities took place during that time and were not diaried. However, selection is inevitable given the effort involved in participation and we consider this bias to be a reasonable price to pay for the high quality of data.

Accelerometry also has its own biases. Specifically it overmonitors high-acceleration activities such as trampolining, and undermonitors low-acceleration activities such as ice skating and cycling, relative to other measures of MVPA. [40, 46–49] It is not clear whether this is likely to produce an over- or underestimate of total MPA and VPA, but allocation of activity by domain may be biased towards those domains with significant levels of ambulation, and away from those domains with low ambulation but high MVPA, such as transportation to school if the student commutes by bicycle.

Epoch length (time over which accelerometric counts are summed) is also not yet standardized. We chose 60 seconds, but other studies of young people [11, 50] have used epochs as short as 5 seconds although 60 is the commonest. Shorter epochs often give higher estimates of moderate, vigorous, and MVPA than longer epochs, although differences are smaller in adolescents than in young children. Edwardson et al [50] found that when epoch length was increased from 5 to 60 seconds, moderate activity was not affected and vigorous activity declined by about 40%, for a slight (10%) decrease in MVPA. Guinhoya et al [11] concurred that the effects of epoch length on PA estimates were stronger for high activity levels than for low ones. This suggests that a shorter epoch length would have given higher estimates of vigorous activity but comparable ones for moderate and MVPA. However, since cardiovascular adaptation to PA is known to take several minutes [32] 60-second epochs may be physiologically the most relevant. 60-second epochs are also most intercomparable with other studies: both recent reviews [11, 51] found that 60 seconds was the most common epoch length. Thus we chose 60 seconds to maximize clinical plausibility and comparability with other studies, but recognize that other lengths are also defensible.

## Conclusions

These German adolescents were comparable to other Europeans in showing low levels of physical activity, with significant contributions from leisure sport and transportation to school. Leisure sport was the most active part of the day and contributed significant amounts of VPA, and participation was comparable between girls and boys and between the two study centers. Although most children had leisure sport, school PE, or both, transportation to school was frequent and thus accounted for a significant fraction of total MVPA. This indicates that even in a population with good access to dedicated sporting activities, frequent active transportation can add significantly to total MVPA.

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## Author Contributions

Conceived and designed the experiments: HS MPS. Performed the experiments: HS JH DB. Analyzed the data: MPS HS. Wrote the paper: MPS HS DN JH DB.

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ORIGINAL ARTICLE
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# Physical activity is not associated with spirometric indices in lung-healthy German youth

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ABSTRACT In lung disease, physical activity improves lung function and reduces morbidity. However, healthy populations are not well studied. We estimate the relationship between spirometric indices and accelerometric physical activity in lung-healthy adolescents.

895 nonsmoking German adolescents without chronic lung disease (45% male, mean±SD age 15.2±0.26 years) from the GINIplus and LISAplus cohorts completed questionnaires, spirometry, 7-day accelerometry and an activity diary. Physical activity was measured as minutes, quintiles and regularity of daily moderate, vigorous and moderate-to-vigorous physical activity (MVPA), participation in sport and active commuting to school. Primary outcomes were forced expiratory volume in 1 s ($FEV_1$), forced vital capacity (FVC), $FEV_1$/FVC and forced expiratory flow at 25–75% of FVC; they were separately correlated with physical activity and adjusted for confounders of respiratory function, including early-life exposures.

Adolescents averaged 40 min MVPA per day, typical for European youth. 79% participated in sports and 51% commuted actively. An association was suggested between 3% higher FVC (~100 mL) and either extreme MVPA quintile or percentage of days with >30 min MVPA ($p<0.05$). However, after Bonferroni correction all associations between spirometry, active lifestyle and physical activity were nonsignificant.

Spirometric indices were not significantly associated with active lifestyle or measures of activity in lung-healthy adolescents after adjustment for confounding and multiple-comparison artefacts.

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## Introduction

Beneficial health effects of physical activity apply across the lifespan, both in the general population [1] and in populations with chronic diseases including diabetes, neurodegenerative and cardiovascular diseases and cancer. Benefits of physical activity for lung function are known for smokers [2, 3] and patients with cystic fibrosis [4], asthma [5, 6] and chronic obstructive pulmonary disease [7]. Accordingly, physical activity has become a standard part of pulmonary rehabilitation [8, 9].

The benefits of activity for healthy lungs are less studied. Better lung function [10] and slower age-related decline [11, 12] have been reported in active adults; improved spirometric indices after exercise interventions have been observed in young adults [13, 14]; and athletes have better lung function than sedentary peers in some, but not all, sports [14]. Active school-aged females experienced faster lung growth, but males did not [15]; active children had better lung function [16]; and physically fit children were less likely to develop asthma [5]. These all suggest that physical activity benefits healthy lungs, but are equally consistent with lung-healthy subjects being preferentially active. However, effects are heterogeneous both between and within studies: benefits sometimes appear to be limited to one sex [15] or, in populations of athletes, to particular sports [14].

Furthermore, neither physical activity nor lung function is measured in the same way across studies. Many studies do not consider lung diseases, particularly asthma, which can interact with activity in complex ways [5, 17–20]. Reported spirometric indices focus on volumes such as forced expiratory volume in 1 s ($FEV_1$) and forced vital capacity (FVC), while flow rates (peak expiratory flow (PEF) and forced expiratory flow (FEF)) are less often addressed. Lastly, physical activity is often assessed by self-report or parental report, which poorly reflect activity as measured by accelerometry [18]. For all these reasons, evidence for the positive association between physical activity and lung function appears to be suggestive, but not conclusive.

The aim of this study was to investigate this association in nonsmoking adolescents without chronic lung disease (asthma or cystic fibrosis). Spirometric indices ($FEV_1$, FVC, $FEV_1$/FVC, and FEF at 25–75% of FVC ($FEF_{25–75\%}$)) were the primary outcomes of our analyses, and we controlled for different early-life factors known to affect lung function. Activity was objectively measured using accelerometry, and activity habits were inferred from participation in sport or active commuting to school.

## Methods

### *Study population*

We combined spirometry, accelerometric physical activity, physical examinations and interviews from GINIplus (German Infant Study on the Influence of Nutrition Intervention (Plus Environmental and Genetic Influences) on Allergy Development) and LISAplus (Lifestyle-Immune System-Allergy: Influence of Life-style Factors on the Development of the Immune System and Allergies in East and West Germany (Plus the Influence of Traffic Emissions and Genetics)), two cohorts of German Caucasians born between 1995 and 1999 and followed-up at the age of 15 years. Further details of the study designs of GINIplus [21] and LISAplus [22] are published elsewhere; abbreviations are defined in the online supplementary material (appendix 1). Both studies were approved by the respective local ethics committees (the Bavarian General Medical Council and the Medical Council of North Rhine-Westphalia) and by written consent from participating families.

GINIplus was initiated to investigate allergy development after intervention with hydrolysed formulas. Of 5991 healthy, full-term newborns recruited in the regions of Munich and Wesel, 2252 (38%) with a family

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history of atopy who consented to participate in a randomised trial (nutritional intervention) were randomised in almost equal numbers to either partially or extensively hydrolysed whey, extensively hydrolysed casein or cow's milk formula. The observation arm, made up of 3739 (62%) unselected children, was given no formula. At 15 years, 3199 adolescents from both study arms were recontacted and approached for accelerometry. Of these, 925 (29%) completed both accelerometry and spirometry; of these, 665 had complete data on confounders and were nonsmokers without known lung disease. Only these complete cases are included in the analyses. Further details on study design, formulas and follow-up are presented in the online supplementary material (appendices 1 and 2) [21, 23].

LISAplus is a population-based cohort of 3097 unselected infants from the cities of Munich, Wesel, Bad Honnef and Leipzig. No intervention, nutritional or otherwise, was used in LISAplus. 1534 subjects were followed-up at the age of 15 years, of which 1107 were from Munich or Wesel and thus approached for accelerometry. Of these, 271 (24%) completed both accelerometry and spirometry, and 230 were nonsmokers, free of lung disease and provided all data for the model analysis. Study design is detailed in Heinrich *et al.* [24].

We thus sampled 895 subjects, 665 from GINIplus and 230 from LISAplus; follow-up is shown in figure 1 and the online supplementary material (appendix 1). Both cohorts are population-based, but the 15-year follow-up is not representative of the underlying study cohorts because of nonrandom loss to follow-up.

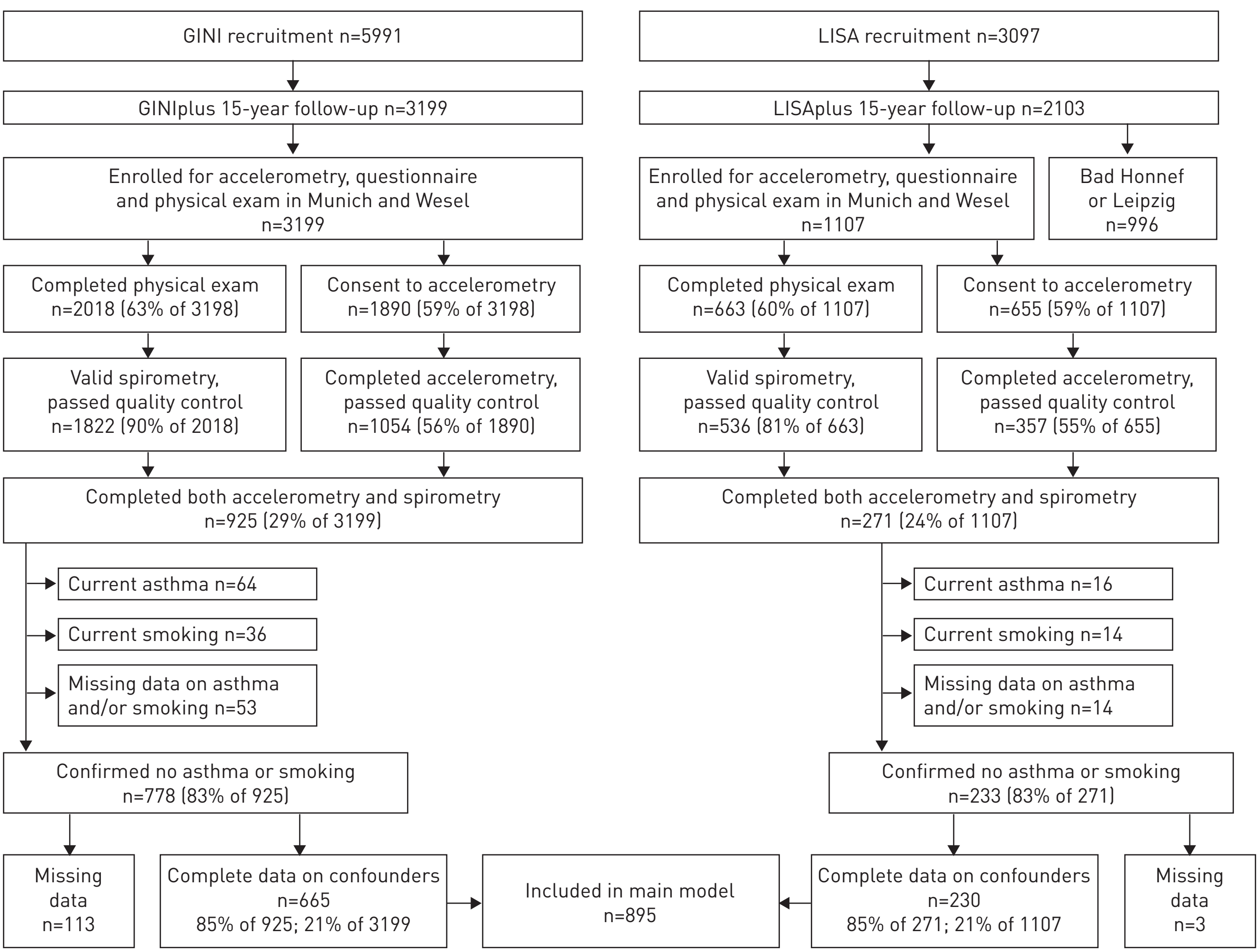


FIGURE 1 GINIplus (German Infant Study on the Influence of Nutrition Intervention (Plus Environmental and Genetic Influences on Allergy Development)) and LISAplus (Lifestyle-Immune System-Allergy: Influence of Life-style Factors on the Development of the Immune System and Allergies in East and West Germany (Plus the Influence of Traffic Emissions and Genetics)) recruitment and follow-up. GINIplus is an ongoing birth cohort study recruited between 1995 and 1999 with the 15-year follow-up addressed in this study (online supplementary material 1 and ginistudie.de). LISAplus is an ongoing birth cohort study recruited between 1995 and July 1998. This study is based on the 15-year follow-up (online supplementary material 1 and lisastudie.de). Details of accelerometry response rate and quality control are provided in the online supplementary material (appendix 1).

Information on sociodemographic confounders (*e.g.* parental education), birthweight, breastfeeding and pre- and postnatal tobacco exposure up to the age of 6 years were obtained from standardised questionnaires from the initial survey (age 4–6 months) and follow-up to 6 years. Height and weight were measured during the physical examination at 15 years. With respect to the considered confounders, questions and protocols were comparable between GINIplus and LISAplus.

### Spirometric protocol

Spirometry was performed seated, wearing a nose clip and after 15 min acclimation to the indoor environment, in line with American Thoracic Society/European Respiratory Society recommendations [25]. Subjects performed at least three but not more than eight trials per test to obtain optimal flow–volume curves. Quality guidelines [25] and visual inspection by physicians were applied to exclude manoeuvres incorrectly performed or with artefacts (for more details see [26] and the online supplementary material (appendix 1)). Spirometric indices were taken from the valid manoeuvre with the largest sum of $FEV_1$ and FVC. Indices measured were $FEV_1$, FVC, $FEV_1$/FVC ratio and flow rates (PEF, FEFs). z-scores were based on Global Lung Initiative (GLI) reference values [27].

### Accelerometric protocol

For a detailed description of accelerometer protocol, quality control and data cleaning, see [28] and the online supplementary material (appendix 1). Accelerometers (ActiGraph GT3X; ActiGraph, Pensacola, FL, USA) were worn at the hip. Sampling rate was 30 Hz; accelerations were stored at 1 Hz and converted into activity levels in 1-min epochs using the algorithm from Freedson *et al.* [29].

In a standardised diary, subjects documented times of getting up and going to bed, sport and active commuting to school. Valid days had ⩾7–10 h of valid recording. Valid subjects provided at least three valid weekdays and one valid weekend day. Of the 1689 subjects who returned the accelerometer, 1411 (8832 days) ultimately provided valid data.

### Physical activity

We considered the following physical activity measures. 1) Average daily minutes of moderate, vigorous and moderate-to-vigorous physical activity (VPA and MVPA, respectively); 2) MVPA quintiles, to check for nonlinearity; 3) regularity of MVPA throughout the week (the health effects of short periods of physical activity may differ from those for long periods [30]. For each subject we averaged the fraction of days with >30, >45 and >60 min MVPA, to create three variables ranging from 0=never to 1=every day); 4) active commuting, defined as walking or bicycling to school at any point during accelerometry. Participation in sport at least once during accelerometry was also considered.

### Exclusion criteria

#### Asthma

Asthma is a lung condition associated with lower physical activity, so to avoid biasing our results, we excluded asthmatics (n=80; fig. 1). Asthma was defined as at least two of the three following characteristics [31]: asthma diagnosed by a doctor at any year since the age of 3 years. Evaluations were performed at ages 4, 6, 10 and 15 years, with the question asked separately for each year of life since the last examination; asthma medication taken in the past 12 months; asthma symptoms (wheezing or shortness of breath) in the past 12 months.

#### Other lung diseases

No children in our study population had cystic fibrosis or other known chronic lung disease.

#### Smoking

Only subjects who self-reported current abstinence from tobacco smoking were included in the study. 50 smokers were identified and excluded (fig. 1).

#### Missing data

We excluded 67 children with missing data on asthma and/or smoking.

### Inclusion criteria

Of 1011 nonasthmatic, nonsmoking 15-year-olds without cystic fibrosis who completed accelerometry and spirometry, 895 (88.5%) had data on all confounders. To maximise comparability between models we restricted our analysis to these complete cases (fig. 1).

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TABLE 1 Population characteristics

| | Males | Females | p-value for sex difference |
|---|---|---|---|
| **Male** | 401 (45) | | ## |
| **Age at exam years** | 15.2±0.25 | 15.2±0.27 | ## |
| **Height at spirometry cm** | 176±7.6 | 167±6.1 | <0.0001 |
| **Weight kg** | 64.4 (63.8; 47–85) | 58.7 (57.2; 46–76) | <0.0001 |
| **BMI kg·m$^{-2}$** | 20.6 (20.0; 17–26) | 20.9 (20.4; 17–26) | ## |
| **Parents highly educated#** | 68 | 70 | ## |
| **Study centre Munich** | 61 | 54 | 0.038 |
| **Nutritional intervention¶** | 36 | 37 | ## |
| **BMI category+** | | | 0.28 |
| Underweight | 7.73 | 6.47 | ¶¶ |
| Normal weight | 81.3 | 84.4 | ¶¶ |
| Overweight | 8.23 | 5.47 | ¶¶ |
| Obese | 2.74 | 3.64 | ¶¶ |
| **$FEV_1$ L** | 3.83±0.65 | 3.23±0.42 | <0.0001 |
| **FVC L** | 4.50±0.73 | 3.66±0.51 | <0.0001 |
| **$FEV_1$/FVC %** | 85±5.8 | 88±5.8 | <0.0001 |
| **$FEV_1$ z-score§** | −0.55±0.99 | −0.48±0.91 | ## |
| **FVC z-score§** | −0.56±0.95 | −0.43±0.91 | 0.035 |
| **$FEV_1$/FVC z-score§** | −0.06±0.94 | −0.075±0.96 | ## |
| **$FEF_{25–75\%}$ z-score§** | −0.43±0.98 | −0.32±0.88 | ## |
| **PEF L·s$^{-1}$** | 7.65±1.3 | 6.56±0.95 | <0.0001 |
| **$FEF_{25\%}$ L·s$^{-1}$** | 6.56±1.3 | 5.93±0.91 | <0.0001 |
| **$FEF_{50\%}$ L·s$^{-1}$** | 4.71±1.2 | 4.26±0.86 | <0.0001 |
| **$FEF_{75\%}$ L·s$^{-1}$** | 2.31±0.78 | 2.15±0.64 | <0.0001 |
| **$FEF_{25–75\%}$ L·s$^{-1}$** | 4.13±1.03 | 3.76±0.76 | <0.0001 |
| **Birthweight g** | 3526±443 | 3422±451 | 0.0006 |
| **Exclusively breastfed** | | | ## |
| Never | 35 | 35 | ¶¶ |
| Months 1–4 only | 10 | 9.11 | ¶¶ |
| Past month 4 | 55 | 56 | ¶¶ |
| **Mother smoked tobacco when pregnant** | 9.47 | 10.3 | ## |
| **Tobacco smoke at home up to age 6 years** | 31 | 30 | ## |
| **Activity levels min·day$^{-1}$ *f*** | | | |
| Moderate | 30.8 (29; 14–54) | 25.3 (24; 9.2–45) | <0.0001 |
| Vigorous | 14.1 (11; 2.0–35) | 10.3 (8.1; 0.86–29) | <0.0001 |
| MVPA | 44.9 (42.0; 17–83) | 35.6 (32.1; 13–67) | <0.0001 |
| **MVPA percentage of days** | | | |
| >30 min | 56 (57; 14–100) | 48 (42; 0–100) | <0.0001 |
| >45 min | 39 (33; 0–86) | 28 (29; 0–71) | <0.0001 |
| >60 min | 26 (20; 0–71) | 16 (14; 0–57) | <0.0001 |
| **Any sport** | 77 | 80 | ## |
| **Any active commuting to school** | 54 | 49 | ## |

Data are presented as n (%), mean±SD, mean (median; 5th–95th percentiles) or %, unless otherwise stated. Centrally distributed variables are presented as mean±SD and p-value from unequal-variance t-test; categorical variables are presented as % for each category, and p-values from Kruskal–Wallis test; binary variables are presented as % and p-value from Wilcoxon's two-tailed rank-sum test; and skewed variables are presented as mean (median; 5th–95th percentiles) and p-value from Wilcoxon's two-tailed rank-sum test. Population is lung-healthy with complete data; it excludes smokers, asthmatics and those missing data. Moderate, vigorous and moderate-to-vigorous physical activity (MVPA) imputed for diarised nonwear of accelerometer due to sport. BMI: body mass index; $FEV_1$: forced expiratory volume in 1 s; FVC: forced vital capacity; $FEF_{25–75\%}$, $_{25\%}$, $_{50\%}$ and $_{75\%}$: forced expiratory flow at 25–75%, 25%, 50% and 75% of FVC, respectively; PEF: peak expiratory flow. #: better-educated parent college admission or higher; ¶: [21, 23]; +: according to 10th, 90th and 97th BMI percentiles from a German reference [32]; §: z-scores from [27]; *f*: accelerometric cutpoints from [29, 33]; ##: p>0.05; ¶¶: p-value given as type 3 for global null hypothesis (top line).

### *Statistical methods*

All analyses were performed using SAS 9.2 (SAS Institute, Cary, NC, USA). Population characteristics (table 1) are presented as mean±SD for centrally distributed variables, and as mean (median; 5th–95th percentile) for skewed variables such as weight, body mass index (BMI) and VPA. p-values for group comparisons were calculated using Wilcoxon's two-tailed rank-sum test for binary and skewed variables, the Kruskal–Wallis test for categorical variables and the t-test for centrally distributed variables.

Statistical models were fit using generalised linear modelling. Spirometric indices and GLI z-scores ($FEV_1$, FVC, $FEV_1$/FVC and $FEF_{25–75\%}$) were modelled as normally distributed functions of known confounders and one physical activity measure at a time. Inspection of quantile (Q)–Q plots confirmed normality. No model contained either more than one physical activity measure or more than one spirometric index. Confounders were chosen *a priori* and left in the models regardless of statistical significance. For further details on statistical analysis see the online supplementary material (appendix 2).

Confounders considered were sex, age, height, weight, BMI, study centre, accelerometer weartime, nutritional intervention, parental education, birthweight, breastfeeding and pre- and postnatal tobacco smoke exposure. Alternative models adjusted for subsets of these confounders (the crude and basic models); adjusted further for air pollution (annual average exposure to nitrogen oxides and particles with a 50% cut-off aerodynamic diameter of 2.5 µm); modelled only the subset of the population without extreme values for spirometry or physical activity; or modelled flows (PEF, $FEF_{25}$, $FEF_{50}$ and $FEF_{75}$) as outcome. Selected models are presented in the main text, and the remainder in the online supplementary material (appendix 3).

At $p \leqslant 0.05$ we have 80% power to detect a difference of ∼100 mL $FEV_1$ or FVC (3%) between the top and bottom physical activity quintiles. This is comparable to the effect size estimated in the literature, so we choose the traditional $p \leqslant 0.05$ to avoid missing an effect. Bonferroni correction is $p \leqslant 0.0003$ (the basic, crude and main models; four spirometric indices; and 12 physical activity measures, counting each MVPA quintile).

## Results

### Study population

Height, weight and BMI of study participants (table 1) fit the German reference population well [32]. Sociodemographic data confirmed a predominance of highly educated and urban families. Over half were from urban Munich rather than rural Wesel, 10% were born to mothers who smoked during pregnancy and one-third were exposed to tobacco smoke at home in the first 6 years. 55% of participants were female, compared to 51% of the 15-year follow-up, but otherwise the baseline population was representative of the follow-up population (online supplementary table 1b). However, the 15-year follow-up differed significantly from the original study population (online supplementary table 1c) suggesting differential loss to follow-up.

### Lung function

Mean±SD $FEV_1$ and FVC in this sample were 3.83±0.65 L and 4.50±0.73 L, respectively, for males, and 3.23±0.42 L and 3.66±0.51 L, respectively, for females. This is about half a standard deviation below the GLI predicted values [27]; however, z-score differences between sexes were small. Offset was smaller (online supplementary table 1d) for the German reference values established in the LUNOKID study [34]. However, the two sets of z-scores correlated extremely closely with each other (all $R^2>0.99$).

### Activity habits

Each day averaged ∼900 min of accelerometry, of which time two-thirds was sedentary, one-third engaged in light activity and ∼5% in MVPA (table 1). Males were more active than females, but had similar participation levels in sport (77% and 80% of males and females, respectively) and active commuting (55% and 49% of males and females, respectively). These values are typical for European youth [35] and well below World Health Organization recommendations [36].

### Physical activity and spirometric indices

At $p \leqslant 0.05$ there was no association between physical activity and any flow index ($FEF_{25–75\%}$ in tables 2–4, others in the online supplementary material (appendix 3)) or between any index and either participation in sport or active commuting to school. There was no evidence for a nonlinear effect of MVPA or for confounding by air pollution. Effect estimates were consistent between models of varying complexity.

FVC was associated with both MVPA quintile and percentage of days with >30 min MVPA. Although type 3 tests often found no significant difference among all quintiles (global null hypothesis), at $p<0.05$ pairwise comparisons often showed significantly higher FVC in the most active quintile than the least active, and there was generally a monotone trend across the others (fig. 2a). In the main model (table 2), children in the top quintile of MVPA averaged 113 mL greater FVC (pairwise $p<0.02$; global null $p>0.10$) than those in the bottom quintile, and getting >30 min MVPA every day, *versus* never doing so, was associated with 113 mL increase in FVC ($p<0.05$.) Effects were similar when outliers were excluded (table 3), when z-scores were modelled as outcome, instead of raw values (table 4) and in simpler models or when air pollution was considered (online supplementary material (appendix 3, tables 1.1–1.3 and 2.1–2.3)).


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TABLE 2 Activity as a correlate of lung function, adjusted for age, sex, height, study centre, nutritional intervention, device weartime, body mass index, parental education, birthweight, exclusive breastfeeding, prenatal tobacco and tobacco smoke at home up to the age of 6 years

| | **$FEV_1$ mL** | | **FVC mL** | | **$FEV_1$/FVC %** | | **$FEF_{25–75\%}$ $mL·s^{-1}$** | |
|---|---|---|---|---|---|---|---|---|
| | **Parameter estimate (95% CI)** | **p-value** | **Parameter estimate (95% CI)** | **p-value** | **Parameter estimate (95% CI)** | **p-value** | **Parameter estimate (95% CI)** | **p-value** |
| **Daily mean minutes** | | | | | | | | |
| MPA | 1.009 (−1.1–3.1) | 0.34 | 1.343 (−0.91–3.6) | 0.24 | −0.0048 (−0.034–0.024) | 0.75 | 1.58 (−2.6–5.8) | 0.46 |
| VPA | 0.979 (−1.6–3.6) | 0.46 | 2.636 (−0.17–5.4) | 0.066 | −0.0344 (−0.070–0.002) | 0.060 | −0.439 (−5.7–4.8) | 0.87 |
| MVPA | 0.700 (−0.66–2.1) | 0.31 | 1.296 (−0.18–2.7) | 0.084 | −0.0114 (−0.030–0.007) | 0.23 | 0.554 (−2.2–3.3) | 0.69 |
| **MVPA quintile[#]** | | 0.22 | | 0.21 | | **0.022** | | **0.050** |
| 1[¶] | 0 | | 0 | | 0 | | 0 | |
| 2[¶] | −5.52 (−89–78) | 0.90 | 58.1 (−33–149) | 0.21 | **−1.45 (−2.6–0.29)** | **0.014** | **−172 (−342–−1.8)** | **0.048** |
| 3[¶] | 43.4 (−40–127) | 0.31 | 63.0 (−28–154) | 0.18 | −0.46 (−1.6–0.70) | 0.44 | 10.1 (−160–181) | 0.91 |
| 4[¶] | −19.0 (−103–65) | 0.66 | 51.1 (−40–142) | 0.27 | | **0.0033** | −155 (−326–14.7) | 0.073 |
| 5[¶] | 67.0 (−18–151) | 0.12 | **113 (21–205)** | **0.016** | −0.86 (−2.0–0.31) | 0.15 | 16.1 (−156–188) | 0.85 |
| **Percentage of days with MVPA** | | | | | | | | |
| >30 min | 96.1 (−2.5–195) | 0.056 | **113 (6.4–221)** | **0.038** | −0.331 (−1.7–1.0) | 0.64 | 117 (−84–318) | 0.26 |
| >45 min | 72.3 (−33–177) | 0.18 | 95.5 (−18–209) | 0.10 | −0.428 (−1.9–1.0) | 0.56 | 106 (109–−107) | 0.33 |
| >60 min | 48.0 (−77–172) | 0.45 | 98.7 (−36–234) | 0.15 | −1.200 (−2.9–0.53) | 0.17 | 23.6 (−230–277) | 0.86 |
| **Any sport** | 34.3 (−31–100) | 0.30 | 46.6 (−25–118) | 0.20 | −0.189 (−1.1–0.72) | 0.68 | 22.5 (−111–156) | 0.74 |
| **Any active transportation[+]** | 23.9 (−32–76) | 0.39 | 40.0 (−21–95) | 0.18 | −0.189 (−0.95–0.54) | 0.68 | 11.9 (−99–120) | 0.83 |

Data presented in bold are statistically significant at $p<0.05$. 95% CI was calculated using Wald's Chi-squared test. Moderate physical activity (MPA), vigorous physical activity (VPA) and moderate-to-vigorous physical activity (MVPA) imputed for diarised nonwear of accelerometer due to sport. Accelerometric cutpoints were calculated using Freedson's algorithm [29, 33]. $FEV_1$: forced expiratory volume in 1 s; FVC: forced vital capacity; $FEF_{25–75\%}$: forced expiratory flow at 25–75% of FVC. [#]: p-value for global null hypothesis (*i.e.* all quintiles equal), quintiles were stratified by sex; [¶]: p-value and parameter estimate for each quintile compared with the lowest (reference); [+]: defined as commuting to school by walking or cycling at least once during accelerometry.

TABLE 3 Activity as a correlate of lung function, outliers excluded, associations for subjects with moderate physical activity (MPA), vigorous physical activity (VPA), moderate-to-vigorous physical activity (MVPA), forced expiratory volume in 1 s ($FEV_1$), forced vital capacity (FVC) and $FEV_1$/FVC all within 2 SD of the sex-specific mean, adjusted for age, sex, height, study centre, nutritional intervention, device weartime, body mass index, parental education, birthweight, exclusive breastfeeding, prenatal tobacco and tobacco smoke at home up to the age of 6 years

| | $FEV_1$ mL | | FVC mL | | $FEV_1$/FVC % | | $FEF_{25–75\%}$ mL·s$^{-1}$ | |
|---|---|---|---|---|---|---|---|---|
| | Parameter estimate (95% CI) | p-value | Parameter estimate (95% CI) | p-value | Parameter estimate (95% CI) | p-value | Parameter estimate (95% CI) | p-value |
| **Daily mean minutes** | | | | | | | | |
| MPA | 1.93 (−0.72–4.6) | 0.15 | 2.05 (−0.80–4.9) | 0.16 | 0.0040 (−0.033–0.041) | 0.83 | 3.01 (−2.6–8.6) | 0.29 |
| VPA | 1.97 (−1.7–5.7) | 0.30 | **4.11 (−0.18–8.1)** | **0.041** | −0.043 (−0.094–0.0090) | 0.11 | −2.15 (−9.9–5.6) | 0.59 |
| MVPA | −1.37 (−0.44–3.2) | 0.14 | **1.94 (0.0041–3.9)** | **0.050** | −0.0083 (−0.034–0.017) | 0.52 | 0.879 (−2.9–4.7) | 0.65 |
| **MVPA quintile#** | | 0.27 | | 0.16 | | **0.024** | | 0.078 |
| 1¶ | 0 | | 0 | | 0 | | 0 | |
| 2¶ | 28.8 (−67–58) | 0.89 | **91.4 (7.4–175)** | **0.033** | **−1.27 (−2.4–−0.18)** | **0.022** | −127 (−291–36) | 0.13 |
| 3¶ | 42.6 (−50–107) | 0.47 | 62.9 (−20–146) | 0.14 | −0.46 (−1.55–0.62) | 0.40 | 9.34 (−153–172) | 0.91 |
| 4¶ | −2.26 (−35–120) | 0.28 | 62.4 (−22–147) | 0.15 | **−1.53 (−2.63–−0.43)** | **0.0064** | −135 (−301–30) | 0.11 |
| 5¶ | 88.4 (−1.7–179) | 0.055 | **109 (13–206)** | **0.026** | −0.14 (−1.40–1.12) | 0.83 | 77.0 (−111–265) | 0.42 |
| **Percentage of days with MVPA** | | | | | | | | |
| >30 min | **109 (7.4–210)** | **0.035** | **115 (6.4–224)** | **0.038** | 0.142 (−1.3–1.6) | 0.84 | 139 (−74–352) | 0.20 |
| >45 min | 104 (−11–219) | 0.076 | 96.2 (−27–219) | 0.13 | 0.483 (−1.1–2.1) | 0.56 | 160 (−81–400) | 0.19 |
| >60 min | 75.9 (−74–225) | 0.32 | 132 (−28–292) | 0.11 | −1.026 (−3.1–1.1) | 0.34 | −12.0 (−325–301) | 0.94 |
| **Any sport** | −15.4 (−79–48) | 0.64 | 10.1 (−58–78) | 0.77 | −0.600 (−1.5–0.30) | 0.19 | −50.0 (−183–83) | 0.46 |
| **Any active transportation+** | −3.10 (−55–49) | 0.91 | 10.8 (−45–67) | 0.71 | −0.333 (−1.1–0.40) | 0.37 | −44.3 (−154–65) | 0.43 |

Data presented in bold are statistically significant at $p<0.05$. 95% CI calculated using Wald's Chi-squared test. MPA, VPA and MVPA imputed for diarised nonwear of accelerometer due to sport. Accelerometric cutpoints were calculated using Freedson's algorithm [29, 33]. $FEF_{25–75\%}$: forced expiratory flow at 25–75% of FVC. #: p-value for global null hypothesis (*i.e.* all quintiles equal), quintiles stratified by sex; ¶: p-value and parameter estimate for each quintile compared with the lowest (reference); +: defined as commuting to school by walking or cycling at least once during accelerometry.

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TABLE 4 Activity as a correlate of Global Lung Initiative z-score [27], adjusted for age, sex, height, study centre, nutritional intervention, device weartime, body mass index, parental education, birthweight, exclusive breastfeeding, prenatal tobacco and tobacco at home up to the age of 6 years

| | $FEV_1$ z-score × 1000 | | FVC z-score × 1000 | | $FEV_1$/FVC z-score × 1000 | | $FEF_{25-75\%}$ z-score × 1000 | |
|---|---|---|---|---|---|---|---|---|
| | Parameter estimate (95% CI) | p-value | Parameter estimate (95% CI) | p-value | Parameter estimate (95% CI) | p-value | Parameter estimate (95% CI) | p-value |
| **Daily mean minutes** | | | | | | | | |
| MPA | 1.93 (−2.6–6.5) | 0.41 | 2.56 (−1.9–7.0) | 0.26 | −0.892 (−5.6–3.8) | 0.71 | 1.56 (−3.1–6.2) | 0.51 |
| VPA | 2.22 (−3.5–7.9) | 0.45 | **5.77 (0.26–11.3)** | **0.040** | −5.88 (−12–0.0041) | 0.050 | −1.24 (−7.1–4.6) | 0.68 |
| MVPA | 1.43 (−1.6–4.4) | 0.35 | 2.67 (−0.21–5.6) | 0.070 | −1.99 (−5.1–1.1) | 0.21 | 0.330 (−2.7–3.4) | 0.83 |
| **MVPA quintile**# | | 0.20 | | 0.14 | | **0.016** | | 0.057 |
| 1¶ | 0 | | 0 | | 0 | | 0 | |
| 2¶ | −7.20 (−192–177) | 0.94 | **121 (−57–300)** | **0.18** | **−252 (−441–−62)** | **0.0093** | −188 (−376–0.23) | 0.050 |
| 3¶ | 113 (−71–298) | 0.22 | 147 (−31–327) | 0.11 | −102 (−292–89) | 0.30 | 21.5 (−167–210) | 0.82 |
| 4¶ | −29.5 (−214–155) | 0.75 | 123 (−55–302) | 0.18 | **−302 (−492–112)** | **0.0018** | −166 (−354–22) | 0.083 |
| 5¶ | 155 (−32–341) | 0.10 | **241 (60–421)** | **0.0089** | −154 (−346–38) | 0.12 | 9.01 (−181–199) | 0.93 |
| **Percentage of days with MVPA** | | | | | | | | |
| >30 min | **218 (0.72–435)** | **0.049** | **252 (42–462)** | **0.019** | −64.7 (−289–160) | 0.57 | 115 (−108–337) | 0.31 |
| >45 min | 155 (−76–386) | 0.19 | 204 (−20–427) | 0.074 | −76.3 (−315–162) | 0.53 | 91.7 (−144–328) | 0.45 |
| >60 min | 88.6 (−186–363) | 0.53 | 203 (−62–469) | 0.13 | −217 (−500–66) | 0.13 | −15.8 (−296–264) | 0.91 |
| **Any sport** | 62.1 (−82–206) | 0.40 | 82.5 (−57–222) | 0.25 | −57.2 (−206–92) | 0.45 | 21.9 (−126–169) | 0.77 |
| **Any active transportation**+ | 56.1 (−62–175) | 0.35 | 72.9 (−42–188) | 0.21 | −31.8 (−154–90) | 0.61 | 16.0 (−105–137) | 0.80 |

Data presented in bold are statistically significant at $p<0.05$. All parameter estimates are multiplied by 1000 for interpretability, *e.g.* subjects who got >30 min moderate-to-vigorous physical activity (MVPA) per day averaged a forced vital capacity (FVC) z-score that was 0.252 units higher. 95% CI calculated using Wald's Chi-squared test. Moderate physical activity (MPA), vigorous physical activity (VPA) and MVPA imputed for diarised nonwear of accelerometer due to sport. Accelerometric cutpoints were calculated using Freedson's algorithm [29, 33]. $FEV_1$: forced expiratory volume in 1 s; $FEF_{25-75\%}$: forced expiratory flow at 25–75% of FVC. #: p-value for global null hypothesis (*i.e.* all quintiles equal), quintiles stratified by sex; ¶: p-value and parameter estimate for each quintile compared with the lowest (reference); +: active transportation defined as commuting to school by walking or cycling at least once during accelerometry.

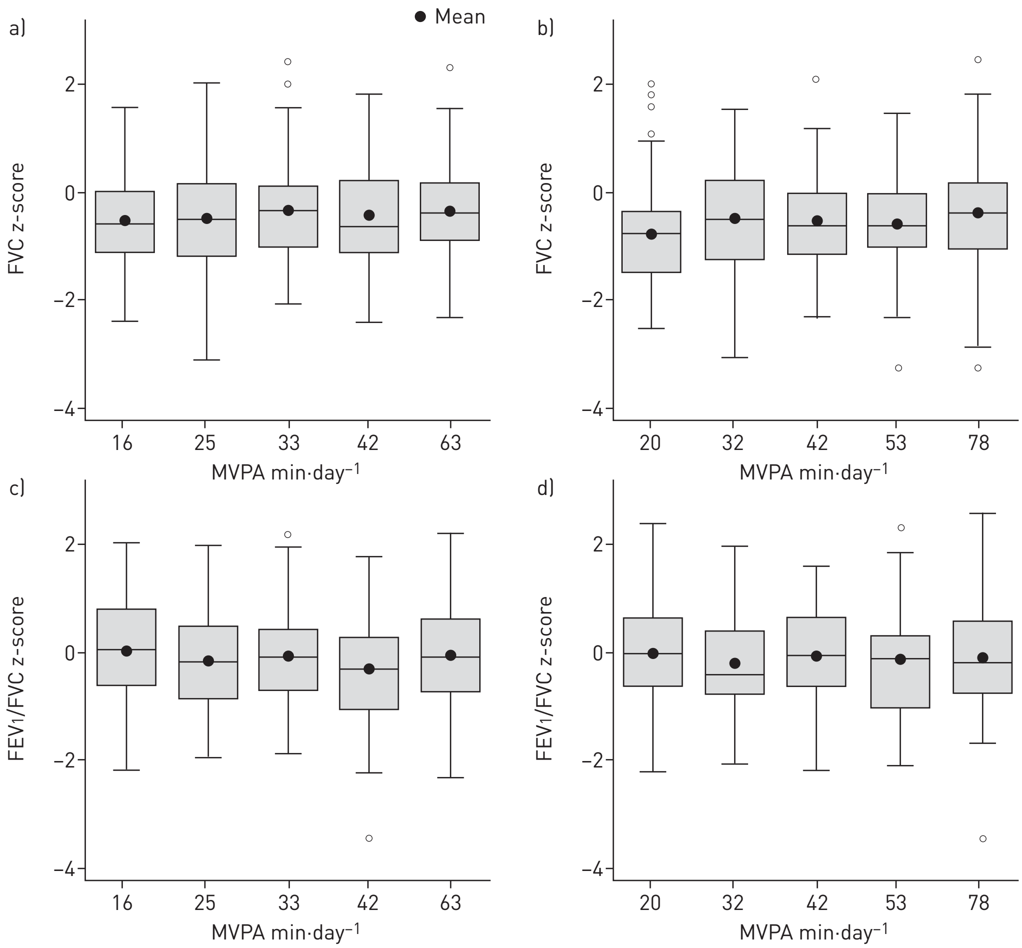


FIGURE 2 Spirometric indices by physical activity quintile. Forced vital capacity (FVC) for a) females and b) males; forced expiratory volume in 1 s ($FEV_1$)/FVC for c) females and d) males. Box and whisker plots show median (25th–75th percentiles) of spirometric z-score and 1.5 interquartile ranges; the mean is represented by a black circle. Spirometric z-scores are from the Global Lung Initiative [27]. Mean daily minutes in MVPA were calculated using Freedson's accelerometric algorithm [29]. Quintiles were calculated separately for each sex.

Relationships with indices other than FVC were often not monotone: for example, the MVPA quintiles that had the most different $FEV_1$/FVC from the least-active (reference) were the second and fourth, not the fifth (highest) (fig. 2b). While PEF was associated at $p \leqslant 0.05$ with VPA and MVPA in the full population, this effect disappeared after the exclusion of outliers. Relationships with spirometric flows (PEF and FEFs) are presented in the online supplementary material (appendix 3, tables 3.1 and 3.2).

After Bonferroni correction, there was no statistically significant relationship between physical activity and any spirometric index.

## Discussion

After correction for multiple comparisons, we found no significant associations in lung-healthy adolescents between physical activity, active lifestyle and spirometric indices. While existing literature suggests that physically active healthy people average 1–10% higher spirometric volumes, particularly FVC, than inactive peers [10, 13, 15, 16, 37], in athletes these effects were found only in some sports [14], and in one study [13] FVC declined by 4% after 8 weeks of aerobic exercise. We found that at $p \leqslant 0.05$ only the association between FVC and either percentage of days with >30 min MVPA or extreme MVPA quintile, was both robust across models and consistent with a monotone trend between spirometry and physical activity. The observed difference of 113 mL FVC (3%) between top and bottom MVPA quintile was consistent with the literature [10, 13, 15, 16, 37]; however, results for other indices often were not plausible, such as larger spirometric differences between intermediate MVPA quintiles than between extreme quintiles. To reduce multiple comparisons we suggest that further research focuses on spirometric indices chosen *a priori*, such as FVC.


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Possible reasons for the discrepancies between studies may include statistical models used, study population, confounding, correction for multiple comparisons or physical activity measurement methods; measurement methods for lung function were comparable. We accelerometrically measured physical activity in adolescents and considered levels, thresholds and lifestyle, while other studies [10, 13, 15, 16, 37] mostly studied younger children, relied on physical activity questionnaires, and/or dichotomised physical activity into active *versus* nonactive.

While we considered nonlinear effects by modelling MVPA quintiles and thresholds in addition to continuous minutes, we may have missed a more complex relationship. The association between FVC and percentage of days with >30 min of MVPA, but no higher threshold, hints at nonlinearity. Although almost the whole population (87% of subjects) had participated in sport and/or commuted actively, physical activity was highly variable: 5th and 95th percentiles were 15 and 75 min per day, respectively, MVPA, and 1.2 and 31 min, respectively, VPA. Nevertheless, the full range of physical activity may not have been sampled. In light of findings in athletes, who experienced ~5% higher spirometric volumes [14], our observed physical activity may have been insufficient to measurably affect lung function.

Furthermore, activity type may be important in determining size or direction of the association between physical activity and lung function: some sports were associated with increased volumes, others were associated with no difference and others with decreases [14]. Although we found no change in spirometry with participation in sport, we did not consider the type of sport, and with regards to total physical activity, one sport associated with increased FVC (~6%) was cycling, which accelerometry is known to undermonitor [38].

### *Strengths and limitations*

The strength of our study is that we applied several different quantifications of physical activity and measured physical activity objectively with accelerometry rather than questionnaires: only 1–10% of the variance of accelerometric physical activity is captured by self-report [18] and this error is not likely to be uniform across subjects. However, accelerometry also has well-known limitations, including the "snapshot" nature of data recorded over the course of a single week and the known undermonitoring of low-acceleration sports [38]. Although participants may be more active when they know measurement is taking place [39], our subjects were no more active on the first weekday of accelerometry than on the others, which suggests that this effect is negligible. Likewise, although spirometry is the standard measurement of lung function, it does not measure mechanical properties of the lung, respiratory pump functions or gas-exchange capacity, although in the healthy lung close correlations have been reported with FVC.

Well-known limitations arise from our cross-sectional design. Selection bias began with the recruitment of German Caucasians born full-term and continued with selective loss to follow-up by the age of 15 years; successful completion of accelerometry, examinations and questionnaires at the age of 15 years may have introduced further bias. Relative to GINIplus and LISAplus at birth, we oversampled females from urban Munich and well-educated families who breastfed more and smoked less, all of which may indicate greater health-consciousness. The intervention arm of GINIplus (selected for atopy risk) was more likely to be followed-up successfully than the unselected observation arm, further suggesting a health-consciousness bias. However, representation of the four different nutritional interventions did not change and $FEV_1$ and FVC did not vary between study formulas [40], suggesting that the intervention itself did not drive results. Thus, while we adjusted for conditions that may affect lung function, and carefully excluded smokers, asthmatics or those with suspected asthma, residual effects cannot be ruled out and our findings may not generalise to all populations.

### *Conclusion*

In a cohort of healthy and active adolescents, we found no clear evidence for an association between spirometric indices and physical activity or activity habits.

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RESEARCH ARTICLE

# Asthma and Rhinitis Are Associated with Less Objectively-Measured Moderate and Vigorous Physical Activity, but Similar Sport Participation, in Adolescent German Boys: GINIplus and LISAplus Cohorts

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**Data Availability Statement:** Data are from the GINIplus study and LISAplus studies, which include patient-specific information. Interested researchers will obtain a de-identified, participant level dataset for the data pertaining to the current study, which will require ethical approval and consent from the GINIplus and LISAplus PIs. Requests should be addressed to Holger Schulz (schulz@helmholtz-muenchen.de).

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## Abstract

### Introduction

Physical activity (PA) protects against most noncommunicable diseases and has been associated with decreased risk of allergic phenotype, which is increasing worldwide. However, the association is not always present; furthermore it is not clear whether it is strongest for asthma, rhinitis, symptoms of these, or atopic sensitization; which sex is most affected; or whether it can be explained by either avoidance of sport or exacerbation of symptoms by exercise. Interventions are thus difficult to target.

### Methods

PA was measured by one-week accelerometry in 1137 Germans (mean age 15.6 years, 47% boys) from the GINIplus and LISAplus birth cohorts, and modeled as a correlate of allergic symptoms, sensitization, or reported doctor-diagnosed asthma or rhinitis.

### Results

8.3% of children had asthma, of the remainder 7.9% had rhinitis, and of the remainder 32% were sensitized to aero-allergens (atopic). 52% were lung-healthy controls. Lung-healthy boys and girls averaged 46.4 min and 37.8 min moderate-to-vigorous PA per day, of which 14.6 and 11.4 min was vigorous. PA in allergic girls was not altered, but boys with asthma got 13% less moderate and 29% less vigorous PA, and those with rhinitis with 13% less moderate PA, than lung-healthy boys. Both sexes participated comparably in sport (70 to

Study on the influence of Nutrition Intervention PLUS environmental and genetic influences on allergy development) and LISAplus (Influence of lifestyle factors on the development of the immune system and allergies Plus the influence of traffic emissions and genetics). We thank the GINIplus and LISAplus Study Groups for all their excellent work. The GINIplus Study Group includes the following: Institute of Epidemiology I, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg (J. Heinrich, I. Brüske, H. Schulz, C. Flexeder, C. Zeller, M. Standl, M. Schnappinger, M. Sußmann, E. Thiering, C. Tiesler); Research Institute, Department of Pediatrics, Marien-Hospital, Wesel (D. Berdel, A. von Berg, B. Filipiak-Pittroff); Ludwig-Maximilians-University of Munich, Dr von Hauner Children's Hospital (S. Koletzko, K. Werkstetter); Department of Pediatrics, Technische Universität München and Deutsche Rentenversicherung Bayern (C.P. Bauer, U. Hoffmann); and IUF-Leibniz Institute for Environmental Research, Düsseldorf (B. Hoffmann, E. Link, C. Klümper, U. Krämer). The LISAplus Study Group includes the following: Institute of Epidemiology I, Helmholtz Zentrum München, German Research Center for Environmental Health (J. Heinrich, I. Brüske, H. Schulz, M. Standl, M. Schnappinger, M. Sußmann, E. Thiering, C. Tiesler, C. Flexeder, C. Zeller); Department of Pediatrics, Marien Hospital Wesel, Wesel (A. von Berg); Pediatric Practice, Bad Honnef (B. Schaaf); Technical University, Munich (C.P. Bauer, U. Hoffmann); Helmholtz Centre for Environmental Research – UFZ, Department of Environmental Immunology/Core Facility Studies, Leipzig (I. Lehmann, M. Bauer, G. Herberth, J. Müller, S. Röder and M. Schilde); Department of Pediatrics, Municipal Hospital 'St. Georg', Leipzig (M. Borte, U. Diez, C. Dorn, E. Braun); and ZAUM – Center for Allergy and Environment, Technical University Munich (M. Ollert, J. Grosch). The GINIplus study was mainly supported for the first 3 years of the Federal Ministry for Education, Science, Research and Technology (interventional arm) and Helmholtz Zentrum Munich (former GSF) (observational arm). The 4 year, 6 year, and 10 year follow-up examinations of the GINIplus study were covered from the respective budgets of the 4 study centres: Helmholtz Zentrum Munich, Research Institute at Marien-Hospital Wesel, Ludwig-Maximilians-University Munich, Technical University Munich, and from 6 years onwards also from IUF - Leibniz Research-Institute for Environmental Medicine at the University of Düsseldorf, and a grant from the Federal Ministry for Environment (IUF Düsseldorf, FKZ 20462296). The LISAplus study was mainly supported by grants from the Federal Ministry for Education, Science, Research and Technology and in addition from Helmholtz Zentrum Munich

84%). Adolescents with wheezing (up to 68%, in asthma) and/or nose/eye symptoms (up to 88%, in rhinitis) were no less active.

## Conclusions

We found that asthma and rhinitis, but not atopy, were independently associated with low PA in boys, but not in girls. These results indicate that allergic boys remain a high-risk group for physical inactivity even if they participate comparably in sport. Research into the link between PA and allergy should consider population-specific and sex-specific effects, and clinicians, parents, and designers of PA interventions should specifically address PA in allergic boys to ensure full participation.

## Introduction

Asthma, allergic rhinitis, and atopic sensitization (collectively "allergic phenotype") are associated with significant medical and social morbidity in the developed world[1]and their increasing prevalence in the last decades has yet to be explained. Several mechanisms have been proposed, [1] but many studies have linked allergic conditions with insufficient physical activity (PA) [2–4]. Children with asthma, particularly boys [5, 6], often get less PA than their peers [2, 5, 6] despite the fact that an "exercise prescription" is recommended for asthma management [3] and normal PA participation is a stated goal of asthma therapy. [7]

Discussed drivers of the relationship between allergy and low PA include inadequately controlled asthma [8] or rhinitis[5] with exacerbation of allergic symptoms by PA; exercise-induced bronchoconstriction (EIB) in individuals with heightened airway sensitivity [9] such as occurs with allergic phenotype; low sport participation among children with asthma[2, 10]; and confounding by environmental and socioeconomic factors associated with both PA and allergy, such as overweight, ethnicity or environmental exposures. [6, 11, 12] As a result children with asthma or rhinitis may deliberately avoid active pursuits, be discouraged from sport by their parents or caregivers [2, 10] and/or be unable to participate in vigorous PA (VPA.) [13] Conversely, some evidence suggests that physical fitness may protect against future development of asthma. [14, 15] However, benefits of PA are proven: physical inactivity in any group is a health risk that should be addressed, whether or not these benefits include prevention of allergy.

The association with allergy, while suggestive, is not conclusive. Some studies fail to find associations between allergy and PA in one sex only [5, 16] [17] and others find no association at all [2]. Protocols are not standardized among studies [2] so different approaches to assessing PA and defining allergies may account for some heterogeneity[2] as may issues of sample population and confounding. Allergy may be quantified as any of the several allergic diagnoses, which may not be standardized [18, 19] or confirmed by physician; or it may be based on symptomsreported by parent or child. [2, 13] Likewise, PA may be reported by the child or their parent [20, 21] or measured objectively by accelerometry,[13] and may be quantified as sport participation or as minutes spent in moderate, vigorous or moderate-to-vigorous activity (MPA, VPA, MVPA); studies relying on subjectively-reported PA data tend to assume that most MPA and VPA take place during well-defined sporting activities [2, 10] which is not always the case [22, 23] [24] and thus may overestimate the importance of sport and active lifestyle as a correlate of allergy. For all these reasons, research is difficult to aggregate and may be considered as inconclusive.

(former GSF), Helmholtz Centre for Environmental Research - UFZ, Leipzig, Research Institute at Marien-Hospital Wesel, Pediatric Practice, Bad Honnef for the first 2 years. The 4 year, 6 year, and 10 year follow-up examinations of the LISAplus study were covered from the respective budgets of the involved partners (Helmholtz Zentrum Munich (former GSF), Helmholtz Centre for Environmental Research - UFZ, Leipzig, Research Institute at Marien-Hospital Wesel, Pediatric Practice, Bad Honnef, IUF – Leibniz-Research Institute for Environmental Medicine at the University of Düsseldorf) and in addition by a grant from the Federal Ministry for Environment (IUF Düsseldorf, FKZ 20462296). This work was supported by the Comprehensive Pneumology Center Munich (CPC-M) as member of the German Center for Lung Research. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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In this study we aim to assess relationships between allergic conditions, allergic symptoms, and PA in a large population-based sample of German adolescents. We compare PA levels in adolescents with reported physician-diagnosed asthma and rhinitis, and IgE-determined aero-allergen sensitization, to those in a group of lung healthy controls. PA was measured throughout a representative week by accelerometry, making it possible to separately establish relationships for different indicators of PA level, particularly vigorous activity. We also examine possible mediators of the relationships we find, including sport participation as an indicator of active lifestyle, and activity limitation by allergic symptoms.

## Methods

### Population Characteristics

We combined data from interviews, physical examinations, and accelerometry from two cohorts of German Caucasians: GINIPlus and LISAPlus, born between 1995 and 1999. Further details on study designs of GINIplus [25, 26] and LISAplus [27] are published elsewhere. Both studies were approved by the respective local Ethics Committees (Bavarian General Medical Council, Medical Council of North-Rhine-Westphalia) and by written consent from participating families.

GINIPlus (German Infant Nutritional Intervention PLUS environmental and genetic influences on allergy development) was initiated to investigate allergy development. Of 5991 infants recruited at birth, 2252 had a family history of atopy and thus were given hydrolysed baby formulas. The remainder was given no formula. At age 15, 3199 adolescents were recontacted and approached for accelerometry. 1890 subjects (59%) consented to accelerometry, of whom 1290 (40%) successfully completed and 1054 (33%) passed quality control. Ultimately 847 of these (26%) were included in the present study. For further details on recruitment, formulas, and followup see von Berg et al. (2015) [28]and Smith et al. (2016) [29]; for details on accelerometry response see Smith et al. (2016.) [23]

LISAPlus (Lifestyle-Immune-System-Allergy; Influence of lifestyle factors on the development of the immune system and allergies plus the influence of traffic emissions and genetics) is a population-based cohort of 3097 unselected infants[30] from the cities of Munich, Wesel, Bad Honnef and Leipzig. 1534 subjects were followed up at age 15, of which 1107 (64%) were from Munich or Wesel and thus approached for accelerometry. 655 subjects (59%) consented to accelerometry, of whom 435 (39%) successfully completed and 357 (32%) passed quality control. Ultimately 290 (24%) were included in the current study. [23]

For a flowchart on accelerometry recruitment, response, and completion see Smith et al. (2016.) [23] Of 1411 subjects who completed accelerometry, [23] 1137 (83%) had complete data and were included in the current paper.

### Measurements of PA

Accelerometry was combined with an activity diary to document activity domains and wear-time. Detailed descriptions of accelerometer protocol, quality control, and data cleaning are given elsewhere. [31, 32] [23] Accelerometers (ActiGraph GT3X, Pensacola, Florida) were worn at the hip. Sampling rate was 30 Hz; accelerations were stored at 1 Hz and converted into activity levels in one-minute epochs using the algorithm for children from Freedson et al, 2005. [33] Diaried weartime was validated against that indicated by the device according to the algorithm of Troiano et al. (2007) [34], using SAS programs from NHANES[31]. Only data from waking time during diaried and validated monitor wear were used. For more details on accelerometry protocol see Smith et al, [23].

Activity diaries contained lines for time of getting up and going to bed, participation in sport, time and reason of removing the monitor, and other activities in a standardized diary, particularly leisure time sport duration and type. Valid days had at least 10 hours of valid recording, or 7 if the subject was awake for between 7 and 10 hours. Valid subjects provided at least 3 valid weekdays, and one valid weekend day. To profile daily activity, we considered average daily minutes of moderate and vigorous PA (MPA, VPA), and sport participation.

## Sociodemographic and Anthropometric Confounders

All multivariable models were corrected for correlates of PA not of primary interest. These were age, height, study center (Munich or Wesel), season of accelerometry, and nutritional intervention. For details see S1 File. Initial analyses suggested sex-specific results, so all presented models are stratified by sex.

## Allergic Respiratory Conditions

Allergic respiratory conditions were asthma, allergic rhinitis and atopic sensitization to aeroallergens, defined as follows:

- Asthma: As in Mölter et al. (2015) [18] and Jarvis et al (2012)[35] current asthma at 15 years was defined as having at least two of the following: doctor diagnosis of asthma ever between age 3–15, current wheezing at 15 years of age, and asthma medication at 15 years of age.
- Allergic rhinitis: Allergic rhinitis was defined as a doctor diagnosis of either allergic rhinitis or hayfever at any time in the past year. Adolescents with asthma or asthma medication were treated in the models as asthma and excluded from the rhinitis group, even if they also had rhinitis.
- Aero-allergen sensitization (atopy): Atopic sensitization was defined as any sensitization to aero-allergens compared with none, defined as at least one RAST positive (IgE $\geq$ 0.35 kU/l) for the following airborne allergens: birch, mugwort, ambrosia, grass, rye, dogs, cats, dust mites (Dermatophagoides pteronyssinus) and indoor mold (Cladosporium herbarum). Models of atopy excluded children with current rhinitis or asthma, or current medication for rhinitis or asthma.
- Lung-healthy (control): Lung-health in this population was defined as: since the age of 3 years no asthma, and in the past year no asthma symptoms (wheezing), no rhinitis, no rhinitis symptoms (nose/eye symptoms; see below), no asthma or rhinitis medications, no positive aero-allergen RAST, or positive bronchodilator response (see Supplement and Miller et al. (2005) [36]for more detail on testing)

No child in the study had cystic fibrosis. For further details on definitions see S1 File.

## Allergic Respiratory Symptoms

- Wheezing: Self-reported wheezing, whistling or chest tightness in the past year was included as an indicator of incompletely diagnosed or treated respiratory disease, particularly asthma, which may discourage vigorous PA.
- Nose and eye symptoms: Self-reported current nose and eye symptoms (runny nose, itchy eyes) in the past 12 months in the absence of a cold were included as an indicator of possible untreated or incompletely treated rhinitis, which may in turn discourage PA.

## Statistical Methods

All calculations were done using SAS 9.2 or 9.3 (Cary, NC.)

Populations (Tables 1 and 2) were compared using nonparametric tests: Kruskal-Wallis for multilevel categorical variables, Wilcoxon's two-tailed rank-sum test for all others. To model corrected relationships, sex-stratified generalized linear models were used to model PA outcomes as statistical functions of respiratory diseases and conditions, corrected for age, height, study center, nutritional intervention, season of accelerometry (categorical) and parental education.

Each PA measure (MPA, VPA, and sport participation) was modeled as function of all confounders not of primary interest, as well as one respiratory condition or diagnosis at a time. Odds of any sport participation during accelerometry were modelled logistically and are presented as odds ratios. Daily minutes MPA and VPA were log-transformed for normality before modeling, and inspection of histograms and q-q plots confirmed normality. Results are presented as percent difference from children without the symptom (in models of symptoms) or as percent difference from apparently lung-healthy controls (in models of asthma, rhinitis, and atopy.)

## Inclusion Criteria

To separate the effects of the different allergic diagnoses, these conditions were modeled separately[37] similar to the comparisons made in Mitchell et al, 2013.[4] Children who confirmed asthma (n = 94) were one group; of the remainder, those who confirmed allergic rhinitis were another group (n = 90); of the remainder, those with positive aero-allergen RAST were the third group (n = 363). Children with each condition were compared only to lung-healthy controls (detailed above; n = 590.) However, all subjects were included in the models of symptoms.

Children who did not confirm any diagnosis, but who also did not fit our criteria for lung-health, were excluded from the analysis. For example, this included children who did not confirm asthma or allergic rhinitis and who did not have a positive RAST, but had a positive bronchodilator response (n = 41) and/or asthma in childhood (n = 49) medications for asthma (n = 2) or rhinitis (n = 5), nose/eye symptoms (n = 51) or wheezing (n = 25.) Ultimately of 1411 subjects who completed accelerometry, 1137 (81%) were included in the paper.

# Results

We combined data from the 15-year followup of two large German birth cohorts, GINIplus [26, 28] and LISAplus, [27, 30] conducted in the suburban region of Wesel (north-west Germany) and the urban area of Munich, primarily aimed at the benefit of nutritional intervention for prevention of allergies (GINIplus) and the influence of lifestyle factors on the development of the immune system (LISAplus). Physical activity levels in this cohort have been previously profiled, as has the allocation of activity by domain. [23]

In the study population of 1137 subjects (47% male), asthma, rhinitis, and atopic sensitization were all more prevalent in boys than girls (Table 1): 9.9 and 6.8% of boys and girls had asthma; of the remainder 9.3 and 6.7% had rhinitis; of the remainder 37 and 28% were atopic (here defined as sensitization to aero-allergens.) Boys got about 20% more moderate, vigorous, and MVPA than girls did, but participated almost equally in sport. Average daily MVPA, of which about 30% was vigorous, was about 45 minutes in boys and 35 minutes in girls. Sport participation was comparable between sexes.

A majority of children with asthma and rhinitis, especially boys, reported being currently medicated for it; but prevalence of symptoms remained high in these groups. (Table 2) 94% of asthmatic boys were on asthma medication and 46% had wheezed in the past year, compared to 78 and 68% of asthmatic girls. 66% of non-asthmatic boys with rhinitis but no asthma were

**Table 1. Population and Selection.**

| Trait | Whole 15-year followup Munich and Wesel Birth cohorts GINIplus[28] and LISAplus.[27] | | Study population | | P for difference if <0.10 | |
|---|---|---|---|---|---|---|
| | Boys | Girls | Boys | Girls | Boys | Girls |
| N | 4306 | | 1137 | | – | |
| Male (N, %) | 2198, 51 | | 538, 47 | | 0.003 | |
| Birthdate (mean) | 21 May 1997 | 5 May 1997 | 6 June 1997 | 3 May 1997 | – | – |
| Birthdate (min—max) | 16 Sep 1995–31 Jan 1999 | 11 Sep 1995–31 Jan 1999 | 25 Sep 1995–22 Jan 1999 | 12 Sep 1995–31 Jan 1999 | – | – |
| Height, cm; mean (SD) | 176 (7.5) | 167 (6.3) | 177 (7.4) | 167 (6.2) | – | – |
| BMI, kg/m$^2$; mean (SD) | 20.8 (3.4) | 21.0 (3.1) | 20.6 (3.0) | 21.0 (3.0) | – | – |
| Nutritional intervention[1], any vs. none (%) | 26 | 25 | 28 | 28 | <0.0001 | <0.0001 |
| BMI category[2] (%); p for global null | | | | | – | – |
| Underweight | 7.8 | 6.6 | 8.8 | 6.5 | * | * |
| Normal | 80 | 84 | 80 | 85 | * | * |
| Overweight | 8.0 | 6.0 | 8.6 | 5.4 | * | * |
| Obese | 4.1 | 3.8 | 2.7 | 3.5 | * | * |
| From Munich (%) | 59 | 59 | 64 | 59 | 0.006 | – |
| Parents highly educated (%) | 65 | 68 | 70 | 72 | 0.01 | 0.06 |
| **Allergy group (N, % of those with data)**; p for global null, among those with data | | | | | <0.0001 | <0.0001 |
| Asthma[3] | 139, 11 | 89, 7.7 | 53, 9.9 | 41, 6.8 | * | * |
| Rhinitis but no asthma[4] | 169, 14 | 134, 12 | 50, 9.3 | 40, 6.7 | * | * |
| Aero-sensitized but no rhinitis or asthma[5] | 410, 34 | 292, 25 | 197, 37 | 166, 28 | * | * |
| Strict lung-healthy (control)[6] | 501, 41 | 646, 56 | 238, 44 | 352, 59 | * | * |
| Missing data (N) | 979 | 947 | 0 | 0 | * | * |
| **In past year** (%): | | | | | | |
| Wheezing | 6.1 | 6.8 | 6.2 | 6.7 | – | – |
| Asthma medication | 5.6 | 3.8 | 9.3 | 5.4 | 0.00002 | 0.01 |
| Rhinitis medication | 11.7 | 9.7 | 9.9 | 4.9 | – | <0.0001 |
| Eye/nose symptoms | 19 | 18 | 19 | 16 | – | 0.03 |
| Positive bronchodilator[7], where performed | 5.0 | 2.8 | 3.0 | 0.98 | 0.01 | 0.0009 |

Study population compared to full 15-year followup

1) Nutritional intervention was used in the first four months of life in the intervention arm of GINIplus. Formulas were partially and extensively hydrolysed whey, extensively hydrolysed casein, or cow's milk. No intervention was used in the observation arm of GINIplus or in LISAplus.

2) BMI categories from 10th, 90th, and 97th percentiles for that age and sex in a German reference population (Kromeyer-Hauschield, 2001).

3) Asthma: As in Jarvis et al (2012)[35]: at age 15 the subject reported at least 2 of the following traits: asthma medication or wheezing in past 12 months, doctor diagnosis of asthma at any time since age 3.

4) Allergic rhinitis: Current rhinitis or hay fever at age 15, but no asthma or asthma medicine

5) Atopy: No asthma, no allergic rhinitis, but one or more positive RAST (IgE □ 0.35) for aero-allergens (birch, mugwort, ambrosia, grass, rye, dogs, cats, dust mites (Dermatophagoides pteronyssinus) and indoor mold (Cladosporium herbarum)

6) Lung-healthy: No asthma ever; no current allergic rhinitis; no wheezing or nose/eye symptoms in past year; no current drugs for asthma or rhinitis; no RAST over 0.35; no positive bronchodilator response.

7) Bronchodilator response is an indicator of current airway hyperresponsiveness, such as may be caused by untreated asthma or recent infection. Testing was performed and defined as in Miller et al (2005) and Flexeder et al (2015)[38]

All measures except bronchodilator response are given only as percentage of subjects with data. P-values from Wilcoxon's two-tailed rank-sum test for binary variables, Kruskal-Wallis for categorical. —if p>0.10, * if pairwise test not performed (see test for global null in top row.)

GINIplus cohort profiled in von Berg et al, 2015[28]; LISAplus cohort profiled in Chen et al, 2007.[27]

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**Table 2. Population and Selection.** Comparison between lung-healthy controls and children with respiratory allergies.

| Trait | Boys | | | | Girls | | | | P-value (Group) if p □ 0.10, for pairwise difference from controls | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Lung-healthy[4] | Atopy[3] | Rhinitis[2] | Asthma[1] | Lung-healthy[4] | Atopy[3] | Rhinitis[2] | Asthma[1] | Boys | Girls |
| N | 238 | 197 | 50 | 53 | 352 | 166 | 40 | 41 | – | – |
| Age, years; mean (SD) | 15.6 (0.5) | 15.5 (0.5) | 15.6 (0.5) | 15.6 (0.5) | 15.6 (0.5) | 15.6 (0.5) | 15.6 (0.5) | 15.7 (0.6) | – | – |
| Height, cm; mean (SD) | 177 (7.4) | 177 (7.3) | 174 (7.7) | 176 (6.9) | 167 (6.0) | 167 (6.6) | 176 (6.9) | 168 (5.8) | 0.08 (1);0.006 (2) | 0.10 (1) |
| BMI, kg/m$^2$; mean (SD) | 20.7 (3.2) | 20.4 (2.8) | 20.4 (3.2) | 21.0 (3.0) | 20.9 (3.0) | 21.1 (2.8) | 21.0 (3.0) | 20.8 (3.0) | – | – |
| Munich, % | 61 | 65 | 76 | 62 | 57 | 64 | 55 | 54 | 0.04 (2) | – |
| Parental education, % | 72 | 69 | 71 | 67 | 71 | 73 | 68 | 78 | – | – |
| **In past year, %:** | | | | | | | | | | |
| Wheezing | 0 | 2.0 | 12.0 | 46 | 0 | 4.9 | 10 | 68 | * | * |
| Asthma medication | 0 | 0 | 0 | 94 | 0 | 0 | 0 | 78 | * | * |
| Rhinitis medication | 0 | 0 | 66 | 38 | 0 | 0 | 61 | 15 | * | * |
| Eye/nose symptoms | 0 | 18 | 88 | 47 | 0 | 27 | 84 | 40 | * | * |
| Bronchodilator response[5]; P for global null | | | | | | | | | * | * |
| Negative | 82 | 79 | 74 | 74 | 85 | 87 | 80 | 73 | * | * |
| Positive | 0 | 2.0 | 6.0 | 11 | 0 | 1.2 | 2.5 | 4.9 | * | * |
| Not performed | 18 | 19 | 20 | 15 | 15 | 12 | 18 | 22 | * | * |
| **Physical activity, min** Mean (Geometric mean) 5$^{th}$, 95$^{th}$ percentile | | | | | | | | | | |
| Moderate | 31.8 (30.2) 14, 54 | 31.1 (29.8) 14, 53 | 28.7 (27.1) 13, 54 | 29.6 (26.8) 9.3, 56 | 26.4 (24.7) 10, 49 | 25.4 (23.6) 8.8, 45 | 23.2 (23.0) 13, 37 | 29.9 (26.2) 12, 50 | – | – |
| Vigorous | 14.6 (11.5) 2.1, 39 | 13.6 (11.4) 2.0, 33 | 12.9 (11.3) 1.9, 30 | 11.2 (8.6) 1.0, 31 | 11.4 (8.8) 0.9, 34 | 10.7 (8.5) 1.0, 30 | 10.5 (8.8) 1.4, 26 | 12.8 (10.2) 1.3, 25 | 0.06 (1) | – |
| MVPA | 46.4 (42.4) 19, 89 | 44.7 (41.7) 18, 79 | 41.6 (38.8) 16, 73 | 40.7 (35.4) 11, 89 | 37.8 (34.1) 13, 70 | 36.1 (32.7) 13, 69 | 33.8 (31.8) 16, 61 | 42.7 (36.3) 14, 71 | 0.05 (1) | – |
| Any reported sport, % | 71 | 77 | 80 | 70 | 70 | 84 | 70 | 83 | – | 0.09 (1); 0.08 (3) |

[1)] Asthma: As in Jarvis et al (2012): at age 15 the subject reported at least 2 of the following traits: asthma medication or wheezing in past 12 months, doctor diagnosis of asthma at any time since age 3.

[2)] Allergic rhinitis: Current rhinitis or hay fever at age 15, but no asthma or asthma medicine

[3)] Atopy: No asthma, no allergic rhinitis, but one or more positive RAST (IgE □0.35) for aero-allergens (birch, mugwort, ambrosia, grass, rye, dogs, cats, dust mites (Dermatophagoides pteronyssinus) and indoor mold (Cladosporium herbarum)

[4)] Lung-healthy: No asthma ever; no current rhinitis; no wheezing or nose/eye symptoms in past year; no current drugs for asthma or rhinitis; no RAST over 0.35 or positive bronchodilator response.

[5)] Bronchodilator response is an indicator of current airway hyperresponsiveness, such as may be caused by untreated asthma or recent infection. Testing was performed and defined as in Miller et al (2005) and Flexeder et al (2015)[38] Reasons for not performing the test included subject refusal and medical contraindications; refusal was the most common.

P-values from Wilcoxon's two-tailed rank-sum test for binary variables, Kruskal-Wallis for categorical.

–if p>0.10, * if pairwise test not performed (see test for global null in top row, or characteristic was used to define groups.)

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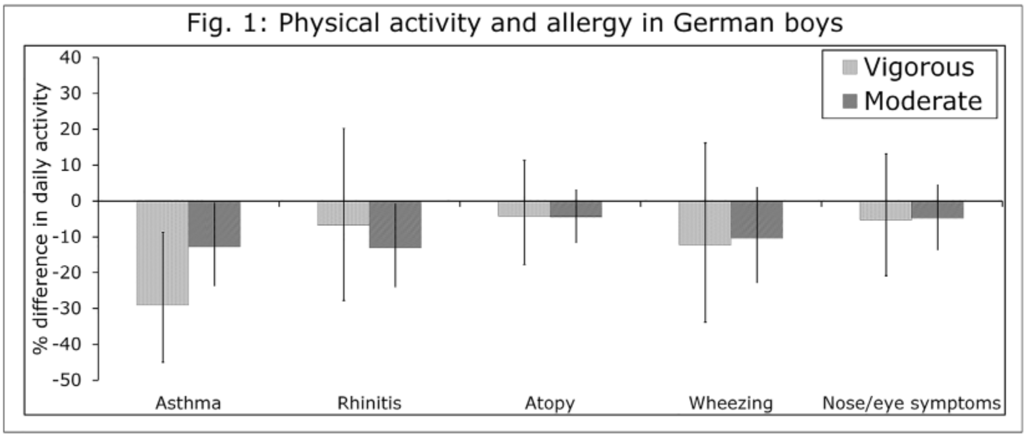


**Fig 1. PA in adolescent German boys with asthma, rhinitis and atopy compared only to lung-healthy controls; boys with self-reported current wheezing or nose/eye symptoms compared to boys without these symptoms.** All models corrected for age, height, nutritional intervention, study center (Munich or Wesel) and parental education. Error bars for 1.96 standard errors.

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medicated for rhinitis and 88% of them had nose/eye symptoms, compared with 61% and 84% of non-asthmatic girls with rhinitis. However, sport participation was comparable across allergy groups (70–80% of boys, 70–84% of girls).

Consistent with earlier work [29] we found that the study population of 1137 subjects was a few percentage points likelier to have had a nutritional intervention, to be female, to have highly educated parents, and to be urban than the whole 15-year followup (Table 1) which we previously compared with the populations recruited at birth. [29] Similar small differences separated lung-healthy controls from children with respiratory conditions (Table 2) but socioeconomic or anthropometric differences between the groups were small.

In boys but not girls, there was a clear trend towards less moderate and vigorous activity as sensitization increased from none, to atopy, to rhinitis, to asthma (Fig 1,Table 2) All associations were consistent whether we considered the mean, the geometric mean, or the 5th and 95th percentiles of PA (Table 2), but were of borderline significance. Control boys averaged 14.7 minutes VPA per day, which was 6% less in those with only atopy; 13% less with rhinitis but no asthma; and 24% less with asthma. This is similar to the observed levels of VPA in lung-healthy girls, who averaged 11.4 (8.8) minutes (Table 2). Moderate activity was also lower in allergic boys: controls got 31.8 minutes MPA per day, which was 2% less in those with only atopy, 10% less with rhinitis, and 7% less with asthma.

However, there were no significant associations between allergic phenotype and PA in girls whether we considered allergic conditions or symptoms. There was also no trend towards increasing or decreasing VPA or MPA across allergic conditions in girls. (Tables 2 and 3).

In corrected models, considering age, height, parental education, study center and nutritional intervention as covariates, boys with asthma got 29.1% less VPA ($p< 0.01$, Table 2, Fig 1) than did control boys. They also got 12.8% less MPA, almost the same as boys with rhinitis (13.1%, both $p = 0.04$). Corrected estimates for the association between MPA, VPA and atopy in the absence of asthma and rhinitis remained negative but were very small (< 5%) and non-significant ($p> 0.20$.) No allergic symptom was significantly ($p = 0.05$) associated with any PA outcome in either sex (Table 2). No allergic diagnosis or symptom was associated with sport participation, and there was no consistent trend towards more or less sport with sensitization.

**Table 3. Corrected Associations between PA and Allergic Phenotype.** Models corrected for age, height, season of accelerometry, nutritional intervention, parental education and study center.

| | Trait | Vigorous activity | | Moderate activity | | Any sport | |
|---|---|---|---|---|---|---|---|
| | | % change | P | % change | P | Odds ratio | P |
| **Boys** | **Conditions** | | | | | | |
| | Asthma[1] (N = 53) | **-29.14** | **0.0076** | **-12.81** | **0.041** | 0.63 | 0.18 |
| | Rhinitis, no asthma[2] (N = 50) | -6.83 | 0.59 | **-13.14** | **0.037** | 1.17 | 0.69 |
| | Atopy, no rhinitis or asthma[3] (N = 197) | -4.29 | 0.57 | -4.53 | 0.23 | 0.91 | 0.66 |
| | Lung-healthy [4] (N = 238) | (reference) | – | (reference) | – | (reference) | – |
| | **Symptoms (all subjects)** | | | | | | |
| | Wheezing (N = 33) | -12.3 | 0.36 | -10.48 | 0.14 | **0.53** | **0.093** |
| | Nose/eye symptoms (N = 102) | -5.34 | 0.55 | -4.97 | 0.29 | 1.24 | 0.41 |
| **Girls** | **Conditions** | | | | | | |
| | Asthma (N = 41) | 23.02 | 0.14 | 9.67 | 0.24 | 2.02 | 0.14 |
| | Rhinitis, no asthma (N = 40) | -1.26 | 0.93 | -5.64 | 0.44 | 0.77 | 0.49 |
| | Atopy, no rhinitis or asthma (N = 166) | -7.54 | 0.33 | -5.96 | 0.16 | 1.46 | 0.11 |
| | Lung-healthy (N = 352) | (reference) | – | (reference) | – | (reference) | – |
| | **Symptoms (all subjects)** | | | | | | |
| | Wheezing (N = 40) | 16.37 | 0.29 | 12.77 | 0.12 | 1.23 | 0.62 |
| | Nose/eye symptoms (N = 93) | -5.32 | 0.57 | -6.83 | 0.18 | 0.90 | 0.70 |

1) Asthma: At age 15 the subject reported at least 2 of the following traits: doctor diagnosis of asthma at any time since age 3, asthma medication in past 12 months, wheezing in past 12 months, as in Jarvis et al (2012)

2) Rhinitis: Current rhinitis or hayfever at age 15, but no asthma or asthma medicine

3) Atopy: No asthma, no rhinitis, but one or more positive RAST (IgE □0.35) for aero-allergens (birch, mugwort, ambrosia, grass, rye, dogs, cats, dust mites (Dermatophagoides pteronyssinus) and indoor mold (Cladosporium herbarum)

4) Lung-healthy: No asthma ever; no current rhinitis; no wheezing or nose/eye symptoms in past year; no current drugs for asthma or rhinitis; no RAST over 0.35 or positive bronchodilator response as defined in Miller et al (2005) and Flexeder et al (2015) [38]

**Bold text** if p□ 0.10. P-values from generalized linear models treating VPA and MPA as lognormal, sport as binary (any vs. none.)

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# Discussion

## Main Findings

In this large study of European adolescents we found that objectively-measured physical activity, particularly vigorous activity, was lower in adolescent boys with asthma and/or rhinitis, who nevertheless participated fully in sport; that symptoms did not appear to constrain PA; and that there were no effects in girls.

## Interpretation in Relation to Previous Work

Like others, [6]'[16] we found sex-specific associations between asthma, rhinitis and PA. However, while Groth et al. (2016) [6] and the current study found that asthma was associated with PA only in boys, Yiallouros et al. (2015)[16] found an effect only in girls, while Sugimoto et al [5] found that rhinitis was associated with lower PA only in boys. This heterogeneity may be explained by the known gender differences in prevalence, symptoms, and progression of asthma [39–42] and/or cultural differences in acceptability of sport [43, 44] especially for girls or children with asthma. [2] Furthermore, asthma diagnosis and treatment may be more available in our own population of Germans than in either the low-income Americans studied in Groth et al. (2016) [6] and Firrincieli et al. (2005)[13], or the Cypriots studied in Yiallouros et al. (2015)[16]. Lastly, our population was 2 years older than those in Groth et al. (2016)[6]

and 7 years older than those in Yiallouros et al. (2015)[16] and age is known to impact on both activity pattern[45] and allergy development. [42]

We concur with the literature [2–4] that allergic phenotype, especially in boys, is often, but not always, associated with low PA; and find that neither respiratory symptoms[4] nor avoidance of sport[17] necessarily drive this difference. Direct comparison of effect sizes is problematic since some studies quantify PA as MVPA, some as VPA only, and some as sport participation; and at least in our cohort these measures of PA had different relationships with allergy. Furthermore many studies, including our own, are near the detection limit at $p = 0.05$ and thus are subject to effect inflation by publication bias. However, children with asthma or asthma symptoms typically got 30–50% less PA or sport in a recent review by Williams et al.[2] Asthma was associated with 30% less self-reported VPA and MPA in boys by Groth et al. (2016)[6] and 41% less accelerometric MVPA in girls by Yiallouros et al. (2015)[16] who like us found no effect of wheezing. Thus, our findings in boys are comparable[6] or at the lower end[2] of reported effects.

Intercomparison of studies is further hampered by the tendency to compare populations without correction for confounding, either by conditions such as overweight or by intercorrelations between allergic conditions. For example, Sugimoto et al. (2012) [5] found a 30% decrease in VPA among boys with rhinitis, but 35% of children with rhinitis also had asthma; and although rhinitis was not independently associated with VPA in our cohort, asthma was. Such comorbidity may have driven the association found by Sugimoto et al. (2012).

The lowered VPA in boys with asthma is consistent with the hypothesis that allergic symptoms or exercise-induced bronchoconstriction (EIB) may constrain PA. Wheezing was associated with 42% less accelerometric PA in Firrincieli et al. (2005)[13] and 30% less self-reported VPA in Groth et al. (2016.) [6] Despite a high percentage of medication use in our population, symptoms of asthma and rhinitis remained prevalent. Although we did not inquire whether it occurred specifically during exercise, wheezing is a common symptom of incompletely controlled asthma, typically occuring during VPA and/or cold weather.[18] In line with this observation, we found that in boys with asthma MPA was almost normal but VPA was much more significantly reduced, an observation also reported by Weisgerber et al. (2008) [46]. Likewise, Sugimoto et al. (2012)[5] found that in a population with a 35% prevalence of asthma MPA was almost normal, but VPA was obviously decreased.

Unlike others, we found that sport participation was not associated with any allergic diagnosis or symptom in either sex. However, we observed high rates of sport participation in general (over 2/3 of children) and previous research with this cohort [22, 47] found that neither female gender nor overweight was associated with sport. When combined with the fact that school sport is mandatory in Germany, it appears that sport is generally well accepted within this population and that barriers to participation are low. This was not the case in British populations studied by Williams et al. (2008), where asthmatic children avoid sport,[2] or are prevented from participating, [2] for fear of exacerbations.

Together, our data show less PA in boys with asthma and/or rhinitis even in the presence of comparable sport participation. Clinicians should fully control asthma and rhinitis in children in order to enable them to participate fully in VPA; and counsel these children and their parents of the possibility, demonstrated in this paper, of full participation in PA and sport. Activity-induced symptoms and consequent limitation of PA should be viewed as indicators to improve the treatment, ensure medication intake as prescribed, and thus eliminate the excuse for inactivity.

## Strengths and Limitations

Our subjects are a generally healthy, prosperous, and uniform group, recruited as follow-up from two birth cohorts and further selected for completion of interviews, a physical exam, wearing of an accelerometer, and meticulous keeping of diaries. Thus these adolescents are likely more compliant and thorough than their peers. They also live in a culture where PA and sport are common: sport participation levels are generally high, and we did not observe any tendency for lower participation in allergic adolescents or those with allergic parents (not shown.) This is known to not be the case elsewhere,[10] and relationships we find are thus necessarily population-specific.

However, since allergic symptoms and doctor diagnoses were reported by either participants or their parents ascertainment bias is a concern. Health-conscious individuals may recognize symptoms or remember diagnoses more accurately, or seek treatment more aggressively: however, relationships were stable in a sensitivity analysis limited to adolescents with negative bronchodilator response (not shown) suggesting that ascertainment bias did not drive results. Likewise, accelerometric data represent a snapshot of activity over a period of a week or less. While we made efforts to include only representative days during school time and to correct for seasonal effects, it is likely that some bias remains.

Lastly, sample size is a concern. Effect inflation by publication bias has been addressed above; to which we add that although our study population was large, it was mostly healthy. We sampled less than 100 adolescents with asthma and found an effect in only half of them (boys.) While no single outlier of either sex drove our results (not shown) and our model treated asthma and rhinitis as mutually exclusive (i.e. the model of rhinitis excluded adolescents with asthma) MPA and VPA were not. Because MPA and VPA tended to intercorrelate within subject (not shown) it is somewhat to be expected that a group of adolescents with low VPA (boys with asthma) also had low MPA.

## Implications for Future Research, Policy and Practice

Our research shows that at least some aspects of the relationship between PA and allergic phenotype are population-specific. Many previously found associations, particularly those between symptoms and PA and between sport and allergy, were not found in our population and thus may be modifiable. However, we confirm that asthma and rhinitis in boys are associated with low PA independent of each other and of reported symptoms, with effects most severe for asthma. We also find that even when allergic symptoms are present, allergic diagnoses do not necessarily preclude adolescents' sport participation. Future research should further explore these links rather than taking them as proven.

Low PA by allergic children is in and of itself a health risk. Coaches, clinicians, and patients may need to collaborate to ensure adequate treatment of allergy and full participation in both sport and PA. To ensure equal access to the health benefits of PA, it may be necessary to target interventions or education to allergic children and/or their parents. PA performance should be specifically addressed by the treating physician, and limitations due to inadequate control of asthma and/or rhinitis should cause either improved treatment schemes and/or regular medication use by the child. Furthermore, counseling as to the need for PA should perhaps target the parents of allergic children, as well as the children themselves.

More generally, the risk of low PA was elevated in girls as compared to boys. Although asthmatic boys' VPA was significantly lower than that of lung-healthy boys, it was almost the same as that of lung-healthy girls. This confirms previous research by us [23]and by others[44] [20] which shows that males are significantly more active than females. Since recommended PA levels are the same for both sexes, [48] this difference suggests that girls are particularly vulnerable to inactivity, and thus perhaps at greater risk for inactivity-related diseases. Future research and interventions should focus on increasing PA in girls.

## Conclusions

In adolescent boys, but not girls, asthma and rhinitis were independently associated with low PA. The association persisted in the absence of differential sport participation and did not appear to be explicable by activity-limiting allergic symptoms. Interventional data are needed to establish existence and direction of causation. Clinicians, parents, and designers of PA interventions should specifically address PA performance of boys with allergic diseases to ensure their full participation in sport.

## Supporting Information

S1 File. Selection, Confounders and Statistics.
(DOC)

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This study was part of the 15-year followup of two German birth cohorts, GINIplus (German Infant Study on the influence of Nutrition Intervention PLUS environmental and genetic influences on allergy development) and LISAplus (Influence of lifestyle factors on the development of the immune system and allergies Plus the influence of traffic emissions and genetics). We thank the GINIplus and LISAplus Study Groups for all their excellent work.

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