Epidemiology of infectious and non-communicable diseases and effect of health interventions on children's physical fitness in Port Elizabeth, South Africa

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

BMI	Body mass index
BMIZ	BMI-for-age Z-score
CAPS	Curriculum and Assessment Policy Statement
CD	Communicable disease
CDC	Centers for Disease Control and Prevention
DALY	Disability-adjusted life year
DASH	Disease, Activity and Schoolchildren's Health
DSBG	Department of Sport, Exercise and Health
DW	Disability weight
ECDoE	Eastern Cape Department of Education
EKNZ	Ethics committees of Northwest and Central Switzerland
EPG	Eggs per gram (of stool)
e.g.	exempli gratia
etc.	et cetera
FGDs	Focus group discussions
GBD	Global Burden of Disease
GIS	Geographical Information System
GHQ-12	General health questionnaire
HAKSA	Healthy Active Kids South Africa

HAZ	Height-for-age Z-score
Hb	Haemoglobin
HBSC	Health behavior in school-aged children
HMS	Human Movement Science
HST	Harvard step test
IDW	Inverse distance weighting
ISRCTN	International Standard Randomised Controlled Trial Number
i.e.	id est
LMICs	Low- and middle-income countries
MVPA	Moderate-to-vigorous intensity physical activity
NCDs	Non-communicable diseases
NTDs	Neglected tropical diseases
NMMU	Nelson Mandela Metropolitan University
NRF	National Research Foundation
NSNP	National school nutrition program
OR	Odds ratio
PA	Physical activity
PAQ-C	Physical activity questionnaire for children
PAR-Q	Physical activity readiness questionnaire
PE	Physical Education
POC-CCA	Point-of-care circulating cathodic antigen
RDT	Rapid diagnostic test
SD	Standard deviation
SES	Socioeconomic status
SNSF	Swiss National Science Foundation
SNOSE	Sequentially numbered, opaque sealed envelopes
SSAJRP	Swiss-South African Joint Research Programme
STH	Soil-transmitted helminth
Swiss TPH	Swiss Tropical and Public Health Institute
T1	Baseline measurements
T2	Follow-up measurements
T3	End-line measurements

VO_2 max	Maximal oxygen uptake
WASH	Water, sanitation and hygiene
WAZ	Weight-for-age Z-score
WC	Western Cape
WHO	World Health Organization

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SUMMARY

Background: Globally, more than 1 billion people are infected with soil-transmitted helminths (STHs; *Ascaris lumbricoides*, hookworm and *Trichuris trichiura*) and *Schistosoma* spp., particularly school-aged children in low- and middle-income countries (LMICs) The symptoms most frequently associated with these parasitic worm infections include abdominal pain, (bloody) diarrhoea, anaemia, growth retardation and cognitive impairment. As traditional lifestyle and diets change with social and economic development, disadvantaged communities in LMICs increasingly also face non-communicable diseases. Particularly in urban settings, obesity-related conditions impose a growing burden and affect people from all socioeconomic strata. Together, this results in a double burden while health systems weaken in many countries, partially explained by high rates of urbanization in face of inadequate infrastructure development. This puts children at an increased risk of compromised health that may hamper their development, wellbeing and socioeconomic future.

Goal and specific objectives: The 'Disease, Activity and Schoolchildren's Health' (DASH) study, a cluster-randomized controlled trial carried out in Port Elizabeth, South Africa, aimed to investigate the relationship between physical fitness and infections with STHs, intestinal protozoa and *Helicobacter pylori* among Grade 4 schoolchildren in quintile 3 primary schools through two 10-week multidimensional school-based physical activity interventions. The specific objectives of this study were (i) to determine the prevalence of intestinal parasite infections and *H. pylori*; (ii) to assess the haemoglobin (Hb) levels and anthropometric indicators; (iii) to comprehensively measure the physical fitness levels; and (iv) to investigate possible associations between infection status and socioeconomic status, self-reported physical activity score, and stunting. Based on the results, we developed a multidimensional intervention programme and assessed its effects on children's cardiorespiratory fitness, body mass index (BMI) and thickness of skinfolds.

Research partnership and funding: The DASH study was a joint research endeavour involving colleagues from three institutions in two countries, (i) the Nelson Mandela University (Department of Human Movement Science, NMU) in South Africa, (ii) the Swiss Tropical and Public Health Institute, and (iii) the Department of Sport, Exercise and Health (Department of Sport, Exercise and Health, DSBG) of the University of Basel in Switzerland. Stool samples were analyzed in the laboratories of the Department of Medical Laboratory Sciences at the NMU with the support of Biomedical Technology (BTech) 4th year students. The study was funded by the Swiss National Science Foundation and the National Research Foundation in South Africa, as part of the Swiss-South Africa bilateral programme and the joint research project funding scheme.

Methods: This cluster-randomized controlled trial was implemented in 26 Grade 4 classes in eight disadvantaged primary schools in Port Elizabeth, South Africa. The selection of the study schools was based on their classification (quintile 3), the size of the Grade 4 classes (at least 100 children), geographical location and population demographics (Xhosa-, Afrikaans- and English-speaking children). The study was conducted in historically black and coloured (mixed race) government primary schools from various areas in Port Elizabeth in the south-eastern part of South Africa. The areas populated by black Africans are commonly referred to as townships and include the areas of Kwazakhele, New Brighton, Zwide and Motherwell. The 'Northern areas' in Port Elizabeth are largely made up of coloured people who were forcefully relocated from the central areas of the city to the outlying northern areas, and include the areas of Schauderville, Gelvandale, Helenvale, Hillcrest and Booysens Park. Fieldwork started in February 2015 (baseline). The midline assessment started in October 2015 and the endline was completed in May 2016. The first stage of the study included 1,009 children aged 9-12 years. Physical fitness was determined using field-deployable tests of the Eurofit fitness test battery. Stool samples were analysed with the Kato-Katz thick smear technique to diagnose STHs, and with rapid diagnostic tests (RDTs) to detect intestinal protozoa and *H. pylori* infections. Hb levels and anthropometric indicators were measured using standard tools and protocols. Demographic data and the socioeconomic status of each participant were captured with a questionnaire. Following the diagnosis of STH infections, children were treated with albendazole (single dose, 400 mg) after each survey. Our multidimensional physical activity intervention programme consisted of (i) physical education lessons twice a week; (ii) weekly dancing-to-music classes; (iii) in-class activity breaks; and (iv) school infrastructure adaptations to promote physical activity. Interventions were implemented twice, each time lasting 10 weeks. Additionally, the school feeding programme was reviewed with an aim to offering more balanced and nutritious food. Primary outcomes included cardiorespiratory fitness indicators measured by a 20 m shuttle run, BMI and thickness of skinfolds. Explanatory variables were socioeconomic status, self-reported physical activity, stunting, anaemia, intestinal protozoa and STH infection.

Results: Complete data at baseline were available for 934 children (92%). In two schools, high prevalence of STH infections were found (*A. lumbricoides* 60% and 72%, respectively; *T. trichiura* 65% each). For boys and girls co-infected with *A. lumbricoides* and *T. trichiura* (n=155) the maximal oxygen uptake (VO_2 max) was estimated to be 50.1 ml kg^{-1} min^{-1} and 47.2 ml g^{-1} min^{-1}, respectively, while it was 51.5 ml kg^{-1} min^{-1} and 47.4 ml kg^{-1} min^{-1} for their non-infected peers (n=278). On average, children without helminth infections had greater body mass (P=0.011), height (P=0.009) and a higher BMI (P=0.024) and were less often stunted (P=0.006), but not significantly less wasted compared to their peers with a single or dual species infection. Among 9-year-old boys, a negative correlation between helminth infections and VO_2 max, grip strength and standing broad jump distance was observed (P=0.038). The overall mean Hb level was 122.2 g l^{-1}. In the two schools with the highest prevalence of STHs, the Hb means were 119.7 g l^{-1} and 120.5 g l^{-1}, respectively.

Across the three measurements, the mean *A. lumbricoides* infection intensities were 9,554 eggs per gram of stool (EPG) in May 2015, 4,317 EPG in October 2015 and 1,684 EPG in May 2016. The corresponding mean feacal egg counts for *T. trichiura* were 664 EPG, 331 EPG and 87 EPG. Results from a sub-study conducted in the two project schools with the highest STH prevalence showed that while albendazole was highly efficacious against *A. lumbricoides* (cure rate (CR): 97.2%; egg reduction rate (ERR): 94.5%), it lacked efficacy against *T. trichiura* (CR: 1.1%; ERR: 46.0%).

With respect to the effect of the multidimensional physical activity intervention programme on BMI, skinfolds and fitness, complete baseline and endline data are available from 579 children (mean age at baseline: 10.0 years). In the intervention group, we observed a significantly lower increase in the mean BMI (estimate of mean change: -0.12 with 95% confidence interval (CI): -0.22 to -0.03; P=0.008) and a reduced increase in the mean thickness of skinfolds (mean change: -1.06; 95% CI: -1.83 to -0.29; P=0.007) from baseline to endline compared to the control group. No significant group differences occurred in mean 20 m shuttle run performance and VO_2 max (P>0.05) estimates.

Conclusions: We could show that intestinal parasite infections have a small but significant negative effect on the physical fitness of children, as expressed by their estimated maximal oxygen uptake. In addition, our results indicate that boys who are infected with multiple intestinal parasite species have lower physical fitness (VO_2 max) levels than their non-infected peers. A significantly higher *T. trichiura* prevalence was noted in stunted children and those with a significantly lower Hb level, compared to children not infected with helminths of this species. A clear impact of STH infections on anthropometric indicators was also observed. A single 400 mg oral dose of albendazole was efficacious against *A. lumbricoides* infections but did not effectively manage *T. trichiura* infections, corroborating earlier research evidence. The local health and education authorities confirmed that deworming has been neglected in recent years. Biannual mass deworming is recommended in order to control the morbidity due to STH infections in two schools, annual deworming should be implemented in another school, while a test-and-treat approach appears appropriate in the other study schools. Moreover, water, sanitation and hygiene (WASH) interventions are warranted. The high spatial heterogeneity suggests that data from additional schools in different neighbourhoods will be needed to identify a more generally applicable intervention strategy.

The promotion of extra-curricular physical activity and healthy nutrition interventions should become an integral part of school health in order to improve children's health in terms of BMI, thickness or skinfolds and cardiorespiratory fitness as indicators for the risk of chronic lifestyle conditions. While our intervention was developed by physical education specialists in consultation with local stakeholders, its effect was limited, suggesting a longer and more intensive implementation might be needed to achieve more relevant impact. Careful adaptation will be necessary before the intervention can be scaled or implemented in other settings.

OPSOMMING

Agtergrond: Wêrelwyd word meer as 1 biljoen mense geïnfekteer deur wurmparasiete wat deur grond oorgedra word (STH’s; *Ascaris lumbricoides,* haakwums en *Trichuris trichiura*) en *Schistosoma* spp. Die simptome wat die meeste geassosieer word met hierdie parasitiese wuminfeksies, sluit in: abdominale pyn, diarree, bloedarmoede, groeivertraging en kognitiewe benadeling. Soos wat tradisionele leefstyle en diëte verander met sosiale en ekonomiese ontwikkeling, ondervind benadeelde gemeenskappe in lae- en middelinkomstelande toenemend nieoordraagbare siektes. Veral in stedelike bevolkings, plaas vetsugverwante toestande ‘n groeiende las en affekteer mense van alle sosio-ekonomiese strata. Gesamentlik veroorsaak dit ‘n dubbele las terwyl gesondheidsisteme in baie lande verswak. Dit veroorsaak ‘n verhoogde risiko vir kinders dat hulle gesondheid in gevaar gestel word, wat hulle ontwikkeling, welsyn en sosio-ekonomiese toekoms benadeel.

Doel en spesifieke doelwitte: Die ‘Siekte, Aktiwiteite en Skoolkinders se Gesondheid (DASH)-studie, ‘n kluster ewekansige, gekontroleerde proefneming, daarop gemik om die verhouding tussen liggaamlike fiksheid en infeksies met grondoordraagbare wurmparasiete (STH’s), ingewandsprotozoa en *Helicobacter pylori* onder Graad 4-skoolkinders in kwintiel 3-primêre skole deur twee 10-weke multidimensionele skoolgebaseerde liggamlike aktiwiteit-intervensies. Die doelwitte van hierdie studie was (i) om die voorkoms van ingewandsparasietinfeksies en *Helicobacter pylori* te bepaal; (ii) om die hemoglobienvlakke en antropometriese indikators te bepaal; (iii) om omvattend die liggaamlike fiksheidsvlakke te bepaal; en (iv) om moontlike verbande tussen infeksiestatus en sosio-ekonomiese status te bepaal, selfaangeduide liggaamlike aktiwiteit stand van sake, en groeivertraging. Die studie is geïmplementeer in benadeelde woonbuurte in Port Elizabeth, Suid-Afrika, van 2014 tot 2017. Gebaseer op die resultate, het ons ‘n multidimensionele intervensieprogram ontwikkel en sy effek op kinders se kardiovaskulêre fiksheid, liggaamsmassaindeks (LMI) en dikte van velvoue, geassesseer.

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Departement van Sport, Oefening en Gesondheid (Departement van Sport, Oefening en Gesondheid, DSBG) van die Universiteit Basel. Stoelgangmonsters is geanaliseer in die laboratoriums van die Departement van Mediese Laboratorium Wetenskappe by die NMU met die ondersteuning van Biomediese Tegnologie (BTech)-vierdejaarstudente.

Metodes: Hierdie kluster ewekansige, gekontroleerde proefneming is geïmplementeer in 26 Graad 4-klasse in 8 benadeelde primêre skole in Port Elizabeth, Suid-Afrika. Die keuse van die bestudeerde skole is gebaseer op hulle klassifikasie (kwintiel 3), die grootte van die Graad 4-klasse (n>100), geografiese ligging en bevolkingsdemografie (Xhosa-, Afrikaans- en Engelssprekende skoolkinders). Die studie is gedoen in histories swart en bruin (gemengde ras) staat- primêre skole van verskeie areas in Port Elizabeth in die suid-oostelike deel van Suid-Afrika. Die areas wat bevolk word deur swart Afrikane word algemeen na verwys as lokasies en sluit die areas van Kwazakhele, New Brighton, Zwide en Motherwell in. Die “Noordelike Areas” in Port Elizabeth bestaan hoofsaaklik uit bruin mense, wat gedwonge verskuif is na die sentrale areas van die stad, na die afgeleë noordelike areas, en dit sluit die areas van Schauderville, Gelvandale, Helenvale, Hillcrest en Booysenspark in. Veldwerk het in Februarie 2015 (basislyn) begin. Die midlyn-assessering het in Oktober 2015 begin en die endlyn is in Mei 2016 voltooi. Die eerste stadium van die studie het 1009 skoolgaande ouderdom kinders vanaf 9 tot 12 jaar ingesluit. Liggaamlike fiksheid is bepaal deur die velduitvoerbare toets van die Eurofit se liggaamlike fiksheid-toetsbattery. Stoelgangmonsters is geanaliseer met die Kato-Katz dik smeertegniek om STH’s te diagnoseer, en met vinnige diagnostiese toetse (RDT’s) om ingewandsprotozoa en *H. pylori*-infeksies. Hemoglobien (Hb)-vlakke en antropometriese indikators is gemeet deur standaardapparate te gebruik. Demografiese data en die sosio-ekonomiese status van elke deelnemer is verkry deur ‘n vraelys. Na die diagnose van STH-infeksies is kinders behandel met albendazole (400mg) na elke ondersoek. Ons multidimensionele liggaamlike aktiwiteit-intervensieprogram het bestaan uit (i) liggaamlike opvoedingslesse twee keer per week; (ii) weeklikse dans-volgens-musiek-klasse; (iii) aktiwiteitspuses in die klas; en (iv) skoolinfrakstruktuurveranderings om liggaamlike aktiwiteit te bevorder. Intervensies is twee keer geïmplementeer, elke keer het dit 10 weke geduur. Bykomend is die skoolvoedingsprogram hersien om meer gebalanseerde en gesonde kos te voorsien. Primêre uitkomste het ingesluit: kardiorespiratoriese fiksheidsindikators gemeet deur ‘n 20m heen en weer-hardlopery, LMI, en die dikte van velvoue.

Verklarende veranderlikes is: sosio-ekonomiese status, selfaangeduide liggaamlike aktiwiteit, groeivertraging, bloedarmoede, ingewandsprotozoainfeksie, en grondoordraagbare wurmparasiet-infeksie.

Resultate: Volledige data op basislyn was beskikbaar vir 934 kinders (92%). In twee skole is hoë STH-voorkomste gevind (*Ascaris lumbricoide*s 60% en 72% onderskeidelik; *Trichuris trichura* 65% elk). Vir seuns en dogters ko-geïnfekteer met *A. lumbricoides* en *T. trichiura* (n=155) was die maksimum suurstofopname (VO_2-maksimum) geskat op 50.1 ml kg^{-1} min^{-1} en 47.4 ml kg^{-1} min^{-1} vir hulle niegeïnfekteerde portuurgroeplede (n=278). Kinders met wurmparasietinfeksie het gemiddeld ‘n groter liggaamsmassa gehad (P=0.011), lengte (P=0.009) en ‘n hoër LMI (P=0.024) en was minder dikwels vertraag ten opsigte van groei (P=0.006), maar nie beduidend minder afgetakel vergeleke met hulle portuurgroep met ‘n enkele of dubbele spesiesinfeksie nie. Onder 9 jaar oue seuns was daar ‘n negatiewe korrelasie tussen wurmparasietinfeksies en VO_2-maksimum, greepsterkte en staande verspringafstand waargeneem (P=0.038). Die algehele gemiddelde Hb-vlak was 122.2 $g1^{-1}$. In die twee skole met die hoogste voorkoms van STH’s was die Hb-gemiddelde 119.7 $g1^{-1}$ en 120.5 $g1^{-1}$ onderskeidelik.

Ten opsigte van al drie mates was die gemiddelde *Ascaris lumbricoides*-infeksieintensiteit 9, 554 eiers per gram van stoelgang (EPG) in Mei 2015, 4,317 EPG in Oktober 2015 en 1,684 EPG in Mei 2016. Die ooreenstemmende getalle vir *Trichuris trichiura* was 664 EPG, 331 EPG en 87 EPG. Resultate van ‘n substudie gedoen in die twee projekskole met die hoogste STH-voorkoms het getoon dat terwyl albendazole hoogs effektief was teen *A. lumbricoides* (herstelvlak (CR): 97.2%; eierverminderingsvlak (ERR): 94.5%), was dit nie so doeltreffend teen *T. trichiura* (CR: 1.1%; ERR: 46.0%).

Met betrekking tot die effek van die multidimensionele liggaamlike aktiwiteit-intervensieprogram van LMI, velvoue en fiksheid, is volledige basislyn- en endlyndata beskikbaar van 579 kinders (gemiddelde ouderdom by basislyn: 10.0 jaar). In die intervensiegroep het ons ‘n beduidend laer toename in die gemiddelde LMI waargeneem (skatting van gemiddelde verandering: -0.12 met 95%-selfvertroueinterval (CI): -0.22 tot -0.03; P=0.008) en ‘n verminderde toename in die gemiddelde dikte van velvoue (gemiddelde verandering: -1.06; 95% CI: -1.83 tot -0.29; P=0.007) van basislyn tot endlyn vergeleke met die kontrolegroep. Geen beduidende groepverskille het in ‘n gemiddelde 20m heen en weer-hardloperyprestasie en VO_2-maksimum (P>0.05)-skattings.

Gevolgtrekkings: Ons kon aantoon dat ingewandsparasietinfeksies ‘n klein, maar betekenisvolle negatiewe effek op die liggaamlike fiksheid van kinders het, soos uitgerdruk deur hulle geskatte maksimale suurstofopname. Verder dui ons resultate aan dat seuns met verskeie ingewandsparasietspesies laer liggaamlike fiksheid het (VO_2-maksimum)-vlakke het as hulle niegeïnfekteerde portuurgroep. ‘n Beduidend hoër *T. trichiura*-voorkoms is in kinders met vertraagde groei raakgesien en diegene met ‘n beduidend laer Hb-vlak, vergeleke met kinders wat nie geïnfekteer is met wurmparasiete van hierdie spesie nie. ‘n Duidelike impak van STH-infeksies op antropometriese indikators is ook waargeneem. ‘n Enkele 400 mg mondelikse dosis van albendazole was effektief teen *A. lumbricoides*-infeksies, maar het nie *T. trichiura*-infeksies effektief beheer nie, wat vorige navorsingsbewyse bevestig. Die plaaslike gesondheids- en opvoedkunde-gesaghebbendes het bevestig dat voorkomende chemoterapie in die onlangse jare verwaarloos is. Tweejaarlikse massa-ontwurming word aanbeveel ten einde die siektesyfer as gevolg van STH-infeksies in twee skole en jaarlikse ontwurming moet geïmplementeer word in ‘n ander skool, individuele diagnose en behandeling lyk gepas in die ander bestudeerde skole. Verder is water, sanitasie en higiëne (WASH)-intervensies nodig. Die hoë ruimtelike heterogeniteit suggereer dat data van addisionele skole in verskillende woonbuurtes nodig sal wees om ‘n meer algemeen toepasbare intervensiestrategie te identifiseer.

Die bevordering van buitemuurse liggaamlike aktiwiteite en gesonde kosintervensies behoort ‘n integrale deel van skoolgesondheid te wees ten einde kinders se gesondheid te verbeter in terme van LMI, dikte van velvoue en kardiorespiratoriese fiksheid, as indikators van die risiko van chroniese leefstyltoestande. Terwyl ons intervensie ontwikkel is deur liggaamsopvoedingspesialiste, tesame met plaaslike belanghebbendes, was die effek beperk, wat suggereer dat ‘n langer en intensiewer implementering nodig mag wees om relevanter impak te hê. Versigtige aanpassing sal nodig wees voor die intervensie uitgebrei kan word of geïmplementeer kan word in ander plekke.

ISISHWANKATHELO

Intsusa: Ehlabathini jikelele, abantu abangaphezu kwebhiliyoni bosuleleka ziintshulube-zidleleleli ezisuka emhlabeni (iintshulube ezinkulu ezirawundi, iintshulube ezibambelelayo, kunye neentshulube ezikumila kusisabhokwe) kuquka zonke ezo zikudidi lweentshulube ezimbaca. Ezona mpawu ziphawulekayo xa umntu esulelwe zezi ntshulube-zidleleli sisisu esibuhlungu, urhudo, ianayemiya, ukungakhuli ngokwaneleyo komzimba kunye nokungaphuhli okwaneleyo kwengqondo. Kumazwe asaphuhlayo, kuye kufunyaniswe nezifo ezingosuleliyo ngenxa yokutshintsha kokutya okutyiwayo nokutshintsha kwendlela eqhelekileyo yokuphila. Kubantu abahlala ezidolophini, kuphawuleka ukuba izigulo ezinokuthanani nokutyeba okugqithiseleyo zingumthwalo yaye zichaphazela wonke ubani kungakhathaliseki ukuba ukuwupi na umgangatho ngokwezoqoqosho. Konke oku, kuye kube ngumthwalo ophindaphindiweyo kwiinkqubo zezempilo eziya zisibabuthathaka kumazwe amaninzi, yaye kubeka iimpilo zabantwana abasakhulayo esichengeni nto leyo enokuba sisithintelo kuphuhlo lwabo, impilontle kunye nekamva labo lezoqoqosho.

Usukelo kunye neenjongo ezithe ngqo: Uhlolisiso olubizwa ngokuba yi-'Disease, Activity and Schoolchildren's Health' (DASH), uvavanyo olulawulweyo lwamaqela akhethwe ngokungacetywanga, lujoliswe ekuphandeni unxulumano phakathi kokomelela komzimba nosulelo ziintshulube-zidleleleli ezisuka emhlabeni, izidalwa eziseli inye zasemathunjini (okanye iiprothozowa zasemathunjini) kunye nebhakhthiriyam efunyanwa esiswini ebizwa ngokuba yi-*Helicobacter pylori* kubantwana abakwibakala lesi-4 kwizikolo zamabakala aphantsi ezikwikhwantile yesi-3 kusetyenziswa iindlela zonyango ezimbini ezibandakanya imisebenzi yentshukumo-mzimba eyahlukahlukeneyo eyenziwa esikolweni kwisithuba seeveki ezili-10. Iinjongo zoluhlolisiso zezi: (i) ukuqonda ukuxhaphaka kosulelo zizidleleleli zasemathunjini ne-*Helicobacter pylori*; (ii) ukuhlola ubungakanani behimaglobhini kunye nezalathisi ze-anthropometric; (iii) ukulinganisa ngokuphelelyo nangokucacileyo amanqanaba okomelela komzimba; kunye (iv) nokuphanda unxulumano olunokubakho phakathi kwemo yosulelo nemo yezoqoqosho, ingxelo yenqaku kwimisebenzi yentshukumo-mzimba exelwa ngumthathinxaxheba kunye nokungakhuli komzimba. Olu phando luphunyezwe kwimimandla ehlelelekileyo yasePort Elizabeth eMzantsi Afrika ukususela ngo-2014 ukuya ku-2017. Ngokusekelwe kwiziphumo, siphuhlise inkqubo yonyango

olwahlukahlukileyo saza senza uvavanyo-hlolo lolu nyango ekomeleleni kwemiphunga neentliziyo zabantwana, kumyinge wobunzima bemizimba yabo (IBM) kunye nobungqingqwa bemigobo yolusu lwabo.

Ulwahlulelwano lophando: Le projekhthi iziinzame ngokubambisana kwamadlelane amaziko awahlukeneyo abandakanya (i) iNelson Mandela Dyunivesithi (iSebe leHuman Movement Science kunye neSebe leDietetics, e-NMU), (ii) iSwiss Tropical and Public Health Institute, kunye (iii) neSebe leSport, Exercise and Health (iSebe leSport, Exercise and Health, e-DSBG) yeDyunivesithi yaseBasel. Sihlalutye iisampuli zelindle kwiilebhu zeSebe le-Medical Laboratory Sciences e-NMU sincediswa ngabafundi abakunyaka wabo we-4 kwizifundo ze-Biomedical Technology (BTech).

Iimethodi: Olu vavanyo olulawulweyo lwamaqela akhethwe ngokungacetywanga**,** luphunyezwe kwiiklasi eziyi-26 zebakala lesi-4 kwizikolo ezihlelelekileyo zamabakala aphantsi ePort Elizabeth eMzantsi Afrika. Ukukhethwa kwezikolo kusekelwe kwinkqubo yokuhlelwa kwazo esekelwe kwimo yazo yezoqoqosho (sikhethe ezikwikhwantile yesi-3), kubukhulu beeklasi zebakala-4 (n>100), indawo apho zifumaneka khona nangokohluka kwamanani abafundi abathetha iilwimi ngeelwimi (abafundi abathetha isiXhosa, isiAfrikansi nesiNgesi).

Olu hlolisiso lwenziwe kwizikolo zikarhulumente ebezisoloko zizezabamnyama nabebala kwiindawo ezahlukeneyo ePort Elizabeth kumzantsi-mpuma weli. Iindawo ezimiwe ngabaMnyama ngokuqhelekileyo zibizwa ngokuba ziilokishi yaye ziquka indawo yakwaZakhele, iNew Brighton, iZwide kunye neMotherwell. Indawo ezikuMantla ePort Elizabeth zimiwe ikakhulu ngabeBala abasuswa ngesinyanzelo kwiindawo ezikumbindi wedolophu babekwa kwiindawo ezisecaleni kumantla edolophu. Ezi ziindawo ezifana neSchauderville, iGelvandale, iHelenvale, iHillcrest kunye neBooysens Park. Uphando lwangaphandle luqalwe kweyoMdumba ku-2015, lwaza uhlolisiso lwedatha lwaqala kweyeDwarha kwakunyaka omnye laza lwaba luyagqitywa uphando lwangaphandle kuCanzibe ngo-2016.

Inqanaba lokuqala lolu hlolisiso lubandakanye abantwana abahamba isikolo abaminyaka iyi-9 ukuya kweyi-12 abayi-1009. Ukomelela komzimba kulinganiswe ngokusetyenziswa iimvavanyo ezisetyenziswa ngaphandle zebhetri lovavanyo i-Eurofitness. Iisampuli zelindle zihlalutywe ngokusebenzisa indlelabuchule kaKato-Katz ukuxilonga-khangela iintshulube-zidleleleli, kunye neemvamvanyo-xilongo ezikhawulezayo (RDTs) ukufumana iiprothozowa zasemathunjini nosulelo lwe-*H. pylori*. Umlinganiselo wehimaglobhini (Hb) kunye nezalathisi ze-anthropometric zilinganiswe kusetyenziswa izixhobo eziqhelekileyo. Idatha enokuthanani neenkcukacha zobuqu nemo yezoqoqosho yomthathinxaxheba ngamnye ifunyanwe ngokusebenzisa ifomu yemibuzo.

Emva kokufunyanwa kweentshulube-zidleleleli, kwabathe zafunyanwa kubo, umntwana ngamnye unyangwe nge-albendazole (ezimiligram eziyi-400) emva komjikelo ngamnye woluphando. Inkqubo yonyango lwethu olwahlukahlukileyo olubandakanya imisebenzi yentshukumo-mzimba ibandakanye oku: (i) iiklasi ngomzimba nomzimba-ntshukumo kabini evekini; (ii) iklasi yokudanisa ngoxa kudlala umculo rhoqo ngeveki; (iii) imisetyenzana eyenzelwa eklasini ngekhefu; kunye (iv) nokulungelelanisa imidlalo yabantwana nezakhiwo ezibangqongileyo esikolweni ukukhuthaza intshukumo-mzimba. Olu nyango lwethu luphunyezwe kabini sihlandlo ngasinye lunikezelwa kwisithuba seeveki eziyi-10 uphando lwethu oluzithabathileyo. Ukongezelela, inkqubo yokondliwa kwabantwana kwezi zikolo iye yahlaziywa ngeenjongo zokunika abantwana ukutya okunesondlo esipheleleyo.

Iziphumo zokuqala zibandakanya imiqondiso yokomelela kwentliziyo nemiphunga elinganiswe ngokubalekiswa iimitha eziyi-20 kwabathathinxaxheba kuvavanyo lwe-shuttle run, i-BMI kunye nobugqigqwa bemigobo yolusu. Iivaribhuli ezichaziweyo yimo yezoqoqosho, ukomelela komzimba okuxelwa ngumthathinxaxheba yena ngokwakhe, ukungakhuli komzimba, ianayemiya, usulelo lwasemathunjini lweeprothozowa kunye nosulelo ziintshulube-zidleleli ezifumaneka emhlabeni.

Iziphumo: Idatha epheleleyo ekuqaleni kophando ebikho yeyabantwana abayi-934 (ngu-92% wabo bathabathe inxaxheba). Kwizikolo ezimbini kufunyanwe ukuxhaphaka kweentshulube-zidleleleli kuphezulu kakhulu (u-60% no-72% wabantwana abafunyenwe besuleleke yi-*Ascaris lumbricoides* ngokulandelelana kwazo ezo zikolo; baza abosuleleke yi-*Trichuris trichiura* bangu-65% sikolo ngasinye). Kumakhwenkwe namantombozana abosulelwe sisidleleleli i-*A. lumbricoides* kunye ne-*T. trichiura* ngaxeshanye (bayi-155 bebonke),kuqikelelwa ukuba owona mkhamo uphezule weoksijini abawusezeleyo (VO_2 max) ngu-50.1 ml kg^{-1} min^{-1} kunye no-47.2 ml kg^{-1} min^{-1} ngokulandelelana kwabo ngoxa ingu-51.5 ml kg^{-1} min^{-1} kunye no-47.4 ml kg^{-1} min^{-1} owogxa babo abangasulelwanga (bayi=278 bebonke). Ngokomyinge, abantwana abangenalosulelo lweentshulube-zidleleleli bebenobunzima bomziba ophezulu

(P=0.001), benobude obufanelekileyo (P=0.009), bene-BMI ephezulu (P=0.024) yaye uninzi lwabo bebenemizimba ekhulayo (P=0.006), kodwa bebengabogqithi kangako ogxa babo abosulelwe sisidleleleli esinye okanye ezimbini ekomeleleni ngomzimba. Phakathi kwamakhwenkwe aneminyaka eyi-9, kuphawulwe unxulumano oluchasanayo phakathi kosulelo lweentshulube-zidleleleli kunye ne- VO_2 max, amandla okubamba kwesandla, kunye nomgama wokutsiba we-Standing Broad Jump (P=0.038).

Umlinganiselo wehimoglobhini (Hb) obungumyinge wabo bonke abathathinxaxheba ubungu-122.2 g l^{-1}, kodwa, kweza zikolo zimbini zifunyenwe zinezinga eliphezulu lokuxhaphaka kosulelo lweentshulube-zidleleleli, imilinganiselo ye-Hb engumyinge ifunyenwe ingu-119.7 g l^{-1} kunye no-120.5 g l^{-1} ngokulandelelana kwayo.

Umyinge wobunzulu bosulelo sisidleleleli i-*Ascaria lumbricoides* ube ngamaqanda ayi-9,554 kwigram nganye yelindle kwekaCanzibe ngo-2015, yangamaqanda ayi-4, 317 kwigram nganye yelindle kweyeDwarha kwakunyaka omnye, yaza yangamaqanda ayi-1, 684 kwigram nganye yelindle kwekaCanzibe ngo-2016. Amanani ahambelanayo esidleleleli i-*T. trichiura:* amaqanda ayi-664, ayi-331 kunye nayi-87 kwigram nganye yelindle ngokulandelelana kwawo nangokuhambelana namaxesha esele siwakhankanyile. Le yimiyinge egubungela amaxesha omathathu bekuthatyathwa imilinganiselo

Imiphumo yophando olulodwa olwenziwe kweza zikolo zimbini zinezinga eliphezulu lokuxhaphaka kweentshulube-zidleleleli lubonise ukuba, nakuba i-albendazole isebenza ngokuphumelelayo ukunyanga usulelo le-*A. lumbricoides* (izinga lonyango (IL): 97.2%; izinga lokwehla kwenani lamaqanda (ILKL): 94.5%), ayinamandla okunyanga i-*T. trichiura* (IL: 1.1%; ILKL: 46.0%). Ngokuphathelele imiphumo yenkqubo yethu yonyango ebandakanya imisebenzi yentshukumo-mzimba eyahlukahlukeneyo nequka uvavanyo-hlolo lwe-BMI, ubungqingqwa bemigobo yolusu, nokomelela komzimba, idatha epheleleyo yasekuqaleni nasekupheleni kophando efunyanwe ebantwaneni abayi-579 sinayo (umyinge weminyaka ngokobudala ekuqaleni kophando yiminyaka eyi-10.0).

Kwela qela silinyangileyo, siphawule ukwanda okuphantsi ngendlela ephawulekayo kumyinge we-BMI (uqikelelo kutshintsho komyinge: -0.12 kunye ne-confidence interval (CI): esuka ku:- -0.22 ukuya ku- -0.03; P=0.008) kunye nokukhula okwehlileyo kumyinge wobungqingqwa bemigobo yolusu (utshintsho lomyinge: -1.06; 95% CI: -1.83 ukuya ku- -0.29; P=0.007) ukususela ekuqaleni ukusa ekupheleni kophando xa silithelekisa nelo lilawuliweyo. Akukho muhloku uphawulekayo kula maqela mabini xa sijonge indlela enze ngayo kuvavanyo lokuxhuma i-shuttle run kunye noqikelelo lowona mkhamo uphezulu weoksijini awusezeleyo (VO_2 max) ($P>0.05$).

Ukuqukumbela: Sikwazile ukubonisa ukuba usulelo lwamathumbu zizidlelelelі lunemiphumo engephi kodwa emibi nephawulekayo ekomeleleni kwemizimba yabantwana njengoko kuchazwa ngamanani owona mkhamo uphezulu weoksijini abawusezeleyo (VO_2 max). Ngaphezu koko, iziphumo zethu zibonakalisa ukuba amakhwenkwe asulelwe zizidlelelelі ezingaphezu kwesinye banemizimba engomelelanga (VO_2 max) xa bethelekiswa kunye noogxa babo abangenalwasulelo. Ukuxhaphaka okuphawulekayo kwe-*T. trichiura* kuqatshelwe ebantwaneni abanemizimba engakhuliyo nabanomlinganiselo ophantsi we-Hb xa bethelekiswa nabo bangasulelwanga ziintshulube-zidlelelelі zolu hlobo.

Imiphumo ecacileyo siyibonisile nakwimiqondiso ye-anthropometric. Ithamo elinye le-Albendazole likwazile ukunyanga usulelo lwe-*A. lumbricoides* kodwa ayikwazi kulweyisa usulelo lwe-*T. trichiura*, nto leyo engqinelana nobungqina bophando lwangaphambili. Abasemagunyeni kumasebe emfundo nelezempilo asekuhlaleni, bagqinile ukuba unyango lwamayeza oluthintelayo lugatyiwe kwiminyaka yakutshanje. Ukusezwa kwabantwana amayeza okukhupha iintshulube kabini ngonyaka rhoqo kuyakhuthazwa kweza zikolo zimbini sikhe sathetha ngazo ukuphepha ukugula okubangelwa lusulelo lweentshulube-zidlelelі yaye kwesinye kukhuthazwa ukuba abantwana basezwe kanye ngonyaka nyaka ngamnye. Uxilongo-khangelo lomntwana ngamnye lwabucala lubonakala lufanelekile kwezinye izikolo eziya zinabantwana abangachatshazelwanga ziintshulube. Ngapha koko, ucoceko nokusetyenziswa kwamanzi acocekileyo kuyimfuneko. I-spatial heterogeneity ibonisa ukuba idatha engakumbi esuka kwezinye izikolo ezikwimimandla esondeleyo isafuneka ukuqulunqa elona qhinga loncedo lifanelekileyo lokujamelana nalo mcelimngeni.

Ukukhuthazwa kwemesebenzi nemidlalo yasemva kwesikolo ebandakanya intshukumo-mzimba kunye neendlela zoncedo ezikhuthaza ukutya okunesendlo nokusempilweni kufanele kube ngundoqo kwimpilo yomntwana wesikolo ngeenjogo zokuphucula impilo yabo ngokunxulumene ne-BMI, ubungqingqwa bemigobo yolusu lwabo kunye nokomelela kwentliziyo nemiphunga njengoko ezi zinto ziyimiqondiso yokuba sengozini yezifo ezinganyangekiyo nezibangelwa yindlela yokuphila. Nakuba uncedo laluphuhlisiwe ziingcaphephe ze-physical education emva kokufakana imilomo nabo babandakanyekileyo, imiphumo yalo ayikhange ibe yaneleyo, nto leyo ethetha ukuba kufuneka uncedo oluya kuhlala ithuba elide nelinzulu ukuze kubekho imiphumo ebonakalayo. Olo ncedo kuya kufuneka ngobulumko lulungelelaniselwe iimfuno zasekuhlaleni xa lusandiswa okanye lisiya kusetyenziswa kwezinye iindawo.

ZUSAMMENFASSUNG

Hintergrund: Weltweit sind mehr als 1 Milliarde Menschen mit vom Boden übertragenen Helminthen (STHs; *Ascaris lumbricoides*, Hakenwürmer und *Trichuris trichiura*) und *Schistosoma* spp. infiziert. Die am häufigsten mit diesen parasitären Wurminfektionen assoziierten Symptome sind Bauchschmerzen, (blutige) Diarrhoe, Anämie, physische und kognitive Beeinträchtigung. Da sich der traditionelle Lebensstil und die Ernährungsgewohnheiten mit der sozialen und wirtschaftlichen Entwicklung ändern, stehen benachteiligte Bevölkerungsgruppen in Ländern mit niedrigem und mittlerem Einkommen zunehmend auch nicht übertragbaren Krankheiten gegenüber. Vor allem in der städtischen Bevölkerung stellen Adipositas-Erkrankungen eine wachsende Belastung dar und betreffen Menschen aus allen sozio-ökonomischen Schichten. Dies führt zu einer doppelten Belastung, während die Gesundheitssysteme in vielen Ländern schwächer werden, was teilweise durch unkontrollierte Urbanisierung erklärt wird. Dies verursacht bei Kindern ein erhöhtes Gesundheitsrisiko, das ihre Entwicklung, ihr Wohlbefinden und ihre sozioökonomische Zukunft beeinträchtigen kann.

Ziel: Die Studie ‚Disease, Activity and Schoolchildren's Health‘ (DASH), eine randomisierte kontrollierte Clusterstudie, zielte darauf ab, die Beziehung zwischen körperlicher Fitness und Infektionen mit vom Boden übertragenen Helminthen, intestinalen Protozoen und *Helicobacter pylori* in Schulkinder der 4. Primarklasse von Quintile 3 Grundschulen durch zwei 10-wöchige mehrdimensionale physische Aktivitätsinterventionen zu untersuchen. Die Ziele dieser Studie waren (i) die Prävalenz von Darmparasiten-Infektionen und *H. pylori* zu bestimmen; (ii) die Hämoglobinwerte und anthropometrische Indikatoren zu bewerten; (iii) die körperlichen Fitnessniveaus umfassend zu messen; und (iv) mögliche Assoziationen zwischen dem Infektionsstatus und dem sozioökonomischen Status, dem selbstberichteten Aktivitätswert und dem ‚Stunting‘ zu untersuchen. Die Studie wurde in Port Elizabeth, Südafrika, von 2014 bis 2017 durchgeführt. Basierend auf den Ergebnissen entwickelten wir ein mehrdimensionales Interventionsprogramm und bewerteten dessen Auswirkungen auf die kardiorespiratorische Fitness, den Body Mass Index (BMI) und die Hautfaltendicke.

Forschungspartnerschaft und Finanzierung: Das Projekt war ein gemeinsames Forschungsprojekt, an dem Kollegen aus drei Institutionen von zwei Ländern beteiligt waren: (i) der Nelson Mandela Universität (Department of Human Movement Science, NMU) in Südafrika, (ii) dem Schweizerischen Tropen- und Public Health-Institut und (iii) dem Departement für Sport, Bewegung und Gesundheit (DSBG) der Universität Basel in der Schweiz. Stuhlproben wurden in den Laboratorien vom Departement für Medizinische Laborwissenschaften an der NMU, mit Unterstützung von Studenten der 4. Jahrgangsstufe der Biomedizinischen Technologiewissenschaften (BTech), analysiert. Die Studie wurde vom Schweizerischen Nationalfonds und dem „National Research Foundation" in Südafrika finanziert, im Rahmen eines bilateralen Forschungsprojekt zwischen der Schweiz und Südafrika.

Methoden: Diese randomisierte kontrollierte Clusterstudie wurde in 26 Klassen der 4. Primarklasse in acht benachteiligten Grundschulen in Port Elizabeth, Südafrika, durchgeführt. Die Auswahl der Studienschulen erfolgte anhand ihrer Klassifikation (Quintile 3), der Grösse der 4. Primarklassen (n>100), der geografischen Lage und der Bevölkerungsdemographie (Xhosa, Afrikaans und Englisch sprechende Schulkinder). Die Studie wurde in historisch schwarzen und farbigen (gemischtrassigen) staatlichen Grundschulen aus verschiedenen Gebieten in Port Elizabeth im südöstlichen Teil von Südafrika durchgeführt. Die von Schwarzafrikanern besiedelten Gebiete werden gemeinhin als Townships bezeichnet und umfassen die Gebiete von Kwazakhele, New Brighton, Zwide und Motherwell. Die ‚nördlichen Gebiete' von Port Elizabeth bestehen grösstenteils aus farbigen Menschen, die zwangsweise aus den zentralen Gebieten der Stadt in die abgelegenen nördlichen Gebiete verlegt wurden und die Gebiete von Schauderville, Gelvandale, Helenvale, Hillcrest und Booysens Park umfassen. Die Feldarbeit begann im Februar 2015 (Baseline). Der mittlere Messzeitpunkt begann im Oktober 2015 und die Schlussmessung wurde im Mai 2016 abgeschlossen. Die erste Phase der Studie umfasste 1'009 Schulkinder im Alter von 9 bis 12 Jahren. Die körperliche Fitness wurde mit Hilfe von feldtauglichen Tests der Eurofit Fitness-Testbatterie bestimmt. Stuhlproben wurden mit der Kato-Katz-Technik mit Abstrich zur Diagnose von STHs und mit Schnelldiagnosetests zum Nachweis intestinaler Protozoen und *H. pylori*-Infektionen analysiert. Hämoglobin (Hb)-Niveaus und anthropometrische Indikatoren wurden unter Verwendung von Standardwerkzeugen gemessen. Demographische Daten und der sozioökonomische Status jedes Teilnehmers wurden mit einem Fragebogen erfasst. Nach der Diagnose von STH-Infektionen wurden Kinder nach jeder Umfrage mit Albendazole (400 mg) behandelt. Unser Interventionsprogramm für mehrdimensionale körperliche Aktivität bestand aus (i) Sportunterricht zweimal pro Woche; (ii) wöchentliche Tanz-Kurse; (iii) Klassenaktivitätspausen; und (iv) schulische Infrastrukturanpassungen zur Förderung körperlicher Aktivität. Die Interventionen wurden zweimal durchgeführt à je 10 Wochen. Zusätzlich wurde das Schulverpflegungsprogramm untersucht, um ausgewogenere und nahrhaftere Lebensmittel anbieten zu können. Zu den primären Endpunkten gehörten kardiorespiratorische Fitnessindikatoren, gemessen anhand eines 20-Meter-Shuttle-Laufs, des BMI und der Hautfaltendicke. Erklärende Variablen waren sozioökonomischer Status, selbstberichtete körperliche Aktivität, ‚Stunting', Anämie, intestinale Protozoeninfektion und durch Boden übertragene Helmintheninfektion.

Ergebnisse: Bei 934 Kindern (92%) waren vollständige Daten zu Studienbeginn verfügbar. In zwei Schulen wurden hohe STH-Prävalenzen vorgefunden (*Ascaris lumbricoides* 60% bzw. 72%; *Trichuris trichiura* jeweils 65%). Für Knaben und Mädchen, die einen Doppelinfekt mit *A. lumbricoides* und *T. trichiura* (n=155) aufwiesen, wurde die maximale Sauerstoffaufnahme (VO_2 max) auf 50,1 ml kg^{-1} min^{-1} bzw. 47,2 ml kg^{-1} min^{-1} geschätzt, während für ihre nicht-infizierten Peers 51,5 ml kg^{-1} min^{-1} und 47,4 ml kg^{-1} min^{-1} resultierten (n=278). Im Durchschnitt hatten Kinder ohne Helmintheninfektionen eine grössere Körpermasse (P=0,011), Grösse (P=0,009) und einen höheren BMI (P=0,024) und waren seltener verkümmert (P=0,006), aber litten nicht signifikant weniger unter Wasting-Syndrom als ihre Altersgenossen mit einer Einzel- oder Doppelinfektion. Bei 9-jährigen Knaben wurde eine negative Korrelation zwischen Helmintheninfektionen und VO_2 max, Grifffestigkeit und der Distanz eines Standsprungs beobachtet (P=0,038). Der mittlere Hb-Gesamtgehalt betrug 122,2 g l^{-1}. In den beiden Schulen mit der höchsten Prävalenz von STHs betrug das Hb-Mittel 119,7 g l^{-1} bzw. 120,5 g l^{-1}.

In den drei Messungen betrug die mittlere *A. lumbricoides*-Infektionsintensität im Mai 2015 9'554 Eier pro Gramm Stuhl (EPG), im Oktober 2015 rund die Hälfte (4'317 EPG) und im Mai 2016 noch 1'684 EPG. Die entsprechenden Zahlen für *Trichuris trichiura* betrugen 664 EPG, 331 EPG und 87 EPG. Die Ergebnisse einer Teilstudie in den beiden Projektschulen mit der höchsten STH-Prävalenz zeigten, dass Albendazole zwar hochwirksam gegen *A. lumbricoides* war (Heilungsrate (CR): 97,2%, Ei-

Reduktionsrate (ERR): 94,5%), jedoch eine fehlende Wirksamkeit gegen *T. trichiura* (CR: 1,1%; ERR: 46,0%) aufwies.

Hinsichtlich der Wirkung des mehrdimensionalen Bewegungsinterventionsprogramms auf den BMI, die Hautfaltendicke und die Fitness liegen vollständige Ausgangs- und Schlussdaten von 579 Kindern vor (mittleres Alter bei Baseline: 10,0 Jahre). In der Interventionsgruppe beobachteten wir einen signifikant geringeren Anstieg des mittleren BMI (Schätzung der mittleren Veränderung: -0,12 mit 95% Konfidenzintervall (CI): -0,22 bis -0,03; P=0,008) und einen reduzierten Anstieg der mittleren Hautfaltendicke (mittlere Veränderung: -1,06; 95% KI: -1,83 bis -0,29; P=0,007) von der Basislinie bis zum Endmesszeitpunkt im Vergleich zur Kontrollgruppe. Keine signifikanten Gruppenunterschiede traten bei der mittleren 20-m-Laufleistung und VO_2 max (P>0,05) auf.

Schlussfolgerungen: Wir konnten zeigen, dass intestinale Parasiteninfektionen einen kleinen, aber signifikanten negativen Effekt auf die körperliche Fitness von Kindern haben, ausgedrückt durch ihre geschätzte maximale Sauerstoffaufnahme. Darüber hinaus weisen unsere Ergebnisse darauf hin, dass Knaben, die mit mehreren intestinalen Parasitenarten infiziert sind, niedrigere körperliche Fitness (VO_2 max) als ihre nicht infizierten Altersgenossen aufwiesen. Eine signifikant höhere *T. trichiura*-Prävalenz wurde bei verkümmerten Kindern und solchen mit einem signifikant niedrigeren Hb-Spiegel beobachtet als bei Kindern, die nicht mit Helminthen dieser Spezies infiziert waren. Ein deutlicher Einfluss von STH-Infektionen auf anthropometrische Indikatoren wurde ebenfalls beobachtet. Eine Einzeldosis von 400 mg Albendazole war wirksam gegen *A. lumbricoides*-Infektionen, konnte jedoch *T. trichiura*-Infektionen nicht wirksam bekämpfen, was frühere Forschungsergebnisse bestätigte. Die lokalen Gesundheits- und Bildungsbehörden bestätigten, dass die präventive Chemotherapie in den letzten Jahren vernachlässigt wurde. Zwei Massenentwurmungen pro Jahr werden empfohlen, um die Morbidität aufgrund von STH-Infektionen in zwei Schulen zu kontrollieren, und eine jährliche Entwurmung sollte in einer anderen Schule durchgeführt werden, und eine individuelle Diagnose und Behandlung erscheint in den anderen Studienschulen angemessen. Darüber hinaus sind Eingriffe in Wasser, Abwasser und Hygiene (WASH) gerechtfertigt. Die hohe räumliche Heterogenität deutet darauf hin, dass Daten von zusätzlichen Schulen in verschiedenen Stadtvierteln benötigt werden, um eine allgemeinere Interventionsstrategie ausfindig zu machen.

Die Förderung ausserschulischer körperlicher Aktivität und gesunder Ernährungs-interventionen sollte ein integraler Bestandteil des Schulalltags werden, um die Gesundheit von Kindern in Bezug auf BMI, Hautfaltendicke und kardiorespiratorische Fitness als Indikatoren für das Risiko chronischer Lebensstilbedingungen zu verbessern. Während unsere Intervention von Sportfachleuten in Absprache mit lokalen Akteuren entwickelt wurde, war ihre Wirkung begrenzt, was darauf hindeutet, dass eine längere und intensivere Umsetzung erforderlich sein könnte, um relevantere Auswirkungen zu erzielen. Eine sorgfältige Anpassung ist erforderlich, bevor das Interventionsprogamms vergrössert oder in anderen Umgebungen ausgeführt werden kann.

RÉSUMÉ

Contexte: À l'échelle mondiale, plus d'un milliard de personnes sont infectées par des helminthes transmis par le sol (STH, *Ascaris lumbricoides*, ankylostomes et *Trichuris trichiura*) et *Schistosoma* spp. Les symptômes les plus fréquemment associés à ces infections parasitaires comprennent les douleurs abdominales, la diarrhée, l'anémie, le retard de croissance et les troubles cognitifs. Alors que le mode de vie traditionnel et les habitudes alimentaires évoluent avec le développement social et économique, les communautés défavorisées des pays à revenu faible ou intermédiaire sont de plus en plus confrontées à des maladies non transmissibles. Particulièrement dans la population urbaine, les conditions liées à l'obésité imposent un fardeau croissant et affectent les personnes de toutes les couches socio-économiques. Ensemble, cela entraîne un double fardeau alors que les systèmes de santé s'affaiblissent dans de nombreux pays. Cela expose les enfants à un risque accru pour la santé pouvant entraver leur développement, leur bien-être et leur avenir socio-économique.

But et objectifs spécifiques: L'étude 'Maladie, activité et santé des écoliers' (DASH), un essai contrôlé randomisé par grappes, vise à étudier la relation entre la condition physique et les infections par les géo helminthes, les protozoaires intestinaux et *Helicobacter pylori sur* des élèves de 4e année primaire du quintile 3 grâce à deux interventions d'activité-physique multidimensionnelles de 10 semaines en milieu scolaire. Les objectifs de cette étude étaient (i) de déterminer la prévalence des infections parasitaires intestinales et *Helicobacter pylori*; (ii) d'évaluer les taux d'hémoglobine et les indicateurs anthropométriques; (iii) de mesurer de manière exhaustive les niveaux de forme physique; et (iv) d'étudier les liens possibles entre le statut d'infection et le statut socio-économique, le score d'activité physique auto déclaré et le retard de croissance. L'étude a été menée entre 2014 et 2017 dans les quartiers défavorisés de Port Elizabeth en Afrique du Sud. Sur la base des résultats, nous avons développé un programme d'intervention multidimensionnel et évalué ses effets sur la condition cardiorespiratoire, l'indice de masse corporelle (IMC) et l'épaisseur des plis cutanés.

Partenariat de recherche: Le projet était une initiative de recherche conjointe impliquant des collègues de trois institutions: (i) l'Université Nelson Mandela (Département des sciences du mouvement humain, NMU), (ii) l'Institut tropical et de santé publique suisse et (iii) le Département de Sport, Exercice et Santé (Département Sport, Exercice et Santé, DSBG) de l'Université de Bâle. Des échantillons de selles ont été analysés dans les laboratoires du département des sciences de laboratoire médical de la NMU avec le soutien des étudiants de 4ème année de Biomedical Technology (BTech).

Méthodes: Cet essai contrôlé randomisé en grappes a été mis en œuvre dans 26 classes de 4e année dans huit écoles primaires défavorisées de Port Elizabeth, en Afrique du Sud. La sélection des écoles était basée sur leur classification (quintile 3), la taille des classes de 4e année (n>100), l'emplacement géographique et la démographie de la population (écoliers Xhosa-, afrikaans et anglophones). L'étude a été menée dans des écoles primaires gouvernementales noires et métisses de diverses régions de Port Elizabeth, dans le sud-est de l'Afrique du Sud. Les zones peuplées par les Africains noirs sont communément appelées townships et comprennent les zones de Kwazakhele, New Brighton, Zwide et Motherwell. Les ‘zones nordiques’ de Port Elizabeth sont en grande partie habitées par des personnes de couleur, lesquelles ont été déplacées de force des zones centrales de la ville vers les régions périphériques du nord et incluent les régions de Schauderville, Gelvandale, Helenvale, Hillcrest et Booysens Park. Le travail de terrain a débuté en février 2015 (base de référence). L'évaluation de la ligne médiane a débuté en octobre 2015 et la mesure finale a été achevée en mai 2016. La première étape de l'étude comprenait 1009 écoliers âgés de 9 à 12 ans. La forme physique a été déterminée à l’aide des tests déployables sur le terrain de la batterie de test de fitness Eurofit. Les échantillons de selles ont été analysés avec la technique de frottis épais Kato-Katz pour diagnostiquer les STH et avec des tests de diagnostic rapide (TDR) pour détecter les protozoaires intestinaux et les infections à *H. pylori*. Les taux d'hémoglobine (Hb) et les indicateurs anthropométriques ont été mesurés à l'aide d'outils standard. Les données démographiques et le statut socio-économique de chaque participant ont été saisis avec un questionnaire. Après le diagnostic d'infection par les géo helminthes, les enfants ont été traités avec de l'albendazole (400 mg) après chaque enquête. Notre programme d'intervention multidimensionnelle sur l'activité physique comprenait (i) des cours d'éducation physique deux fois par semaine; (ii) des cours hebdomadaires de danse; (iii) les pauses actives en classe; et (iv) les adaptations de l'infrastructure scolaire visant à promouvoir l'activité physique. Les interventions ont été mises en œuvre à deux reprises, chaque fois pendant 10 semaines. De plus, le programme d'alimentation scolaire a été revu dans le but d'offrir une alimentation plus équilibrée et plus nutritive. Les principaux résultats comprenaient des indicateurs de la condition cardiorespiratoire, mesurés par une course navette de 20 m, l'IMC et l'épaisseur des plis cutanés. Les variables explicatives étaient le statut socio-économique, l'activité physique auto déclarée, le retard de croissance, l'anémie, l'infection par les protozoaires intestinaux et l'infection par les helminthes transmis par le sol.

Résultats: Les données complètes au départ étaient disponibles pour 934 enfants (92%). Dans deux écoles, des prévalences élevées de STH ont été trouvées (*Ascaris lumbricoides* 60% et 72% respectivement, *Trichuris trichiura* 65% chacun). Pour les garçons et les filles co-infectés par *A. lumbricoides* et *T. trichiura* (n=155), l'absorption maximale d'oxygène (VO_2 max) a été estimée à 50,1 ml kg^{-1} min^{-1} et 47,2 ml kg^{-1} min^{-1} respectivement alors qu'il était de 51,5 ml kg^{-1} min^{-1} et 47,4 ml kg^{-1} min^{-1} pour leurs compairs non infectés (n=278). En moyenne, les enfants sans infections par helminthes avaient une masse corporelle supérieure (P=0,011), une taille (P=0,009) et un IMC plus élevé (P=0,024) et souffraient moins souvent d’un retard de croissance (P=0,006), cependant, n’étaient pas significativement plus affaiblis que leurs pairs avec une infection à une ou deux espèces. Chez les garçons de 9 ans, une corrélation négative entre les infections par helminthes et le VO_2 max, la force de préhension et la distance du saut en longueur a été observée (p=0,038). Le taux moyen global d'Hb était de 122,2 g l^{-1}. Dans les deux écoles où la prévalence des STH était la plus élevée, les moyennes d'Hb étaient respectivement de 119,7 g l^{-1} et de 120,5 g l^{-1}.

Parmi les trois mesures, les intensités moyennes d'infection à *Ascaris lumbricoides* étaient de 9554 œufs par gramme de selles (EPG) en mai 2015, 4317 EPG en octobre 2015 et 1684 EPG en mai 2016. Les chiffres correspondants pour *Trichuris trichiura* étaient 664 EPG, 331 EPG et 87 EPG. Les résultats d'une sous-étude menée dans les deux écoles du projet ayant la prévalence la plus élevée, ont montré que l'albendazole était très efficace contre *A. lumbricoides* (taux de guérison: 97,2%, taux de réduction des œufs: 94,5%), cependant manquait d’efficacité contre *T. trichiura* (CR: 1,1%; ERR: 46,0%).

En ce qui concerne l'effet du programme d'intervention sur l'activité physique multidimensionnelle sur l'IMC, les plis cutanés et la condition physique, des données complètes de base et finale sont disponibles auprès de 579 enfants (âge moyen au départ: 10,0 ans). Dans le groupe d'intervention, nous avons observé une réduction significative de l’augmentation de l’IMC moyen (estimation de la variation moyenne: -0,12 avec intervalle de confiance à 95%: -0,22 à -0,03; p=0,008) et une augmentation réduite de l'épaisseur moyenne des plis cutanés (changement moyen: -1,06, IC à 95%: -1,83 à -0,29, p=0,007) entre le début et la fin du traitement par rapport au groupe témoin. Il n'y a pas eu de différences significatives entre les groupes en ce qui concerne les performances moyennes de la navette de 20 m et les estimations du VO_2 max ($P>0,05$).

Conclusions: Nous avons pu montrer que les infections parasitaires intestinales ont un effet négatif faible mais significatif sur la condition physique des enfants, tel qu'exprimé par leur absorption maximale d'oxygène estimée. De plus, nos résultats indiquent que les garçons qui sont infectés par des espèces de parasites intestinaux multiples ont des niveaux de condition physique (VO_2 max) plus bas que leurs pairs non infectés. Une prévalence de *T. trichiura* significativement plus élevée a été notée chez les enfants souffrant d'un retard de croissance et ceux ayant un taux d'Hb significativement plus faible, comparativement aux enfants non infectés par les helminthes de cette espèce. Un impact clair des infections par les géo helminthes sur les indicateurs anthropométriques a également été observé. Une dose unique de 400 mg d'albendazole par voie orale a été efficace contre les infections à *A. lumbricoides*, mais n'a pas permis de traiter efficacement les infections à *T. trichiura*, ce qui corrobore les données de recherche antérieures. Les autorités locales de santé et d'éducation ont confirmé que la chimiothérapie préventive avait été négligée ces dernières années. Dans deux écoles, un traitement vermifuge biannuel est recommandé afin de contrôler la morbidité due aux infections par les géo helminthes, dans une autre école, le déparasitage annuel doit être mis en place et, dans les autres écoles, le diagnostic individuel et le traitement adapté sembles appropriés. De plus, les interventions d'eau, d'assainissement et d'hygiène (WASH) sont justifiées. L'hétérogénéité spatiale élevée suggère que des données provenant d'écoles supplémentaires dans différents quartiers seront nécessaires pour identifier une stratégie d'intervention plus généralement applicable.

La promotion de l'activité physique extrascolaire et des interventions nutritionnelles saines devrait devenir partie intégrante du programme scolaire afin d'améliorer la santé des enfants en termes d'IMC, d'épaisseur de plis cutanés et de condition cardiorespiratoire comme indicateurs du risque de conditions de vie chroniques. Alors que notre intervention a été développée par des spécialistes de l'éducation physique en consultation avec les parties prenantes locales, son effet était limité, ce qui suggère qu'une mise en œuvre plus longue et plus intensive pourrait être nécessaire pour obtenir un impact plus pertinent. Une adaptation minutieuse sera nécessaire avant que l'intervention puisse être accrue ou mise en œuvre dans d'autres contextes.

This PhD thesis is dedicated to my family

1 INTRODUCTION

1.1 Healthcare challenges in low- and middle-income countries

Countries with populations predominantly in the low- and middle-income brackets often face the continuing challenges of poverty-related infectious diseases (Yap *et al.*, 2015). As traditional lifestyles and diets change with socioeconomic development, low- and middle-income countries face a *dual burden* of communicable and non-communicable diseases, often exacerbated by weak healthcare systems (Boutayeb, 2006; Santosa *et al.*, 2014) (Figure 1.1). The World Health Organization (WHO) estimates that more than one billion of the world's population is chronically infected with soil-transmitted helminths, and that around 200 million people are infected with schistosomes (World Bank, 2017a; WHO, 2017a). The global rates of humans with intestinal helminth infections are estimated as follows: for roundworm (*Ascaris lumbricoides*) approximately 807 - 1,121 million; whipworm (*Trichuris trichiura*) approximately 604 - 795 million; and hookworm (*Necator americanus* and *Ancylostoma duodenale*) approximately 576 - 740 million (CDC, 2017b).

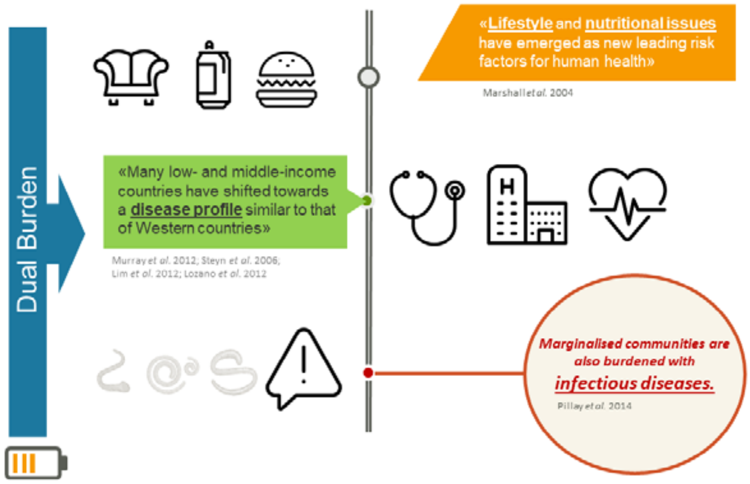

Figure 1.1 The double burden – Many low- to middle-income countries are undergoing a rapid demographic and nutritional transition.

Rates of exposure and susceptibility to soil-transmitted helminth infections (other than hookworms) in human communities are not uniform. However, data from a survey among poor communities in Jamaica, presented in Figure 1.2, shows that schoolchildren are most at risk of (intense) infections with prevalence levels reaching up to 90% at 8 to 15 years of age, whereas at the age of 60 years (up to 80%) the infection prevalence levels were a little lower (Bundy, 1988).

Furthermore, as the intensity of infection is related to morbidity and the developmental stage of the host,

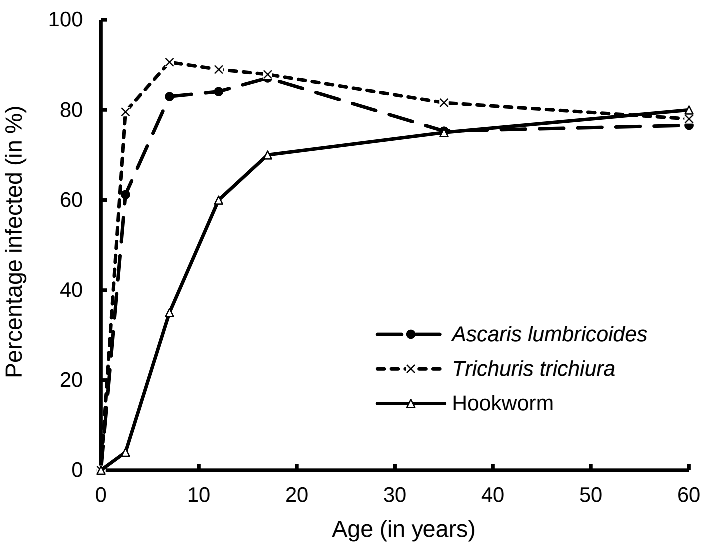

Figure 1.2 Age-related soil-transmitted helminth infections in poor human Jamaican communities (adapted from (Bundy, 1988).

the risk of health consequences from soil-transmitted helminth infections is concentrated in the 8 to 15 years age-group (hookworm, however, often peaks at a later stage of life) (Bundy, 1988). In low- and middle-income countries, soil-transmitted helminth infections account for an estimated 12% of the total disease burden for girls and boys in socio-economically deprived areas aged around 5 years, and for 11% when they reach 14 years of age (Drake *et al.*, 2000; World Bank, 2017a). A recent WHO estimation (WHO, 2017b) is that roughly 300 million humans live with extensive helminth infection rates and suffer from severe morbidity (Figure 1.3), resulting in more than 150,000 annual deaths (Crompton, 1999; Montresor *et al.*, 2002). These numbers are high: soil-transmitted helminth infections represent one of the largest contributors to the disease burden of 5- to 14-year-old children (Bundy, 1988).

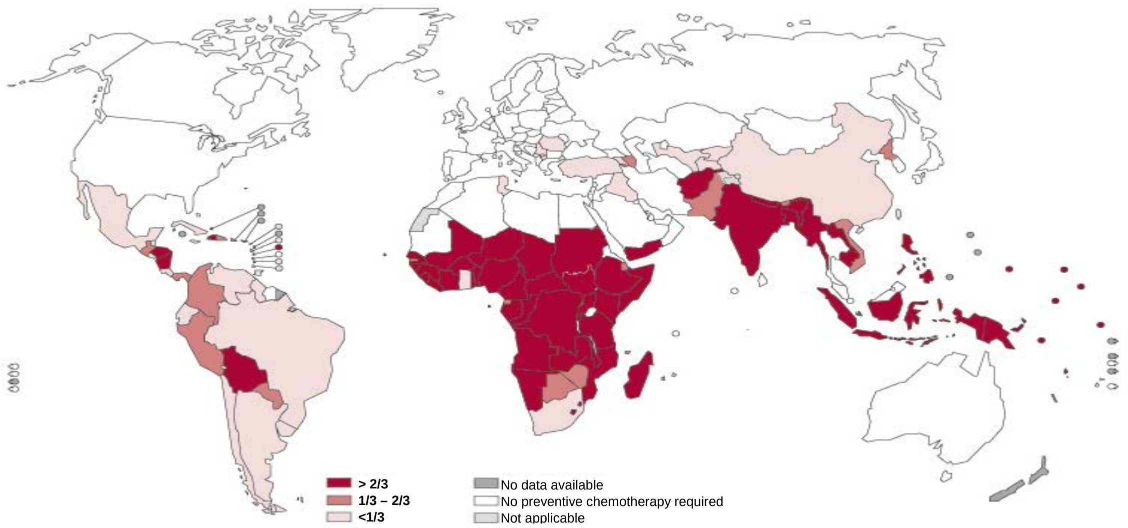

Figure 1.3 Distribution of soil-transmitted helminthiases and proportion of children (aged 1–14 years) in each endemic country requiring treatment (WHO, 2017).

Chronic parasitic helminth infections potentially threaten children's psychological and physical development as well as potentially causing, or exacerbating, malnutrition and retarding child-development (Stephenson *et al.*, 2000). Anthelminthic treatments may, in turn, reverse growth and nutritional deficits caused by worm infections if adequate macro- and micro-nutrient availability allows the children to catch up in terms of growth and development (World Bank, 2017a). Intervention studies show that roundworm infections are associated with growth deficits in school-aged children and that *Trichuris trichiura* infections of moderate intensity may cause growth retardation and anaemia (Drake *et al.*, 2000). Children with Trichuris dysentery syndrome presented *'catch-up growth'* after *Trichuris trichiura* infection treatment. Other intervention studies have shown a positive effect of deworming in terms of iron status and anthropometric parameters in preschool and school-aged helminth infected children (Drake *et al.*, 2000). Furthermore, ill health caused by parasitic helminth infections may also negatively affect the child's mental functions (World Bank, 2017a). There are, reputedly, also risks of iron deficiency, anaemia, stunting and cognitive development (World Bank, 2017a). However, this may be true only for those children with the most intense parasitic infections, or for those already vulnerable in other ways, such as from undernourishment (Drake *et al.*, 2000). The Cochrane systematic reviews do not show significant health effects of deworming for the majority of affected individuals (Taylor-Robinson *et al.*, 2015; Taylor-Robinson and Garner, 2017).

The life cycles of soil-transmitted helminths are complex, and the parasites have adapted well to their environment. Adult worms of *Ascaris lumbricoides* or *Trichuris trichiura* live in the intestines of infected humans, as shown in Figure 1.4 (CDC, 2017). They produce thousands of eggs each day and these are passed through faeces into the environment (WHO, 2017a). In areas where sanitation is lacking, these eggs contaminate the soil and water (Jourdan *et al.*, 2017). Worm eggs are picked up by children who play on the contaminated soil and then put their unwashed hands in their mouths (WHO, 2017b). Eggs can also be ingested either with vegetables that are not carefully cooked, peeled or washed or through a contaminated water source.

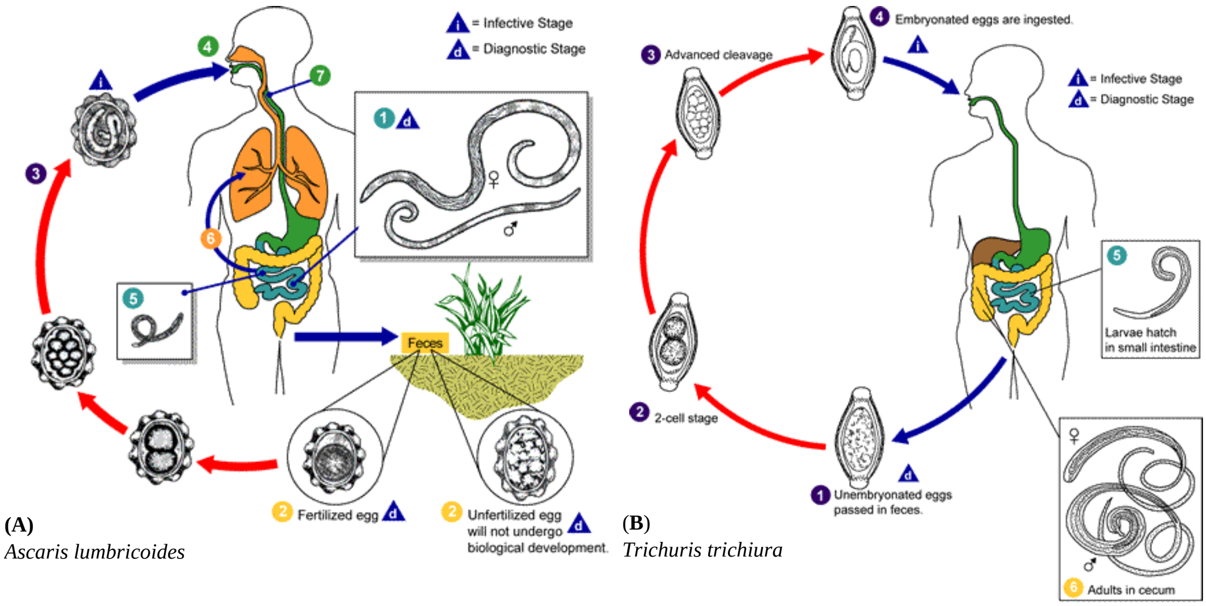

Figure 1.4 Biology - Life cycle of (**A**) *Ascaris lumbricoides* (roundworm) and (**B**) *Trichuris trichiura* (whipworm) (Source: CDC, 2017).

Hookworm infection, however, is usually obtained by barefoot running on soil-contaminated with faeces, as shown in Figure 1.5 (CDC, 2017). The eggs in the soil can mature, hatch, and release larvae. The larvae ripen from the rhabditiform into the filariform, which can then penetrate human skin.

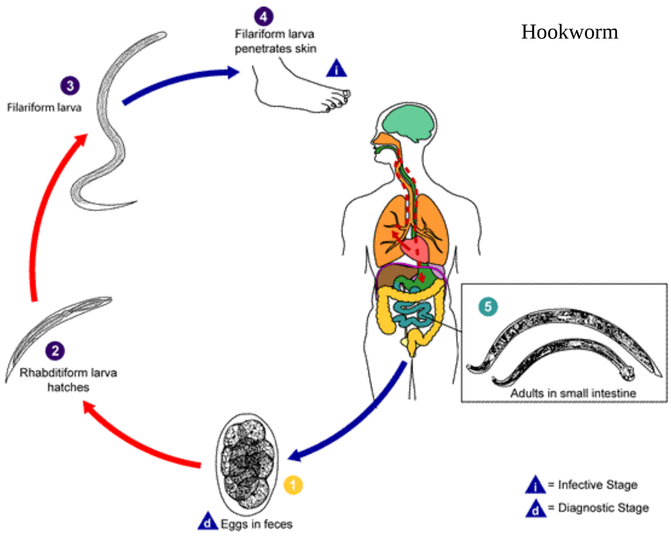

Figure 1.5 Biology – The Life cycle of hookworm (Source: CDC, 2017).

In addition to transmissible diseases, non-communicable diseases, such as diabetes, cardiovascular diseases, obesity-related conditions, dementia and cancers impose a growing burden on the population of low- and middle-income countries, and may impact on the health care systems of developing countries (Marshall, 2004; WHO, 2014). Evidence-based research shows that a sedentary lifestyle is one of the main risk factors for the development of chronic diseases. This lifestyle increases global mortality and accounts for 6% of deaths worldwide (WHO, 2014). The estimated probability of dying prematurely from cardiovascular diseases, cancer, chronic respiratory diseases or diabetes between the ages of 30 and 70 is presented in Figure 1.6 (from Economist; Source: WHO, 2015).

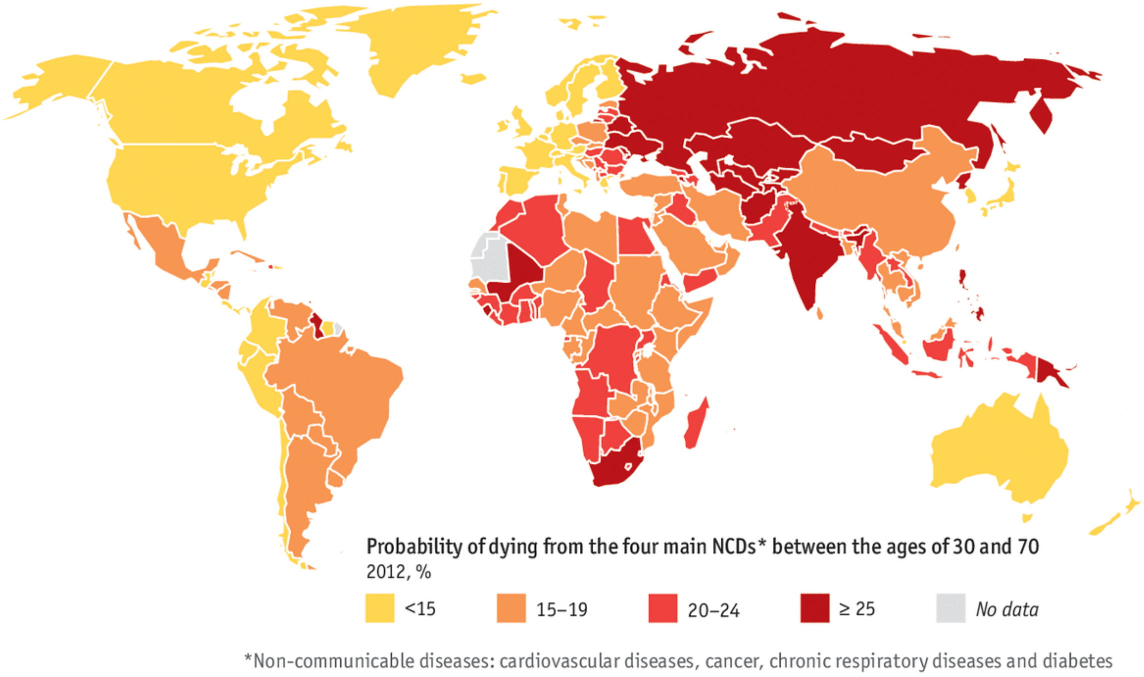

Figure 1.6 Probability of dying prematurely from non-communicable diseases (from Economist; Source: WHO, 2015).

Whereas overweight and obesity account for 5% of the global mortality rate (WHO, 2014), physical inactivity is considered the main cause of 21-25% of all breast and colorectal cancers, 27% of all diabetic diseases and about 30% of all ischaemic heart diseases (Hancock, 2011). It is predicted that by 2020 non-communicable diseases will cause seven out of every ten deaths in developing countries (Boutayeb, 2006). Researchers predict that, due to the sedentary lifestyle of children in low- and middle-income countries, children in these countries will have a lower life expectancy than their parents. Globalization, technological developments and urbanization also cause health-damaging environmental conditions. Factors such as processed and high-energy foods, motorized transport to the workplace, office work, elevators, and escalators lead to increased inactivity (Lob-Corzilius, 2007). Experts predict that by the year 2030, 1.3 billion people or approximately 15% of the global population will be classified as overweight (Puoane *et al.*, 2012; Okop *et al.*, 2016). Furthermore, the lack of active life-style role models in modern families may contribute significantly to this development. Study findings show that children of active parents move more than children of inactive parents (Graf *et al.*, 2003; Graf *et al.*, 2006). Research over the past few decades has provided a greater understanding of factors influencing whether or not a person or community is physically active (Figure 1.7) (Edwards and Tsouros, 2006).

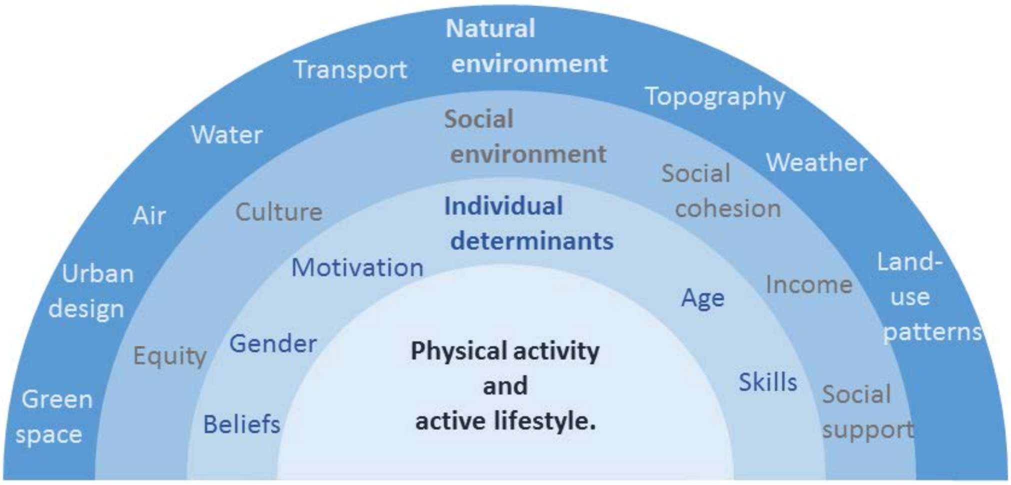

Figure 1.7 Layers of influence affecting engagement in physical activity (Edwards and Tsouros, 2006).

This development needs to be addressed by the global health community in the new age of Sustainable Development Goals (SDGs), especially to ‘ensure a healthy life and promote the well-being of all ages’ (Affairs, 2014; Yap *et al.*, 2015). Insufficient physical activity is amongst the leading risk factors for death worldwide, and a key risk factor for NCDs, such as cardiovascular diseases, diabetes and cancer. Furthermore, it is well known that physical activity has significant health benefits and contributes to preventing NCDs. Moreover, physical inactivity and inappropriate diet, such as low fruit intake and excess salt consumption, have emerged as new risk factors, accounting for 10% of the global burden of disease as expressed in disability-adjusted life years (DALYs) (Lim *et al.*, 2012). Overweight has replaced under-nutrition as a risk factor for the first time in history (Lim *et al.*, 2012; Lozano *et al.*, 2012; Murray *et al.*, 2013). Since childhood malnutrition has recently been eradicated in most areas of the world, further extensive dissemination of the overweight problem and its concomitant non-communicable diseases is, and will increasingly become, the central task for the WHO. The WHO has indeed proposed the following recommendations for children between 5 to 17 years of age: in general, at least 60 min of moderate to vigorous physical activity per day (WHO, 2017b). The bulk of the activity should be aerobic and be linked to activities that strengthen muscles and bones, occurring at least three times a week (WHO, 2017b). Those who are regularly physically active suffer less from illness than inactive people, are less likely to be prone to illness, have a higher life expectancy and a higher quality of life (Schwarzer, 2004). The American Heart Association recommends that cardiovascular health should be monitored through three biomarkers: cholesterol, blood pressure and fasting glucose (Lloyd-Jones *et al.*, 2010). Figure 1.8 shows that underlying risk factors, such as physical inactivity, alcohol abuse, smoking and unhealthy diets, are causally associated with non-communicable diseases (*e.g.*, cardiovascular diseases, chronic respiratory diseases, diabetes, and cancer) (WHO, 2017).

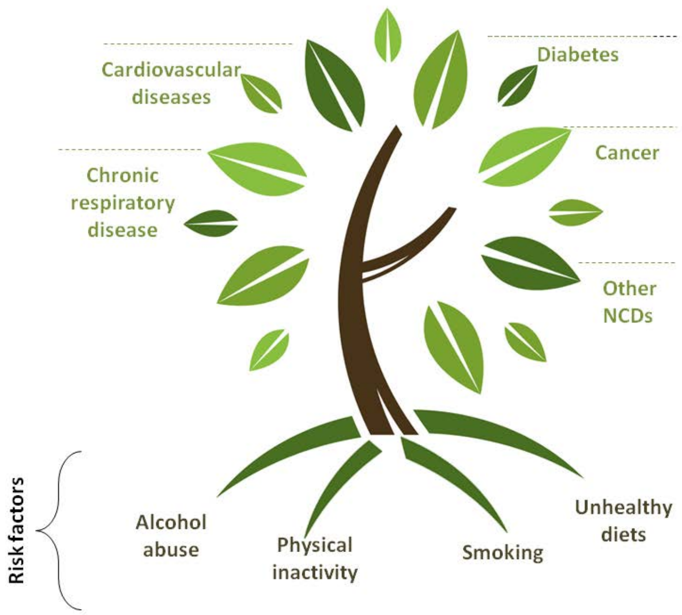

Figure 1.8 Non-communicable diseases are associated and linked with four particular risk factors (Source: WHO, 2017).

Physical inactivity has been identified as one of the most relevant risk factors for NCDs (Monyeki and Kemper, 2008). It should be noted, though, that global averages are subjected to a high degree of heterogeneity and therefore a relatively large inaccuracy is included in the data. However, what happens at national or even regional level is crucial for locally tailored research interventions that help to reduce disease risk factors and improve the health and well-being of local populations.

1.2 South Africa

1.2.1 Health issues in South Africa

Health in South Africa should be viewed within a broader context of different levels of prosperity. As soon as poverty affects a population, health is fundamentally affected by the lack of access to basic needs such as water, adequate nutrition, effective sanitation, adequate housing, access to vaccination programmes or health care and education (Mayosi and Benatar, 2014). South African public hospitals are often in a poor condition as public health infrastructure has become dysfunctional due to under-financing, neglect and mismanagement (Mayosi and Benatar, 2014; WHO, 2017b). This is most clearly visible in the Eastern Cape province but also occurs in other regions of South Africa. The Eastern Cape harbours over 40 district hospitals, but each with low bed occupancies and inadequate professional staff in order to achieve quality care (HST, 2017). Improved access to basic health care and increased socio-economic situations contribute to the prospect of a healthier life: however, where health care is not adequate, both absolute and relative poverty contribute to poor health (Mayosi and Benatar, 2014). Social grants have downscaled absolute poverty, but 45% of the South African population still lives on amounts starting from as low as $2 per day, the defined limit for absolute poverty (Mayosi and Benatar, 2014). The Gini coefficient (from 0 to 1; where 0 indicates the overall equality of income and 1 the maximum inequality) increased from 0.6 in 1995 to almost 0.7 in 2009, indicating that relative poverty has become worse (World Bank, 2017c). Furthermore, approx. 10% of the South African population earns approximately 58% of the entire national income at the top of the scale, while 70% at the lower end earn only about 17% (Mayosi and Benatar, 2014; World Bank, 2017c). In societies with lower relative poverty levels, the differences in health care and well-being are less pronounced (characterized by a low Gini coefficient) than in countries where the divide reflects an inequality.

Over recent years, improvement and substantial growth have occurred in South Africa. Furthermore, a Black African middle class has emerged and expanded, and a significant increase in social assistance was implemented for the poorest and unemployed inhabitants (Lemon, 2017). However, more than 10 million people in South Africa still live with less than $1 a day. This technically reflects a food shortage and people living below the level cannot buy enough food for adequate nutrition

(Mayosi and Benatar, 2014; World Bank, 2017b). Nowadays, South Africa harbours the world's biggest poverty and prosperity disparities.

In the immediate past major South African public health concerns were the human immunodeficiency virus (HIV) or the immune deficiency syndrome (AIDS) endemic, and tuberculosis, both of which affect the non-white population most. Much research and significant resources have been focussed on these areas. However, a global burden of disease (GBD) study recently summarized three main aspects of the changing disease burden in South Africa (GBD, 2014): First, the causes of premature death have significantly changed due to the rising HIV/AIDS infection rates and the increasing contribution of violence, injuries, diabetes and other non-communicable diseases (Mayosi and Benatar, 2014; Pillay-van Wyk *et al.*, 2016). The highest proportion of disability-adjusted life years is attributable to alcohol consumption, high body mass index and hypertension (GBD, 2014). Second, South Africa continues to be poor in terms of life expectancy at birth, years of life lost due to premature death, years lived with disability, and age-adjusted death rate (Figure 1.9) (GBD, 2017). In terms of life expectancy, South Africa was and still is a divided country: 14 years ago, life expectancy at birth was 46.6 years for the total population, whereas life expectancy for the white population of South Africa was much higher and, due to better access to health information and to healthcare, similar to that of most Western countries. In particular, the majority of South Africa’s murders are mainly in the townships of non-white people by other non-whites, which contributes to this dichotomy (Bor *et al.*, 2013).

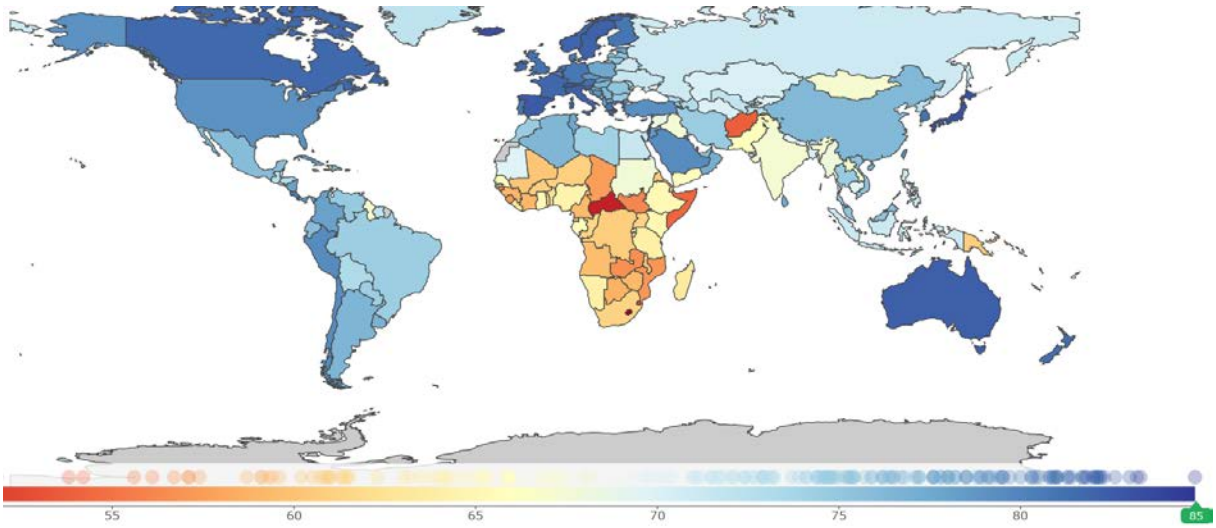

Figure 1.9 Life expectancy (x-axis in years) and probability of early death (both sexes) on a national level (GBD, 2017).

Third, non-communicable diseases occur in both rural and urban environments but are more predominant in urban areas amongst poor people. Consequently, this rising burden, together with a demographic change and an increasing proportion of retirees aged over 65, is boosting the pressure on health services. It is likely that the burden of non-communicable diseases will further increase, while treatment for HIV/AIDS continues to improve and the associated mortality will further be reduced.

Studies conducted in schools located in disadvantaged neighbourhoods and focusing on the physical activity patterns of primary schoolchildren have confirmed that physical activity levels are insufficient (Walter, 2011). Due to an increasingly sedentary lifestyle and in accordance with international developments (Katzmarzyk *et al.*, 2008), the fitness of South African children is decreasing and overweight is the result (Hurter and Pienaar, 2007). Overweight and obesity have been found to be more common in urban environments in South Africa than in rural areas (Shisana *et al.*, 2013) but are generally increasing in South Africa (McVeigh *et al.*, 2004; Armstrong *et al.*, 2006; Walter, 2011). After the democratic government was elected in 1994, revisions in the school curriculum meant that physical education lost its stand-alone subject status in the South African schools. It is included in the learning area called Life Skills (together with other disciplines), based on the guidelines of the South African Curriculum and Assessment Policy Statement (CAPS) (Rajput and Van Deventer, 2010). Under the apartheid government, physical education lessons were given a stand-alone status and some emphasis, but especially in advantaged schools. It was therefore a privilege for only a segment of the population with the masses effectively ignored. Physical education at schools was viewed by anti-apartheid activists as one of the instruments used to further develop the ideological agenda of the apartheid government, at one with the militarized cadet system implemented in white schools. The advent of democracy in 1994 was accompanied by high expectations of undoing the injustices of the past, and physical education was incorporated into a general life-skills learning area, which is non-examinable. However, the delivery of physical education and sport in schools has not benefited the learners in its new format in the curriculum, particularly in less advantaged schools which did not have a strong tradition of the subject. One hour per week is allocated to physical education in the primary and intermediate grades. In comparison to most other countries worldwide, the South African curriculum allocates little time to physical education (Pühse and Gerber, 2005). The deficiency of physical education is further aggravated by the fact that a considerable number of schools do not follow the CAPS prescriptions (Du Toit *et al.*, 2007). For instance, Reddy *et al.* 2003 reported that only every second South African child has physical education classes on the timetable and that only half of these engage in vigorous physical activity at school (Reddy *et al.*, 2003). Furthermore, the physical environments of schools located in poor neighbourhoods are generally not conducive to the promotion of physical activity. There are inadequate recreation and sport facilities, a non-existent physical education programme and a lack of qualified teachers (Yap *et al.*, 2015). This, in turn, has a negative impact on the activity patterns and thus the health of children (Van Deventer, 2004). Kimani-Murage *et al.* reported in 2010 from a low-income South African setting that increasing levels of physical inactivity in girls occurred together with early stunting in adolescence (Kimani-Murage *et al.*, 2010). This phenomenon was especially prevalent among black girls and those who reported the highest rate of physical inactivity (Puoane *et al.*, 2005; Walter *et al.*, 2011).

The Healthy Active Kids South Africa (HAKSA) Report Card 2014 states that two out of three women in South Africa are insufficiently active, as is one out of three men. Almost half of all adults and children are not sufficiently active (less than an hour of exercise per day) to avoid chronic diseases such as heart attacks, diabetes or lung disease. Overweight and obesity have doubled amongst male adolescents over the past six years. Only half of all children participate in organized sports and leisure activities and, on average, a South African child watches three hours of television a day (Draper *et al.*, 2014). The recently published HAKSA Report Card 2016 supports these statements. Moreover, it identifies an urgent need for practice-based evidence building and the evaluation of existing interventions (Uys *et al.*, 2016). Using data from the World Health Survey (2003) researchers have estimated that, among South Africans older than 15 years, about 30% of ischemic heart disease, 27% of colorectal carcinoma, 22% of ischemic stroke, 20% of type 2 diabetes and 17% of breast cancer are as a result of physical inactivity (Joubert *et al.*, 2007). Physical activity has been associated with multiple health benefits in both adults and children (Hardman and Marshall, 2005; Pühse and Gerber, 2005). Research suggests that participating in regular physical activity and being in a good physical state of health reduces the risk of cardiovascular diseases and type 2 diabetes, and also helps to control body weight, having, therefore, a positive impact on muscles and bones and contributing to improved psychological well-being (WHO, 2017c). Because physical inactivity during childhood can lead to poor health effects in adulthood (Tian *et al.*, 2015) there is a pressing need to promote physical activity among school-aged children: this may minimise risk factors for non-communicable diseases (Olshansky *et al.*, 2005).

Based on these findings, international organizations (*e.g.*, Centers for Disease Control and Prevention, USA, in addition to WHO) recommend that children aged between 5 and 17 years should accumulate at least 60 min of moderate to vigorous physical activity per day (CDC, 2017a). A number of factors hinder South African children from achieving this goal, including the fact that in South Africa physical education is rarely taught in disadvantaged schools (Demombynesa and Özler, 2005; Fataar, 2007; Makoelle, 2014; Olivier *et al.*, 2016) aggravating health promotion among children. And since there is a lack of basic sports equipment in disadvantaged schools the children have no incentive to engage in sporting activities (Mchunu and Roux, 2010). At the same time, infectious diseases that are intimately linked to poverty are also prevalent among disadvantaged South African schoolchildren (Draper *et al.*, 2010), resulting in a negative impact on children's physical fitness, cognitive abilities and nutritional status (Hürlimann *et al.*, 2014; Yap *et al.*, 2014). Where deficient nutrition is added as a risk factor, the burden on personal health is further increased (Toriola *et al.*, 2012; Tathiah *et al.*, 2013).

In South Africa, such a dual disease burden threatens to put children at risk of vulnerable health, growth deficits, and reduced well-being (Yap *et al.*, 2015). Furthermore, previous surveys have revealed that the South African population has moved towards a disease profile resembling Western countries, with increasing proportions of deaths attributed to chronic diseases of lifestyle (Steyn and Damasceno, 2006). Concurrently, tuberculosis is still escalating in South Africa, and the HIV/AIDS pandemic puts additional pressure on the already overburdened South African healthcare system (McVeigh and Meiring, 2014).

In order to provide further detailed information on the study area, the next section provides a brief outline of South African history, which indicates that many of the socio-economic and health problems have an historical and socio-political basis.

1.2.2 A brief outline of South Africa's recent history

The South African Union in 1910 emerged from the Anglo-Boer War. The Union focused on the citizens of European descent (the English and the Boers from the two conflicting sides), and did not cater for black South Africans in terms of citizenship or facilities. Emerging from this, the National Government, elected in 1948, promulgated laws to enforce its policies of “apartheid” or “separateness”, and promulgated laws that separated people of different ethnicities: blacks – and especially black Africans – were disadvantaged in the social, political, educational, health and economic spheres. It was only in 1994 with the election of politician and anti-apartheid revolutionary Nelson Mandela as President of South Africa – and the passing of a progressive constitution – that the ‘apartheid laws’ were completely abolished (Roberts, 1994; Limb, 2008). The following quote depicts the prevailing notion during the apartheid era:

> *“In South Africa, to be poor and black was normal, to be poor and white was a tragedy”* (Mandela, 1994).

Apartheid’s legalised and enforced social division into black, coloured, Asian and white people is still reflected in South African society, despite the 1994 political settlement. South Africa is still struggling with race-based socio-economic inequalities, characterized by a high rate of unemployment and of crime, and a poor health and public education system (Fataar, 2007; Toit *et al.*, 2011; Mayosi *et al.*, 2012; Nattrass, 2014).

Although black and coloured South Africans nowadays do have the same rights and, in law at least, the same possibilities as whites, large socioeconomic differences are still to be found, especially in the agglomeration of areas in South African cities. During apartheid, blacks were forced to live in ‘Townships’ and their possibilities for movement were limited (Weber *et al.*, 2010). There were beaches accessible only to white people, while black or coloured people were threatened with a fine or even jail for entering these areas (Weber *et al.*, 2010). After the disintegration of apartheid in 1994, the life situation of black people has not generally improved. Many townships still exist where unemployment, poverty and high crime rates prevail (Weber *et al.*, 2010). Among the main problems in Port Elizabeth since the multiracial elections of 1994 were a lack of foreign and government investment and a general increase in crime. Port Elizabeth has been, and remains fraught with problems similar to the whole of South Africa. One year after the turn of the millennium the Nelson Mandela Bay Metropolitan Municipality administration was formed consisting of the Port Elizabeth, the Uitenhage and the Despatch areas, and including the surrounding agricultural farmland. Nowadays, the Nelson Mandela Bay Metropolitan Municipality area harbours a population of over 1.3 million (Weber *et al.*, 2010).

1.3 Research needs

Only a few studies in South Africa have focused on physical education promotion programmes as well as preventive measures for cardio-vascular and communicable disease risk factors. This is particularly true for poor schools in socio-economically impoverished neighbourhoods. The authors of the HAKSA report 2016 conclude that in South Africa there is an urgent need for building evidence and for the evaluation of existing and scaled up interventions (Uys *et al.*, 2016).

The perception that it is easier for healthy children to learn and that they also therefore show an elevated learning efficiency is empirically manifested and well accepted (Basch, 2011). Given that previous studies (Hürlimann *et al.*, 2014; Yap *et al.*, 2014) have enriched the understanding of how intestinal helminth infections impact negatively on children's cognitive performance, nutritional status, psychosocial health and physical fitness, – and may, therefore, lower cardiorespiratory fitness – it is hypothesized, for this study, that by deworming and promoting a setting-specific physical activity programme and a healthy diet, one can positively influence the health (*e.g.* an elevated cardiorespiratory fitness level) and wellbeing, as well as learning outcomes of children.

The premise is that a combination of interventions – health and lifestyle interventions, designed after an initial survey, and rendering the school infrastructure more suitable for physical activity – will have a positive impact on children's health and wellbeing. An active lifestyle reduces the risk factor for children to develop non-communicable diseases later in life, such as *e.g.* overweight. In addition, we want to find out which kind of infectious diseases occur in the targeted area of investigation and how these change as a result of relevant treatment (*e.g.* deworming).

Further intensive research on parasitic infections in a poor part of Port Elizabeth, South Africa, offers a unique chance to investigate its impact on children's psychosocial health, physical fitness and cognitive performance (Yap *et al.*, 2015). Therefore, an investigation of risk factors in childhood for the development of non-communicable diseases later in life in adulthood seems to be justified. This research endeavours to provide an evidence base to establish setting specific health interventions in order to institutionalize and even expand such interventions.

1.4 Key goal of the PhD thesis

Accordingly, the overall goal of this project is to survey the distribution of selected intestinal parasite infections, mainly soil-transmitted helminth infections, and risk factors for non-communicable conditions, and to assess their impact on schoolchildren's physical fitness, cognitive performance and psychosocial health over time in disadvantaged primary schools of Port Elizabeth, South Africa, before, during and after the introduction of setting-specific interventions focusing on deworming, a nutritional supplement, a physical education and health and hygiene education programme (Yap *et al.*, 2015). Moreover, the association between the measured risk factor variables for non-communicable diseases (*e.g.* cardiorespiratory fitness, skinfold thickness, BMI, anaemia, diabetes) and the implemented lifestyle interventions among Grade 4 schoolchildren in Port Elizabeth, South Africa, were investigated.

1.5 Specific objectives of the PhD thesis in detail

The aforementioned overall goal will be achieved by pursuing two specific objectives:

(i) To conduct a longitudinal study assessing the prevalence of intestinal parasites, risk factors for diabetes and hypertension, anthropometry and the level of cardiorespiratory fitness, cognitive performance and psychosocial health among 1000 primary schoolchildren; and

(ii) To design setting-specific interventions, such as deworming, a nutritional intervention, a physical education programme and a health and hygiene education programme in order to contribute to the understanding of *health literacy*, and to assess their effects on the measured health parameters.

Table 1.1 depicts the various hypotheses formulated for the relevant research question and corresponding specific objectives set for the study.

			Research Questions	Specific Objectives	Hypotheses
A - Baseline survey	**Schoolchildren aged around 10 years**	**I**	What is the extent of risk factors for non-communicable diseases (*e.g.* risk factors for diabetes, anaemia and malnutrition)? What is the prevalence of hypertension? And at what level is the cardiorespiratory fitness, upper, and lower body strength?	To estimate mean values of the following variables among primary schoolchildren in Port Elizabeth: Blood glucose levels, blood pressure, weight, height, haemoglobin, grip strength, standing broad jump, and cardiorespiratory fitness.	Study population shows a high prevalence of malnutrition (*e.g.* stunting) but low blood glucose levels. Furthermore, overweight or obese children show lower cardiorespiratory fitness, grip strength, and standing broad jump.
		II	What is the prevalence of helminth infections (*e.g.* soil-transmitted-helminth) or selected parasitic diseases (*e.g.* intestinal protozoa) among Grade 4 schoolchildren in Port Elizabeth?	To estimate the prevalence of the following variables among primary schoolchildren in Port Elizabeth: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm, *Cryptosporidium* spp., *Giardia intestinalis,* and *Helicobacter pylori*.	Schoolchildren in disadvantaged schools in Port Elizabeth show a low prevalence of helminth infections. Nevertheless, it is assumed that there will be hot spots of soil-transmitted-helminth-infections, and/or specific protozoa infections.
B - Intervention and follow-up	**Schoolchildren aged around 10^{+} years**	**III**	What is the specific effect of the deworming campaign? Is there a change of the measured variables with regard to the prevalence of parasitic intestinal diseases at 3 different time points among Grade 4 schoolchildren in Port Elizabeth? What will be the re-infection rate of the selected parasitic diseases?	To estimate prevalence at 3 different time points, and thus also the change, of the following variables among Grade 4 primary schoolchildren in Port Elizabeth: *Ascaris lumbricoides*, *Trichuris trichiura*, hookworm, *Cryptosporidium* spp., *Giardia intestinalis,* and *Helicobacter pylori*.	It is assumed, that after deworming, the prevalence of the selected parasitic diseases will decrease. After a few weeks, however, we assume that there will be re-infections, and the prevalence levels of the selected parasitic diseases increase again.
		IV	Is there an association between the measured risk factor variables for non-communicable diseases (*e.g.* cardiorespiratory fitness, skinfold thickness, BMI, anaemia, diabetes) and the implemented lifestyle interventions among Grade 4 schoolchildren in Port Elizabeth? What is the effect of setting-specific interventions (*e.g.* lifestyle intervention as health education or physical-activity promotion) on improving children's health, and wellbeing?	To conduct assessments of anthropometric indicators (*e.g.* height, weight and body composition), physical fitness levels, cognitive performance, and psychosocial health. To assess the change in blood glucose levels, blood pressure, weight, height, and haemoglobin among Grade 4 schoolchilden in Port Elizabeth.	After implementing the interventions, risk factors, as *e.g.* prevalence levels of non-communicable diseases (*e.g.* overweight, anaemia, and/or diabetes), will decrease and variables on children's health (*e.g.* cardiorespiratory fitness), and wellbeing will show an improvement.

An integrated approach, consisting of targeted and complementary health interventions, might decrease the incidence of intestinal parasite infections and non-communicable disease risk factors. As a result, children's physical health and well-being improve and this contributes to the enhancement of their cognitive performance and learning abilities. As a whole, it is intended to consolidate and contribute to the understanding of health literacy, which refers to the personal characteristics and social resources of every human being (Ophelia, 2017). It is needed for individuals but also for communities to access, understand and to use the given information in order to make better decisions about their own health (Dodson *et al.*, 2014). In addition, health literacy includes the ability to make, and to communicate, these decisions (Figure 1.10) (Dodson *et al.*, 2014).

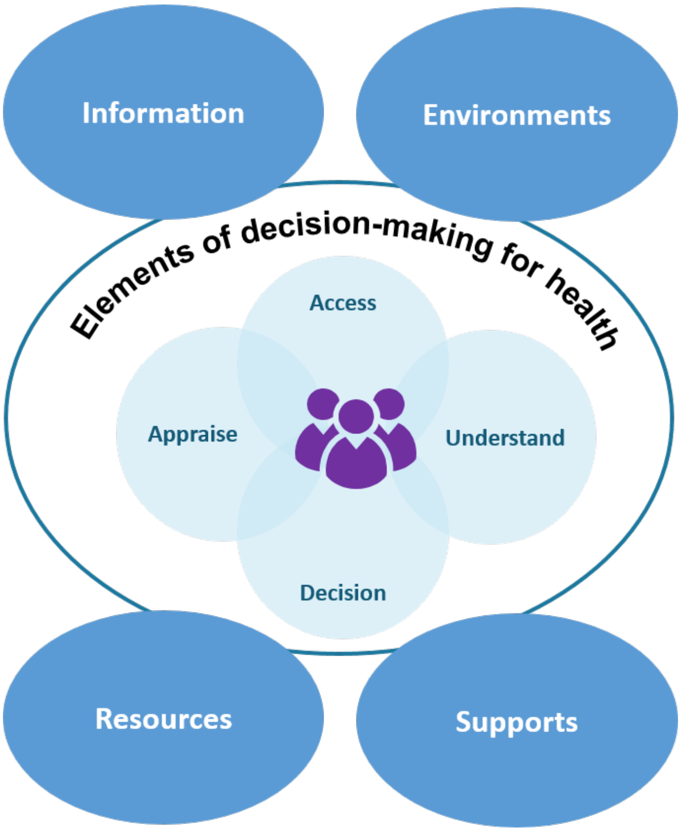

Figure 1.10 When people make health decisions as they interact with information, environments, resources, and supports, this is called health literacy.

1.6 Collaborative framework in the context of SSAJRP

In 2013, the Swiss National Science Foundation (SNSF) launched, within the context of the Swiss-South African Joint Research Programme (SSAJRP), a call for joint research projects (JPRs) in collaboration with the partner organization from South Africa, the National Research Foundation (NRF) (SNSF, 2017). Since 2008, the SSAJRP has promoted technical and scientific cooperation between Switzerland and South Africa based on the principles of scientific excellence, mutual interest and reciprocity due to matching funds (NRF, 2017). This programme is one of several bilateral research cooperation programmes, organized by the State Secretariat for Education, Research and Innovation (SERI) of Switzerland (SNSF, 2017). The SSAJRP supports research partnerships, the so-called joint research projects (JRPs), between scientists from Switzerland and South Africa to encourage knowledge transfer and innovation in either countries (NRF, 2017). It also supports scientists in transforming their applied research into market application and discovering their entrepreneurial potential (SNSF, 2017).

Projects have a duration of three years, and Switzerland fosters financing of up to CHF 230,000 per project (SNSF, 2017). As part of the SNSF projects, grants cover the costs of equipment, research funds and salaries. Based on a call in 2013, 65 submitted applications were jointly assessed by the SNSF and the NRF of South Africa. Ultimately, 25 applications were successful and approved, including this project. The SNSF is responsible for all the costs of the Swiss research component, which corresponds to a total of CHF 5.5 million, and the NRF funded the South Africa component (SNSF, 2017). The projects to be funded were distributed as follows across the different topics of the call:

- Public health and biomedicine: 10
- Biotechnology and nanotechnology: 5
- Environmental technology (Greentech and Cleantech): 6
- Humanities and social sciences: 4

1.7 Study area and population

The Disease, Activity and Schoolchildren's Health (DASH) study was carried out in Port Elizabeth, Eastern Cape province, South Africa (geographical coordinates: 34°07'54'' to 33°57'29'' S latitude and 25°36'00'' to 25°55'49'' E longitude). Port Elizabeth is one of the largest cities in South Africa and it is situated in the Eastern Cape province (770 km east of Cape Town) within a subtropical climate with light rain throughout the year. In accordance with the *Köppen climate classification*, Port Elizabeth shows an oceanic climate, which is mostly pleasant throughout the year with moderate cold and rare extreme heat (Arnfield, 2016).

Recruitment of schools commenced in September 2014. Overall, 103 quintile 3 primary schools were eligible for participation (note that quintile 1 refers to poor schools while quintile 5 refers to least poor schools; Figure 1). Eight schools were selected based on (i) sufficiently large Grade 4 classes (n>100 children); (ii) geographical location; (iii) representation of the various target communities; and (iv) commitment to support the project activities.

The study population consisted of coloured children (mixed race ancestry), usually Afrikaans speaking, and black African children, mainly Xhosa speaking. Children's ages ranged between 8 and 12 years (Yap *et al.*, 2015). The following inclusion criteria were employed: (i) willingness to participate; (ii) written informed consent by a parent/guardian; (iii) no participation in other clinical trials during the study period; and (iv) no suffering from medical conditions preventing participation in the physical activity tests, as determined by qualified medical professionals.

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2 METHODOLOGY OF THE DASH STUDY

2.1 Disease, activity and schoolchildren's health (DASH) in Port Elizabeth, South Africa: a study protocol

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2.2 Abstract

Background: An in-depth epidemiological investigation on intestinal parasite infections in an impoverished area of Port Elizabeth, South Africa provides a unique opportunity for research on its impact on children's physical fitness, cognitive performance and psychosocial health. Additionally, we will screen risk factors for the development of diabetes and hypertension in adulthood.

Methods/Design: A 2-year longitudinal cohort study will be conducted, consisting of three cross-sectional surveys (baseline and two follow-ups), in eight historically black and coloured (mixed race) primary schools located in different townships in Port Elizabeth, South Africa. Approximately 1000 Grade 4 primary schoolchildren, aged 8 to 12 years, will be enrolled and followed. At each survey, disease status, anthropometry and levels of physical fitness, cognitive performance and psychosocial health will be assessed. After each survey, individuals diagnosed with parasitic worm infections will be treated with anthelminthic drugs, while children with other infections will be referred to local clinics. Based on baseline results, interventions will be tailored to the local settings, embedded within the study and implemented in half of the schools, while the remaining schools will serve as controls. Implementation of the interventions will take place over two 8-week periods. The effect of interventions will be determined with predefined health parameters.

Discussion: This study will shed new light on the health burden incurred by children in deprived urban settings of South Africa and provide guidance for specific health interventions. Challenges foreseen in the conduct of this study include: (i) difficulty in obtaining written informed consent from parents/guardians; (ii) administration of questionnaires in schools where three languages are spoken (Afrikaans, Xhosa and English); (iii) challenges in grasping concepts of psychosocial health among schoolchildren using a questionnaire; and (iv) loss to follow-up due to the study setting where illiteracy, mobility and violence are common. Finally, designing the health interventions together with local principals and teachers will allow all concerned with the research to bolster a sense of community ownership and sustained use of the interventions after the study has ceased.

Trial registration: Controlled-trials.com; identifier: ISRCTN68411960 (date assigned: 14 February 2014).

Keywords: Anthropometry, Cognitive performance, Diabetes, Health interventions, Intestinal parasite infections, Physical fitness, Physical activity, Psychosocial health, South Africa.

2.3 Background

As traditional lifestyle and diet change alongside socioeconomic developments, countries are starting to experience a double burden of communicable and non-communicable diseases in the face of weak health systems (Boutayeb, 2006; Santosa *et al.*, 2014). Many countries still struggle to meet the existing challenges stemming from infectious diseases, such as malaria and intestinal parasite infections. Meanwhile, non-communicable diseases, such as diabetes, cardiovascular diseases, obesity-related conditions and cancers, impose a growing burden on them (Marshall, 2004). This phenomenon has been recognised by the global health community and must be addressed in the new era of the sustainable development goals (SDGs), particularly "to ensure healthy lives and promote well-being for all at all ages" (Affairs, 2014), while the unfinished agenda of the communicable diseases during the millennium development goal (MDG) era must be accelerated.

In South Africa, investigations of physical activity patterns of primary schoolchildren attending schools in disadvantaged neighbourhoods have confirmed that physical activity levels are insufficient (Walter, 2011). These school environments are usually not conducive for the promotion of physical activity due to inadequate sport and recreation facilities, a lack of qualified teachers and an irregular physical education program. In 2010, Kimani-Murage *et al.* (Kimani-Murage *et al.*, 2010) reported that in a low-income South African setting, the co-prevalence of early stunting and adolescent obesity in girls is a result of increasing levels of physical inactivity. This observation was particularly prevalent among black girls, who were found to have the highest rates of physical inactivity (Walter *et al.*, 2011). As physical inactivity during childhood can lead to poor health outcomes in adulthood (Tian *et al.*, 2015), there is a pressing need to promote physical activity among school-aged children in disadvantaged communities in order to prevent obesity-related conditions and other non-communicable diseases. Additionally, infectious diseases that are intimately connected with poverty may also occur in disadvantaged South African schools (Draper *et al.*, 2010). These infections can have a negative impact on children's nutritional status, cognitive abilities and physical fitness (Hürlimann *et al.*, 2014; Yap *et al.*, 2014). Such a dual burden of disease can put children at a high risk of compromised health, poor subjective well-being, hampering their growth and economic perspectives.

In particular, it is hypothesized that, first, intestinal parasite infections have a negative influence on the physical fitness, cognitive performance, nutritional status and psychosocial health of school-aged children in deprived urban South Africa. Second, the development of setting-specific health interventions can decrease the incidence of parasitic infections and insulin resistance as well as elevated blood pressure, and thereby the risk of developing non-communicable conditions later in life, such as diabetes and hypertension (Figure 2.1).

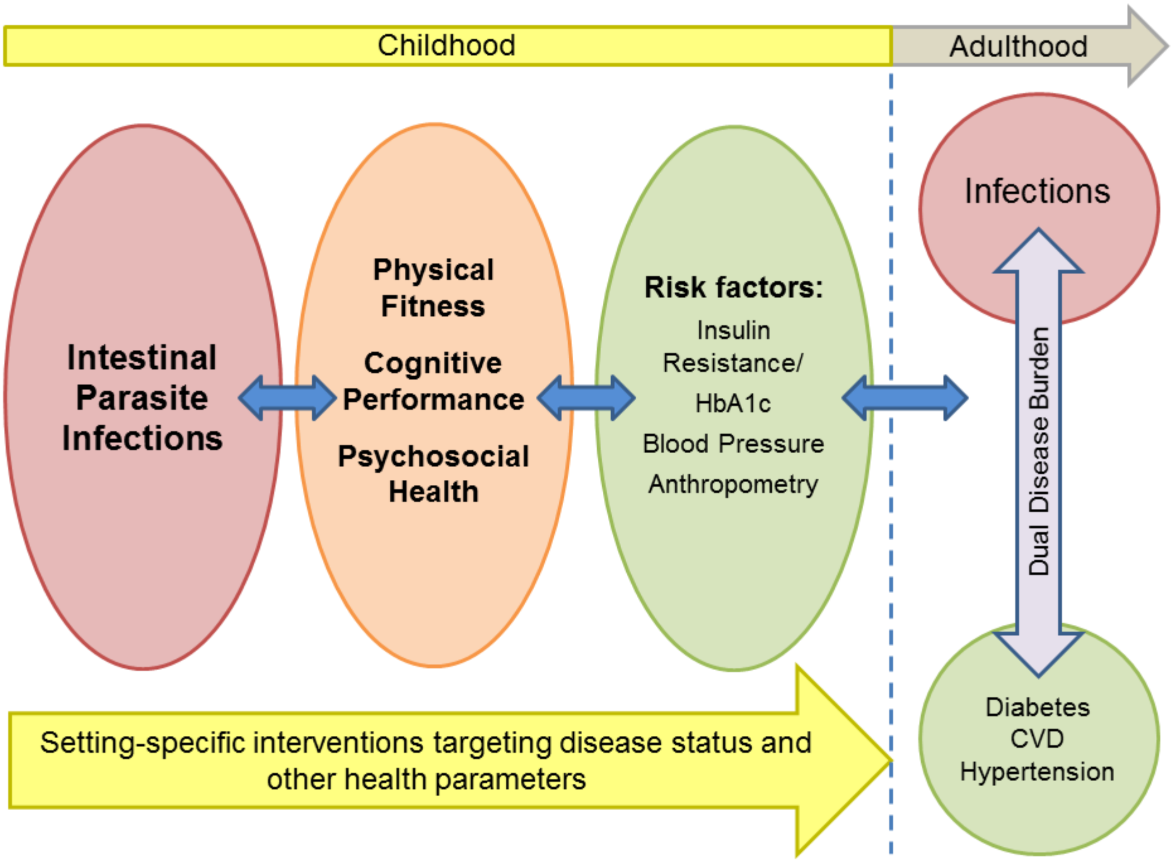

Figure 2.1 A conceptual framework for the DASH study.

An in-depth epidemiological study on intestinal parasite infections in an impoverished part of Port Elizabeth, South Africa, will provide a unique opportunity for research on its impact on children's physical fitness, cognitive performance and psychosocial health. In addition, a search for risk factors for the development of diabetes and hypertension in adulthood seems justified. From this research, an evidence-base will be created to design setting-specific health interventions. The purpose of this article is to present the detailed protocol of the proposed study.

2.4 Goal and objectives

The goal of this project is to survey the distribution of selected intestinal parasite infections and risk factors for non-communicable conditions, and assess their impact on schoolchildren's health over time in the face of tailored interventions in eight townships of Port Elizabeth, South Africa before, during and after the introduction of setting-specific interventions. We will pursue two specific objectives:

(i) to conduct a longitudinal study assessing the prevalence of intestinal parasites, risk factors for diabetes and hypertension, anthropometry and the level of physical fitness, cognitive performance and psychosocial health among schoolchildren; and

(ii) to design setting-specific interventions and assess their effect on the measured health parameters.

2.5 Methods/Design

Study area

The study will be conducted in historically black and coloured (mixed race) government primary schools from various areas in Port Elizabeth in the south-east part of South Africa (Figure 2.2).

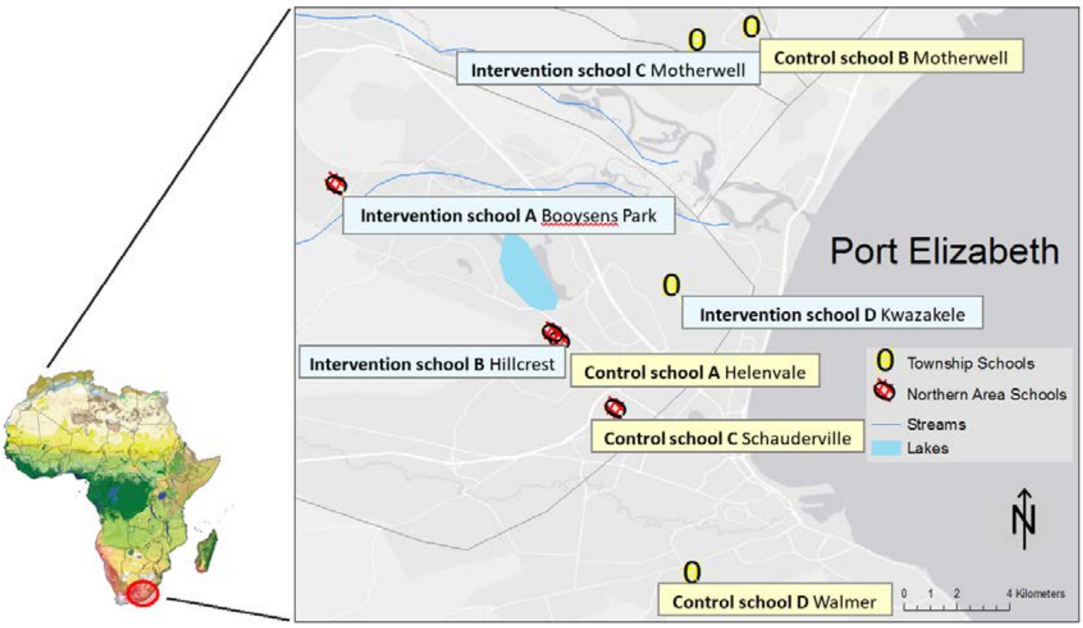

Figure 2.2 Study area and location of schools participating in the DASH study.

The areas populated by black Africans are commonly referred to as townships and include the areas of Kwazakhele, New Brighton, Zwide, and Motherwell. The “Northern areas” in Port Elizabeth are largely made up of coloured people who were forcefully relocated from the central areas of the city to the outlying northern areas, and include the areas of Schauderville, Gelvandale, Helenvale, Hillcrest and Booysens Park (Southern Africa Development, 2013; Agherdien *et al.*, 1997). Government schools in South Africa are classified into 5 groups, called quintiles, mainly for the purpose of allocating financial resources, with quintile 1 being the poorest and quintile 5 being the “least poor”. Schools in quintiles 1, 2 and 3 are proclaimed as no-fee schools, while schools in quintiles 4 and 5 are fee-paying schools (Release *et al.*, 2013). The eight schools who will be participating in the DASH study belong to quintiles 3. Furthermore, the study area has been detrimentally affected by extreme poverty and high rates of unemployment, due to past government policies, as well as current public health and economic challenges faced by the country (Walter *et al.*, 2011).

Study design

The study duration spans from February, 2015 to June, 2017 (Figure 2.3). The longitudinal cohort study consists of three cross-sectional surveys (baseline, mid- and final follow-up). At each survey time point, disease status, anthropometry and levels of physical fitness, cognitive performance and psychosocial health are measured. After each survey, infected individuals are either treated with anthelminthics (400 mg albendazole, single dose) for soil-transmitted helminths (Keiser and Utzinger, 2008) and/or referred to local clinics for the management of other intestinal parasite infections.

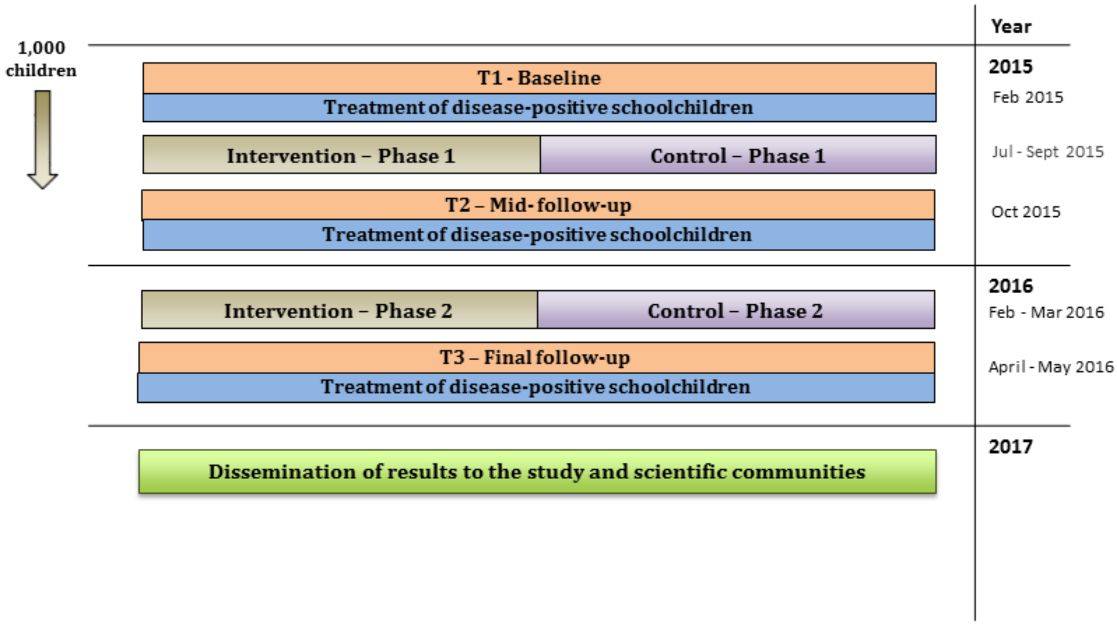

Figure 2.3 A pictorial display of the design and timeline of the DASH study.

Based on results from the baseline survey, a package of setting-specific interventions is designed together with local students, teachers, school volunteers and parents. The intervention package consists of three main components:

(i) <u>Physical activity</u> (Draper *et al.*, 2010; Kriemler *et al.*, 2010): Regular physical activity opportunities, including two physical education (PE) lessons a week, weekly dancing-to-music classes, and in-class activity breaks will be incorporated into the main school curriculum and a physical activity friendly school environment will be created. These approaches could help improve children’s physical fitness, and positively affect their psychosocial health (Muraven *et al.*, 1999; Oaten, 2004; Baumeister *et al.*, 2006; Oaten and Cheng, 2006; Gailliot *et al.*, 2007).

(ii) <u>Health education</u> (Bieri *et al.*, 2012): A series of classroom-based lessons will be developed to help increase the awareness for intestinal parasite infections among the schoolchildren and educate them on treatment and prevention methods, such as proper hygiene, sanitation habits and the importance of consuming clean water and food. It is also planned that schoolchildren will produce a theatre play to convey key messages they have learnt through the health education.

(iii) Nutritional interventions: A series of classroom-based lessons will be developed to help increase the awareness of the importance of healthy nutrition. In addition, an analysis of the school feeding programme will be done to identify ways to improve their current diet to be healthier. The schoolchildren will also be given a ready to use supplementary food (RUSF) in the form of an enriched lipid-based paste. The cooks in the schools will also be trained in basic nutrition and hygiene during preparation of the school meals.

The interventions will be embedded within the longitudinal study and be implemented in half of the schools, while the remaining schools will serve as controls. The intervention schools were either selected due to the soil-transmitted helminth prevalence, number of Grade 4 learners, geographical location and affiliation to a particular ethnic group or commitment of teachers or school staff. Implementation of the interventions will take place twice; in July-September, 2015, after the baseline survey, and in February-March, 2016, after the first follow-up. The first follow-up will allow the implementation feasibility of the designed interventions to be determined through focus-group discussions with teachers and students, while the subsequent surveys will allow assessing their impact on the measured health parameters.

Sample size

The sample size calculation for the study was based on achieving sufficient precision in estimating the prevalence of soil-transmitted helminth infections. We conducted our calculation under the following assumptions for the cross-sectional baseline study:

i) a prevalence of soil-transmitted helminth infections, p, of approximately 3%;

ii) an average number of children per school, B, of 150; and

iii) an intra-class correlation coefficient for the clustering of outcomes within schools, ICC, of 0.15.

Requiring the standard error of the respective prevalence, SE, not exceeding 2.5%, we obtained a necessary sample size n of 1,088 children, using the formula (Kish, 1965)

$$n \geq \frac{p \cdot (1-p)}{SE^2}(1 + (B-1) \cdot ICC) \qquad \textbf{(Equation 1)}$$

As a consequence, eight clusters (schools) will be needed considering the fact, that with a total of 1,200 children from eight schools, we can accommodate 10% loss to follow-up**.**

Study participants

Children will be invited to participate if they meet the following inclusion criteria: (i) are willing to participate in the study; (ii) have a written informed consent by a parent/guardian; (iii) are not participating in other clinical trials during the study period; and (iv) do not suffer from medical conditions, which will prevent participation in the study, as determined by qualified medical personnel. Approximately 1000 Grade 4 primary schoolchildren, aged around 8 to 12 years, from 8 schools will be recruited during the baseline survey.

School selection, participant recruitment and written informed consent

School authorities will be briefed about the project and their approval sought. Subsequently, a description of the project will be delivered by hand to 103 government primary schools and principals will be encouraged to allow their schools to participate in the study. Those schools with positive written responses will be invited to a comprehensive information meeting with the study investigators. Thereafter, interested schools will be visited and the study investigators will talk to the school management from these schools to find out whether the school environment is conducive for the performance of the study. Selection of schools will be based on size of the Grade 4 classes (n>100), geographical location and population demographics (Xhosa-, Afrikaans- and English-speaking schoolchildren). School principals and teachers of the selected schools will be notified about the study aims, procedures and potential risks and benefits. Schoolchildren, parents or legal guardians of learners will then be informed and schoolchildren encouraged to participate in the study. Before the launch of the study, a patient information sheet in English, including translation into the local language (Xhosa or Afrikaans), will be given to all potential participants and their parents/guardians, explaining the objectives, procedures and potential risks and benefits of the study. The name and contact address of the main investigator on site will be provided for any specific follow-up question. Oral assent from each participating schoolchild will be sought, while individual written informed consent will be required from parents/guardians. For illiterate parents, the information sheet will be read aloud and, if need be, an oral translation of the information sheet into all the local languages (Xhosa, Afrikaans or English) will be given. Participation is voluntary, and hence, children can withdraw from the study at any time without consequences and further obligation. Finally, demographic data and socioeconomic status of each participant will be obtained via the use of a questionnaire.

Assessment methods

Figure 2.4 summarises the assessment methods to be used in this study. For each cross-sectional survey, a specific combination of the following procedures will be selected and conducted by well-trained staff, adhering to standardised and quality-controlled protocol.

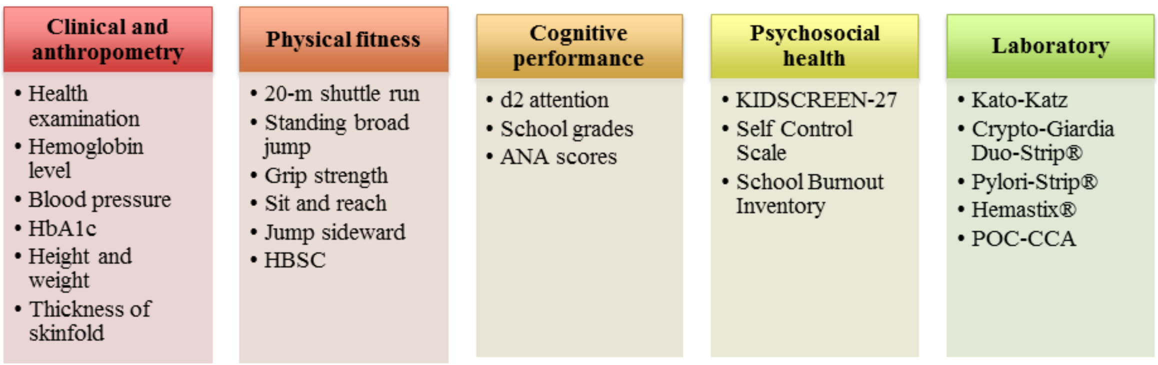

Figure 2.4 A summary of the measurements and tests performed under the DASH study.

Health examinations

(i) Clinical examination of children will include detailed medical history taking and physical examination. Features of patient history will focus on fevers, constitutional symptoms, abdominal pain and change in bowel movements. Physical examination is directed towards evidence of anaemia (e.g. conjunctival pallor), detailed abdominal examination (e.g. tenderness, hepatomegaly and splenomegaly) and evidence of pulmonary hypertension (e.g. jugulovenous pressure and cardiac auscultation).

(ii) Four questions about food security in the past two days, based on a simplified version of the Household Food Insecurity Access Scale (HFIAS) will be asked (Coates *et al.*, 2007).

(iii) For the detection of anaemia, the hemoglobin concentration will be measured once (to the nearest 0.1 g/l) using a HemoCue® Hb 301 system (HemoCue®AB; Ängelholm, Sweden). A fresh set of alcohol swab, safety lancet and microcuvette will be used for each child. After swabbing the fingertip with alcohol, the field investigator will prick it with a safety lancet and squeeze gently for two drops of blood. The first drop will be wiped away with the alcohol swab, while the second drop will be taken up by the microcuvette and read by the device. The Eurotrol Hb 301 Control will be used to verify the precision and accuracy of the measuring system (Since there will be other tests, which involve the use of whole blood from a finger prick, we will ensure an organised procedure so that each child is only pricked once.)

(iv) For the measurement of blood pressure, each child's blood pressure will be measured once with the Omron® digital blood pressure monitor, while the child is seated. The cuffs will be wrapped around the left arm such that one finger could fit between the cuff and the arm. The bottom of the cuff is about 4.0 cm above the elbow and the palm should be facing up while blood pressure is being measured.

(v) For the measurement of glycated haemoglobin (HbA1c) level, a point-of-care instrument employing the Afinion test (Alere Technologies) will be used. This test is based on boronate affinity separation and the use of fluorescence quenching, with results available in about 3 minutes. This method meets the generally accepted performance criteria for HbA1c as defined by the National Glycohemoglobin Standardization Program (NGSP) and has no interference from HbC, HbS, HbE and HbD traits results. Of note, the HbA1c level reflects the average plasma glucose concentration levels over the previous 8-12 weeks before measurement with no prior fasting required. A fresh set of alcohol swab, safety lancet and HbA1c test cartridge will be used for each child. After swabbing the fingertip with alcohol, the field investigator will prick it with a safety lancet and squeeze gently for two drops of blood. The first drop will be wiped away with the alcohol swab, while the second drop will be taken up by the test cartridge and read by the Alere Afinion AS 100 Analyzer. Identical Afinion HbA1 control blood will be used as an internal control and tested at regular intervals to control for potential laboratory drift.

Anthropometric measurements

(i) Each schoolchild will be asked to take off their shoes and sweater before standing on the digital weighing scale. Body weight will be measured once and recorded to the nearest 0.1 kg.

(ii) With the shoes off, each child will stand against a stadiometer with their back erect and shoulders relaxed. Body height will be measured once and recorded to the nearest 0.5 cm.

(iii) Body mass index (BMI) and two specific Z-scores will be calculated, as follows: (i) BMI = weight (kg) / (standing height [meters (m)]^2); (ii) BMI-for-age (BMIZ); an indicator for weight-for-height proportion (WHO growth reference for children older than 60 months) (WHO, 2007); (iii) Height-for-age (HAZ); an indicator for stunting (WHO growth reference for children older than 60 months).

(iv) The thickness of the skinfold will be measured at two sites, namely triceps and subscapular (Niederer *et al.*, 2009; Puder *et al.*, 2011). Before measurement, the field investigator will show the Harpenden skinfold caliper to the child and clamp it normally on the child’s finger to show that the process will not hurt. During the measurement, the child will stand with arms and shoulders relaxed. With the thumb and forefinger, the field investigator will gently pinch the skin (a vertical skinfold) slightly above the middle of the back of the arm (triceps) and clip the caliper (mouth of caliper is perpendicular to skinfold). After counting for 2 sec, the reading should stabilize, and hence, it will be recorded. The field investigator will release the pinch but let the fingers stay in the same position on the arm and repeat the measurements two additional times. The three values obtained should be no more than ±5% different from each other. If this is not the case, the measurements will be repeated. The final reading is an average of the three values. The same procedure applies for the subscapular site directly underneath the shoulder blade.

Physical fitness tests and self-reported physical activity

Previous studies in South Africa have used the Eurofit fitness testing battery (Europe, 1983). For the purpose of this project, specific tests from the Eurofit fitness testing battery will be conducted in outdoor settings.

(i) The children's cardiorespiratory fitness will be measured with the 20-m shuttle run test (Léger *et al.*, 1988). In brief, a 20-m flat running course will be measured with a measuring tape and marked with cones. Ten running lanes will be designated. Before the start of the test, children will be told to indicate any body discomfort and anyone who feels sick or not comfortable will not take part in the test. The pre-recorded sound signals will be played to the children and they will be initiated to do trial run of two intervals (2 x 20 m). Once children are familiar with the test procedures, they will be asked to run, in groups of five or ten, back and forth on the 20 m flat course by following the pre-set pace of sound signals. Starting with a running speed of 8.5 km/h, the frequency of the signal will be gradually increased so that every minute, the pace increases by 0.5 km/h. When children fail to follow the pace in two consecutive intervals, they will be asked to stop and the stage and the distance completed (full laps) will be recorded. The age of the participating child and the speed at which the child stopped running will be converted into VO_2 max estimates, which is the maximum volume of oxygen that can be utilized within 1 min during exhaustive exercise, with an equation put forth by Léger *et al*. (Léger *et al.*, 1988).

(ii) Lower body strength will be estimated with the standing broad jump test. Before the start of the test, the field investigator will demonstrate how exactly the standing broad jump is performed. Each child will stand behind a straight line and then jump as far forward as possible with both legs. Children will have 2 tries (with a 30 sec rest in between) and the longest jump will be recorded (to the nearest 1 cm). The distance of the jump is measured from the starting line to the heel of the most back foot.

(iii) Upper body strength will be determined with the grip strength test. The TKK® dynamometer will be used for this test. Before the start of the test, the hand span (distance from the tip of the thumb to the tip of the little finger) of the child's dominant hand will be measured (to the nearest 0.5 cm) and the grip span on the dynamometer adjusted accordingly (Ruiz *et al.*, 2006; Espana-Romero *et al.*, 2008). The field investigator also demonstrates how to grip the dynamometer to the child. Each child will have two tries (with a 30 sec rest in between) to grip the dynamometer as hard as possible with both hands and the maximum readings (measured to the nearest 0.5 kg) will be recorded. Additionally, the dominant hand will be noted.

(iv) The Sit-and-Reach Test (SRT) will be conducted as an indication of flexibility. This test measures flexibility of the hamstring muscles (back of the thigh) and, to a minor extent, the lower back muscles. The study participant will be asked to sit on the floor with stretched legs and feet against the sit-and-reach box. The hands are placed over each other and with the hips bent forward as far as possible, the fingers should move as far as possible to the front. The distance between the fingertips and the back edge of the box will be measured.

(v) For the measurement of coordination skills and speed strength of the leg muscles, we will use the jump-sideward test. The task for the participant is to jump laterally with both legs at the same time as many times as possible within 15 seconds across a wooden bar. A field investigator demonstrates the test in advance and five jumps can be practiced.

(vi) The children will be asked questions about experiencing physical activity, such as doing sports, specific activities during school, playing with friends in their free time and walking to school. A recall period of 7 days will be used. The questions will be adapted from the Health Behaviours in School Age Children Survey (HBSC), an instrument used to gain insight into young people's well-being, health behaviours and their social context (WHO, 2014).

Cognitive performance

Three measures will be considered as indicators of cognitive and academic performance, namely a standardized attention test (d2), children's school grades, and the results of standardized national tests (ANA).

(i) The d2 test will be employed to measure attention performance. This test is among the most widely used measures of attention, particularly visual attention, in Europe and the USA (Brickenkamp, 1998). The d2 paper-and-pencil version, which can be performed in a group setting, assesses several dimensions of cognitive performance: (i) total number of items processed (TN), a highly reliable measure of processing speed; (ii) percentage of errors (E%), measuring the qualitative aspects of performance; and (iii) the total number of items processed minus errors (TN-E), as an indication of the implications of the combined speed and accuracy scores for attentional and inhibitory control. Criterion, construct and predictive validity of the d2 test among children aged 9 years and above are well documented (Bates and Lemay, 2004; Wassenberg *et al.*, 2008; Gallotta *et al.*, 2012). Moreover, the test offers an extensive list of norms, according to age, sex and education.

(ii) In cooperation with the schools, we will obtain school test grades from the following subjects: English, mathematics, home language and life orientation. The sum-score of the four subjects will be used to estimate academic achievement.

(iii) The Annual National Assessments (ANA) are standardised tests for literacy and numeracy in the foundation phase (Grades 1-3) and Mathematics and languages in the intermediate phase (Grades 4-6). For the purpose of our study, Mathematics and home language ANA scores will also be used as a measure for academic achievement.

Questionnaires for assessment of psychosocial health

To assess children's psychosocial health, the following paper-and-pencil questionnaires will be applied:

(i) The KIDSCREEN-27 will be used to assess children's physical and psychological well-being, moods and emotions, self-perception, autonomy, parent relation and home life, financial resources, peers and social support, school environment and bullying. The questionnaire includes 27 items and has been proven to be a valid instrument to assess psychosocial health of children aged 8-18 years across various countries (Ravens-Sieberer *et al.*, 2005; Hong *et al.*, 2007; Ravens-Sieberer *et al.*, 2008).

(ii) Six items of the short version of the Self-Control Scale (SCS) will be used to assess individual differences in the capacity for self-control (Tangney *et al.*, 2006). The human capacity of self-control has been described as one of the most powerful and beneficial adaptations of the human psyche (Baumeister *et al.*, 2006; Tangney *et al.*, 2006; Hagger *et al.*, 2009; Duckworth, 2011; Moffitt *et al.*, 2011). The exertion of self-control strengthens the relationship between the self and the environment, which is an important prerequisite for individuals' satisfaction with life, well-being and positive development (Duckworth *et al.*, 2010; Miller *et al.*, 2011). Evidence for the reliability and validity of the SCS has been demonstrated previously (Tangney *et al.*, 2006).

(iii) The 9-item School-Burnout Inventory (SBI) (Salmela-Aro *et al.*, 2009a) will be applied to measure symptoms of school burnout. It has been shown that school burnout predicts subsequent depressive symptoms (Salmela-Aro *et al.*, 2009b) and that low levels of physical activity are associated with increased school burnout among adolescents (Elliot *et al.*, (in press)). The SBI consists of 10 items and is a multifaceted instrument with three subscales: (i) exhaustion at school; (ii) cynicism towards the meaning of school; and (iii) sense of inadequacy at school. Answers are given on a 5-point Likert-scale ranging from 1 (never) to 5 (always). Evidence in support of the factorial and construct validity of the SBI can be found in the literature (Salmela-Aro *et al.*, 2009a; Salmela-Aro *et al.*, 2009b; Salmela-Aro *et al.*, 2008; Salmela-Aro and Tynkkynen, 2012).

Parasitological examinations

In order to determine the prevalence of various intestinal parasites, both stool and urine samples will be collected from each participant. The samples will be subjected to a suite of standardised, quality-controlled diagnostic work-up (Knopp *et al.*, 2008; Sherkhonov *et al.*, 2013).

(i) A single stool sample will be collected from each child and analysed on the same day. The procedures are as follows. Each student will be given a container, labelled with a unique identification number, in which they will be asked to deposit a stool sample of not more than half the container's size with their own stool at home and bring it to the school for collection the following morning. In a first step, stool sample (at least 15 g) will be visually examined for the presence of *Taenia* spp. proglottids as well as signs of blood, mucus and diarrhoea. Second, duplicate 41.7 mg Kato-Katz thick smears will be prepared from each stool sample (Yap *et al.*, 2012). Slides will be allowed to clear for 30-45 minutes before being examined under a microscope by experienced laboratory technicians. The number of helminth eggs will be counted and recorded for each species separately. Helminth egg counts will be multiplied by a factor 24 to obtain a proxy for infection intensity, as expressed by the number of eggs per 1 g of stool (EPG) (Knopp *et al.*, 2008; Utzinger *et al.*, 2011). Possible helminth species to be detected include the three main species of soil-transmitted helminths (i.e. *Ascaris lumbricoides*, hookworm and *Trichuris trichiura*), *Fasciola hepatica* and *Schistosoma mansoni*. The presence of other helminth eggs will be noted, but not quantified.

(ii) For the detection of *Cryptosporidium* spp. and *Giardia intestinalis*, a Crypto-Giardia Duo-Strip® rapid diagnostic test (RDT) (CORIS, BioConcept; Gembloux, Belgium) will be performed on a stool sample, which has been diluted with a commercial buffer (Polman *et al.*, 2015).

(iii) For the detection of *Helicobacter pylori*, a Pylori-Strip® RDT (CORIS, BioConcept; Gembloux, Belgium) will be performed on a stool sample, which has been diluted with a commercial buffer.

(iv) A single urine sample will be collected from each child. All children will be given a container, labelled with a unique identification number, which they will be asked to fill up full with their urine. Distribution and collection of filled containers will occur on the same day. Each sample will be analysed visually for macrohaematuria and tested with Hemastix® strips to detect blood in urine as a proxy for *Schistosoma haematobium*. A point-of-care circulating cathodic antigen (POC-CCA) urine casette test (Rapid Medical Diagnostics; Cape Town, South Africa) will be used to detect the presence of *S. mansoni* infections (Coulibaly *et al.*, 2011).

(v) For quality control, a random sample of 10% of all Kato-Katz and urine filtration slides will be re-examined by a senior technician (Speich *et al.*, 2015). In case of discordant results, the slides will be read a third time and results discussed among the technicians until agreement has been reached.

Following Table 2.1 depicts the various variables to be collected and applied cut-offs for the relevant research question and corresponding specific objectives set for the study.

Table 2.1 Summary of variables to be collected and applied cut-offs based on literature review (continues on the next page).

Variables to be collected				Observation period		
		Units	**Cut-offs**	**T1** 2015	**T2** 2015	**T3** 2016
Schistosomiasis	*Schistosoma mansoni*	eggs/g of stool	Light int. 1-99 epg; Moderate int. 100-399 epg; Heavy int. >399 epg	X	X	X
	Schistosoma haematobium	eggs/ml of urine	Light int. <50 eggs/10ml of urine; Heavy int. >49/10ml of urine or visible hematuria	X		
Soil-transmitted-helminthiasis	*Ascaris lumbricoides*	eggs/g of stool	Light int. 1-4999 epg; Moderate int. 5000-49999 epg; Heavy int. >49999 epg	X	X	X
	Trichuris trichiura	eggs/g of stool	Light int. 1-999 epg; Moderate int. 1000-9999 epg; Heavy int. >9999 epg	X	X	X
	Fasciola hepatica	eggs/g of stool	+/-	X	X	X
	Hookworm egg count	eggs/g of stool	Light int. 1-1999 epg; Moderate int. 2000-3999 epg; Heavy int. >3999 epg	X	X	X
	Taenia spp. proglottids	eggs/g of stool	+/-	X	X	X
Gastro-intestinal infections	Presence of intestinal protozoa (*Cryptosporidium* spp. and *Giardia intestinalis*)	+/-	+/-	X	X	X
	Presence of the bacterium *Helicobacter pylori*	+/-	+/-	X	X	X
Personal characteristics	Age	Years/ months		X	X	X
	Sex	male/ female		X	X	X
Functional signs	Diarrhoea events	#	#	X	X	X
	Presence of mucus	+/-	+/-	X		X
	Presence of fever	+/-	Oral temp. >37.8ºC	X	X	X
	Presence of abdominal pain, change in bowel movements	+/-	+/-	X	X	X
Physical examination	Detailed physical examination (e.g. tenderness, hepatomegaly, splenomegaly)	+/- on a scale	+/- on a scale	X		X

Variables to be collected		**Units**	**Cut-offs**	**Observation period** T1 2015	T2 2015	T3 2016
Blood measurements	Anaemia (e.g. conjunctival pallor; haemoglobin concentration in the blood)	g/L	Non-anaemia >114g/L; Mild 110-114g/L; Moderate 80-109g/L; Severe <80g/L	X	X	X
	Evidence of elevated blood pressure (jugulovenous pressure, cardiac auscultation, blood pressure)	+/- on a scale mm Hg	High blood pressure: >95th percentile of children who are the same sex, age and height	X	X	X
Diabetes	Presence of diabetes (HbA1c level)	mmol/mol HbA1c	Non-diabetes <6%; Prediabetes 6-6.4%; Diabetes >6.5%	X	X	X
Malnutrition	2 Z-scores: BMI-for-age (BMIZ), Height-for-age (HAZ)	for years; cm for years	Wasting is defined as ≤-2 in BAZ score; Stunting is defined as ≤-2 HAZ score	X	X	X
Anthropometry	Height	cm		X	X	X
	Weight	kg		X	X	X
	Body mass index (BMI); 2 Z-scores: BMI-for-age (BMIZ), Height-for-age (HAZ)	kg/m^2; for years; cm for years	WHO guide-lines (BMIZ; HAZ)	X	X	X
	Upper arm circumference	cm		X	X	X
	Body composition (thickness of the skinfolds at the triceps and subscapular, directly underneath the shoulder blade)	mm		X	X	X
	Muscle mass at targeted sites (e.g. deltoid, vastus medialis)	mm		X	X	X
Cardiorespiratory fitness	VO_2 max (Maximum volume of oxygen uptake)	ml * O_2/min	Wilmore JH and Costill DL (2005)	X	X	X
Muscle strength	Upper body grip strength	Nm	Eurofit	X	X	X
Flexibility	Sit & reach test	cm	Eurofit	X	X	X
Lower body strength	Standing broad jump test	cm	Eurofit	X	X	X
Coordination & Speed	Jump sideward test	#	Eurofit	X	X	X

Variables to be collected				Observation period		
		Units	Cut-offs	**T1** 2015	**T2** 2015	**T3** 2016
Questionnaires	Hunger scale	-	WHO	**X**	**X**	**X**
	Socio-economic and demographic profile	-		**X**		**X**
	Physical activity and behavioral patterns (HBSC*)	-		**X**	**X**	**X**
	The test of attention d2; cognitive performance (quantitative data)	-		**X**	**X**	**X**
	Children's physical and psychological well-being (Kidscreen) (psychosocial health level; quantitative data)	-		**X**	**X**	**X**
	Individual differences in the capacity for self-control (SCS) (quantitative data)	-		**X**	**X**	**X**
ANA* and EoYR*	Measuring symptoms of school burnout (quantitative data)	Standardized school marks		**X**		**X**

*ANA: Annual National Assessment; *EoYR: End of the Year Results and *HBSC: Health Behaviours in School Age Children

Data collection and management

The type of data to be collected include: (i) quantitative data on the prevalence of intestinal parasites, measurements of blood pressure and glycated hemoglobin level, anthropometry and the level of physical fitness, cognitive performance and psychosocial health; (ii) socioeconomic status and demographic data, including the geographical location (latitude and longitude expressed in decimal degrees) of the students' households; and (iii) qualitative data on the feasibility and acceptability of the intervention measures implemented via focus-group discussions.

Data will be double-entered, cross-checked with EpiData 3.1 (EpiData Association; Odense, Denmark) and merged into a single database using STATA version 13.0 (STATA Corp.; College Station, TX, USA).

Data analysis

The primary objectives of the statistical analysis will be to assess (i) the prevalences of infections and conditions, and their associations with physical fitness, nutritional status, cognitive performance and psychosocial health at baseline and over time; and (ii) the effects of interventions on disease status and other health parameters. The secondary objective will be to assess the feasibility and acceptability of the health interventions implemented.

Parasitological status will be assessed in terms of prevalence and intensity of infection with specific parasite species and the extent of multiparasitism. Clinical and anthropometric indicators, physical fitness, cognitive performance and psychosocial health scores will be characterised by their mean and standard deviation if they are normally distributed and by their median and interquartile range otherwise. Questionnaire data pertaining to the psychosocial health will be expressed as percentages. All indicators will be compared between physically fit/non-infected and physically unfit/infected children and between intervention and control schools.

To assess the effects of the different interventions on the parasitological status, clinical and anthropometric indicators, physical fitness, cognitive performance and psychosocial health, the following statistical procedures will be employed:

(i) Mixed logistic regression models with random intercepts for schools will be used to compare binary data, such as parasitological status and clinical indicators, between the intervention and control groups.

(ii) Linear mixed models with random intercepts for schools will be used for numeric data, such as anthropometric measurements, physical fitness, cognitive performance, and psychosocial health scores and haemoglobin concentration measurements.

These models will include sex and age of the child, socioeconomic status of the parents or health status or fitness at the baseline survey as well as variables which were not perfectly randomised and might therefore act as confounders. Moreover, as intervention effects might depend on baseline characteristics of the child, stratified analyses and analyses involving interaction terms will be performed. The potential effect modifiers tested include sex, age, socioeconomic status of the parents or health status or fitness at the baseline survey.

Ethical approval and considerations

Ethical approval for the study has been obtained from the Ethics Committee Northwest and Central Switzerland (EKNZ) in Basel, Switzerland (reference no. 2014-179; obtained on 1 August 2014), and the following ethics committees in Port Elizabeth, South Africa:

(i) NMMU Human Ethics Committee (Human) (reference no. H14-HEA-HMS-002; obtained on 4 July 2014);

(ii) Eastern Cape Department of Education (obtained on 13 August 2014); and

(iii) Eastern Cape Department of Health (obtained on 7 November 2014).

Besides obtaining written informed consent, confidentiality of the study participants will be ensured by giving each participant a unique project-ID number so that all collected data of the schoolchildren will remain anonymous. Data will be used exclusively for scientific research and samples will be discarded after laboratory analyses have been completed. Paper records of the study are kept in locked cupboards in South Africa, accessible only by the main investigators. After 5 years, these records will be destroyed. Data entered into computerised files will be accessible only to authorised investigators or medical personnel directly involved with the study. At the end of the project, successful and appropriate interventions will be provided to the control schools so that the whole community can benefit from this project.

2.6 Discussion

The baseline survey of this study has been conducted in February-March 2015. Subsequently, eight schools, with approximately 1000 schoolchildren, were selected for the study. During this first survey time point, several challenges were met and needed to be addressed. First, the study is conducted in impoverished and harsh environments, where illiteracy and violence are common (Deaton and Tortora, 2015; Deaton, 2007). In these challenging socioeconomic conditions, the recruited schoolchildren may often be subjected to the lack of sufficient care or neglect by their parents (Case and Deaton, 2005; Case and Deaton, 1999; Steptoe *et al.*, 2015). As such, it was difficult to obtain support and written informed consent from the parents/guardians even if the schoolchildren have provided their oral assent. To address this issue, we prepared and conducted several pre-study workshops in the selected schools. The study purposes were explained in detail to the school principals, teachers and parents/guardians, in order to garner their strong support. We also adapted our study as much as possible in response to ideas voiced by teachers and parents to tailor the study further to the needs of the people concerned. Second, three languages, namely Afrikaans, Xhosa and English, are being spoken by the communities in the study area. For example, certain schoolchildren might prefer to speak and write in English, while others from the same school prefer Afrikaans. In addition, Xhosa-speaking children often preferred the tests to be administered in English, with explanations in Xhosa. This proved to be challenging when questionnaires were administered. Furthermore, although the questionnaires were pre-tested with some schoolchildren, the content of the questionnaires employed, particularly the ones focusing on psychosocial health indicators, did not fully match the educational level of the schoolchildren, making it hard for them to understand and answer the questions. To address these issues, we employed native speakers to perform the translation and to pre-test the translated questionnaires among teachers and students before the start of the study. During the actual administration of the questionnaires, we had the help of teachers and school volunteers to explain the questions to the children in their preferred language.

During our sample size calculation, we accounted for a 10% loss to follow-up. Moving forward with the follow-ups and second phase of intervention, we might expect a more substantial loss (30-40%) to follow-up as people show considerable mobility in this setting. We will address the potential bias resulting from differential loss to follow-up using inverse probability weighting, i.e. by assigning each follow-up participant the inverse of their prior probability of participation in the follow-up as weight in the follow-up analyses. In addition, multiple imputation will be used to deal with missing data where appropriate. However, it is difficult to predict the extent of the movement of people and hence, our presumed loss to follow-up might not be accurate.

Based on the obtained results, we have designed the health interventions together with local principals and teachers. Such collaboration is aimed at bolstering a sense of community ownership and empowerment, where the community feels that they are taking steps to improve the health of their children. We hope that this approach will further encourage the continued participation of the children and their parents/guardians during the study and sustained use of the interventions after the study has ceased.

In conclusion, the DASH study described here will provide a snapshot on the status of intestinal parasite infections and risk factors for diabetes and hypertension in selected disadvantaged primary schools in Port Elizabeth, South Africa. To our knowledge, such data are currently not available, and hence, our study fills an important void and generates new local evidence. By linking children's parasitic infection status with the physical fitness, nutritional status, cognitive performance and psychosocial health, this wealth of information will help shed new light on the health consequences incurred by the children and provide guidance for further health interventions in this area. Implementation of setting-specific interventions within the longitudinal study will further highlight the feasibility and scalability of these health interventions in the study area.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

PY, IM, PS and JU designed the study, established the methods and questionnaires and wrote the original study protocol. All other authors contributed to the development of the study protocol. UP is the principal investigator. CW, IM, PY and DS were the main coordinators of the study. IM, PY, DS, NSNH, LS, AG, BPD, MG, SG, TH, DB, RDR, UP and CW conducted the study. CW is responsible for community sensitization; IM is liable for drug administration. IM managed data entry, cleaning and preparation of the database for statistical analysis, supported by HS. PY, IM and JU wrote the first draft of the manuscript. All authors read and provided comments on the drafts and approved the final version of the paper prior to submission.

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CHAPTER 3

3.1 Intestinal parasites, growth and physical fitness of schoolchildren in poor neighbourhoods of Port Elizabeth, South Africa: a cross-sectional survey

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3.2 Abstract

Background: As traditional lifestyle and diets change with social and economic development, disadvantaged communities in low- and middle-income countries increasingly face a double burden of communicable and non-communicable diseases while health systems weaken. We studied the relationship between physical fitness and infections with soil-transmitted helminths (STHs), intestinal protozoa and *Helicobacter pylori* among schoolchildren in Port Elizabeth, South Africa.

Methods: We conducted a cross-sectional survey among 1,009 children, aged 9 to 12 years, from eight primary schools in socioeconomically disadvantaged neighbourhoods of Port Elizabeth. Physical fitness was determined using field-deployable tests of the Eurofit fitness test battery. Stool samples were analysed with the Kato-Katz thick smear technique to diagnose STHs and with rapid diagnostic tests (RDTs) to detect intestinal protozoa and *H. pylori* infections. Haemoglobin (Hb) levels and anthropometric indicators were measured.

Results: Complete data were available for 934 children (92 %). In two schools, high STH prevalences were found (*Ascaris lumbricoides* 60 % and 72 %; *Trichuris trichiura* 65 % each). For boys and girls co-infected with *A. lumbricoides* and *T. trichiura* (n = 155) the maximal oxygen uptake (VO_2 max) was estimated to be 50.1 ml kg^{-1} min^{-1} and 47.2 ml kg^{-1} min^{-1}, compared to 51.5 ml kg^{-1} min^{-1} and 47.4 ml kg^{-1} min^{-1} for their non-infected peers (n = 278), respectively. On average, children without helminth infections had greater body mass (P = 0.011), height (P = 0.009) and a higher body mass index (BMI) (P = 0.024) and were less often stunted (P = 0.006), but not significantly less wasted compared to their peers with a single or dual species infection. Among 9-year-old boys, a negative correlation between helminth infections and VO_2 max, grip strength and standing broad jump distance was observed (P = 0.038). The overall mean Hb level was 122.2 g l^{-1}. In the two schools with the highest prevalence of STHs the Hb means were 119.7 g l^{-1} and 120.5 g l^{-1}, respectively.

Conclusions: Intestinal parasite infections appear to have a small but significant negative effect on the physical fitness of infected children, as expressed by their maximal oxygen uptake. A clear impact on anthropometric indicators was observed.

Keywords: Anthropometric indicators, Haemoglobin, Intestinal protozoa, Intestinal polyparasitism, Physical fitness, Soil-transmitted helminths, South Africa

3.3 Background

Globally, more than 1 billion people are infected with soil-transmitted helminths (STHs; *Ascaris lumbricoides*, hookworms and *Trichuris trichiura*) and *Schistosoma* spp. (Colley *et al.*, 2014; Hotez *et al.*, 2014; Yap *et al.*, 2014). The symptoms most frequently associated with these parasitic worm infections include abdominal pain, diarrhoea, anaemia, growth retardation and cognitive impairment (Utzinger *et al.*, 2012), ultimately resulting in reduced physical fitness and work productivity (Yap *et al.*, 2012). Important risk factors for STH and *Schistosoma* spp. infections are a lack of clean water, sanitation and hygiene (WASH) (Grimes *et al.*, 2014; Strunz *et al.*, 2014). Permissive conditions are commonly found in socioeconomically deprived neighbourhoods in low- and middle-income countries, including in South Africa (Pillay *et al.*, 2014). Intestinal protozoa such as *Cryptosporidium parvum*, *Entamoeba* spp. and *Giardia intestinalis* are associated with poor living conditions (Steinmann *et al.*, 2010). Their transmission mostly occurs through faecal contamination of food and water (Shirley *et al.*, 2012). They may lead to symptoms such as abdominal pain, diarrhoea and nausea. Many low- and middle-income countries struggle to control such infectious diseases stemming from traditional challenges (Murray *et al.*, 2012). In South Africa, a country that shows considerable health inequity in global terms (e.g. Gini index of 0.63 in 2011 (WHO, 2017)), socioeconomically deprived communities with a high burden of infectious diseases live in close proximity to affluent ones with a disease burden profile typical of western societies. Among both populations, non-communicable diseases (e.g. diabetes, cardiovascular- and obesity-related conditions and cancers) are rapidly increasing, fuelled by unhealthy lifestyles including poor nutritional habits and sedentary lifestyles (Marshall, 2004). South Africa's 2014 Report Card on Physical Activity for Children and Youth (Draper *et al.*, 2014) highlights the current concerns for the health and well-being of children and youth in relation to declining physical activity levels and increasing rates of consumption of soft-drinks and fast food.

Low levels of in-school physical activity have been documented for children in Port Elizabeth in the frame of a study by Walter et al. (Walter, 2011) who focused on primary schoolchildren in disadvantaged schools. Low quality and often inaccessible sport and recreation facilities, a lack of qualified teachers and an irregular physical education schedule complicate the promotion of age-appropriate physical activity among schoolchildren at disadvantaged schools. The resulting dual burden of diseases (i.e. non-communicable chronic conditions and infectious diseases) puts children at an increased risk of compromised health that may hamper their development, wellbeing and future prospects (Marshall, 2004; Boutayeb, 2006; Santosa *et al.*, 2014). Moreover, this dual burden is a challenge for the health system.

The “Disease, Activity and Schoolchildren’s Health” (DASH) study in Port Elizabeth, South Africa, aims to investigate this dual disease burden (i.e. non-communicable chronic conditions and infectious diseases) among children in selected primary schools located in disadvantaged neighbourhoods (Yap *et al.*, 2015). Here, we report the findings pertaining to parasite infections and physical activity from a cross-sectional survey among 9 to 12-year-old children. The objectives of this cross-sectional survey were (i) to determine the prevalences of intestinal parasite infections and *Helicobacter pylori*; (ii) to assess the haemoglobin levels and anthropometric indicators; (iii) to comprehensively measure the physical fitness levels; and (iv) to investigate possible associations between infection status and other measured variables.

3.4 Methods

Study site and school selection

The study was carried out at eight primary schools in socioeconomically disadvantaged neighbourhoods of Port Elizabeth, in the Western region of the Eastern Cape province of South Africa (geographical coordinates: 34°07′54″ S to 33°57′29″ S latitude and 25°36′00″ E to 25°55′49″ E longitude, altitude: extends from 0 m to approximately 100 m above sea level) in February 2015. The study population consisted of coloured children (of mixed race ancestry, and generally Afrikaans speaking) and black African children (largely Xhosa speaking), residing in areas previously demarcated for these specific race groups, in accordance with past Apartheid legislation. Colloquially, these respective areas are referred to as the northern areas (for coloured people) and townships (for black African people). The people living in these areas are still detrimentally affected by the legacy of Apartheid (Agherdien *et al.*, 1997). A total of 103 quintile 3 primary schools (where quintile 1 denotes the poorest and quintile 5 the “least poor” schools, with the degree of poverty referring to the neighbourhood around school locations) were contacted to explore interest in study participation. Positive responses were received from 25 schools. Eight schools were finally included in the study, with selection based on (i) size in terms of the number of students; (ii) geographical location; (iii) representation of the different target communities; and (iv) commitment to support the project activities.

Study design

The DASH study is a cohort study with a physical intervention component to determine whether WASH and an education and nutrition programme can reduce parasitic prevalences and improve physical fitness levels among 9 to 12-year-old children (Yap *et al.*, 2015). A single stool and a single urine sample were collected for parasitological work-up to diagnose helminth and intestinal protozoa infections using light microscopy. Anthropometric indicators (i.e. height and weight) and haemoglobin (Hb) concentrations were assessed by trained examiners or nurses. Physical fitness was determined by measuring the participants’ performance in a grip strength test for upper body strength, standing broad jump test for lower body strength and 20 m shuttle run test for cardiorespiratory endurance.

Study procedures

Stool containers with unique identifiers were handed out to schoolchildren together with the instruction to return them with a small portion (at least 15 g) of their own morning stool. Containers were collected between 9 and 10 a.m. and transferred to a laboratory of the NMMU in Port Elizabeth for diagnostic work-up on the same day. Stool samples were first visually examined for the presence of *Taenia* spp. proglottids, signs of blood, mucus and diarrhoea. Duplicate 41.7 mg Kato-Katz thick smears were prepared from each stool sample (Katz *et al.*, 1972). Slides were read under a microscope by experienced laboratory technicians who counted the number of eggs of each helminth species. The two slides were read by different technicians, the results compared for quality control and, in case of inconsistencies (i.e. positive *versus* negative or egg counts differing by more than 20 %), the slides were re-read. Helminth egg counts were multiplied by a factor of 24 to obtain a proxy for infection intensity, as expressed by the number of eggs per 1 g of stool (EPG) (Knopp *et al.*, 2008).

At the time of stool collection, children were given an empty urine collection container and asked to return it with a urine sample within the next 30 min. Filled containers were transferred to the laboratory and analysed on the same day. Samples were first inspected visually for macrohaematuria and then tested with Hemastix® strips (Siemens Healthcare Diagnostics GmbH; Eschborn, Germany) to detect blood in urine as a proxy for *Schistosoma haematobium* infections. A point-of-care circulating cathodic antigen (POC-CCA) urine cassette test (Rapid Medical Diagnostics; Cape Town, South Africa) was used for the diagnosis of *S. mansoni* infections (Coulibaly *et al.*, 2011).

For the detection of *C. parvum* and *G. intestinalis*, a Crypto-Giardia Duo-Strip® rapid diagnostic test (RDT) was performed on the stool sample, while for the discovery of *H. pylori*, a Pylori-Strip® RDT was employed (both tests from CORIS, BioConcept; Gembloux, Belgium).

The Hb concentration was measured once, to the nearest 0.1 g l^{-1}, with the HemoCue® Hb 301 system (HemoCue®AB; Ängelholm, Sweden). In brief, after swabbing the child's fingertip with alcohol, a field worker pricked the fingertip with a safety lancet and squeezed gently to obtain two drops of blood. The first drop was wiped away with the alcohol swab and the second drop was taken up with the microcuvette.

For the anthropometric measurements, each child was asked to take the shoes and sweater before standing on a digital weighting scale (Micro T7E electronic platform scale, Optima Electronics; Georg, South Africa). Body weight was measured once to the nearest 0.1 kg. The height of each child was assessed with a Seca stadiometer (Surgical SA; Johannesburg, South Africa) whereby the child was standing with the back erect and shoulders relaxed. Body height was taken to the nearest 0.1 cm.

Specific standardised tests from the Eurofit fitness test battery (Europe, 1983) were conducted as follows. Upper body strength was determined through the grip strength test, with both right and left hands. Measurements were taken with the Saehan hydraulic hand dynamometer (MSD Europe BVBA; Tisselt, Belgium) set at handle position two. The examiner demonstrated how to grip the dynamometer with both arms at a 90 degree angle, while sitting straight and being relaxed. Each participant had three attempts, with about a 30 s rest in between, to grip the dynamometer with alternating hands as hard as possible. The maximum reading, measured to the nearest 1 kg, was recorded. The grip strength of both hands was measured. Additionally, the dominant hand was noted.

Lower body strength was estimated with the standing broad jump test. Before the start, the examiner demonstrated the test. Each child stood behind a straight line and jumped as far as possible with both legs forward. Participants had two attempts, with about a 30 s rest in between. The longer jump measured from the starting line to the heel of the foot closest to the starting line and rounded to the nearest 1 cm, was recorded.

The children’s endurance was measured with the 20 m shuttle run test (Léger *et al.*, 1988), using the test protocol from Léger et al. (Léger *et al.*, 1984) for which a great number of scientific international benchmarks exist (Tomkinson *et al.*, 2003; Olds *et al.*, 2006). The 20 m flat grass running course was measured with a measuring tape and marked with different coloured cones. Five running lanes were created. The majority of the schoolchildren wore school or street shoes, whereas a minority ran barefoot. Shortly before the start of the test, the children were asked if anyone was sick or did not feel well. These children were excluded from the test. Next, the pre-recorded sound signals were played and the children did a trial run of two intervals (40 m). Once they were familiar with the test procedures, they were asked to run in groups, back and forth on the 20 m flat course, following the pace of the sound signals. Starting with a running speed of 8.5 km h^{-1}, the frequency of the signal increased gradually such that every min, the pace increased by 0.5 km h^{-1}. When a child failed to follow the pace in two consecutive intervals, she or he was asked to stop. The number of 20 m laps run to the last fully completed lap was noted as the final score.

Statistical analysis

Data were double-entered, validated using EpiData version 3.1 (EpiData Association; Odense, Denmark) and merged into a single database. Statistical analysis was performed using STATA version 13.0 (STATA Corp.; College Station, TX, USA). Maps were created with ArcGIS version 10.2.1 (ESRI; Redlands, CA, USA).

Statistical significance was defined as $P < 0.05$. The parasitological status was described in terms of prevalence and infection intensity (mean EPG) of individual parasite species and the extent of multiparasitism (concurrent infections with more than one helminth or protozoan species). Anthropometric indicators, Hb concentrations and fitness performance scores were expressed as means and standard deviations (SD). Differences between groups were assessed using mixed linear models. The likelihood-ratio test was used to compare models. To describe the anthropometry of the children, body weight and height values were used to calculate the body mass index (BMI), defined as weight (in kg)/height^2 (in m^2), the sex-adjusted BMI-for-age Z-score (BMIZ) as an indicator for wasting and sex-adjusted height-for-age Z-score (HAZ) as an indicator for stunting (de Onis *et al.*, 2007).

The age of the participating child and the speed at which the child stopped running in the 20 m shuttle run test were converted into a third variable, the maximal oxygen uptake or VO_2 max (Léger *et al.*, 1988). All statuses and indicators were compared between non-infected and infected children, the latter also further stratified by degrees of multiparasitism. Comparisons between schools were done using the χ^2 test or the one-way ANOVA, as appropriate. Mixed linear and mixed logistic regression models with random intercepts for schools were used to analyse quantitative and binary data, respectively. These analyses included group comparisons with and without adjustment for covariates. For a simple interpolation of georeferenced data of children's homes, the inverse distance weighting (IDW) method was used to obtain smoothed values of infection intensity, which is based on the assumption that two geographically close sites are more similar than two locations far apart.

3.5 Results

Demographic baseline characteristics

All 1,009 Grade 4 primary children of the eight selected schools from the northern part of Port Elizabeth were invited to participate. As illustrated in Figure 3.1, complete data were available from 934 children (92 %). Reasons for exclusion were age outside the target range of 9 to 12 years, no stool or urine sample submitted for diagnostic work-up, lack of clinical examination, reported health problems precluding participation in the physical fitness tests (e.g. chronic asthma), or incomplete physical test battery. Children infected with either *C. parvum* or *G. intestinalis* and those who reported abdominal pain, blood in the stool or diarrhoea, those with special lung sounds (e.g. chest wheezing or creeping), ringworm infection or showed signs of tachycardia, were referred to the local clinic. All subsequent analyses refer to the final cohort of 934 children, which included 462 girls (49.5 %) and had a mean age of 10.0 years. No statistically significant difference was observed between the eight schools with regard to the mean age and sex ratio (both $P > 0.05$).

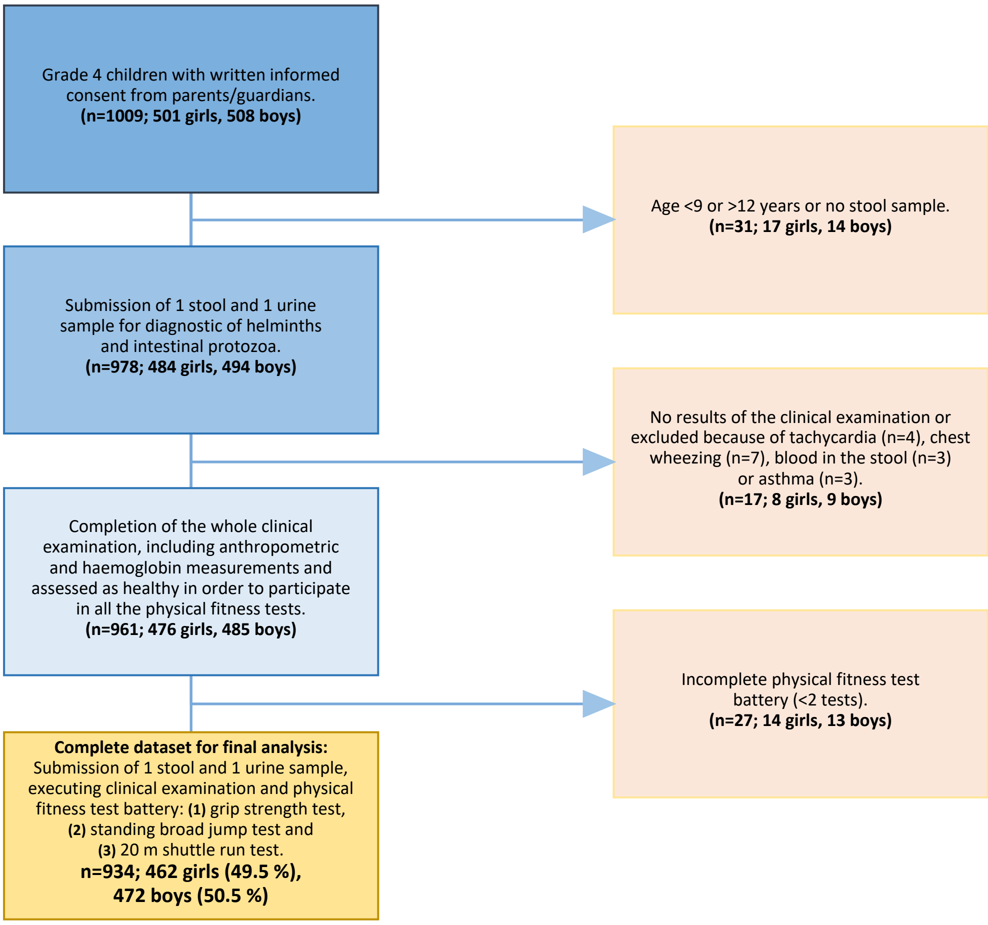

Figure 3.1 Study cohort and compliance of Grade 4 primary schoolchildren from eight schools in disadvantaged neighbourhoods of Port Elizabeth, South Africa in early 2015.

Infections with helminths, intestinal protozoa and *H. pylori*

Overall, 248 children (26 %) were infected with *A. lumbricoides* and 207 (22 %) with *T. trichiura*. One child had a *S. haematobium* infection, while *Taenia* spp., hookworm and *S. mansoni* were not observed. A total of 144 children (15 %) were infected with at least one intestinal protozoan species: the *G. intestinalis* prevalence was 13 % and *C. parvum* prevalence was 3 %. *H. pylori*-prevalence was found at all schools, ranging from 25 % up to 65 % (Figure 3.2). Multiparasitism was common: 158 of the 384 infected children (41 %) harboured at least two parasite species, mostly *A. lumbricoides* and *T. trichiura*. Thirty triple-species infection were also detected (8 %).

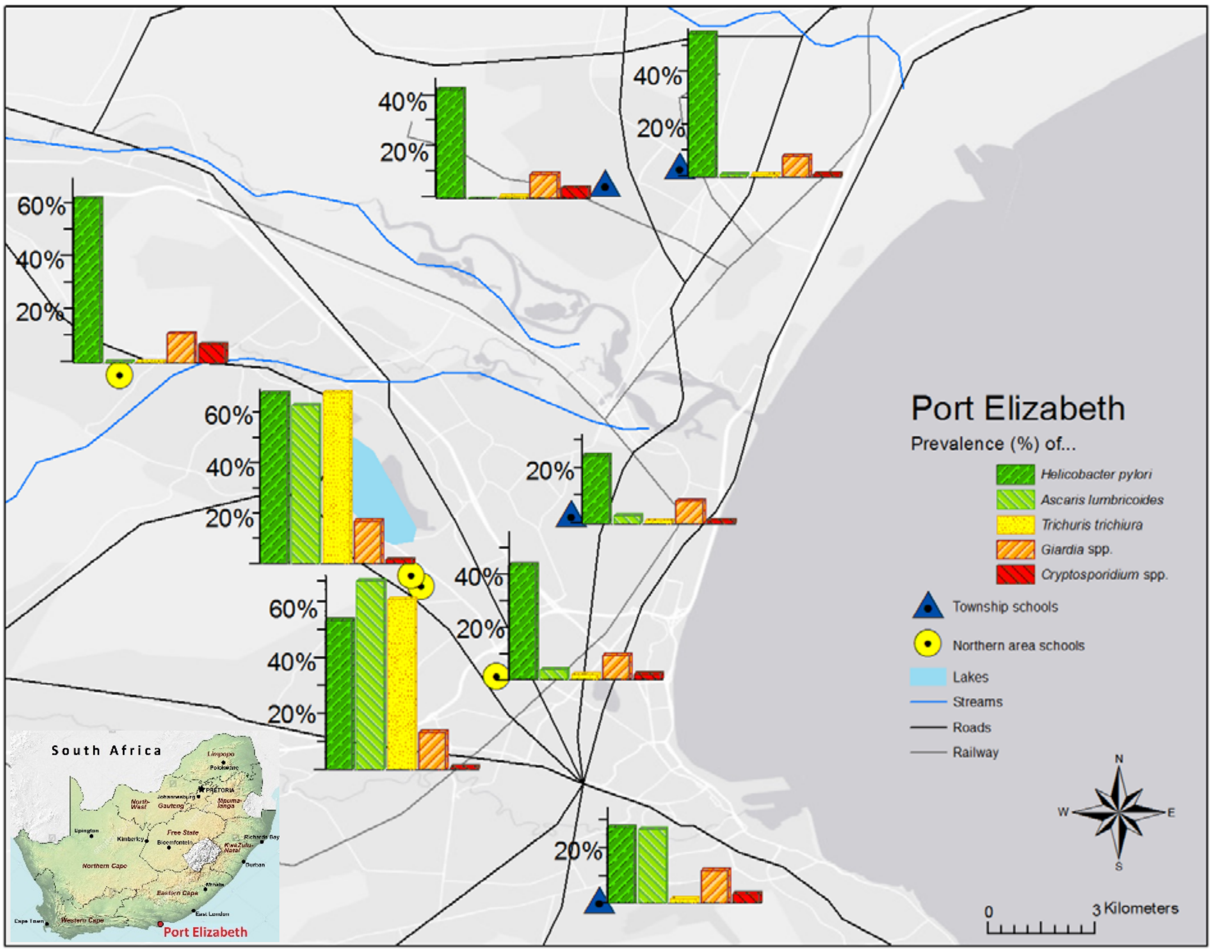

Figure 3.2 Prevalence of helminth, intestinal protozoan and *Helicobacter pylori* infection in eight primary schools in Port Elizabeth, South Africa, in early 2015.

Stratification by sex revealed that boys had higher prevalences and mean EPG values compared to girls for both *A. lumbricoides* and *T. trichiura* (Table 3.1). *T. trichiura* infections were of highest mean intensity in children aged 11 years (mean 940 EPG), while *A. lumbricoides* infections were of highest intensity in 12-year-old children (mean 18,630 EPG). Infections were spatially clustered: the prevalence of *T. trichiura* and *A. lumbricoides* at school B in Hillcrest was 65 % and 60 %, respectively, and at school A in Helenvale 65 % and 72 %, which was significantly higher than in the other schools (*T. trichiura*: $\chi^2 = 592.53$, $df = 7$, $P < 0.001$; *A. lumbricoides*: $\chi^2 = 475.34$, $df = 7$, $P < 0.001$) (Fig. 2). Similarly, infection intensities were highest in schools A and B (Figure 3.3). At school B in Hillcrest and at school A in Helenvale, the prevalence of *G. intestinalis* was 16 % and 14 %, respectively and the respective prevalence of *H. pylori* was 65 % and 57 %.

Anthropometric indicators and Hb concentration

The mean height, weight and BMI of the study cohort were 133.2 cm, 30.5 kg and 17.0 kg m^{-2}, respectively. Stunting was observed in 10 % of the children, while wasting was found in 4 % of the children. We found statistically significant differences in anthropometric indicators when comparing children without a helminth infection with those with a single species infection of either *A. lumbricoides*, *T. trichiura* or a co-infection (Table 3.2). Non-infected children had greater body mass ($\chi^2 = 11.09$, $df = 3$, $P = 0.011$), height ($\chi^2 = 11.60$, $df = 3$, $P = 0.009$) and a higher BMI ($\chi^2 = 9.49$, $df = 3$, $P = 0.024$) and were less likely to be stunted ($\chi^2 = 12.29$, $df = 3$, $P = 0.006$) but not less wasted ($\chi^2 = 2.83$, $df = 3$, $P = 0.418$) compared to their peers with a single or dual species infection. Children concurrently infected with *A. lumbricoides* and *T. trichiura* had similar anthropometric and haemotologic measures compared to children with a single *T. trichiura* infection.

Table 3.1 *Ascaris lumbricoides* and *Trichuris trichiura* prevalence and infection intensity (as mean of duplicate Kato-Katz thick smears) among 934 primary schoolchildren from Port Elizabeth, South Africa, in early 2015, stratified by sex and age.

		Sex			Age (years)				
		Male (*n* = 472)	**Female (*n* = 462)**		**9 (*n* = 282)**	**10 (*n* = 375)**	**11 (*n* = 216)**	**12 (*n* = 61)**	
		n (%)	*n* (%)	*P*[a]	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*P*[a]
A. lumbricoides	Prevalence[b]	134 (28)	114 (25)	0.305	43 (15)	108 (29)	74 (34)	23 (38)	0.691
	Infection intensity[d]								
	Mean EPG[e] (95 % CI)	10,866 (7,907–14,934)	9,256 (6,633–12,915)	0.333	8,411 (4,357–16,238)	9,038 (6,309–12,948)	10,899 (7,306–16,258)	18,630 (11,725–29,602)	0.252
	Light (1–4,999)	36 (8)	36 (8)		10 (4)	41 (11)	18 (8)	3 (5)	
	Moderate (5,000–49,999)	67 (14)	58 (13)		26 (9)	43 (11)	39 (18)	17 (28)	
	Heavy (≥ 50,000)	31 (7)	20 (4)		7 (2)	24 (6)	17 (8)	3 (5)	
T. trichiura	Prevalence[c]	114 (24)	93 (20)	0.065	31 (11)	88 (23)	68 (32)	20 (33)	0.208
	Infection intensity[d]								
	Mean EPG[e] (95 % CI)	757 (572–1,002)	747 (557–1,002)	0.950	737 (471–1,155)	640 (467–877)	940 (661–1,336)	744 (322–1,723)	0.446
	Light (1–999)	65 (14)	55 (12)		16 (6)	55 (15)	36 (17)	13 (21)	
	Moderate (1,000–9,999)	44 (9)	35 (8)		15 (5)	32 (9)	27 (13)	5 (8)	
	Heavy (≥ 10,000)	5 (1)	3 (1)		0 (0)	1 (0.3)	5 (2)	2 (3)	

[a]All *P*-values are calculated using either mixed linear or mixed logistic regression, as appropriate, adjusted for clustering of schools

[b]*A. lumbricoides* prevalence irrespective of co-infections

[c]*T. trichiura* prevalence irrespective of co-infections

[d]Stratified according to WHO guidelines

[e]Geometric mean among the infected (95 % confidence interval)

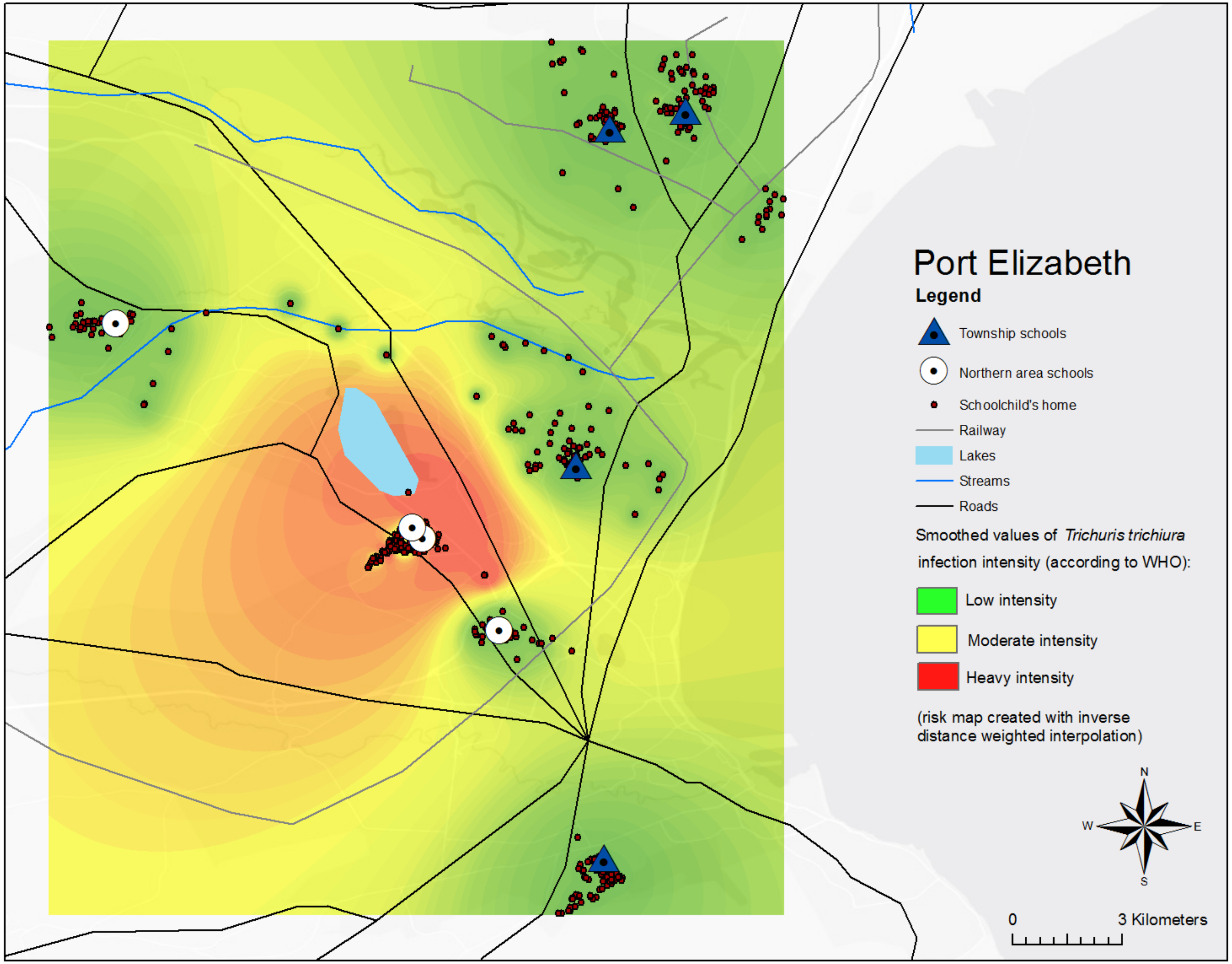

Figure 3.3 *Trichuris trichiura* infection intensities (stratified according to WHO guidelines) in the northern part of Port Elizabeth, South Africa, in February 2015, smoothed and based on 648 geographical coordinates of schoolchildren's homes.

Table 3.2 Anthropometric indicators and haemoglobin concentrations among 934 primary schoolchildren, stratified by Ascaris lumbricoides and/or Trichuris trichiura infection status, from Port Elizabeth, South Africa, in February 2015.

	Non-infected children	***A. lumbricoides* single infection**	***T. trichiura* single infection**	***A. lumbricoides - T. trichiura* co-infection**	
	***n* = 635**	***n* = 248**	***n* = 207**	***n* =156**	***P*[a]**
Anthropometric					
Mean[a] weight [kg] (95 % CI[c])	31.6 (31.0–32.2)	28.4 (27.7–29.1)	27.8 (27.0–28.5)	27.8 (26.9–28.6)	0.011
Mean[b] height [cm] (95 % CI[c])	133.9 (133.3–134.5)	131.8 (130.9–132.6)	131.1 (130.1–132.1)	131.1 (130.0–132.2)	0.009
Mean[b] BMI [kg m^{-2}] (95 % CI[c])	17.5 (17.2–17.7)	16.2 (16.0–16.5)	16.0 (15.7–16.3)	16.1 (15.7–16.4)	0.024
n (%) wasted[d]	15 (2.4)	17 (6.9)	16 (7.7)	12 (7.7)	0.418
n (%) stunted[e]	37 (5.8)	47 (19.0)	47 (22.7)	36 (23.1)	0.006
Haemotologic					
Mean[a] haemoglobin [g l^{-1}] (95 % CI[b])	123.1 (122.3–123.8)	120.4 (119.2–121.6)	119.5 (118.3–120.6)	119.5 (118.2–120.8)	0.009

[a]All *P*-values are calculated using either mixed linear or mixed logistic regression, as appropriate, adjusted for clustering of schools

[b]Arithmetic mean

[c]95 % confidence interval

[d]Wasting is defined as ≤ -2 in BMIZ score

[e]Stunting is defined as ≤ -2 HAZ score

The overall mean Hb level was 122.2 g l^{-1}. Hb levels were significantly lower in children harbouring a single or dual species helminth infection (χ^2 = 11.70, *df* = 3, *P* = 0.009). In school B in Hillcrest, the mean Hb level was 119.7 g l^{-1}, and at school A in Helenvale, 120.5 g l^{-1}, respectively. These values were significantly lower compared to the overall mean Hb level of the eight schools enrolled in our study.

Physical fitness levels and parasitological status

Non-infected boys achieved statistically significantly higher mean grip strength test results than non-infected girls (13.2 kg *versus* 11.7 kg; χ^2 = 31.71, *df* = 1, *P* < 0.0001) (Figure 3.4; Additional file 1: Table S1). Older children (11–12 years) had significantly higher mean grip strength test results compared to their younger counterparts (9–10 years) (χ^2 = 150.25, *df* = 1, *P* < 0.0001). Irrespective of age and sex, children with multiple parasite infections had slightly, but not statistically significantly, lower mean grip strength compared to non-infected children.

Infection status was not associated with lower achievement in the standing broad jump test, irrespective of age and sex. The VO_2 max estimated from the 20 m shuttle run test was higher in non-infected boys than girls (51.5 ml kg^{-1} min^{-1} and 47.4 ml kg^{-1} min^{-1}; χ^2 = 167.43, *df* = 1, *P* < 0.0001), but unrelated to age.

With regard to infection with *A. lumbricoides* and *T. trichiura*, irrespective of the co-infection state (Table 3.3), the estimated mean VO_2 max for 9 year old children infected with *T. trichiura* was statistically significantly lower than the VO_2 max of their non-infected peers (48.1 ml kg^{-1} min^{-1} *versus* 49.6 ml kg^{-1} min^{-1}; χ^2 = 4.29, *df* = 1, *P* = 0.038). Estimates for infected children of higher age were lower compared to non-infected children of the same age, but the difference did not reach statistical significance.

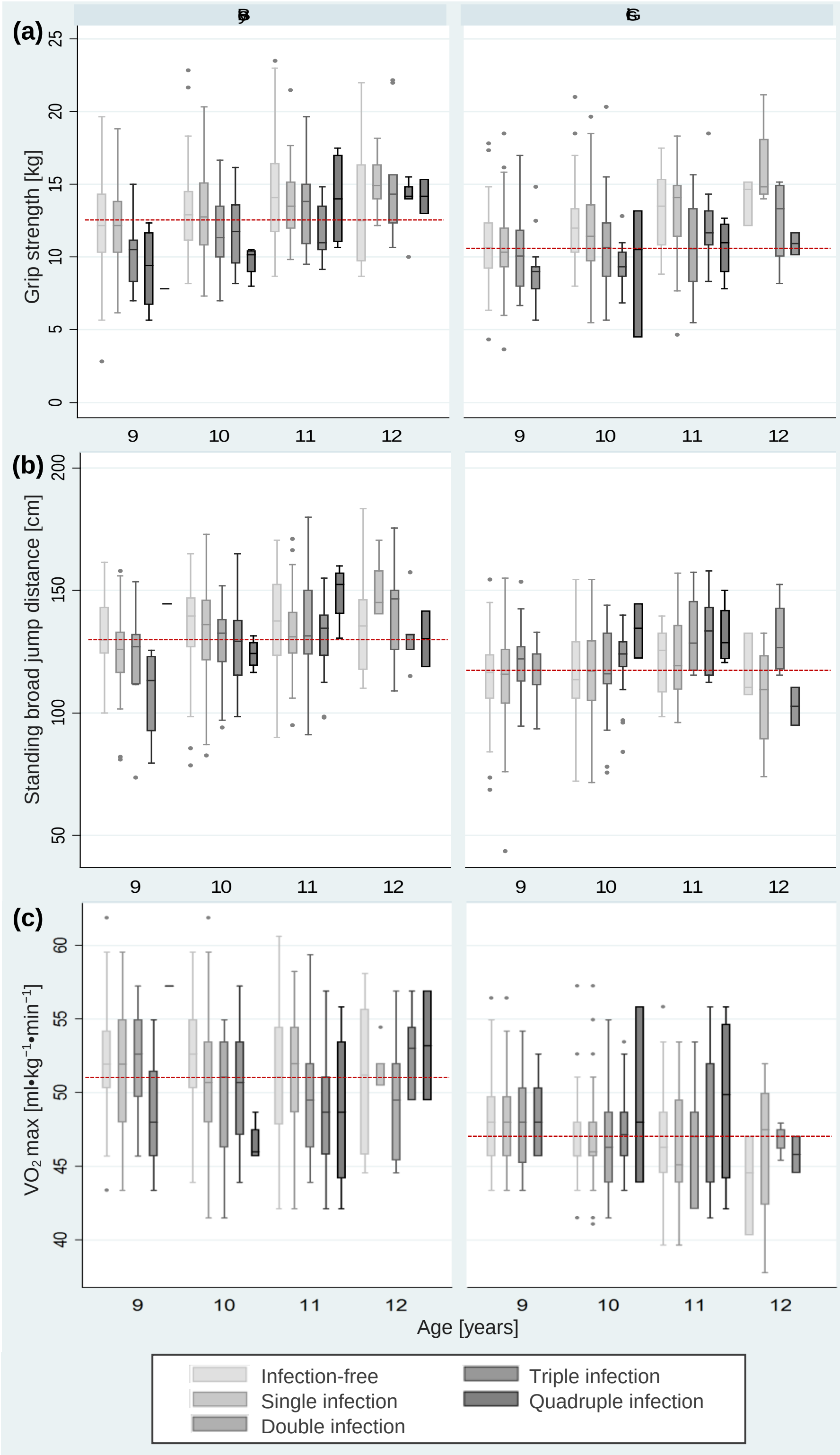

Figure 3.4 Physical fitness test results (namely (**a**) grip strength, (**b**) standing broad jump and (**c**) 20 m shuttle run test) among 934 Grade 4 schoolchildren, stratified by sex, age and infection status, in Port Elizabeth, South Africa, in early 2015. Note: The darker the boxplot is, the more parasite species are hosted by a child; bright boxplots represents infection-free, black boxplots represents quadruple infections; the dashed red line represents the mean.

Table 3.3 Mean maximal oxygen uptake (VO_2 max) estimates (ml kg^{-1} min^{-1}) among 934 primary schoolchildren from Port Elizabeth, South Africa, in February 2015, stratified by sex, age and *Ascaris lumbricoides* and *Trichuris trichiura* infection status.

	A. lumbricoides			***T. trichiura***		
	Non-infected (*n* = 686)	**Infected (*n* = 248)**	***P*[b]**	**Non-infected (*n* = 727)**	**Infected (*n* = 207)**	***P*[b]**
Sex						
Male (*n* = 472)	51.1	50.0	0.113	51.1	49.8	0.204
(95 % CI)	(50.7–51.5)	(49.3–50.6)		(50.7–51.5)	(49.1–50.6)	
Female (*n* = 462)	47.5	47.4	0.946	47.5	47.4	0.911
(95 % CI)	(47.2–47.8)	(46.7–48.0)		(47.1–47.8)	(46.7–48.1)	
Age (years)						
9 (*n* = 282)	49.6	48.6	0.104	49.6	48.1	0.038
(95 % CI)	(49.1–50.0)	(47.5–49.6)		(49.1–50.0)	(47.0–49.3)	
10 (*n* = 375)	48.9	48.8	0.955	48.9	48.9	0.778
(95 % CI)	(48.4–49.4)	(48.2–49.5)		(48.4–49.4)	(48.2–49.6)	
11 (*n* = 216)	49.2	48.8	0.489	49.3	48.4	0.151
(95 % CI)	(48.4–49.9)	(47.7–49.8)		(48.6–50.0)	(47.3–49.5)	
12 (*n* = 61)	49.9	49.0	0.424	49.2	50.2	0.548
(95 % CI)	(48.7–51.0)	(47.0–51.1)		(48.0–50.5)	(48.2–52.1)	

[a]All mean VO_2 estimates are expressed in ml kg^{-1} min^{-1} and are adjusted for age, with 95 % confidence intervals in parentheses when appropriate

[b]All *P*-values are calculated using either mixed linear or mixed logistic regression, as appropriate, adjusted for clustering of schools

In the multiple linear regression model presented in Table 3.4, sex and age were statistically significantly and negatively associated with mean VO_2 max estimates. The mean VO_2 max estimate of girls overall was 3.48 ml kg^{-1} min^{-1} lower than the VO_2 max estimate of boys ($P < 0.001$). The mean VO_2 max estimate also decreased by 0.40 ml kg^{-1} min^{-1} per year ($P = 0.004$). Non-significantly higher mean VO_2 max estimates were found in *H. pylori*-infected children compared to their non-infected peers.

Table 3.4 Associations between mean maximal oxygen uptake (VO_2 max) estimates (ml kg^{-1} min^{-1}) and age, sex and infection status as predictor variables across eight schools. Data are derived from 934 primary schoolchildren from Port Elizabeth, South Africa, in early 2015.

	Multiple linear regression		
Explanatory variables	**Coefficient**	**95 % confidence interval**	***P***
A. lumbricoides (reference: not infected)	-0.37	-1.23 to 0.50	0.403
Age (in years)	-0.40	-0.68 to -0.13	0.004
Dual infected (reference: not infected)	-0.42	-1.27 to 0.43	0.332
T. trichiura (reference: not infected)	-0.46	-1.61 to 0.70	0.442
Sex (reference: male)	-3.48	-3.95 to -3.01	< 0.0001

P-value of mixed-effects linear regression model $P < 0.0001$, adjusted for clustering within schools

3.6 Discussion

We found notable levels of helminth and intestinal protozoa infections in 9 to 12-year-old children in eight schools of poor neighbourhoods in Port Elizabeth, South Africa. Children infected with *T. trichiura* had significantly lower body weight, were less tall and had a lower BMI compared to their non-infected peers (all $P < 0.05$). The same trend was observed for *A. lumbricoides*-infected children.

Helicobacter pylori infections were classified by World Health Organization (WHO) as a carcinogen of class 1 (definite carcinogen) in 1994 (1994). Non-significant associations between an infection with this bacterium and the growth of children were noted, confirming findings by Abdelrazak and Richter et al. (Abdelrazak and Walid, 2015; Richter *et al.*, 2001). Boys, but not girls, with a *T. trichiura* or *A. lumbricoides* infection had significantly lower mean VO_2 max estimates than non-infected peers (Figure 3.5). Grip strength and standing broad jump test results were also statistically significantly lower in 9 to 10-year-old boys, whereas in girls no difference was seen.

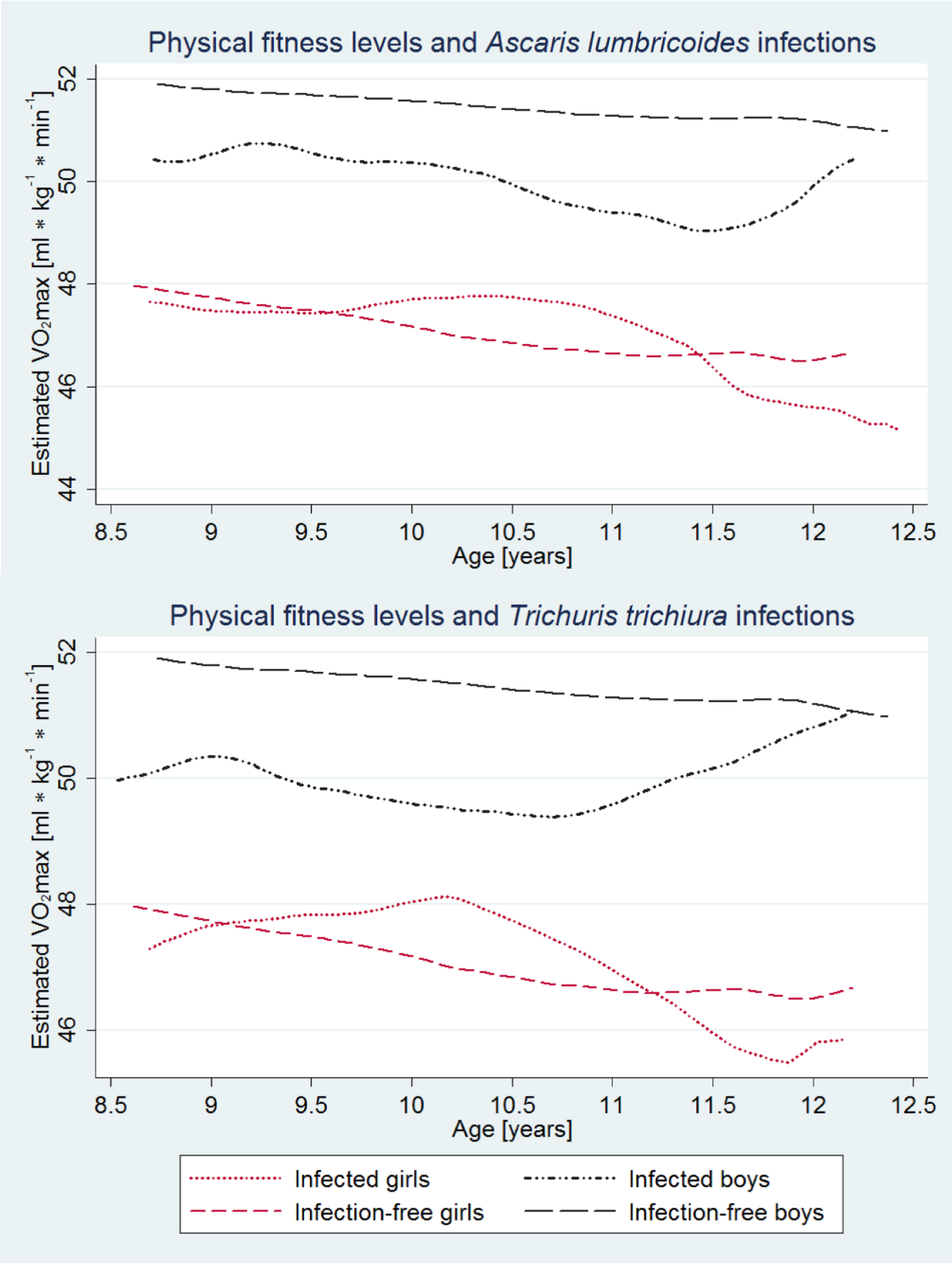

Figure 3.5 Physical fitness levels as estimated by maximal oxygen uptake (VO_2 max) of children infected with either *A. lumbricoides* (n = 248) or *T. trichiura* (n = 207), compared to physical fitness levels of infection-free peers among Grade 4 schoolchildren in Port Elizabeth, South Africa, in early 2015. Note: Curves were generated using a polynomial smooth. Infection-free is here defined as no *A. lumbricoides*, *T. trichiura*, *Cryptosporidium* spp. and *Giardia* spp. infection (n = 278).

The mean number of completed levels/stages of the 20 m shuttle run test corresponds closely to the mean results reported from other studies in different settings, e.g. the KISS- or the Sportcheck-study with Swiss primary schoolchildren of similar age (Kriemler *et al.*, 2010; Meyer *et al.*, 2014; Imhof *et al.*, 2015). Yap et al. reported slightly lower VO_2 max results, 45.6 ml kg^{-1} min^{-1} for boys and 44.7 ml kg^{-1} min^{-1} for girls, from 194 children aged 9 to 12 years and living in south-west Yunnan province in the People's Republic of China (Yap *et al.*, 2014). With regard to *T. trichiura* infections, Yap et al. (Yap *et al.*, 2012) found more pronounced impacts on weight, height and BMI than the present study.

The 20 m shuttle run test was the selected measurement method for the assessment of cardio-respiratory fitness in a resource-constrained setting due to its easy and trouble-free application (Léger *et al.*, 1988). An alternative test, though with smaller samples, is the Harvard step test (HST) (Gallagher JR, 1943; Stephenson *et al.*, 1990). However, using different and technically more elaborated methods such as the cycle ergometer test used by Aandstad et al. (Aandstad *et al.*, 2006), the estimated maximal oxygen uptake in 9 and 10-year-old children in Tanzania and Norway is significantly higher compared to the VO_2 max of the 20 m shuttle run test ($P < 0.001$), namely for boys 58.6 ml kg^{-1} min^{-1} (95 % CI: 57.3–60.0 ml kg^{-1} min^{-1}) and for girls 54.7 ml kg^{-1} min^{-1} (95 % CI: 52.9–56.5 ml kg^{-1} min^{-1}) (Aandstad *et al.*, 2006). The estimated VO_2 max values generated from the 20 m shuttle run test tend to be high in relation to other direct VO_2 max measurement methods, such as maximal watt cycle ergometer test, treadmill or spirometry in laboratory settings. This shift in absolute level of VO_2 max is not expected to influence the association signals with infection status, though.

Comparing calculated standing broad jump result means of 118 cm for girls and 132 cm for boys of the present survey with results of the Armstrong et al. study (Armstrong *et al.*, 2011), also conducted in South Africa with 2,819 girls and 3,573 boys of the same age, Armstrong and colleagues measured noticeably longer standing broad jump distances, namely 152 cm for girls and 164 cm for boys.

The highest prevalence of stunting was observed in schools in the region of Hillcrest (22 %) and Helenvale (19 %), where also the highest prevalences of *A. lumbricoides* and *T. trichiura* were detected. However, these observations need to be interpreted with caution since current infection status is correlated with long-term growth indicators. Potentially, systematic differences in socioeconomic status and malnutrition levels exist between the study schools.

Only few studies have investigated the distribution of STHs in South Africa. Higher prevalences of hookworm and schistosome infections have been reported from warmer KwaZulu-Natal, located further north than Port Elizabeth (2015; Karagiannis-Voules *et al.*, 2015) compared to the results from our study. In our cohort of primary schoolchildren, heavy *T. trichiura* and *A. lumbricoides* intensities were observed in areas built in the 1950s to accommodate 6,000 predominantly coloured people but where a recent survey estimated that more than 30,000 people are living in the area (Armstrong *et al.*, 2011). The area is characterised by unhygienic living conditions (poor sanitation and litter), high unemployment and gangsterism. Based on our results, biannual mass deworming should be implemented in the Hillcrest and Helenvale region in order to reduce STH prevalences and thus lower the risk of morbidity, complemented by interventions focusing on WASH (Strunz *et al.*, 2014).

Our study has several limitations. First, results reported here stemmed from a cross-sectional survey and as such we only identified associations rather than causality. Also, current infection status and current effects of past, long-term effects such as stunting are not directly linked. Secondly, it is still debated whether cardiorespiratory performance of children, measured here as maximal oxygen uptake (VO_2 max), is receptive enough for change (Rowland, 1985) due to varying personal living conditions. Thirdly, only single stool samples were collected from each participant. Hence, some infections, particularly those of light intensity, were possibly missed, as seen in other studies where multiple biological samples and a combination of diagnostic methods were employed (Knopp *et al.*, 2008; Steinmann *et al.*, 2008; Booth *et al.*, 2003). Despite these limitations, the study confirms the practicability of the methods employed as suggested by previous experiences in different African and Asian settings, where school-aged children liked to perform physical fitness tests (Ziegelbauer *et al.*, 2010; Bustinduy AL, 2011; Müller *et al.*, 2011).

In the 2004 Global Burden of Disease (GBD) study, heavy *A. lumbricoides* and *T. trichiura* infections have both been assigned a zero disability weight (DW) as each of the two infections for itself alone is very rarely fatal, whereas the cognitive impairment resulting from both infections clearly differ, namely 0.463 for *A. lumbricoides* and 0.024 for *T. trichiura* on a scale from 0 (no disability) to 1 (death) (WHO, 2004). In the Global Burden of Disease update 2013, a disease burden of 14.2 disability-adjusted life years (DALYs) per 100,000 person-years is estimated for children below the age of 15 years in South Africa who are infected with *A. lumbricoides*, while the respective estimate for children infected with *T. trichiura* is almost 10-fold higher (140 DALYs per 100,000 person-years) (IHME, 2016). As we observed similar prevalences for *A. lumbricoides* and *T. trichiura* (Karagiannis-Voules *et al.*, 2015; Pullan *et al.*, 2014), it appears that the disease burden of the latter helminth infection in under 15-year-old South African children is higher.

3.7 Conclusions

This cross-sectional survey of the DASH study provides new insight into helminth and intestinal protozoa infections, physical fitness and growth of Grade 4 children in quintile 3 primary schools from disadvantaged communities in Port Elizabeth, South Africa. Our results indicate that boys who are infected with multiple intestinal parasite species have lower physical fitness levels than their non-infected counterparts, as expressed by the maximal oxygen uptake (VO_2 max). A significantly higher *T. trichiura* prevalence was noted in stunted children and those with a significantly lower Hb level, compared to children not infected with this species. Biannual mass deworming in order to control the morbidity due to STH infections is recommended in school B in Hillcrest and school A in Helenvale.

Abbreviations

BMI, body mass index; BMIZ, BMI-for-age Z-score; DALY, disability-adjusted life year; DASH, Disease, Activity and Schoolchildren's Health; DW, disability weight; EKNZ, Ethics committees of northwest and central Switzerland; EPG, eggs per gram (of stool); GBD, global burden of disease; HAZ, height-for-age Z-score; Hb, haemoglobin; HST, Harvard step test; IDW, inverse distance weighting; ISRCTN, International Standard Randomised Controlled Trial Number; NMMU, Nelson Mandela Metropolitan University; NRF, National Research Foundation; POC-CCA, point-of-care circulating cathodic antigen; RDT, rapid diagnostic test; SD, standard deviation; SNSF, Swiss National Science Foundation; SSAJRP, Swiss-South African Joint Research Programme; STH, soil-transmitted helminth; VO_2 max, maximal oxygen uptake; WASH, water, sanitation and hygiene; WHO, World Health Organization

Declarations

Ethics statement

This study was cleared by the ethics committees of Northwest and Central Switzerland (EKNZ; reference no. 2014-179, approval date: 17 June 2014), the Nelson Mandela Metropolitan University (NMMU; study number H14-HEA-HMS-002, approval date: 4 July 2014), the Eastern Cape Department of Education (approval date: 3 August 2014) and the Eastern Cape Department of Health (approval date: 7 November

2014). The study is registered at ISRCTN registry under controlled-trials.com (unique identifier: ISRCTN68411960, registration date: 1 October 2014).

The school principals, teaching staff and potential participants were briefed on the purpose, procedures, potential risks and benefits of the study. Meetings with parents or guardians were held to explain the project. Children who were absent from school on the clinical examination day or suffering from any chronic illness were excluded from the physical fitness testing prior to the 20 m shuttle run test. Oral assent from each participating child was sought and individual written informed consent was obtained from parents/guardians. For illiterate parents/guardians, the information sheet available in English, Xhosa and Afrikaans was read aloud in the appropriate language or, if needed, an oral translation of the information sheet into another local language was provided. Participation was voluntary, and hence, children could withdraw from the study at any time without further obligations. To ensure confidentiality, each study participant was given a unique identification number. Children with serious health problems were referred to the local clinic. STH infections were managed free of charge according to WHO and national treatment guidelines.

Consent for publication

Not applicable.

Availability of data and material

The datasets are available from the corresponding author on request.

Conflicting interests

The authors declared that they have no financial, professional or personal conflicting interests related to this article.

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Authors' contributions

IM, PY, PS, NP-H, MG, RdR, UP, CW and JU designed the study, established the methods and questionnaires and wrote the original study protocol. All other authors contributed to the development of the study protocol. IM, PY, BPD, NSNH, MG, RdR, UP and CW conducted the study. CW was responsible for community sensitisation. IM managed data entry, cleaning and preparation of the database for statistical analysis, supported by CS and HS. IM wrote the first draft of the manuscript. All authors read and provided comments on the drafts and approved the final version of the paper prior to submission.

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Additional Table S1

Table S1 Grip strength, standing broad jump and 20 m shuttle run test, among 934 Grade 4 schoolchildren from Port Elizabeth, South Africa, in early 2015, stratified by multiple infection status sex and age.

		Sex		Age (years)			
		Male (n = 472)	**Female (n = 462)**	**9 (n = 282)**	**10 (n = 375)**	**11 (n = 216)**	**12 (n = 61)**
		Mean [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])
(1) Grip strength test	**Non-infected [kg]**	**13.2** (135; 3.4)	**11.7** (143; 2.7)	**11.3** (96; 3.1)	**12.4** (107; 2.8)	**13.6** (57; 3.3)	**14.2** (18; 3.4)
	Infected [kg]						
	Single	**12.9** (178; 2.9)	**11.7** (186; 3.0)	**11.3** (130; 2.6)	**12.3** (146; 2.8)	**13.2** (72; 3.0)	**16.0** (16; 3.2)
	Double	**12.7** (82; 3.2)	**10.9** (73; 2.9)	**10.5** (34: 2.6)	**11.3** (61; 2.9)	**12.9** (45; 2.9)	**14.2** (15; 3.8)
	Triple	**11.7** (69; 2.3)	**10.1** (51; 2.2)	**9.1** (21; 2.0)	**10.8** (54; 2.2)	**11.8** (36; 2.0)	**13.3** (9; 2.3)
	Quadruple	**12.6** (8; 3.5)	**10.1** (9; 2.7)	**7.8** (1; n.a.)	**9.8** (7; 2.6)	**12.8** (6; 3.7)	**12.9** (3; 2.4)
(2) Standing broad jump test	**Non-infected [cm]**	**134.2** (135; 18.0)	**116.4** (143; 16.5)	**119.9** (96; 18.0)	**124.8** (107; 19.2)	**131.2** (57; 20.0)	**134.2** (18; 18.4)
	Infected [cm]						
	Single	**130.4** (178; 17.3)	**116.2** (186; 17.6)	**119.5** (130; 18.5)	**123.7** (146; 18.8)	**126.1** (72; 17.6)	**134.5** (16; 22.9)
	Double	**131.3** (82; 17.9)	**122.4** (73; 16.3)	**122.7** (34; 15.9)	**122.7** (61; 17.6)	**133.1** (45; 16.5)	**137.5** (15; 17.3)
	Triple	**129.8** (69; 16.7)	**121.9** (51; 15.6)	**114.4** (21; 14.5)	**126.4** (54; 15.4)	**134.2** (36; 15.8)	**124.2** (9; 17.2)
	Quadruple	**132.1** (8; 12.6)	**128.0** (9; 16.0)	**144.5** (1; n.a.)	**128.6** (7; 9.3)	**134.9** (6; 12.9)	**118.3** (3; 23.5)

		Sex		Age (years)			
		Male (n = 472)	**Female (n = 462)**	**9 (n = 282)**	**10 (n = 375)**	**11 (n = 216)**	**12 (n = 61)**
		Mean [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])	**Mean** [a] (n; SD [b])
(3) 20 m Shuttle run test	**Non-infected [ml kg^{-1} min^{-1}]** [c]	**51.5** (135; 4.2)	**47.4** (143; 3.3)	**49.6** (96; 3.9)	**49.0** (107; 4.1)	**49.9** (57; 5.1)	**49.1** (18; 4.5)
	Infected [ml kg^{-1} min^{-1}]						
	Single	**50.9** (178; 4.0)	**47.5** (186; 3.1)	**49.6** (130; 3.6)	**48.8** (146; 4.2)	**48.9** (72; 4.0)	**49.8** (16; 3.7)
	Double	**50.1** (82; 3.7)	**47.2** (73; 3.3)	**49.1** (34; 3.7)	**48.7** (61; 3.7)	**48.3** (45; 4.2)	**48.9** (15; 3.6)
	Triple	**50.0** (69; 3.9)	**47.9** (51; 3.2)	**47.9** (21; 2.7)	**49.3** (54; 3.5)	**49.0** (36; 4.4)	**51.0** (9; 3.8)
	Quadruple	**49.1** (8; 5.4)	**48.3** (9; 5.5)	**57.2** (1; n.a.)	**48.0** (7; 3.8)	**47.7** (6; 5.8)	**49.5** (3; 7.4)

[a] **Arithmetic mean** (sample size (n); standard deviation (SD))

[b]All standard deviations (SD) are calculated using univariate analysis as appropriate

[c] All mean VO_2 estimates are expressed in ml kg^{-1} min^{-1} and are adjusted for age

n.a.: not applicable; n.r.: not represented

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CHAPTER 4

4.1 Low efficacy of albendazole against *Trichuris trichiura* infection in schoolchildren from Port Elizabeth, South Africa

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4.2 Abstract

Background: Albendazole is one of two standard drugs for the control of soil-transmitted helminthiasis.

Methods: A total of 149 schoolchildren from Port Elizabeth, South Africa, were examined for soil-transmitted helminth infections using duplicate Kato-Katz thick smears before and 2 weeks after administration of albendazole (400 mg).

Results: *Trichuris trichiura* was the predominant soil-transmitted helminth species (prevalence 60.4%), followed by *Ascaris lumbricoides* (47.4%). While albendazole was highly efficacious against *A. lumbricoides* (cure rate (CR): 97.2%; egg reduction rate (ERR): 94.5%), it lacked efficacy against *T. trichiura* (CR: 1.1%; ERR: 46.0%).

Conclusions: Our study confirms low efficacy of single-dose albendazole against *T. trichiura*. There is a need for safe and efficacious drugs against *T. trichiura*.

Keywords: Albendazole, *Ascaris lumbricoides*, Drug efficacy, Kato-Katz technique, South Africa, *Trichuris trichiura*

4.3 Introduction

South Africa is considered a moderate-burden country for soil-transmitted helminth (STH) infections; yet, there is a paucity of data (Karagiannis-Voules *et al.*, 2015). Within the frame of a 3-year prospective epidemiological study entitled “Disease, Activity and Schoolchildren’s Health (DASH)” that is focusing on schoolchildren from poor neighbourhoods in Port Elizabeth, South Africa (Yap *et al.*, 2015; Müller *et al.*, 2016), a sub-study was implemented to assess the efficacy against STH infections of the anthelminthic drug albendazole.

4.4 Materials and methods

The study was carried out in Helenvale, situated in the northern part of Port Elizabeth, a coastal city located in the Eastern Cape province of South Africa (geographical coordinates: 34°07′54″ to 33°57′29″ S latitude and 25°36′00″ to 25°55′49″ E longitude) (Yap *et al.*, 2015; Müller *et al.*, 2016). Established in the 1950s, Helenvale is one of the oldest townships stemming from the apartheid era as a group area for coloured people. It is considered to be one of the poorest and most unsafe neighbourhoods of the city, characterised by high unemployment, low levels of education, illicit drugs, alcohol abuse and gangsterism. Grade 4 schoolchildren, aged 9-14 years, from a disadvantaged school (quintile 3) were included in the study.

The school principal, teaching staff, schoolchildren and their parents/guardians were informed about the purpose and procedures of the study. Written informed consent (either in English, Xhosa or Afrikaans) was obtained from children’s parents/guardians, while children assented orally. Children could withdraw at any time without further obligations.

Consenting children were provided stool containers with unique identifiers and invited to return the containers filled with a small portion of their morning stool the next day. Duplicate 41.7 mg Kato-Katz thick smears were prepared from each stool sample (Katz *et al.*, 1972). Two slides were examined quantitatively under a microscope. Species-specific helminth egg counts were multiplied by a factor of 24 to obtain a proxy for infection intensity, as expressed by the number of eggs per gram of stool (EPG).

Subsequently, a single oral dose of 400 mg albendazole (INRESA; Bartenheim, France) was administered to all children participating in the study owing to a STH prevalence of over 20%.(WHO, 2006) Ingestion of the drug was directly observed. Two weeks after administration, all treated children were invited to resubmit another stool sample to be re-examined with the same diagnostic procedures.

Data were double-entered and validated using EpiData version 3.1 (EpiData Association; Odense, Denmark). Statistical analysis was done using STATA version 13.0 (STATA Corp.; College Station, TX, USA). Drug efficacy was expressed as cure rate (CR; proportion of participants who were helminth-egg positive before treatment and became egg-negative 2 weeks post-treatment) and egg reduction rate (ERR; reduction of the arithmetic mean helminth egg count after treatment compared to the baseline). A 95% confidence interval (CI) was calculated for prevalence estimates. Statistical significance was defined as P <0.05, while P-values were calculated using Pearson's χ^2 or paired t-test, as appropriate.

4.5 Results and discussion

Complete data were available from 149 children; 76 girls (51.0%) and 73 boys. At baseline, 90 children were found to be infected with *Trichuris trichiura* (60.4%) and 71 with *Ascaris lumbricoides* (47.7%). No hookworm infections were found. Infection intensities were mainly light or moderate (Table 4.1).

Table 4.1 Prevalence and intensity of *T. trichiura* and *A. lumbricoides*, before and after treatment with a single dose of 400 mg albendazole, among 9- to 14-year-old schoolchildren in Port Elizabeth, South Africa, 2015.

		Baseline		2 weeks after treatment[a]	
	n	***T. trichiura***	***A. lumbricoides***	***T. trichiura***	***A. lumbricoides***
Prevalence of infection [% (95% CI)]					
Sex					
Males	73	71.2 (59.6-80.6)	54.8 (43.1-66.0)	69.9 (58.1-79.4)	1.4 (0.2-9.5)
Females	76	50.0 (38.7-61.3)	40.8 (30.1-52.4)	50.0 (38.7-61.3)	1.3 (0.2-9.1)
Total	**149**	**60.4 (52.3-68.0)**	**47.7 (39.7-55.8)**	**59.7 (51.6-67.4)**	**1.3 (0.3-5.3)**
CR[b] [%]					
		n.a.	n.a.	**1.1**	**97.2**
Arithmetic mean EPG [n (95% CI)]					
Total	**149**	**1,081.5** (639.3-1,523.8)	**10,959.2** (7,324.9-14,593.6)	**583.8** (273.0-930.6)	**628.8** (-251.0-1,508.7)
ERR[c] [%]					
		n.a.	n.a.	**46.0**	**94.3**
Intensity of infection					
Infected [n]		90	71	89	2
Light[d]		59	24	68	0
Moderate[e]		28	38	20	1
Heavy[f]		3	9	1	1

[a] Treatment according WHO and national guidelines (single oral dose of 400 mg albendazole)
[b] CR: cure rate (percentage of egg-positive children at baseline who became egg-negative after treatment)
[c] ERR: egg reduction rate (reduction in the arithmetic mean faecal egg count at treatment follow-up compared to before treatment)
[d] *A. lumbricoides*, 1-4,999 EPG; *T. trichiura*, 1-999 EPG
[e] *A. lumbricoides*, 5,000-49,999 EPG; *T. trichiura*, 1,000-9,999 EPG
[f] *A. lumbricoides*, ≥50,000 EPG; *T. trichiura*, ≥10,000 EPG

The highest prevalence of *T. trichiura* was observed among 11-year-old children (67.1%). Boys were significantly more often infected with *T. trichiura* than girls (71.2% *versus* 50.0%; $\chi^2 = 7.02$, $df = 1$, P

= 0.008). Boys were also more often infected with *A. lumbricoides* than girls (54.8% *versus* 40.8%), but this difference was not statistically significant (P = 0.087).

A single dose of 400 mg albendazole lacked efficacy against *T. trichiura*. Only one of the 90 infected children at baseline appeared completely cured from this STH species at follow-up (observed CR: 1.1%). In terms of infection intensity, the arithmetic mean faecal egg count of *T. trichiura* was reduced from 1,082 to 584, owing to a moderate ERR of 46.0% ($t_{(148)}$ = 2.48, P = 0.007). The number of moderate and heavy *T. trichiura* infections (≥1,000 EPG) declined from 31 (20.8%) before treatment to 21 (14.1%) after the administration of albendazole.

A single dose of albendazole was highly efficacious against *A. lumbricoides*. At treatment follow-up, only two children were found positive for this STH species (CR 97.2%). The arithmetic mean *A. lumbricoides* egg count dropped from 10,959 EPG to 628 EPG, an ERR of 94.3% ($t_{(148)}$ = 5.68, P <0.001). The prevalence of moderate and heavy *A. lumbricoides* infections (≥5,000 EPG) decreased from 31.5% before to 1.3% after-treatment.

The current study confirms that a single 400 mg oral dose of albendazole is highly efficacious against *A. lumbricoides*, but lacks efficacy against *T. trichiura* among school-aged children (Keiser and Utzinger, 2010). In 2009, Stothard and colleagues reported low CRs for single-dose albendazole against *T. trichiura* among preschool-aged children on Zanzibar Island (Stothard *et al.*, 2009). Recently, combination therapy (oxantel pamoate plus albendazole) showed higher CR and ERR compared to standard albendazole or mebendazole treatment (Speich *et al.*, 2014).

Only few studies have examined the distribution of STHs in South Africa. For instance, Karagiannis-Voules and colleagues reported slightly higher STH prevalences further North, in the province of KwaZulu-Natal (Karagiannis-Voules *et al.*, 2015). Given the high prevalence and intensity of STH infections observed in our study, specific public health interventions are warranted but according to education authorities, preventive chemotherapy using either albendazole or mebendazole against STHs has thus far been neglected in the Helenvale neighbourhood.

Our study has several limitations. First, we only focussed on Grade 4 children attending a disadvantaged quintile 3 school in Port Elizabeth. Hence, our findings cannot be generalized for a broader population. Second, only single stool samples were collected before and after anthelminthic drug administration. It is conceivable that some infections, particularly those of light intensity, were missed.

Taken together, our findings from Port Elizabeth in South Africa suggest that a single 400 mg oral dose of albendazole is efficacious against *A. lumbricoides* but does not effectively manage *T. trichiura* infections in children. To control STH infections among school-aged children, public health measures are required, such as preventive chemotherapy, along with improvements in water, sanitation and hygiene (WASH). Moreover, there is a pressing need to use alternative and develop novel drugs and drug combinations that are safe and efficacious against *T. trichiura*.

Author contributions: IM, PS, RdR, MG, UP, CW and JU designed the study protocol. IM, LB, LZ and CW conducted the field work. CW was responsible for community sensitisation. IM, JU and PS analysed and interpreted the data, and drafted the manuscript. All authors critically reviewed and approved the manuscript prior to submission. IM and PS are the guarantors of the paper.

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Competing Interests: None declared.

Ethical approval: The study was cleared by the ethics committees of Northwest and Central Switzerland (EKNZ; reference no. 2014-179, approval date: 17 June 2014), the Nelson Mandela Metropolitan University (NMMU; study number H14-HEA-HMS-002, approval date: 4 July 2014), the Eastern Cape Department of Education (approval date: 3 August 2014) and the Eastern Cape Department of Health (approval date: 7 November 2014). The study is registered at ISRCTN registry under controlled-trials.com (unique identifier: ISRCTN68411960, registration date: 1 October 2014).

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CHAPTER 5

5.1 Shrinking risk profiles after deworming of children in Port Elizabeth, South Africa, with special reference to *Ascaris lumbricoides* and *Trichuris trichiura*

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5.2 Abstract

Risk maps facilitate discussion among different stakeholders and provide a tool for spatial targeting of health interventions. We present maps documenting shrinking risk profiles after deworming with respect to soil-transmitted helminthiasis among schoolchildren from disadvantaged neighbourhoods in Port Elizabeth, South Africa. Children were examined for soil-transmitted helminth infections using duplicate Kato-Katz thick smears in March 2015, October 2015 and May 2016, and subsequently treated with albendazole after each survey. The mean infection intensities for *Ascaris lumbricoides* were 9,554 eggs per gram of stool (EPG) in May 2015, 4,317 EPG in October 2015 and 1,684 EPG in May 2016. The corresponding figures for *Trichuris trichiura* were 664 EPG, 331 EPG and 87 EPG. Repeated deworming shrank the risk of soil-transmitted helminthiasis, but should be complemented by other public health measures.

Keywords: Albendazole, *Ascaris lumbricoides*, *Trichuris trichiura,* risk profiling, South Africa.

Video link: https://youtu.be/SEaz8RC3t4s

5.3 Background

Soil-transmitted helminths (STH), such as *Ascaris lumbricoides*, hookworm and *Trichuris trichiura* are among the most common parasite infections in humans (Bethony *et al.*, 2006). Indeed, more than 4 billion people are at risk of infection globally and more than a billion are infected (Pullan *et al.*, 2014). STH infections are most prevalent in poor communities in low- and middle-income countries, where these parasitic worms are of direct public health relevance because of their negative impact on children's health and development. The highest prevalence and intensity of STH infections are typically observed in school-aged children (Woolhouse, 1998). However, hookworm infection might peak in older age groups (Bethony *et al.*, 2006). Morbidity due to STH infections can be prevented through periodic administration of anthelminthic drugs – a strategy known as 'preventive chemotherapy' (WHO, 2006). School-aged children, and increasingly also preschool-aged children and women of reproductive age, are the key target groups for preventive chemotherapy. The school platform has been shown to be a cost-effective approach for regular deworming, as it offers a readily available, extensive and sustained infrastructure with a skilled workforce that is in close contact with the target age group, the community and authorities alike (Lo *et al.*, 2015).

South Africa has a moderate burden of soil-transmitted helminthiasis (Karagiannis-Voules *et al.*, 2015), yet, there is a paucity of quality data on the risk STH infections in school-aged children with regard to deworming interventions. At the regional level, there is a concentration of data coming from Western Cape province, *i.e.* around Cape Town, and the KwaZulu-Natal province, *i.e.* around Durban (GAHI, 2017), whilst there is a lack of data from the southern part of Eastern Cape, *i.e.* around Port Elizabeth. Precise estimates of the number of people with STH infections are important as they are needed to guide treatment campaigns (Scholte *et al.*, 2013). Of particular utility in this regard are spatially explicit risk maps which facilitate targeted interventions. Indeed, the development and use of risk maps is being recommended by the World Health Organization (WHO) to support planning and implementation of preventive chemotherapy (WHO, 2006). Risk maps must, however, be updated over time to reflect changing risk profiles resulting from treatment interventions and other public health measures, such as water, sanitation and hygiene (WASH) approaches and information, education and communication (IEC).

The 'Disease, Activity and Schoolchildren's Health' (DASH) study is focusing on schoolchildren from deprived neighbourhoods in Port Elizabeth (geographical coordinates: 34°07′54″ to 33°57′29″ S latitude and 25°36′00″ to 25°55′49″ E longitude) in South Africa (Yap *et al.*, 2015; Müller *et al.*, 2016; Gall *et al.*, 2017). Within the frame of this 3-year investigation, a longitudinal study was implemented to document spatial and temporal changes in the distribution of STH infection as a result of repeated anthelminthic treatment among schoolchildren from Port Elizabeth.

A baseline cross-sectional survey carried out in March 2015 constituted the time point 1 data assessment (T1), a mid-line survey seven months later in October 2015 was designated T2 and an end-line survey after another seven months in May 2016 marked point T3 (Yap *et al.*, 2015; Müller *et al.*, 2016). Grade-4 schoolchildren aged 9-12 years from eight disadvantaged quintile-3 schools were included in the study. Note that South African schools are divided into quintiles reflecting the socioeconomic status of the community in which the school is located (quintile-1 schools are the poorest and quintile-5 schools are the least underprivileged). Preparation of the study, including identification of schools, commenced in September 2014. Eight schools were selected based on (i) sufficiently large Grade-4 classes (n>100 children); (ii) geographical location (accessibility); (iii) representation of the various target communities; and (iv) commitment to support the project activities over the duration of the 14-month study. The study population consisted of coloured children, *i.e.* of mixed-race ancestry (generally Afrikaans-speaking) and black Africans children (largely Xhosa-speaking). The schools are situated in areas colloquially known as the 'northern areas' (for coloured people: four schools) and townships (for black African people: four schools). These areas are considered to be adversely affected by high unemployment rates and low levels of educational attainment and socioeconomic status as well as criminality.

We informed school principals, teaching staff, schoolchildren and their parents/guardians about the purpose, procedures and potential risks and benefits of the study. Written informed consent was obtained from the parents/guardians. Assenting children were provided with uniquely identifiable empty stool containers and invited to return them the next day filled with a fresh morning stool specimen. Duplicate

41.7 mg Kato-Katz thick smears were prepared on glass slides from each stool sample (Yap *et al.*, 2012) and subsequently independently examined by experienced microscopists. We multiplied species-specific helminth egg counts by 24 to obtain an approximation of the infection intensity that was expressed in eggs per gram of stool (EPG) (Leuenberger *et al.*, 2016). At the end of each of the three cross-sectional surveys, a single 400 mg oral dose of albendazole (INRESA; Bartenheim, France) was administered to children testing positively for STH. All children were treated regardless of infection status in schools where the infection prevalence was equal or larger than 50%, according to national and international treatment guidelines (WHO, 2006). Ingestion of albendazole was monitored by health staff and children remained under medical supervision for 24 hours.

Data were double-entered and cross-checked using EpiData version 3.1 (EpiData Association; Odense, Denmark). Children with complete data records, *i.e.* duplicate Kato-Katz thick smears at each of the three cross-sectional surveys were included in the final analysis. Spatially explicit risk maps were created using ArcGIS version 10.2.1 (ESRI; Redlands, CA, USA). Statistical analysis (χ^2-tests, average calculations, computations of minimum and maximum as well as standard deviation (SD)) was done using STATA version 13.0 (STATA Corp.; College Station, TX, USA). For a simple interpolation of georeferenced data (obtained from coordinates of the children's homes), the inverse distance weighting (IDW) method was employed to obtain smoothed values of infection intensity. The IDW is based on the assumption that two geographically close sites are more similar than two locations further apart. It should be noted that IDW is a univariate approach, and hence does not consider individual and environmental risk factors.

Complete data records were available for 638 children in the eight surveyed schools. Interestingly, no hookworm infections were found, while infections with *A. lumbricoides* and *T. trichiura* showed spatial clustering. At the baseline cross-sectional survey in March 2015, the prevalence of *T. trichiura* and *A. lumbricoides* at school A in Helenvale was 65% and 72%, respectively, while in school B in Hillcrest, the corresponding prevalence values were 65% and 60%. Compared to the other six schools, these prevalence levels were significantly higher, both for *T. trichiura* (χ^2 = 592.5, degree of freedom (df) = 7, P<0.001) and *A. lumbricoides* (χ^2 = 475.3, df = 7, P<0.001). Similarly, infection intensities were highest in schools A and B (red area in Figure 5.1) both for *T. trichiura* (χ^2 = 185.4, df = 7, P<0.001) and *A. lumbricoides* (χ^2 = 166.7, df = 7, P<0.001). At the mid-line (October 2015) and endline surveys (May 2016), the reduction of infection intensity for both types of STH was significant as shown by the considerably larger green area in Figure 5.1, both for *T. trichiura* ($F_{(7, 631)} = 94.6$, $P<0.001$) and *A. lumbricoides* ($F_{(7, 631)} = 92.2$, $P<0.001$).

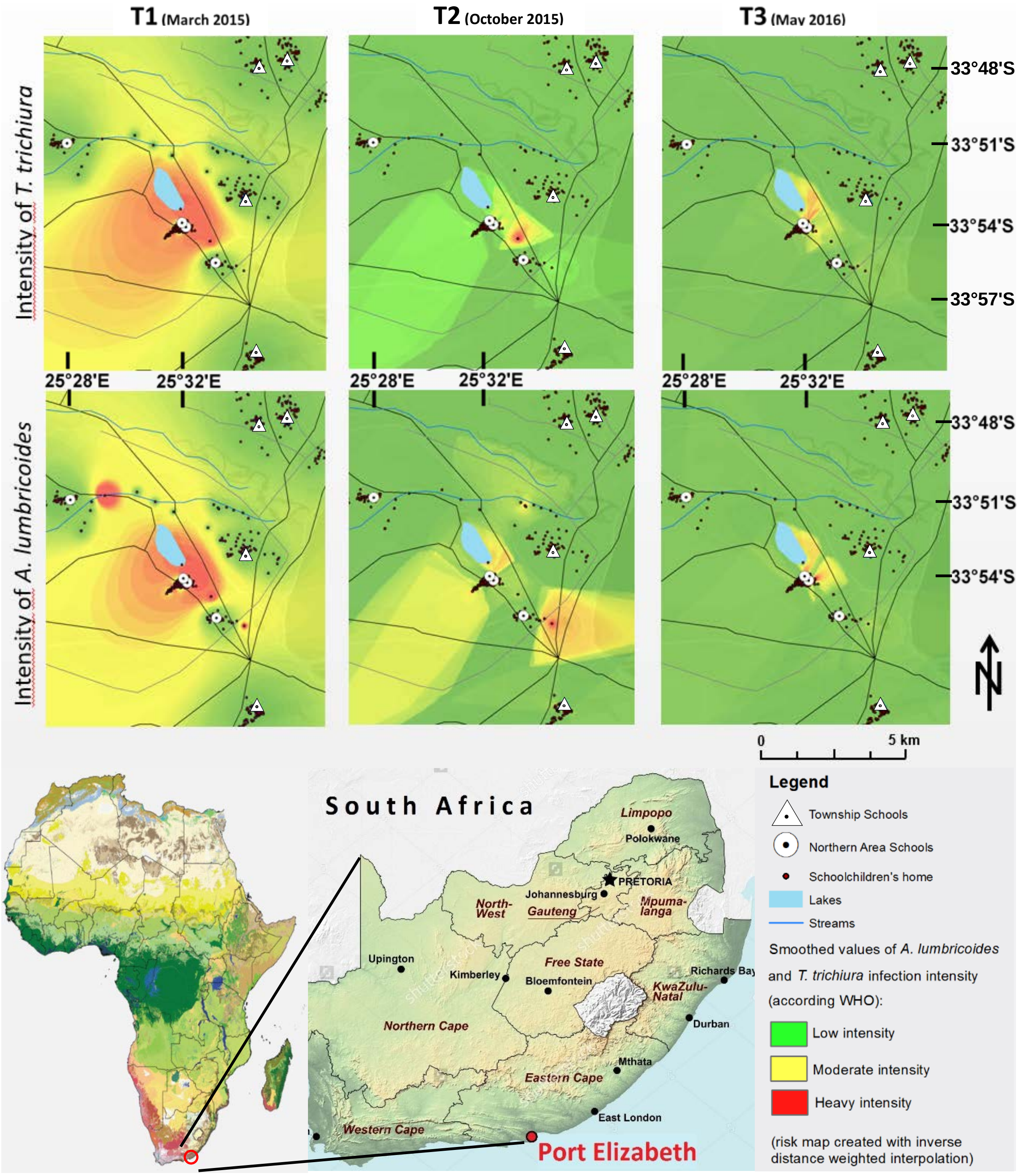

Figure 5.1 *Ascaris lumbricoides* and *Trichuris trichiura* infection intensities, stratified according to World Health Organization guidelines. The study was carried out in the northern part of Port Elizabeth, South Africa between March 2015 and May 2016. Smoothed maps based on 638 geographical coordinates of schoolchildren's homes are given.

Note. Low intensity of infection: *A. lumbricoides*, 1-4,999 EPG; *T. trichiura*, 1-999 EPG
Moderate intensity of infection: *A. lumbricoides*, 5,000-49,999 EPG; *T. trichiura*, 1,000-9,999 EPG
High intensity of infection: *A. lumbricoides*, ≥50,000 EPG; *T. trichiura*, ≥10,000 EPG

At baseline, we recorded a mean *A. lumbricoides* infection intensity among infected schoolchildren of 9,554 EPG (SD = 26,245 EPG) (Table 5.1). Seven months after a first round of deworming, the mean infection intensity of *A. lumbricoides* was more than halved to 4,317 EPG (SD = 15,665 EPG). Another seven months later, at the end-line survey in May 2016, the mean infection intensity was further reduced to 1,684 EPG (SD = 8,082 EPG). With regard to *T. trichiura* infections, the mean infection intensities among infected schoolchildren were 664 EPG (SD = 2,787 EPG) at baseline, halved to 331 EPG (SD = 1,457 EPG) at mid-line and reduced to 87 EPG (SD = 382 EPG) at the end. The highest *A. lumbricoides* egg count was 217,608 EPG, while the highest *T. trichiura* egg count was 33,900 EPG, both observed during the baseline cross-sectional survey.

Table 5.1. Change of infection intensities of *Ascaris lumbricoides* and *Trichuris trichiura* among 638 schoolchildren from disadvantaged communities in Port Elizabeth, South Africa over the 14-month study period.

Intensity of infection	Observations (n)	Mean[a]	IQR[b]	Minimum	Maximum
A. lumbricoides					
EPG[c] T1	638	9,554	324	0	217,608
EPG[c] T2	638	4,317	0	0	118,728
EPG[c] T3	638	1,684	0	0	100,956
T. trichiura					
EPG[c] T1	638	664	0	0	33,900
EPG[c] T2	638	331	0	0	17,892
EPG[c] T3	638	87	0	0	6,108

[a]Calculated among infected children only

[b]Interquartile range (difference between 75th and 25th percentiles)

[c]Eggs per gram of stool

5.4 Outlook

Specific public health interventions are warranted given the high prevalence and intensity of two of the three STH species, *i.e.*, *A. lumbricoides* and *T. trichiura*, observed during a baseline cross-sectional survey among children in two out of eight schools surveyed in poor neighbourhoods. Discussions with local health and education authorities revealed that preventive chemotherapy (with either albendazole or mebendazole) against STH has been neglected in recent years. Our data confirm that multiple rounds of deworming targeting school-aged children is an effective approach. Following national and international guidelines, we recommend the following treatment strategies: (i) individual testing and treatment of infected children are indicated if the STH prevalence is below 20% (seen in five of the schools); (ii) annual deworming if the prevalence ranges between 20% and 50% (seen in one school); and (iii) biannual treatment of all learners if the prevalence exceeds 50% (seen in two schools). The high spatial heterogeneity noted suggests that data from additional schools in different neighbourhoods will be needed to determine a locally appropriate intervention strategy, which ideally should not only be carried out by the school community but cover the entire local population at risk. Lastly, such activities should be complemented by efforts to strengthen hygiene awareness and to improve related behaviour such as hand washing with soap along with improved water and sanitation infrastructure – collectively known as WASH interventions – in schools and households alike (Strunz *et al.*, 2014).

Our findings should be interpreted in the light of several limitations. First, only a single stool sample was collected before each round of deworming, and subjected to duplicate Kato-Katz thick testing. Hence, some STH infections, particularly those of light intensity, were missed (Steinmann *et al.*, 2008). It follows that the ‘true’ infection prevalence is likely to be even higher than reported in our study. Second, we focussed only on Grade-4 children attending disadvantaged quintile-3 schools. Generalizability of our findings to a broader population is thus not possible. Third, we employed an IDW method for risk mapping. This univariate approach has shortcomings as it does not consider individual and environmental risk factors. Hence, a Bayesian-based geostatistical approach should be considered, ideally using zero-inflated models to account for the excess number of children without STH infections in six of the eight surveyed schools (Vounatsou *et al.*, 2009). Fourth, the current risk maps do not deal with the uncertainty in the estimates as variation in risk due to child-specific traits (*e.g.*

behavioural and genetic characteristics), as described, for example, by (Diggle *et al.*, 2007). Finally, the reduction in STH infection intensities cannot be attributed solely to deworming interventions, since the complex temporal interaction between host and parasite can only be displayed to a limited extent in the mathematical model presented here.

Box 1. Purpose of the documentation and risk maps.

- To visualize the spatial and temporal changes in the STH infection risk profile patterns among school-aged children between March 2015 and May 2016 in the light of three rounds of deworming.
- To facilitate access to this information for a broad range of stakeholders (staff of the project schools, parents/guardians, epidemiologists and health specialists) in Port Elizabeth, as well as public health policy makers and the Department of Health and Education in South Africa.

Box 2. Applied software.

- ArcGIS version 10.2.1 (ESRI; Redlands, CA, USA).
- Microsoft PowerPoint 2013 (Microsoft Corporation; Redmond, WA, USA).
- Camtasia Studio 9 (TechSmith Corporation; Okemos, MI, USA).

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Ethical approval: The survey was approved by the ethics committees of Northwest and Central Switzerland (EKNZ; reference no. 2014-179, approval date: 17 June 2014); the Nelson Mandela Metropolitan University (NMMU; study number H14-HEA-HMS-002, approval date: 4 July 2014); the Eastern Cape Department of Education (approval date: 3 August 2014) and the Eastern Cape Department of Health (approval date: 7 November 2014). The study is registered at ISRCTN registry under controlled-trials.com (unique identifier: ISRCTN68411960, registration date: 1 October 2014).

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CHAPTER 6

6.1 Effect of a multidimensional physical activity intervention on body mass index, skinfolds and fitness in South African children: Results from a cluster randomised controlled trial

Original article

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Conflict of interest:
The authors declare no conflict of interest.

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6.2 Abstract

Background: Obesity-related conditions impose a considerable and growing burden on low- and middle-income countries, including South Africa. We aimed to assess the effect of twice a 10-week multidimensional school-based physical activity intervention on children's health in Port Elizabeth, South Africa.

Methods: A cluster randomised controlled trial was implemented from February 2015 to May 2016 in grade 4 classes in eight disadvantaged primary schools. Interventions consisted of physical education lessons, moving-to-music classes, in-class activity breaks and school infrastructure enhancement to promote physical activity. Additionally, deworming and school feeding were offered. Primary outcomes included cardiorespiratory fitness, body mass index (BMI) and skinfold thickness. Explanatory variables were socioeconomic status, self-reported physical activity, stunting, anaemia and parasite infections. Complete data were available from 746 children.

Results: A significantly lower increase in the mean BMI Z-score (estimate of difference in mean change: -0.17; 95% confidence interval (CI): -0.24 to -0.09; $P<0.001$) and reduced increase in the mean skinfold thickness (difference in mean change: -1.06; 95% CI: -1.83 to -0.29; $P=0.007$) was observed in intervention schools. No significant group difference occurred in the mean change of cardiorespiratory fitness ($P>0.05$).

Conclusions: These findings show that a multidimensional school-based physical activity intervention can reduce the increase in specific cardiovascular risk factors. However, a longer and more intensive intervention might be necessary to improve cardiorespiratory fitness.

Keywords: Body mass index; cardiorespiratory fitness; intestinal protozoa; physical activity programme; school-aged children; soil-transmitted helminths; South Africa

6.3 Introduction

Non-communicable diseases (NCDs) and obesity-related conditions, such as diabetes and cardiovascular diseases, impose a considerable and rapidly growing burden on low- and middle-income countries (LMICs) (Marshall, 2004). Physical inactivity and unhealthy diet, particularly low vegetable and fruit intake and excess salt and sugar consumption, have emerged as new leading risk factors, accounting for 10% of the global burden of disease (Lim et al., 2012). In 2010, for the first time, overweight replaced under-nutrition as a risk factor in the Global Burden of Disease (GBD) study (Lim et al., 2012). Indeed, overweight is a rapidly growing epidemic affecting all socioeconomic strata and ethnicities (Ogden et al., 2006). Factors that contribute to the increase in average body fat are excessive energy intake governed by fast food consumption, and a decrease in energy expenditure through physical inactivity, partially explained by sedentary behaviour (*e.g.*, television viewing and personal transport by automobile) (Robinson, 1999, Ekelund et al., 2004). A meta-analysis by Guerra and colleagues with data from 11 randomised trials suggests that, regardless of the potential benefits of physical activity in the school environment, school-based physical activity interventions did not have any significant effects on body mass index (BMI) (Guerra et al., 2013), while another non-randomised trial by Li *et al.* reported favourable effects (Li et al., 2014).

Representative surveys revealed that the South African population has moved towards a disease profile similar to Western countries, where a considerable proportion of preschool- and school-aged children are overweight or obese, and increasing proportions of deaths among adults are attributed to chronic diseases of lifestyle (Steyn and Damasceno, 2006, Kipping et al., 2008). South Africa’s 2018 Report Card on Physical Activity for Children and Youth highlights the current concerns for health and wellbeing of children and youth related to declining physical activity levels (Uys et al., 2016). Moreover, South Africans consume about three times the global average of soft drinks, and intake of fast food is reported at least three times a week by more than two thirds of adolescents (Uys et al., 2016). Meanwhile, socioeconomically deprived communities with a high burden of infectious diseases persist in South Africa (Müller et al., 2016b, Gall et al., 2017, Becker et al., 2017).

In the paper presented here, we examined whether participation in the ‘Disease, Activity and Schoolchildren’s Health’ (DASH) multidimensional physical activity intervention programme would improve children's cardiorespiratory fitness and counteract an excess increase of BMI and skinfold thickness. We took into account baseline adjustments for potential sociodemographic confounders and soil-transmitted helminth infection status. The overarching purpose of the DASH study was to investigate the dual disease burden (*i.e.*, NCDs and infectious diseases) among children in primary schools in disadvantaged neighbourhoods (Yap et al., 2015).

6.4 Methods

6.4.1 Study area and population

The study was carried out in Port Elizabeth in the Eastern Cape province of South Africa (geographical coordinates: 34°07’54’’ to 33°57’29’’ S latitude and 25°36’00’’ to 25°55’49’’ E longitude). Recruitment of schools commenced in September 2014 and two 10-week multidimensional physical activity interventions were implemented in July-September 2015 and February-April 2016. Overall, 103 quintile 3 primary schools were eligible for participation. South Africa’s public schools are classified into five groups, with quintile five standing for the least poor and quintile one standing for the poorest. The quintiles are determined through the national poverty table, prepared by the treasury. Areas are being ranked on the basis of income levels, dependency ratios and literacy rates in the area. The quintile ranking of a school determines the no-fee status of the school and also the amount of money that a school receives, with the poorest schools receiving the greatest per-learner allocation (Hall and Giese, 2009).

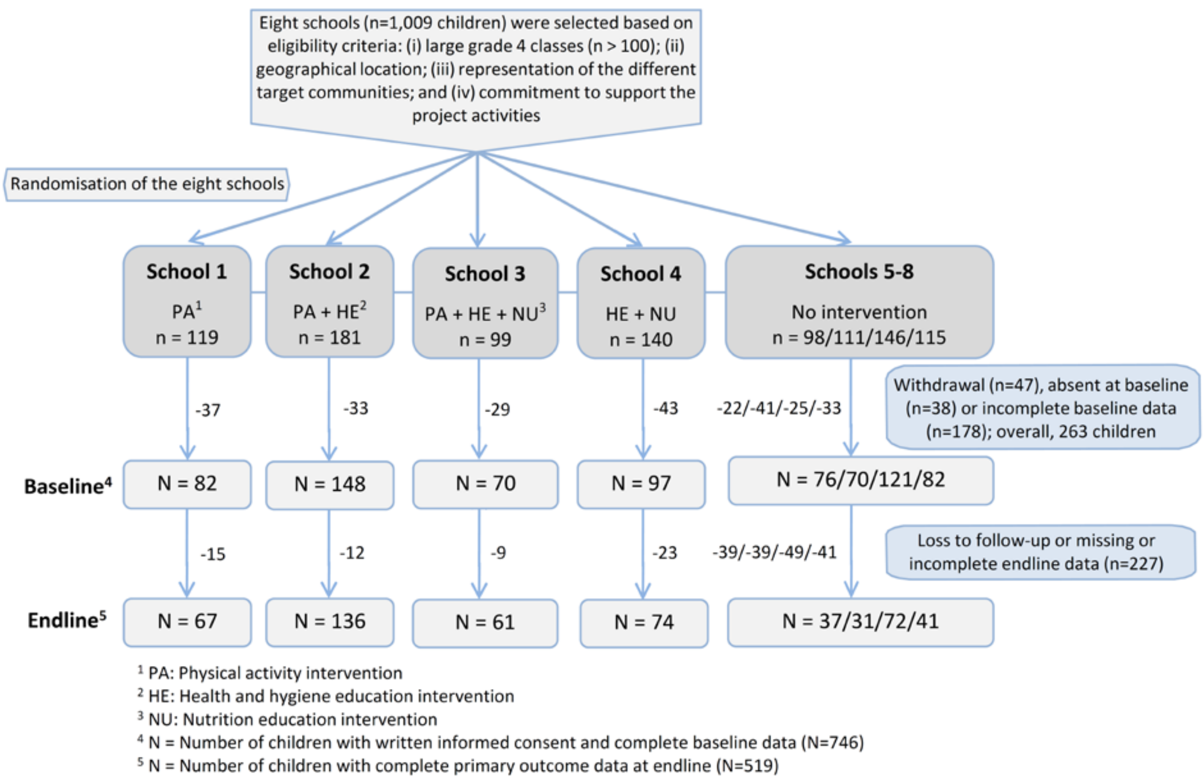

Figure 6.1 Selection of intervention sites (schools) for the “*Disease, Activity and Schoolchildren’s Health*” (DASH) study, including flow chart of study participants with detailed information on all intervention arms from the randomisation of schools to the endline assessment of schoolchildren, Port Elizabeth, South Africa, 2015 and 2016.

From the 103 quintile 3 schools, 25 schools expressed an interest, as documented in a response letter. Those 25 schools were invited to an information sharing meeting that was attended by 15 schools. Among the 15 schools, seven did not satisfy the chief criterion of having at least 100 learners in grade 4, and hence, were excluded. Eight schools were selected based on (i) sufficiently large grade 4 classes (n>100 children); (ii) geographical location; (iii) representation of the various target communities; and (iv) commitment to support the project activities (Figure 6.1). In South Africa, physical education is generally neglected in disadvantaged schools due to resource limitations and priority given to academic subjects, although two weekly lessons are officially included in the curriculum.

The study population consisted of coloured children (mixed race ancestry), usually Afrikaans speaking, and black African children, mainly Xhosa speaking. Children's age ranged between 9 and 14 years with mean age of 11.2 years (standard deviation 0.9 years) (Yap et al., 2015). The following inclusion criteria were employed: (i) willingness to participate; (ii) written informed consent by a parent/guardian; (iii) no participation in other clinical trials during the study period; and (iv) not suffering from medical conditions preventing participation in a maximum exercise test, as determined by qualified medical personnel.

6.4.2 Study design and randomisation

Enrolment of schools was conducted by the research team. The DASH study was designed as a cluster randomised controlled trial. In order not to contaminate intervention effects, schools rather than classes were randomised (Table S1). Generating the allocation sequence by a simple randomisation of the schools was carried out by the research team on the basis of a computer-generated random number list. Among the eight available schools, three different interventions were implemented in four different combinations. One of the interventions, which is the primary focus of the current paper, involved additional physical activity lessons (PA), while the other two consisted in a health and hygiene education (HE) and a nutrition education (NE) programme, respectively. First, four schools not to get any intervention were randomly selected, and then each of the four remaining schools was randomly allocated to one of the following intervention combinations: a) PA+HE+NU, b) PA+HE, c) PA alone, and d) HE+NU (Yap et al., 2015, Gall et al., 2018) (Table S2). The PA intervention was thus carried out in three of the eight schools. No financial incentives were provided; neither to the school authorities, nor to the participating children.

6.4.3 Interventions

We developed a multidimensional physical activity intervention in collaboration with education authorities, teachers and students from the participating schools. As shown in Figure 6.2, the multidimensional physical activity intervention programme consisted of four components: (i) two 40 min physical education lessons per week; (ii) one weekly 40 min moving-to-music lesson; (iii) regular in-class physical activity breaks incorporated into the main school curriculum; and (iv) enhancement of the school environment to be more physical activity friendly (*e.g.*, installation of activity stations and a variety of painted games).

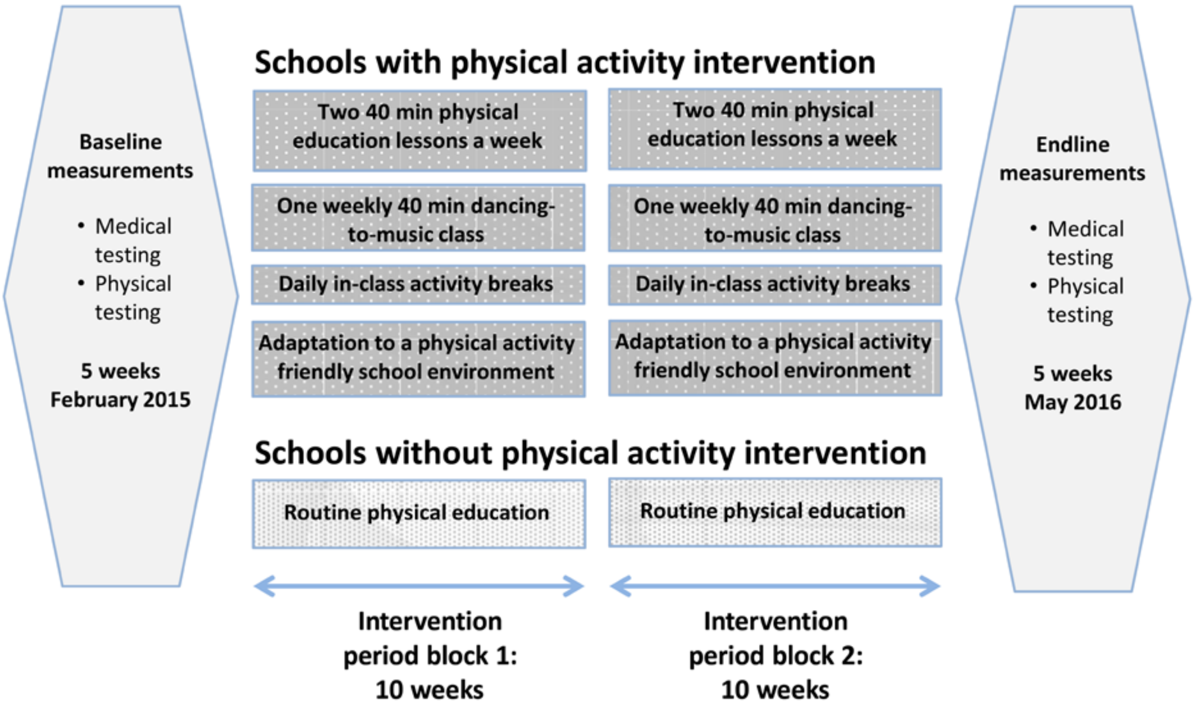

Figure 6.2 Timetable and content of the children's assessments and the multidimensional physical activity intervention programme, Port Elizabeth, South Africa in 2015 and 2016. The total duration of physical activity for schools with physical activity intervention was 55 hours, compared to 15 hours for schools without physical activity intervention.

The intervention components were applied in schools during official hours, and were taught in collaboration with the life orientation teachers. The dancing lessons were led by students from the Nelson Mandela University (NMU). The control group continued to follow their usual school curriculum. At the beginning of the study, we carried out project information sharing sessions with principals, teachers, parents and school governing bodies. Workshops with the life orientation teachers and class teachers were organised to discuss the materials and information provided during the intervention. Physical education lessons were given twice per week covering two 10-week periods. From the first 10-week intervention block to the second, the research team optimised the intervention components to render them more efficient with an increased intensity. All the lessons adhered to the requirements of the South African Curriculum and Assessment Policy Statement (CAPS). Teachers designated to provide the physical education were assisted by a trained physical education coach for one of the two weekly lessons, while the teachers thereafter taught the subsequent lesson on their own. A physical education lesson lasted 40 min, starting with a 5 min warm-up and concluding with a cool-down towards the end of the lesson. The physical education classes were taught outside on either grass or cemented areas and most children wore light sports clothing. Sports equipment for the lessons (*e.g.*, bean bags, colour bands, skipping ropes, cones and diverse balls) was donated to the schools. In addition to the physical activity intervention, two supplementary programmes were conducted in selected schools. The first one was a health and hygiene education programme to increase children's awareness for communicable diseases and the second one a nutrition education and supplementation programme to contribute to the awareness of healthy diet, as described in the study protocol published elsewhere (Yap et al., 2015) and summarised in the supplementary material of the current piece (Table S2).

6.4.4 Ethics statement

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki and was cleared by the ethics committees of Northwest and Central Switzerland (reference no. 2014-179), the Nelson Mandela University (study number H14-HEA-HMS-002), the Eastern Cape Department of Education and the Eastern Cape Department of Health. The study is registered at ISRCTN registry under controlled-trials.com (identifier: ISRCTN68411960). There were no injuries or other adverse events during the physical activity lessons. Soil-transmitted helminth infections were managed according to guidelines put forth by the World Health Organization (WHO) and national treatment recommendations.

6.4.5 Procedures

Baseline and endline measurements took place at eight disadvantaged quintile 3 primary schools before and after the implementation of the multidimensional physical activity intervention. Primary outcome measures included anthropometric indicators (*i.e.*, height, weight and skinfolds; the latter including triceps and subscapular) and cardiorespiratory fitness. Secondary outcomes were socioeconomic status (SES), self-reported physical activity, haemoglobin (Hb) and infection with soil-transmitted helminths and intestinal protozoa.

Children's body weight was measured once to the nearest 0.1 kg (Micro T7E electronic platform scale, Optima Electronics; George, South Africa). Height was assessed to the nearest 0.1 cm with a Seca stadiometer (Surgical SA; Johannesburg, South Africa). Height and BMI (defined as weight [kg]/height $[m]^2$) were standardised according to WHO guidelines, resulting in HAZ (height for sex and age) and BMIZ (BMI for sex and age) scores (de Onis et al., 2007). Stunting was defined as sex-adjusted height-for-age Z-score (HAZ) <-2, overweight as BMIZ score of +1 to +2, and obesity as BMIZ score of >+2. Skinfold-thickness was measured three times at triceps and subscapular positions, using a Harpenden skinfold caliper (Niederer et al., 2009, Puder et al., 2011).

Cardiorespiratory fitness was assessed using the 20 m shuttle run test, adhering to a standard test protocol (Léger et al., 1988, Léger et al., 1984). Most of the schoolchildren wore school or street shoes, while some ran barefoot. In brief, when a child failed to follow the pace for two consecutive intervals, the child was asked to stop running. As the final score, we noted the number of fully completed 20 m laps and converted the results in VO_2 max values, according to a standard protocol (Léger et al., 1984).

We measured Hb concentration once to the nearest 0.01 g dl^{-1} with a HemoCue® Hb 301 system (HemoCue®AB; Ängelholm, Sweden). After swabbing the child's fingertip with alcohol, a nurse or qualified field worker pricked the fingertip with a safety lancet and squeezed gently to obtain two drops of blood. The first drop was wiped away with the alcohol swab and the second drop was collected with a microcuvette. Anaemia was defined as an Hb concentration ≤11.4 g dl^{-1} (Gwetu et al., 2017).

The parasitological work-up is detailed in the study protocol (Yap et al., 2015). In brief, the Kato-Katz technique was used on the stool samples to identify and count the number of soil-transmitted helminth eggs that were reported for each species separately. Additionally, a Crypto-Giardia Duo-Strip® rapid diagnostic test (RDT) (CORIS, BioConcept; Gembloux, Belgium) was performed for the detection of *Cryptosporidium* spp. and *Giardia intestinalis* (Katz et al., 1972). Deworming was offered to infected children or the entire school, depending on school prevalence according to WHO and national treatment guidelines (Müller et al., 2016a). The SES index is based on household asset ownership and housing characteristics, determined by a questionnaire completed by the participants, which also examined self-reported physical activity (Health Behaviour in School-aged Children; HBSC) (see supplementary material, Table S3) (Vyas and Kumaranayake, 2006). The detailed test description is provided in the study protocol (Yap et al., 2015).

6.4.6 Statistical analysis

Details of the sample size calculation have been described elsewhere (Yap et al., 2015). In brief, sample size was based on achieving sufficient precision in assessing the prevalence of soil-transmitted helminth infections at baseline, taking into account clustering within schools and classes as well as loss to follow-up, amounting to a total of 1,200 participants. We used linear mixed models with random intercepts of schools and classes to analyse changes in quantitative outcomes (cardiorespiratory fitness, BMIZ, skinfolds and self-reported physical activity) from baseline to follow-up. The effects of the three interventions, physical activity lessons, health and hygiene education and nutritional education, on these changes were simultaneously estimated using separate indicator variables for the three types of intervention. These analyses were adjusted for sex, age, HAZ, SES index, Hb, intestinal protozoa (*Cryptosporidium* spp. and/or *G. intestinalis*) and STH infection (*Ascaris lumbricoides* and/or *Trichuris trichiura*). To capture potential ceiling effects, we also ran models adjusting for the baseline values of the respective outcome variable.

In addition, we assessed intervention effects on the occurrence of symptoms or infections at follow-up i) among children having shown the respective condition already at baseline and ii) among children who did not show the respective condition before. Mixed logistic regression models were used to analyse intervention effects on the occurrence of the respective condition at follow-up in the respective subsample. They included the same random intercepts and covariates as the previously described linear mixed models.

To analyse intervention effects on the prevalence of symptoms or infections, we used mixed logistic regression models including the occurrence of the respective condition at baseline and follow-up as repeated outcomes. These models were adjusted for the same baseline covariates as the previous models and included a random intercept for each child in addition to the random intercepts of schools and classes. To distinguish baseline and follow-up observations, an indicator variable for period with values 0 for baseline and 1 for follow-up was introduced. Intervention effects on the prevalence of a given condition were estimated using interaction terms between the intervention indicator variables and this period variable. In accordance with the focus of the present paper, only the estimated effects of the physical activity intervention are reported in the main text, while the effects of the other two interventions are reported in the on-line supplement (https://www.mdpi.com/1660-4601/16/2/232#supplementary).

Furthermore, differences at baseline between the intervention and control group with regard to primary outcome measures, such as obesity, skinfolds and cardiorespiratory fitness, were investigated. We also examined potential heterogeneity of the intervention effects across subgroups (*e.g.*, males *vs.* females; lower *vs.* higher SES). This was done by stratification into two categories of the respective variable (using a median split in case of quantitative characteristics) (Woringer and Schutz, 2003). An additional analysis, excluding one of the schools, was conducted according to a factorial design (see supplementary material, Table S4). Statistical analyses were performed using STATA version 13.0 (STATA Corp.; College Station, TX, USA). Statistical significance was defined as $P<0.05$.

6.5 Results

Of the 1,009 grade 4 schoolchildren with written informed consent from their parents/guardians, complete baseline data were available from 746 children (Figure 6.1). Reasons for exclusion were withdrawal, absence during baseline data collection and incomplete baseline data (*e.g.*, reported health problems precluding participation in the cardiorespiratory fitness test). All subsequent analyses pertained to the 746 children (372 girls, 49.9%; and 374 boys, 50.1%; mean age 10.0 years). 519 children presented a full data record after endline, of which 264 children participated in the physical activity intervention. No adverse events occurred during the physical activity intervention.

Table 6.1 summarises the baseline characteristics of the study participants, stratified by schools with physical activity intervention and schools without physical activity intervention. No significant differences in primary outcome measures, such as obesity, skinfolds and cardiorespiratory fitness at baseline were detected, when comparing schools with and without physical activity intervention (all $P>0.05$).

Table 6.1 Baseline characteristics of 746 children from Port Elizabeth, South Africa, in February 2015.

	Total (n=746)	Schools with physical activity intervention (n=300)	Schools without physical activity intervention (n=446)
In numbers (percentages)			
Girls	372 (49.9)	150 (50.0)	222 (49.8)
Overweight[a]	102 (13.7)	38 (12.7)	64 (14.3)
Obese[b]	39 (5.3)	15 (5.0)	24 (5.4)
Stunted[c]	86 (11.5)	46 (15.3)	40 (9.0)
Anaemic[d]	138 (18.5)	67 (22.3)	71 (15.9)
Infected with intestinal protozoa[e]	120 (16.1)	61 (20.3)	59 (13.2)
Infected with soil-transmitted helminths (STHs)[f]	235 (31.5)	132 (44.0)	103 (23.1)
In means (SD)			
Age in years	10.0 (0.9)	10.1 (0.9)	9.9 (1.0)
Height in cm	133.3 (7.1)	132.6 (7.1)	133.8 (7.0)
Skinfolds in mm	9.0 (4.5)	9.0 (4.5)	9.0 (4.4)
Shuttle run in laps	36.3 (17.3)	35.6 (17.0)	36.8 (17.4)
VO_2max[g] in $ml \times kg^{-1} \times min^{-1}$	46.1 (4.3)	45.8 (4.1)	46.3 (4.3)
Overall SES index[h]	0.0 (2.8)	-0.1 (2.7)	0.0 (2.9)
Poorest	-4.8 (2.3)	-4.5 (2.5)	-5.0 (2.1)
Second quintile	-0.3 (0.6)	-0.2 (0.6)	-0.4 (0.6)
Less poor	1.0 (0.2)	1.0 (0.2)	1.0 (0.2)
Fourth quintile	1.7 (0.2)	1.7 (0.2)	1.7 (0.2)
Least poor	2.3 (0.2)	2.3 (0.2)	2.3 (0.2)
Score of self-reported physical activity	8.4 (3.8)	9.1 (3.7)	7.8 (3.8)

[a] Overweight: >+1 SD (equivalent to BMI 25 kg/m^2 at 19 years)
[b] Obesity: >+2 SD (equivalent to BMI 30 kg/m^2 at 19 years)
[c] Stunting is defined as height-for-age Z-score (HAZ) score <-2
[d] Anaemic is defined as haemoglobin concentration in blood ≤11.4 g dl^{-1}
[e] Infected with one or two intestinal parasite species (*Cryptosporidium* spp. and/or *Giardia intestinalis*)
[f] Infected with one or two soil-transmitted helminth (STH) species (*A. lumbricoides* and/or *T. trichiura*; no hookworm infections were diagnosed)
[g] Using age-adjusted test protocol from Léger *et al.*[17]
[h] Socioeconomic status (SES) is based on self-reported household characteristics and assets, and calculated based on factor scores of principal component analysis (PCA)

Cardiorespiratory fitness and body composition results are presented in Table 6.2, along with adjusted estimates of intervention effects defined as difference in mean changes. We observed a significantly lower increase in mean BMIZ (estimated difference in mean change: -0.17; 95% confidence interval (CI): -0.24 to -0.09; P<0.001) and reduced increase in the mean thickness of skinfolds (difference in mean change: -1.06; 95% CI: -1.83 to -0.29; P=0.007) from baseline to endline when comparing children from the intervention group with their peers in the control group (intervention effects on primary outcome measures from baseline to midline and from midline to endline can be found in the supplementary material Table S5 and S6, respectively).

Table 6.2 Cardiorespiratory fitness and obesity outcome measures among children from Port Elizabeth, South Africa, at baseline (February 2015) and after a multidimensional physical activity intervention at the 16-month endline survey (May 2016). Values are unadjusted means (standard deviations) unless specified otherwise and estimated effects of the physical activity intervention on the mean changes in the respective outcome measures between baseline and endline, adjusted for the respective baseline value of sex, age, HAZ, SES index, Hb, soil-transmitted helminth (*A. lumbricoides* and/or *T. trichiura*) and intestinal protozoa (*Cryptosporidium* spp. and/or *G. intestinalis*) infection.

Variables	Schools with physical activity intervention		Schools without physical activity intervention		Intervention effect[a]		
	Baseline (n=300)	Endline (n=264)	Baseline (n=446)	Endline (n=255)	Estimate[b] (95% CI)	P-value	ICC[c]
Cardiorespiratory fitness							
Shuttle run (laps)	35.6 (17.0)	34.5 (17.9)	36.8 (17.4)	35.3 (18.7)	-0.56 (-4.67 to 3.56)	0.79	0.04
VO_2max[d] ($ml \times kg^{-1} \times min^{-1}$)	45.8 (4.1)	43.5 (4.7)	46.3 (4.3)	44.0 (4.8)	-0.14 (-1.17 to 0.88)	0.78	0.03
Obesity							
BMIZ[e]	-0.1 (1.2)	-0.1 (1.3)	0.0 (1.2)	0.2 (1.3)	-0.17 (-0.24 to -0.09)	<0.001	<0.01
Skinfolds[f] (mm)	9.0 (4.5)	9.6 (4.6)	9.0 (4.4)	10.1 (5.9)	-1.06 (-1.83 to -0.29)	0.007	0.02
Mean of self-reported physical activity[g]	9.1 (3.7)	9.0 (3.1)	7.8 (3.8)	9.9 (3.4)	-1.08 (-2.36 to 0.18)	0.09	0.04

[a] Schoolchildren from the intervention group accomplished a multidimensional physical activity intervention programme between baseline and endline, as described in Figure 2; adjustment was also made for two health and nutrition education programmes conducted at some of the schools in either group

[b] Estimate of respective intervention effect on the change in the respective outcome measure from baseline to endline, with 95%-confidence interval, P-value and ICC. The underlying linear mixed models included binary factor variables for each of the two interventions A (physical fitness intervention) and B (combination of a health education and a nutritional intervention) providing the respective effect estimates, along with baseline values of age, sex, height-for-age Z-score (HAZ), haemoglobin, socioeconomic (SES) index, protozoa- and soil-transmitted helminth (STH) infection status and random effects for classes and schools

[c] Proportion of unexplained variance attributable to clustering within schools and classes (intraclass correlation coefficient; ICC)

[d] Using age-adjusted test protocol from Léger *et al.*[17]

[e] Sex-adjusted BMI-for-age Z-score (BMIZ)

[f] Average of six measurements (triceps and subscapular three times each)

[g] Score generated based on self-reported physical activity in the personal free time over the past 7 days and intense exercises outside structured school hours (range: from 1 to 14; 14 being the most active)

Mean changes in 20 m shuttle run test results and VO_2 max were comparable between the two groups with a positive but statistically non-significant tendency for the intervention group. Self-reported physical activity remained stable in the intervention group but increased in the control group, resulting in a non-significant difference in mean change of -1.08 (95% CI: -2.36 to 0.18; P=0.09). Intra-class correlations were all <0.05, showing a low level of unexplained variability between schools and classes. In the intervention group, the frequency of overweight children slightly declined from 12.7% (out of 300) to 11.5% (out of 278), while obesity slightly increased from 5.0% (out of 300) to 6.5% (out of 278). In the control group, both the prevalence of overweight and obese children increased (overweight from 14.4% [out of 446] to 17.2% [out of 405] and obesity from 5.4% [out of 446] to 8.5% [out of 405]). Stratified estimates of intervention effects on primary outcome measures are presented in Figure 6.3.

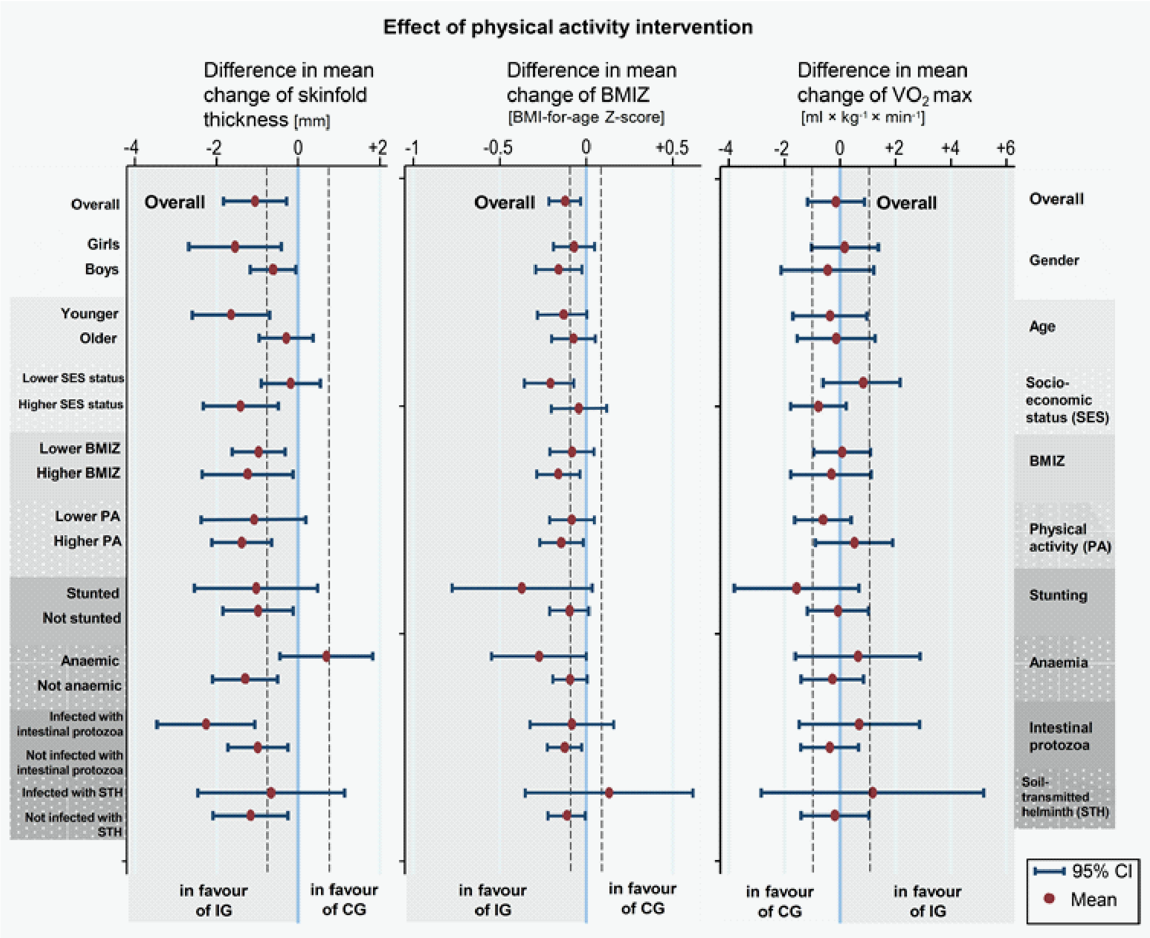

Figure 6.3 Estimated intervention effects on VO_2 max, sex- and age-adjusted Z-score of body mass index (BMI) and thickness of skinfolds in different strata of children from baseline (February 2015) to 16-month endline (May 2016). Intervention effects were defined as differences in the mean longitudinal changes of the respective outcomes associated with the physical activity intervention.

In particular, differential intervention effects on skinfold thickness were observed according to sex (with a higher benefit among girls), age (with higher benefit among younger children) and to SES (with higher SES being advantageous) as well as between anaemic and non-anaemic children in which the intervention had opposite effects.

Table 6.3 summarises the baseline and endline measurements of binary outcome variables (all secondary outcomes) affecting cardiorespiratory fitness or body composition, along with a description of the intervention effects on the re-occurrence (proportion of lasting cases), new occurrence (proportion of new cases) and prevalence (proportion of cases) of the respective conditions, as expressed by ORs. For none of the binary outcomes considered, the change in prevalence between baseline and endline, the new occurrence or the re-occurrence at follow-up was significantly associated with the intervention. At baseline, the prevalences of stunting, anaemia and infection with either soil-transmitted helminths or intestinal protozoa were 6.3%, 6.4%, 20.9% and 7.1% higher in the intervention (n=300) than in the control group (n=446), while after 16 months, the same indicators were 5%, 0.9%, 27.3% and 10.3% higher, respectively.

Table 6.3 Stunting, anaemia and intestinal parasite infections among children from Port Elizabeth, South Africa, at baseline (February 2015) and the 16-month endline survey (May 2016) for schools with and without physical activity intervention. Values are numbers (percentages) unless specified otherwise.

Binary variables	Schools with physical activity intervention		Schools without physical activity intervention		Intervention effect[a]	
	Baseline (n=300)	Endline (n=264)	Baseline (n=446)	Endline (n=255)	Odds ratio[b] (95% CI)	P-value
Stunted[c]	46 (15.3)	47 (17.8)	40 (9.0)	48 (12.8)	New occurrence: 0.68 (0.23 to 2.07)	0.50
					Re-occurrence: 0.68 (0.12 to 3.96)	0.67
					Prevalence: 0.76 (0.09 to 6.53)	0.81
Anaemic[d]	67 (22.3)	37 (14.0)	71 (15.9)	50 (13.4)	New occurrence: 1.36 (0.53 to 3.49)	0.52
					Re-occurrence: 0.82 (0.25 to 2.62)	0.73
					Prevalence: 0.93 (0.38 to 2.30)	0.87
Infected with soil-transmitted helminths (STHs)[f]	132 (44.0)	108 (40.9)	103 (23.1)	51 (13.6)	New occurrence: 2.33 (0.03 to 186.00)[g]	0.71
					Re-occurrence: 3.44 (0.04 to 298.70)[g]	0.59
					Prevalence: 1.92 (0.47 to 7.80)	0.36
Infected with intestinal protozoa[e]	61 (20.3)	54 (20.5)	59 (13.2)	38 (10.2)	New occurrence: 1.37 (0.65 to 2.90)	0.41
					Re-occurrence: 1.55 (0.58 to 4.17)	0.38
					Prevalence: 1.23 (0.47 to 3.22)	0.68

[a] Schoolchildren from the intervention group accomplished a multidimensional physical activity intervention programme between baseline and endline, as described in Figure 2; adjustment was also made for two health and nutrition education programmes conducted at some of the schools in either group

[b] Re-occurrence (proportion of lasting cases) and new occurrence (proportion of new cases): adjusted OR of the respective outcome at endline between intervention and control groups among children with respectively without the outcome at baseline in a mixed logistic regression model with random intercepts at the unit of school and class. Prevalence (proportion of cases): OR of the interaction term between follow-up period and intervention in a mixed logistic regression model with random intercepts at the unit of class and child. Variables adjusted additionally for in these models were age, sex, height-for-age Z-score (HAZ), haemoglobin, SES index, intestinal protozoa, and soil-transmitted (STH) infection status at baseline

[c] Stunting is defined as HAZ score <-2

[d] Anaemic is defined as haemoglobin concentration in blood ≤11.4 g dl^{-1}

[e] Infected with one or two intestinal parasite species (*Cryptosporidium* spp. and/or *Giardia intestinalis*)

[f] Infected with one or two soil-transmitted helminth species (*A. lumbricoides* and/or *T. trichiura*; no hookworm infections were diagnosed)

[g] The wide 95% CIs reflect strong heterogeneity between schools, with the vast majority of STH-infected children occurring in only two of the eight schools

6.6 Discussion

A twice-repeated 10-week multidimensional physical activity intervention contributed to a lower increase of BMI and thickness of skinfolds in schoolchildren from disadvantaged neighbourhoods in Port Elizabeth, South Africa. However, contrary to our hypothesis, no detectable effects were observed on cardiorespiratory fitness at the 16-month endline survey. Result modification for skinfold thickness and BMI by sex suggests that gender-specific interventions may be necessary. Although girls benefited more from the intervention in terms of skinfold thickness, they profited less regarding BMI. Without specific physical activity interventions, females might become obese during adolescence, a time of life when males are usually more physically active (*e.g.*, playing soccer), and hence, specific interventions readily tailored to females might need to kick in later.

A Cochrane review revealed that school-based physical activity programmes are generally effective in increasing physical activity and physical fitness in children and adolescents aged 6-18 years (van Sluijs et al., 2007). Furthermore, physical activity programmes may also be useful to improve systolic blood pressure and heart rate (López et al., 2018, Resaland et al., 2018). However, the authors concluded that the magnitude of the effect is small. Moreover, while the review included 44 studies, all of them were carried out in America, Europe and the People's Republic of China, which precludes generalisation to an African context. Indeed, there is a paucity of research conducted among school-aged children in LMICs, including South Africa. Yet, setting-specific insights regarding the effectiveness of school-based initiatives are necessary to promote physical activity, which in turn might improve children's health and wellbeing. We are aware of relevant previous research done in South Africa, specifically the HealthKick study (Draper et al., 2010). The HealthKick study was conducted in primary schools in low-income settings, but the prime focus was on healthy nutrition. A common observation in LMICs is the paucity and often low quality of sport and recreation facilities, coupled with a lack of qualified teachers offering physical education classes. Absence or only irregular physical education complicate the promotion of age-appropriate physical activity, particularly in disadvantaged schools (UNESCO, 2013).

Previous studies in South Africa focusing on school-based interventions promoting a healthy lifestyle have shown disappointing results and the implementation of successful projects is even more difficult in children with lower SES, where the benefit could potentially be largest (van Sluijs et al., 2007). Infectious diseases and lack of physical activity among school-aged children and adolescents are important factors that influence growth. Furthermore, it adds to the complexity that anthropometry and physical fitness are impacted by a wide range of environmental and behavioural factors, including infectious diseases and declining physical activity in adolescence. Of note, several studies have highlighted a possible compensation of supervised physical activities in the school against spontaneous physical activity outside of school hours (Møller et al., 2014, Frémeaux et al., 2011). The findings of these studies support the hypothesis that more activity in school at one time is compensated for by less activity during leisure time. However, efforts should be made to increase the overall activity levels in youth because primary prevention against overweight during this time of life is essential. Previous investigations of physical activity patterns of primary schoolchildren in disadvantaged neighbourhoods in South Africa have confirmed insufficient physical activity levels (Walter, 2011). For example, Kimani-Murage and colleagues reported that in a low-income South African setting, the co-existence of early stunting and adolescent obesity in females is a result of increasing physical inactivity (Kimani-Murage et al., 2010). This combination was particularly prevalent among black females, who showed the highest rates of physical inactivity (Walter et al., 2011). As physical inactivity during childhood can lead to poor health outcomes in adulthood, promotion of physical activity among school-aged children is pivotal to prevent obesity-related conditions and related increased morbidity later in life (Baker et al., 2007). The effect sizes of our physical activity intervention with respect to BMIZ and skinfold thickness raises hope that high intensity physical activity programmes in schools with a manageable duration can be used to combat excessive weight gain during adolescence. Additionally, in the face of weak healthcare systems, infectious diseases that are intimately connected with poverty are still widespread in disadvantaged South African schools (Draper et al., 2010). Such dual burdens constitute a major challenge for the healthcare system, and infections might themselves have a negative impact on children's nutritional status and cardiorespiratory fitness (Hürlimann et al., 2014, Yap et al., 2014).

Compared to results from recent studies in Switzerland, the cardiorespiratory fitness of the South African study cohort was slightly below average. Swiss children achieved the same cardiorespiratory fitness level at 7 years of age, 3 years earlier than their South African peers (Kriemler et al., 2010, Imhof et al., 2015). In contrast, Lang *et al.* reported slightly better reference values in South African than Swiss children (Lang et al., 2016). Comparing our reference values with data obtained from a systematic literature review that included 50 countries, our values were slightly higher (Tomkinson et al., 2017). Also, Yap *et al.* reported slightly lower VO_2 max results from south-west Yunnan province in the People's Republic of China, namely 45.6 $ml \times kg^{-1} \times min^{-1}$ for 9- to 12-year-old males and 44.7 $ml \times kg^{-1} \times min^{-1}$ for females of the same age (Yap et al., 2014). The high prevalence of chronic infections going hand-in-hand with fatigue and anaemia may contribute in part to the lower level of physical activity and complicate the performing of physical activity interventions. Furthermore, result modification of skinfold thickness by anaemia suggests that anaemia should be managed before accomplishing physical activity interventions, or else children might feel too tired to benefit from specific physical activity interventions.

Implementing a multidimensional physical activity intervention in schools in poor neighbourhoods was a challenging endeavour. Indeed, marginalised inhabitants of Port Elizabeth are still affected by the former Apartheid system (Southern Africa Development, 2013). A novelty of our study was the focus on health indicators of young primary schoolchildren in disadvantaged neighbourhoods, in communities with low SES and a high risk of inhabitants to develop obesity.

We were able to create, implement and measure the effect of a multidimensional physical activity intervention programme within an existing and productive research partnership, ensuring local relevance and acceptability and thus promoting sustainability. This intervention was perceived positively by the teachers (evaluation result: 4.2 on a 5-point Likert scale; 1 being poor and 5 excellent) and teachers and other education authorities expressed an interest to pursue the physical activity programme in the long term. The schoolchildren especially liked the weekly dance-to-music classes, perhaps as children are intrinsically motivated to move to music. The implementation of the intervention resulted in favourable effects on body composition, one of the major public health targets in LMICs (Kipping et al., 2008). Moreover, while school-based physical activity promotion has a long tradition in Western countries, the study presented here is among the few physical activity interventions implemented in an African context. Importantly, only few physical activity intervention programmes proved to be effective with regard to lowering the increase of BMI and body fat, the latter measured as thickness of skinfolds, in school-aged children (Kamath et al., 2008). We therefore assume that a multidimensional intervention might be particularly beneficial.

Our study has several limitations. First, the relevant motivation of teachers (Erturan-Ilker et al., 2018) to facilitate physical education classes was variable and influenced by unequal class sizes, the lack of formal qualifications for physical education and the fact that physical education lessons are generally not taught on a regular basis. Second, to achieve higher effects, an extended duration of the intervention, coupled with more extensive involvement of the school communities, school volunteers and parents/guardians may be needed, which might require changes in policies (van Sluijs et al., 2007). Third, no objective measurements of physical activity using accelerometers were pursued, which would have presented an objective and fine-grained picture (Meyer et al., 2013). Fourth, the sample size was relatively small and the intervention was only implemented in three out of eight schools for two 10-week periods because of logistic reasons. Fifth, concealment and blinding were not possible in our study design. Cluster randomised trials have a greater potential for bias than studies that allow concealment and blinding. Despite these limitations, the study provides evidence for the feasibility of designing, implementing and evaluating a multidimensional physical activity intervention in a low-resource setting (Bustinduy et al., 2011, Müller et al., 2016b).

Physical education in schools needs to consider local resources, conditions and preferences, while adhering to minimal standards to be effective. Our intervention was developed by physical education specialists in consultation with local stakeholders. Careful adaptation will be necessary before the intervention can be implemented and scaled up in other settings. Moreover, a longer duration, preferably covering the entire school year and expansion to include all school grades is imperative. Lastly, the promotion of extra-curricular physical activity and healthy nutrition should become an integral part of the programme. New donors have agreed to fund such an expanded intervention in South Africa and two additional countries in East and West Africa and the research-cum-action has started.

6.7 Conclusions

Our cluster randomised controlled trial provides evidence that a well-designed multidimensional physical activity programme can lower the increase in BMI and thickness of skinfolds in school-aged children from disadvantaged communities in Port Elizabeth, South Africa, but no significant effects on cardiorespiratory fitness were observed. To increase effectiveness and sustainability of the results, the intervention should be extended to cover the entire school term and adapted to additional age groups. As overweight is caused by diverse lifestyle behaviours, there is a need for longitudinal monitoring, with age, gender and school-grade specific assessments. Furthermore, dissemination of this school-based physical activity programme in South Africa may help to reduce risk factors for the development of chronic diseases among socially deprived children.

Supplementary Materials

The following are available online at https://www.mdpi.com/1660-4601/16/2/232# supplementary, Table S1: Descriptive results, stratified by physical activity intervention and control; Table S2: Intervention measures at eight primary schools in Port Elizabeth, South Africa; Table S3: Socioeconomic status among 746 schoolchildren aged 9-14 years from disadvantaged neighbourhoods in Port Elizabeth, South Africa in February 2015: Final results from the principal component analysis; Table S4: Additional analysis according to a factorial design[a] achieved after exclusion of one of the schools. Estimated parallel effects of a) physical fitness intervention and b) combined health education and nutritional intervention on the mean changes in the respective outcome measures between baseline and endline; Table S5: Cardiorespiratory fitness and obesity outcome measures from schoolchildren in Port Elizabeth, South Africa, at baseline (February 2015) and after a physical activity intervention (7-month midline; September 2015). Values are unadjusted means (standard deviations) unless specified otherwise and estimated effects of the physical activity intervention on the mean changes in the respective outcome measures between baseline and midline; Table S6: Cardiorespiratory fitness and obesity outcome measures from schoolchildren in Port Elizabeth, South Africa, at midline (September 2015) and after a physical activity intervention (16-month endline; May 2016). Values are unadjusted means (standard deviations) unless specified otherwise and estimated effects of the physical activity intervention on the changes in the respective outcome measures between midline and endline.

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Authors' Contributions

Conceptualisation, IM, CS, KE, MG, NP-H, RduR, HS, PS, JU, PY, CW and UP; Methodology, IM, CS, KE, MG, NP-H, RduR, HS, PS, JU, PY, CW and UP; Writing – original draft preparation, IM, CS, KE, MG, NP-H, RduR, HS, PS, JU, PY, CW and UP; Writing – review & editing, all authors; Investigation, IM, SG, DS, LA, SN, NJ, NSNH, PY, MG, RduR, UP and CW; Data curation, IM, SG, DS, LA, SN, NJ, CS, HS; Formal analysis, CS, IM; All authors provided comments on the drafts and have read and approved the final version of the paper prior to submission and re-submission. IM and UP are guarantors of the paper.

Conflicting Interests

All authors declare no competing interests.

Availability of Data and Material

The datasets are available from the corresponding author on reasonable request.

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6.9 Appendix

Table S1 Supplementary Material S1.

Schools with physical activity intervention (n=300; 3 schools, 11 classes)			Schools without physical activity intervention (n=446; 5 schools, 15 classes)	
Baseline February 2015	**Endline** May 2016	**Primary outcomes**	**Baseline** February 2015	**Endline** May 2016
300	278	BMI	446	405
300	272	Cardiorespiratory fitness	446	397
300	277	Average of six skinfolds	446	403
		Secondary outcomes		
300	277	Haemoglobin	446	401
300	300	Socioeconomic status	446	446
300	278	Self-reported physical activity	446	403
300	279	Stunting	446	402
300	264	Intestinal protozoa infection	446	374
300	264	STH infection	446	375

Table S2 Supplementary Material S2.

Study arm	Schools with physical activity intervention	Schools without physical activity intervention
Physical activity	School 1	
Physical activity and health/hygiene education	School 2	
Physical activity, health/hygiene education and nutrition education	School 3	
(No physical activity), health/hygiene education and nutrition education		School 4
(No physical activity)		Schools 5, 6, 7 and 8

Table S3 Supplementary Material S3.

Variable description	Absolute frequency (N)	Relative frequency (P)	Coefficient in factor score
Asset ownership			
Washing machine for clothes	530	0.71	0.13
Fridge	680	0.91	0.19
Freezer for food	599	0.80	0.17
Radio	596	0.80	0.07
Land line phone	231	0.31	0.07
Television	723	0.97	0.10
Cell phone	721	0.97	0.10
Car	455	0.61	0.14
Computer	457	0.61	0.16
Housing			
Shack in informal settlement	86	0.12	-0.25
Backyard shack	36	0.05	-0.06
Privately built house	50	0.07	0.06
RDP house[a]	301	0.40	0.11
Council house	273	0.37	0.05
House of zinc	84	0.11	-0.22
House of bricks	630	0.84	0.26
House of wood	32	0.04	-0.12
Bathroom	422	0.57	0.24
Electricity inside the house	722	0.97	0.18
Toilet inside the house	496	0.67	0.27
Flush toilet	627	0.84	0.25
Pit toilet, bucket or communal toilet	119	0.16	-0.25
Tabs inside house	555	0.74	0.25
Tab in the yard	120	0.16	-0.13
Water tank or communal tab	71	0.10	-0.22
Cooking with electricity	697	0.93	0.18
Cooking with gas, paraffin stove or fire	49	0.07	-0.18

[a] In South Africa: Reconstruction and Development Programme house

Table S4 Supplementary Material S4.

Variables	Physical activity intervention[b] Estimated effect [d] (95% CI)	P-value	Combination of health education and a nutritional intervention[c] Estimated effect[d] (95% CI)	P-value	ICC[e]
Cardiorespiratory fitness					
Shuttle run (laps)	-0.69 (-5.20 to 3.81)	0.76	-4.83 (-9.48 to -0.18)	0.04	0.044
VO_2max[f] ($ml \times kg^{-1} \times min^{-1}$)	-0.17 (-1.32 to 0.97)	0.76	-1.30 (-2.48 to -0.12)	0.03	0.038
Obesity					
BMIZ[g]	-0.16 (-0.24 to -0.09)	<0.001	-0.04 (-0.12 to 0.04)	0.28	0.00
Skinfolds[h] (mm)	-1.06 (-1.91 to -0.21)	0.02	0.67 (-0.19 to 1.54)	0.13	0.024
Mean in self-reported physical activity[i]	-1.05 (-2.36 to 0.26)	0.12	0.70 (-0.63 to 2.03)	0.3	0.055

[a] The two interventions distinguished in this analysis were a physical fitness intervention on the one hand (referred to as A) and the combination of a health education and a nutritional intervention (referred to as B) on the other hand. They were each represented by a binary factor in the analysis. After one school with physical fitness and health education intervention was excluded, there were 4 schools without any intervention and one school for each of the other combinations of the two factors (i.e., A, B and A+B)

[b] The physical fitness intervention consisted in physical education lessons taking place twice a week; weekly moving-to-music classes; in-class activity breaks; and school infrastructure adaptation to promote physical activity in two phases of 10 weeks each, as described in Figure 2 and it was applied in 3 of the 8 schools between baseline and endline. One of these schools was excluded from the present analysis because the physical activity intervention was combined with the health education programme only and not with the combined health education and nutritional intervention

[c] The combined health education and nutritional intervention (referred to as factor B) consisted in a series of classroom-based lessons to help increase the awareness for intestinal parasite infections and education on treatment and prevention methods, such as proper hygiene, sanitation habits and consuming clean water/food and to help increase the awareness for healthy nutrition. Furthermore, an analysis of the school feeding programme was done and the cooks in the schools were trained in basic nutrition and hygiene during preparation of the school meals. The schoolchildren were given a ready to use supplementary food (RUSF) in the form of an enriched lipid-based paste. The combination of these two additional programmes was applied in 2 of the 8 schools, once with additional application of the physical fitness intervention and once without

[d] Estimate of respective intervention effect on the change in the respective outcome measure from baseline to endline, with 95%-confidence interval. The underlying linear mixed models included binary factor variables for each of the two interventions A and B providing the respective effect estimates, along with baseline value of the respective outcome variable and baseline values of age, sex, height-for-age Z-score (HAZ), haemoglobin, socioeconomic (SES) index, protozoa- and soil-transmitted helminth (STH) infection status and random effects for classes and schools

[e] Proportion of unexplained variance attributable to clustering within schools and classes (ICC; intraclass correlation

coefficient)

[f] Using age-adjusted test protocol from Léger *et al.*[17]

[g] Sex-adjusted BMI-for-age Z-score (BMIZ)

[h] Average of six measurements (triceps and subscapular three times each)

[i] Score generated based on self-reported physical activity in the personal free time over the past 7 days outside school hours (range: from 1 to 14; 14 being the most active)

Table S5 Supplementary Material S5.

Variables	Schools with physical activity intervention		Schools without physical activity intervention		Intervention effect[a]		
	Baseline (n=300)	Midline (n=294)	Baseline (n=446)	Midline (n=417)	Estimate[b] (95% CI)	P-value	ICC[c]
Cardiorespiratory fitness							
Shuttle run (laps)	35.6 (17.0)	32.3 (18.4)	36.8 (17.4)	33.9 (18.2)	-1.53 (-4.59 to 1.53)	0.33	0.02
VO_2 max[d] ($ml \times kg^{-1} \times min^{-1}$)	45.8 (4.1)	43.9 (4.7)	46.3 (4.3)	44.6 (4.7)	-0.54 (-1.31 to 0.22)	0.16	0.01
Obesity							
BMIZ[e]	-0.1 (1.2)	0.1 (1.1)	0.0 (1.2)	0.2 (1.2)	-0.01 (-0.08 to -0.05)	0.73	0.01
Skinfolds[f] (mm)	9.0 (4.5)	8.9 (4.3)	9.0 (4.4)	10.5 (6.5)	-1.68 (-2.61 to -0.75)	<0.001	0.02
Mean of self-reported physical activity[g]							

[a] Schoolchildren from the intervention group accomplished a multidimensional physical activity intervention programme between baseline and midline, as described in Figure 2; Estimate of respective intervention effect on the change in the respective outcome measure from baseline to midline, with 95%-confidence interval. The underlying linear mixed models providing the respective effect estimates, included baseline value of the respective outcome variable and baseline values of age, sex, height-for-age Z-score (HAZ), haemoglobin, socioeconomic (SES) index, protozoa- and soil-transmitted helminth (STH) infection status and random effects for classes and schools; Adjustment was also made for two health and nutrition education programmes conducted at some of the schools in either group

[b] Estimate of respective intervention effect on the change in the respective outcome measure from baseline to midline, with 95%-confidence interval, P-value and ICC. The underlying linear mixed models included binary factor variables for each of the two interventions A (physical fitness intervention) and B (combination of a health education and a nutritional intervention) providing the respective effect estimates, along with baseline values of age, sex, HAZ, haemoglobin, SES index, protozoa- and STH infection status and random effects for classes and schools

[c] Proportion of unexplained variance attributable to clustering within schools and classes (intraclass correlation coefficient; ICC)

[d] Using age-adjusted test protocol from Léger *et al.*[17]

[e] Sex-adjusted BMI-for-age Z-score (BMIZ)

[f] Average of six measurements (triceps and subscapular three times each)

[g] Score generated based on self-reported physical activity in the personal free time over the past 7 days and intense exercises outside structured school hours (range: from 1 to 14; 14 being the most active)

Table S6 Supplementary Material S6.

Variables	Schools with physical activity intervention		Schools without physical activity intervention		Intervention effect[a]		
	Midline (n=294)	Endline (n=264)	Midline (n=417)	Endline (n=255)	Estimate[b] (95% CI)	P-value	ICC[c]
Cardiorespiratory fitness							
Shuttle run (laps)	32.3 (18.4)	34.5 (17.9)	33.9 (18.2)	35.3 (18.7)	2.88 (-0.42 to 6.17)	0.09	0.004
VO_2 max[d] ($ml \times kg^{-1} \times min^{-1}$)	43.9 (4.7)	43.5 (4.7)	44.6 (4.7)	44.0 (4.8)	0.92 (0.10 to 1.73)	0.03	<0.001
Obesity							
BMIZ[e]	0.1 (1.1)	-0.1 (1.3)	0.2 (1.2)	0.2 (1.3)	-0.16 (-0.25 to -0.07)	0.001	0.02
Skinfolds[f] (mm)	8.9 (4.3)	9.6 (4.6)	10.5 (6.5)	10.1 (5.9)	0.51 (-0.25 to 1.28)	0.19	0.03
Mean of self-reported physical activity[g]	10.2 (2.9)	9.0 (3.1)	9.0 (3.3)	9.9 (3.4)	-1.11 (-2.39 to 0.18)	0.09	0.07

[a] Schoolchildren from the intervention group accomplished a multidimensional physical activity intervention programme between midline and endline, as described in Figure 2; The underlying linear mixed models providing the respective effect estimates, included midline value of the respective outcome variable and midline values of age, sex, height-for-age Z-score (HAZ), haemoglobin, socioeconomic (SES) index, protozoa- and soil-transmitted helminth (STH) infection status and random effects for classes and schools; Adjustment was also made for two health and nutrition education programmes conducted at some of the schools in either group

[b] Estimate of respective intervention effect on the change in the respective outcome measure from midline to endline, with 95%-confidence interval, P-value and ICC. The underlying linear mixed models included binary factor variables for each of the two interventions A (physical fitness intervention) and B (combination of a health education and a nutritional intervention) providing the respective effect estimates, along with midline values of age, sex, HAZ, haemoglobin, SES index, protozoa- and STH infection status and random effects for classes and schools

[c] Proportion of unexplained variance attributable to clustering within schools and classes (intraclass correlation coefficient; ICC)

[d] Using age-adjusted test protocol from Léger *et al.*[17]

[e] Sex-adjusted BMI-for-age Z-score (BMIZ)

[f] Average of six measurements (triceps and subscapular three times each)

[g] Score generated based on self-reported physical activity in the personal free time over the past 7 days and intense exercises outside structured school hours (range: from 1 to 14; 14 being the most active)

7 DISCUSSION

7.1 Overview of the sub-studies and outline of the discussion

The ‘Disease, Activity and Schoolchildren’s Health’ (DASH) project was implemented as a joint research project involving staff from three institutions, namely the (i) Department of Human Movement Science at Nelson Mandela University in Port Elizabeth, South Africa; (ii) the Swiss Tropical and Public Health Institute, an associated institute of the University of Basel; and (iii) the Department of Sport, Exercise and Health (DSBG) at the University of Basel. The objectives of the present PhD thesis are summarized in chapter 2. In brief, we studied the epidemiology of selected intestinal parasite infections with a particular emphasis on soil-transmitted helminth infections (STHs) (chapters 3, 4 and 5). Additionally, we determined risk factors for non-communicable conditions, assessed their impact on schoolchildren’s physical fitness and monitored the impact of setting-specific interventions over a 14-month period (chapter 6). Table 7.1 summarizes the studies included in this PhD thesis. Experiences, limitations and lessons learned during the four years of the DASH project implementation are highlighted towards the end of this chapter. Finally, strategies for the promotion of physical activity programmes, taking into account the results of the DASH project, are offered for consideration, along with recommendations regarding the scaling-up of related interventions.

Table 7.1 Overview over the studies implemented in Port Elizabeth, South Africa and included in this PhD thesis, stratified according to the Swiss TPH continuum from innovation to application.

<table>
<tr><th>Chapter</th><th>Innovation</th><th>Validation</th><th>Application</th></tr>
<tr><td>2</td><td colspan="3">Quantification of the effect of disease burden and setting-specific interventions on schoolchildren’s physical fitness. Contribution to the health literacy among the study population.</td></tr>
<tr><td>3</td><td colspan="2">Identification of STH endemic areas and assessment of the association between intestinal parasites and the growth and physical fitness of schoolchildren.</td><td></td></tr>
<tr><td>4</td><td></td><td>Assessment of the efficacy of albendazole against Trichuris trichiura infection in the study population.</td><td></td></tr>
<tr><td>5</td><td></td><td colspan="2">Description of the temporal dynamics of the risk profiles of the study population, with special reference to Ascaris lumbricoides and T. trichiura. Discussion of communication and training tools, including a video to create awareness of communicable diseases and to facilitate access to the study results for a broad range of stakeholders.</td></tr>
<tr><td>6</td><td></td><td colspan="2">Evaluation of the efficacy of a multidimensional physical activity intervention on body mass index, skinfolds and physical fitness.</td></tr>
</table>

7.2 Infection prevalence of STHs, intestinal protozoa and *Helicobacter pylori*

We observed notable levels of helminth and intestinal protozoa infections among the study population of 9- to 12-year-old children in eight schools from poor neighbourhoods in Port Elizabeth, South Africa. The same trend was observed for *A. lumbricoides*-infected children. *H. pylori*-prevalence was prominent, and found at all schools, ranging from 25% to 65%.

H. pylori infections were classified by the World Health Organization (WHO) as a carcinogen of class 1 (definite carcinogen) in 1994 (WHO, 1994). Non-significant associations between an infection with this bacterium and the measured growth indicators of the children were noted, confirming previous findings by Richter et al. (2001) and Abdelrazak and Walid (2015).

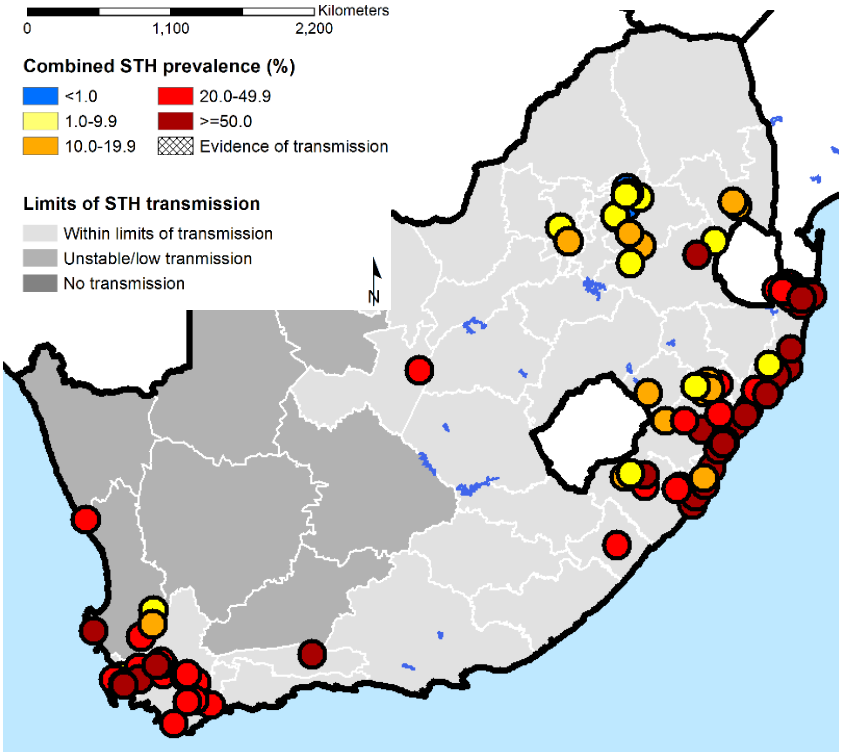

Figure 7.1 Distribution of soil transmitted helminth survey data in South Africa in August 2017 (GAHI, 2017).

Only a few studies have investigated the distribution of STHs in South Africa (Figure 7.1). As the current map of the Global Atlas of Helminth Infections (GAHI) of the London School of Hygiene and Tropical Medicine (LSHTM) shows, there is a lack of data for the Eastern Cape province of South

Africa. High prevalences of hookworm and schistosome infections have been reported from warmer KwaZulu-Natal, located further North than Port Elizabeth (Karagiannis-Voules *et al.*, 2015), whereas these parasitic worms were not commonly observed in our study. However, heavy *T. trichiura* and *A. lumbricoides* infection intensities were observed in the Hillcrest and Helenvale settlements built in the 1950s to accommodate 6,000 predominantly coloured people that are today inhabited by more than 30,000 people (Armstrong *et al.*, 2011).

(a) **(b)** **(c)**

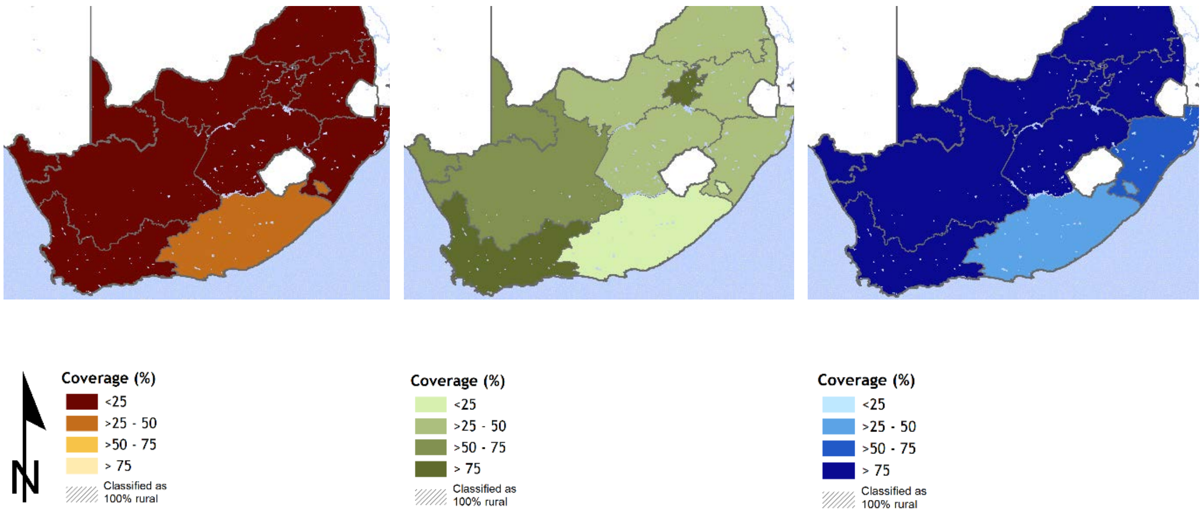

Figure 7.2 (a) Open defecation in South Africa (2017); **(b)** use of an improved sanitation facility in South Africa (2017), and **(c)** use of an improved drinking water source in South Africa (2017) (GAHI, 2017).

The areas where the highest intestinal helminth infection prevalences were observed is characterised by unhygienic living conditions (poor sanitation and litter), high unemployment and drug and alcohol related gangsterism. At a macro-level, this is also reflected at provincial level where the Eastern Cape province stands out as an area with a relatively high prevalence of open defecation, with low access to improved sanitation and drinking water sources (Figure 7.2). Based on our results, it is recommended that biannual mass deworming should be implemented among school-aged children in the Hillcrest and Helenvale areas in order to reduce STH prevalences and thus lower the risk of morbidity due to high- and moderate-intensity STH infections. Interventions focusing on water, sanitation and hygiene (WASH) should complement the deworming.

7.3 Effects of deworming on the prevalence of intestinal helminth infections measured at three different time points

At the end of each of the three cross-sectional surveys, a single 400 mg oral dose of albendazole was administered to children testing positively for STH. According to national and international treatment guidelines (WHO, 2006), all children were treated, regardless of infection status, in schools where the infection prevalence was equal to or larger than 50%. Ingestion of albendazole was monitored by health staff, and children remained under medical supervision for 24 hours. At baseline, we recorded a mean *A. lumbricoides* infection intensity among infected schoolchildren of 9,554 eggs per gram of stool (EPG). Seven months after a first round of deworming, the mean infection intensity of *A. lumbricoides* had been more than halved to 4,317 EPG. Another seven months later, during the end-line survey in May 2016, the mean infection intensity had further declined to 1,684 EPG. With regard to *T. trichiura* infections, the mean infection intensities among infected schoolchildren were 664 EPG at baseline, double the level of 331 EPG at mid-line. The final value was 87 EPG. The highest *A. lumbricoides* egg count was 217,608 EPG, while the highest *T. trichiura* egg count was 33,900 EPG, both observed during the baseline cross-sectional survey. Furthermore, a single dose of albendazole was highly efficacious against *A. lumbricoides*. At treatment follow-up only two children were found positive for this STH species (cure rate (CR) 97.2%). The arithmetic mean of the *A. lumbricoides* egg count dropped from 10,959 EPG to 628 EPG after the first round of treatment, an egg reduction rate (ERR) of 94.3%. The prevalence of moderate and heavy *A. lumbricoides* infections (≥5,000 EPG) decreased from 31.5% before, to 1.3% after, the first treatment.

The current study confirms that a single 400 mg oral dose of albendazole is highly efficacious against infection with *A. lumbricoides*, but lacks efficacy against *T. trichiura* among school-aged children (Keiser and Utzinger, 2010; Moser et al., 2017). In 2009, Stothard and colleagues reported low CRs for single-dose albendazole against *T. trichiura* among preschool-aged children on Zanzibar Island (Stothard *et al.*, 2009). Recently, combination therapy (oxantel pamoate plus albendazole) showed higher CR and ERR compared to standard albendazole or mebendazole treatment (Speich *et al.*, 2014).

Our findings suggest that a single 400 mg oral dose of albendazole is efficacious against *A. lumbricoides* in the study setting but does not effectively manage *T. trichiura* infection prevalence in children. To control STH infections among school-aged children, complementary public health measures are required, such as improvements in WASH. Moreover, there is a pressing need to use alternatives and to develop novel drugs and drug combinations that are safe and efficacious against *T. trichiura*.

7.4 Soil-transmitted helminths and their association with non-communicable diseases, cardiorespiratory fitness and upper and lower body strength

The overall mean haemoglobin (Hb) level of the study cohort was 122.2 g l^{-1}. Hb levels were significantly lower in children harbouring a single or dual species helminth infection. In two schools, a high prevalence of STH infections was observed, namely in school B in Hillcrest where the mean Hb level was 119.7 g l^{-1}, and at school A in Helenvale where it was 120.5 g l^{-1}. These values were significantly lower than the overall mean Hb level of the eight study schools. However, these associations need to be interpreted with caution since current infection status was measured and correlated with long-term growth and health indicators. Systematic and independent differences in socioeconomic status and nutrition levels may exist between the study schools.

The mean height, weight and BMI of the study cohort were 133.2 cm, 30.5 kg and 17.0 kg m^{-2}, respectively. We found statistically significant differences in anthropometric measurements when comparing children without a helminth infection with those with a single species infection of either *A. lumbricoides*, or *T. trichiura* or a co-infection. Children infected with *T. trichiura* had significantly lower body weight, were less tall and had a lower BMI compared to their non-infected peers (all $P < 0.05$). Non-infected children were heavier, higher and had a higher BMI compared to their peers with a single or dual species infection. They were also less likely to be stunted but not less wasted. Children concurrently infected with *A. lumbricoides* and *T. trichiura* had similar anthropometric and haematologic measures compared to children with a single *T. trichiura* infection. Stunting was observed in 10% of the children, while wasting was found in 4% of the children. Again, the highest prevalence of stunting was observed in schools in the regions of Hillcrest (22%) and Helenvale (19%), where it appears to be a major problem at a young age in our study population. Boys, but not girls, with a *T. trichiura* or *A. lumbricoides* infection had significantly lower mean VO_2 max estimates than their non-infected peers.

Overweight and obese children showed lower cardiorespiratory fitness, grip strength and standing broad jump than their normal weighted peers. Grip strength and standing broad jump test results were also statistically significantly lower in 9- to 10-year-old boys, whereas in girls no difference was observed.

The mean VO_2 max values, as estimated based on the number of completed levels/stages of the 20 m shuttle run test, namely 35.8 cumulative shuttles, correspond closely to the mean results reported from other studies in different settings, *e.g.* the KISS- or the Sportcheck-study with Swiss primary schoolchildren of similar age (Kriemler *et al.*, 2010; Meyer *et al.*, 2014; Imhof *et al.*, 2015). Yap *et al.* (2014) reported slightly lower VO_2 max results, 45.6 ml kg^{-1} min^{-1} for boys and 44.7 ml kg^{-1} min^{-1} for girls, after assessing 194 children aged 9-12 years in the south-western part of Yunnan province, People’s Republic of China (Yap *et al.*, 2014). With regard to *T. trichiura* infections, Yap *et al.* (2012) found more pronounced impacts on weight, height and BMI than the present study (Yap *et al.*, 2012). With regard to the standing broad jump results, 118 cm for girls and 132 cm for boys, Armstrong *et al.* (2011) reported noticeably longer standing broad jump distances, namely 152 cm for girls and 164 cm for boys among 2,819 South African girls and 3,573 boys of the same age.

7.5 Effects of lifestyle interventions, such as health education and physical-activity promotion, on improving children’s health and wellbeing

The twice-applied 10-week multidimensional physical activity intervention contributed to a lower increase of BMI and thickness of skinfolds in the study cohort. However, no detectable effects were observed on cardiorespiratory fitness. Differences in the magnitude of the effect on skinfold thickness and BMI for study participants of different sex suggest that gender-specific interventions may be necessary. Although females benefited more from the intervention in terms of skinfold thickness, they profited less regarding BMI. Without specific physical activity interventions, females might be at a particular risk of obesity during adolescence, a time of life when males are usually more physically active (*e.g.* playing soccer), and hence, specific interventions might need to be implemented around that time.

In South Africa, a large-scale intervention trial involving Grade 4 students (n = 887) from eight intervention and eight control schools has been carried out in the frame of the HealthKick study (Draper *et al.*, 2010). The study has provided insights into the effectiveness of school-based initiatives to promote physical activity and the potential of strengthening schoolchildren's health. It pursued similar goals as our study, specifically the promotion of physical activity and healthy nutrition. However, the approach differed in many ways. The HealthKick survey was based on a social-ecological model, focused on behaviour change in- and outside the schools, targeted children and their parents/caregivers, and encouraged school principals, staff and individuals affiliated with the school to assess whether action was needed with respect to nutritional and physical activity, to identify priorities and to set feasible goals. The aim of DASH was to implement an intervention toolkit to reduce children's *double burden* of diseases (infectious diseases and risk factors for non-communicable diseases (NCDs)).

Contrary to the HealthKick study, the DASH intervention primarily focused on children and the creation of healthy school environments by implementing a series of clearly defined and standardized intra-mural measures (Yap *et al.*, 2015). The evaluation of the HealthKick project pointed out that educators play a key role in implementing a school-based intervention, but that developing capacity within school staff and stakeholders is not straightforward (Draper *et al.*, 2010). The public education system (schools, etc.) of South Africa – especially in areas disadvantaged by Apartheid – is continuously underfunded and understaffed, whereas the far better resourced public schools in advantaged areas, as well as private schools, served only the wealthiest inhabitants of the country (Ataguba and Akazili, 2010). In particular, few staff members in disadvantaged public schools were willing to take on an active role because they considered action planning as additional work, which resulted in limited cooperation. As a consequence, the outcomes of the HealthKick survey were disappointing in the sense that no significant improvements were found with regard to dietary diversity and unhealthy snacking, as well as physical fitness and self-reported physical activity (Uys *et al.*, 2016). Therefore, the authors conclude that such a low-intensity intervention does not seem to be effective in a South African primary school setting, and that focusing on physical activity and healthy nutrition outside the school context may not be ideal for children from low-income households because these children may have very little influence on their food choices and their lifestyle-related behaviours.

In addition, we assume that, amongst other factors, criminality and gangsterism may be a hindrance to our study population maintaining an active lifestyle. Reducing crime in a preventive way through multilevel interventions (*i.e.*, economic, political and safety development initiatives to increase time available for physical activity and also to benefit to preventive health care) may promote an active lifestyle and therefore yield a decline in the risk factors for obesity (Powell-Wiley *et al.*, 2017).

However, a few studies confirmed an increase of physical activity levels in South African schoolchildren living in poor neighbourhoods, if concerted action is undertaken. For instance, in 2012, Naidoo and Coopoo (2012), found that among 10- to 15-year-old children, flexibility, strength and physical activity could be increased by an 18-month physical activity intervention. Similarly, Lennox and Pienaar (2013) demonstrated that physical activity levels and aerobic fitness significantly increased among learners who had participated twice a week in an extra-mural aerobic exercise intervention programme. Monyeki *et al.* (2012) were able to show that a 10-month physical activity programme with two 30 min sessions of structured exercise per week had positive effects on body fat among 9- to 13-year-old learners. The results also showed that positive effects on the quality of life could be achieved in socially disadvantaged areas through appropriate interventions. For example, Tian *et al.* (2014) examined the effect of a 12-week sports intervention programme on physical and motor fitness in Grade 7 schoolchildren in Potchefstroom, South Africa. The main outcome of the study showed that the children's physical performance significantly improved after implementation of the intervention (Tian *et al.*, 2014). However, in general, according to an international study from Tomkinson *et al.* (2017), there has been a substantial decline in cardiorespiratory fitness in children since the beginning of the eighties, which is suggestive of a meaningful decline in population health. New data on cardiorespiratory fitness are needed from children in low- and middle-income countries (LMICs) to more confidently determine this international trend.

In South African quintile-3 schools and communities, sports and leisure facilities are often inadequate and/or inaccessible. A lack of qualified teachers and the absence or irregular implementation of physical education schedules complicates the promotion of age-appropriate physical activity, particularly in disadvantaged schools. Since physical education specialists are no longer being appointed at schools, generalist teachers, who have often scant knowledge and understanding of physical education, are required to teach Life Skills which includes, amongst other areas, a limited focus on physical education. The major problem reported by the Life Skills teachers is that they are not qualified to teach all the learning outcomes of Life Skills, and educators feel that it is ‘impossible to be a specialist in the five subject areas’ comprising Life Skills (Du Toit *et al.*, 2007). In response, an association for physical educators, called the South African Association of Human Movement Sciences (SAAHMS), was constituted in 2008 (Rajput and Van Deventer, 2010). However, this association has not been active for a number of years and in 2015, the South African University Physical Education Association (SAUPEA) was formed. This new association should ideally liaise with teachers and the responsible education officials to forge a way forward for school sport and physical education. The Department of Education should now foster stronger linkages with teaching staff, revisit the way physical education is taught in the National Curriculum Statements, and ensure that qualified teachers are employed to teach physical education (Rajput and Van Deventer, 2010).

After implementing the four intervention modules of the DASH study, variables on children's health (*e.g.* BMI or percentage body fat), and wellbeing showed an improvement. Additionally, risk factors for NCDs (*e.g.* overweight, anaemia, and/or diabetes indicators) decreased. To increase effectiveness and sustainability of the results, the intervention should be extended to cover the entire school year, and should be expanded to all school grades.

7.6 Strengths and limitations of this PhD thesis

We were able to design, implement and measure the effect of a multidimensional physical activity intervention programme on schoolchildren's health and wellbeing in close collaboration with local partners, ensuring local relevance and acceptability and promoting sustainability. This intervention, carried out by experienced sports teachers – and thus with good teaching quality ensured – was perceived positively by the teachers (evaluation result: 4.2 on a 5-point Likert scale, 1 being poor and 5 excellent). Teachers expressed interest in pursuing the physical activity programme in the longer-term. The implementation of the intervention resulted in favourable effects on body composition, one of the major public health issues in LMICs (Kipping *et al.*, 2008). Moreover, while school-based physical activity promotion has a long tradition in Western countries, the study presented here is among the few physical activity interventions implemented in an African context. Importantly, only a few of the previous physical activity intervention programmes proved to be effective with regard to lowering the increase in BMI and body fat, the latter measured as thickness of skinfolds, in school-aged children (Kamath *et al.*, 2008). We therefore assume that a multidimensional intervention of the type we pursued might be particularly beneficial.

A further strength of the DASH study was the relatively high number of study participants, which makes the study findings robust. Indeed, a total of 1,009 schoolchildren were examined in the baseline survey in 2015, and a high proportion could be followed-up throughout the study. Furthermore, the measurements were carried out by a small research team to minimize inter-observer variation, and data were entered twice to ensure consistency, minimize input errors and thereby increase overall data quality. In addition, the longitudinal tracking of the same schoolchildren by means of three measuring time points provided a substantial amount of information not easily collected through the more common cross-sectional studies. To complement the database, a final 4th measurement is scheduled for 2018 before the study cohort completes the compulsory primary school phase.

There were no specific risks associated with participation in this study. Submission of stool and urine samples by schoolchildren might be perceived as embarrassing. However, we tried to manage this issue by communicating openly and providing clear explanations on the reasons why the stool samples were necessary and important for our study (to detect parasitic worm infections). Fingerpricks, the pricking of a finger with a lancet to obtain a small quantity of capillary blood to test for anaemia and diabetes through rapid diagnostic tests, causes only transient and slight pain and is a widely used approach among school-aged children across Africa. Albendazole, one of two donated drugs for preventive chemotherapy against STHs, rarely causes adverse events. All medical procedures were supervised by medical staff prepared to manage or refer any untoward symptoms.

The design of the study has several inherent limitations. Firstly, the motivation of teachers to facilitate physical education classes varied and was influenced by class size, a lack of formal qualifications as a physical education teacher and the fact that physical education lessons are not taught on a regular basis. The concentration of the children was often short-lived, and, in spite of the presence of translators, language barriers as well as low literacy levels amongst the children sometimes posed problems that might have resulted in incorrect answers.

Secondly, to achieve more robust effects, an extended duration of the intervention coupled with more extensive involvement of the school communities, school volunteers, parents/guardians, and policies might have been needed (van Sluijs *et al.*, 2007). Thirdly, no objective measurements of physical activity using accelerometers were made, although this would have allowed us to obtain a more objective and fine-grained picture (Meyer *et al.*, 2013).

Fourthly, the intervention was only implemented in four out of eight schools as it was a cluster randomized controlled trial, which means that the participating schools rather than the individual students were randomly assigned either to the intervention or to the control group. This minimized contamination so that disturbance could be controlled for and comparability of the results was ensured (Beller, 2008). Selection from a larger number of schools would have been preferable.

Fifthly, our main study was a cohort study on infectious disease with different interventions embedded. These different sub-studies may have interacted, since different interventions were tested in the same population and one intervention may have had effect-moderating effects on another. As a result, the data analysis became complex for which we accounted by introducing interaction terms and adjustments.

Sixthly, it is debatable whether the cardiorespiratory performance of children, measured here as maximal oxygen uptake (VO_2 max), is receptive enough for short-term change (Rowland, 1985) despite varying personal living conditions and other factors not affected by the intervention. In addition, it remains uncertain whether the children reached their performance limit in the 20 m shuttle run test, as no heart rate monitors were worn. For example, in a study in Côte d'Ivoire, children who were not able to reach a heart rate of 180 bpm when conducting the test were excluded from the study (Müller *et al.*, 2011). Such an approach might have increased the accuracy of the data. However, operational circumstances made it impossible to use heart rate monitors. Large classes, as well as multiple languages spoken and communication barriers may have resulted in the instructions lasting longer than initially planned, and hence in a less favourable teaching-to-activity ratio. This limitation has already been described in another study (Uys *et al.*, 2016), which found that so-called 'low-intensity' interventions are not effective and do not lead to any improvement in physical performance and movement behaviour.

Seventhly, and finally, only single stool samples were collected from each participant, and only a single diagnostic tool was used. Hence, some infections, particularly those of light intensity, were possibly missed, as seen in other studies where multiple samples and a combination of diagnostic methods were employed (Booth *et al.*, 2003; Knopp *et al.*, 2008; Steinmann *et al.*, 2008). Despite these limitations, the study confirmed the feasibility of the methods employed, corroborating previous experiences in different African and Asian settings where school-aged children liked to perform physical fitness tests (Ziegelbauer *et al.*, 2010; Bustinduy *et al.*, 2011; Müller *et al.*, 2011).

8 COMMUNITY IMPACT OF THE DASH STUDY

Interviews were carried out with key persons in the study area from Port Elizabeth, South Africa, namely with (i) a former Grade 5 Teacher and Head of Department (HOD) (Grades 4 to 7) from Hillcrest Primary School; (ii) the Head of the Department of Medical Laboratory Sciences at the Nelson Mandela University; and (iii) the Director of the Centre for Community Schools (CCS), Faculty of Education at the Nelson Mandela University, and former principal of Sapphire Road Primary.

8.1 Former Grade 5 Teacher and Head of Department (HOD) (Grades 4 to 7) from Hillcrest Primary School

"*Hillcrest Primary School has 1,084 learners attending the school. The neighbourhood is densely populated and overcrowded, with a high rate of unemployment. Gangsterism and drug abuse is rife and teenage pregnancy rates are high. Gangs often have "turf" wars over the trade of illegal drugs. These factors greatly affect the community, pupils and teachers at the school. Absenteeism is common due to many issues including parental neglect and the lack of shelter, clothes, school uniforms or shoes. Some* *learners are sometimes so hungry, they collapse during assembly. Learners are often traumatised by the prevalence of crime, including rape, murder, domestic violence and gang wars. The intervention programmes from DASH improved the learners' concentration, confidence and appearance, as well as their toilet routine, including hand washing hygiene. Teachers and learners thoroughly enjoyed the dance lessons which were conducted once a week. Teachers believe that it is easier to teach a happy learner and found that through the intervention package, learners appeared to be happier and more co-operative during class. The deworming of the learners created an element of safety and health amongst the teachers. I would recommend the DASH programme to other schools, since the school has improved in terms of physical education and personal health. The school's nutrition has also improved in terms of utensil choice and cleanliness in the kitchen, as well as the menu that is chosen. Our learners were dewormed twice in 2016 and once in 2017. A second deworming will be conducted in September 2017. The new playground installations are very valuable and used extensively by all the schoolchildren.*"

8.2 Head of the Department of Medical Laboratory Sciences at the Nelson Mandela University

"*The staff and students in the Medical Laboratory Science (MLS) department helped complete specific diagnostic tests on urine and stool samples collected during the DASH research project. Some of the diagnostic procedures are not routinely performed in the department and insight was gained through extensive training. Two groups of students assisted during the testing. These students were in the process of completing their BTech: Biomedical Technology (4^{th} year) on a full time basis. The first group consisted of five female students that came from different local communities in the Nelson Mandela Metropole. The second group of students consisted of five male students that came from Malawi to complete their BTech qualification on a full time basis at Nelson Mandela University. The participation in the DASH project had a multi-fold impact, such as enhancing the diagnostic experience of the MLS department and by raising awareness for the parasitic burden linked to the local schools in the Nelson Mandela Metropole.*"

8.3 Director of the Centre for the Community Schools (CCS), Faculty of Education at the Nelson Mandela University

"*As a school principal, the project was extremely valuable for the school as an organization on several levels. The project informed us about the impact of health and physical wellbeing not only on the life of the child, but on how it affected our learners' cognitive development as well. What made the project unique from other projects was that it did not only identify these difficulties, but provided complementary tools to be responsive to the challenges identified. Although there were challenges, our schooling community saw the DASH project as a great complementary tool. The findings of the project were shared with our parents, in parent meetings, and the broader community, through newsletters. As Director of the CCS, I am now able to share the knowledge gained through DASH with other schools across the country, and I am looking forward to engaging with the next phase of the project.*"

9 CONCLUSIONS

The insights from the DASH study shed light on the burden of both infectious and chronic diseases as well as low physical activity among disadvantaged children in Port Elizabeth, South Africa. Our results indicate that boys who are infected with multiple intestinal parasite species have lower physical fitness levels than their non-infected counterparts, as expressed by the maximal oxygen uptake (VO_2 max). A significantly higher *T. trichiura* prevalence was noted in stunted children and those with a significantly lower Hb level, compared to children not infected with this species. According to our results, STH infections affect the schoolchildren in multiple ways. Infected children have lower BMI, are more stunted and have a lower cardiorespiratory fitness.

Specific public health interventions are warranted given the high prevalence and intensity of two of the three STH species, *i.e. A. lumbricoides* and *T. trichiura*, observed during a baseline cross-sectional survey among children in two out of eight study schools. Discussions with local health and education authorities revealed that preventive chemotherapy (with either albendazole or mebendazole) against STH has been neglected in recent years. Biannual mass deworming in order to control the morbidity due to STH infections is recommended in school B in Hillcrest and school A in Helenvale. Our data confirm that multiple rounds of deworming targeting school-aged children is an effective approach. Therefore, we recommend following detailed treatment strategies according to national and international guidelines: (i) individual testing and treatment of infected children are indicated if the STH prevalence is below 20% (seen in five of the schools); (ii) annual deworming if the prevalence ranges between 20% and 50% (one school); and (iii) biannual treatment of all learners if the prevalence exceeds 50% (two schools). The high spatial heterogeneity noted suggests that data from additional schools in different neighbourhoods will be needed to determine a locally appropriate intervention strategy, which ideally should not only be carried out by the school community but cover the entire local population at risk. Furthermore, our results suggest that a single 400 mg oral dose of albendazole is efficacious against *A. lumbricoides* but does not effectively manage *T. trichiura* infection in children. Alternative treatment regimens should therefore be explored. The high spatial heterogeneity of infections suggests that data from additional schools in different neighbourhoods will be needed to determine a locally appropriate intervention strategy, which ideally should not only be carried out by the school community but should also cover the entire local population at risk. Such activities should be complemented by efforts to strengthen hygiene awareness and to improve related behaviours such as hand washing with soap, along with improved water and sanitation infrastructure – collectively known as WASH interventions – in schools and households alike.

Moreover, a well-designed, multidimensional physical activity programme was shown to lower the average increase in BMI and the thickness of skinfolds in school-aged children. To increase effectiveness and sustainability of the results, the intervention should be extended to cover the entire school year and be expanded to all school grades. Our intervention was developed by physical education specialists in consultation with local stakeholders, and careful modification will be necessary before the intervention could be implemented in another setting and/or go to scale. Physical education in schools needs to consider local resources, conditions and preferences, while adhering to minimal standards, to be effective. In any case, promotion of extra-curricular physical activity and healthy nutrition should become an integral part of the programme.

Besides, physical education should be reintroduced as a stand-alone subject in the school curriculum and be promoted as an examinable subject, taught by specialist teachers. The specialist teachers will be able to implement appropriate programmes and monitor the learners' progress. Higher Education Institutions should provide physical education as a major subject, or a learning area specialization, that will ensure that qualified and highly skilled physical education teachers are brought back into the teaching body. The qualification must ensure that teachers have a sound theoretical and practical knowledge of physical education. There should be a re-evaluation of available sports facilities to facilitate physical education lessons, with every school provided with the required facilities for physical education at a basic level.

As overweight is caused by diverse lifestyle choices, there is a need for longitudinal monitoring and age-, gender- and school-grade specific assessments. However, our findings suggest that the dissemination of a school-based physical activity programme – inspired by our findings from South Africa – are likely to help to reduce risk factors for the development of chronic diseases among children living in socioeconomically deprived neighbourhoods.

10 OUTLOOK AND FURTHER RESEARCH NEEDS

A first attempt to increase health literacy in South African children was undertaken in the DASH research project, which was supported by the Swiss National Science Foundation in Switzerland and the National Research Foundation in South Africa as part of the Swiss-South Africa Joint Research Programme. Promoting wellbeing among children is a complex and challenging endeavour. One way of addressing infectious diseases and co-existing non-communicable diseases – which constitute a dual disease burden – and disrupting the vicious cycle of poverty and poor health is to incorporate health promotion measures within existing school structures. This study focused on Grade 4 primary schoolchildren and the development of a healthy school environment by implementing a series of standardized intra-mural measures. The intervention programme consisted of four main components, including a medical examination, anthelminthic treatment, and – in case of serious health risks – referral to the local clinic. Moreover, there was a special emphasis on physical activity (*e.g.* playful games and moving-to-music), nutrition supplementation and health education (*e.g.* healthy nutrition, health and hygiene education). The preliminary findings suggest that: the prevalence of parasitic worm infection was high in several schools; children infected with STHs had lower maximal oxygen uptake (VO_2 max) compared to their non-infected peers; albendazole is highly efficacious against *A. lumbricoides* infection prevalence, but lacks efficacy against *T. trichiura* infection; and the physical activity intervention component resulted in a significantly delayed increase in children's BMI. However, no objective measurements of physical activity using accelerometers were made, which would have resulted in a more objective and fine-grained picture. Nonetheless, qualitative data revealed that the DASH intervention package was well received at all schools.

After successful implementation of the DASH research project, the next logical step would be to capitalize on the findings by scaling-up the intervention programme. This is being achieved by creating tools and structures which allow for an effective dissemination of the programme, by further monitoring and improving the effectiveness of the intervention programme with the support of selected model schools, and by exploring ways for effective community involvement. The overarching goal of this phase – named the *KaziBantu* project (which means 'active people' project in Swahili and Xhosa) – will be to assess the efficacy and effectiveness of a school-based intervention programme on communicable diseases (*e.g.* helminth infections), risk factors for NCTs (*e.g.* type 2 diabetes, obesity and hypertension), health behaviours (*e.g.* physical activity and nutrition) and psychosocial health (*e.g.* mental well-being, stress, cognitive performance) in school-aged children in disadvantaged neighbourhoods from Port Elizabeth, South Africa. This study will expand the previous research in the sense that the intervention included in the initial DASH research project (20 weeks, focussed on Grade 4 learners) will be scaled-up in order to be implemented with learners across the entire primary school system (Grades 1 to 7). Moreover, to assess the efficacy, the intervention will be evaluated over a longer time period, an entire school year. Finally, to examine the effectiveness of the intervention, the participating schools will take increasing responsibility with regard to the implementation of the intervention during the course of the project. In addition, a second goal will be to develop and pilot-test an additional school-based health intervention programme for schoolteachers themselves. Based on a comprehensive health assessment among schoolteachers, key objectives for workplace health promotion will be formulated and translated into a workplace health promotion programme. The effectiveness of this teacher workplace health promotion programme will be tested among teachers of the involved intervention and control schools. The Novartis Foundation (Basel, Switzerland), as a new donor, has agreed to fund such an expanded intervention and a kick-off meeting took place in Port Elizabeth in October 2017. The *KaziBantu* school health promotion programme will be designed in such a way that we will be able to disseminate the programme to other regions in South Africa and to other (African) countries.

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12 APPENDIX

12.1 Informed consent form in English, Afrikaans and Xhosa

15 October 2014

Impact of disease burden and setting-specific interventions on schoolchildren’s cardio-respiratory physical fitness and psychosocial health in Port Elizabeth, South Africa

INFORMED CONSENT FORM

Project title: Impact of disease burden and setting-specific interventions on schoolchildren’s cardio-respiratory physical fitness and psychosocial health in Port Elizabeth, South Africa

Statement by the researcher/person taking consent

I have accurately outlined the purpose, objectives and procedures of the study and given enough information including the potential benefits and risks to the parent/legal guardian of the potential participant.

I confirm that the parent/legal guardian of participant Mr/Ms: ___________________________

School Nr.: _______________________ Telephone Nr.: ______________________________ was given an opportunity to ask questions and that all questions have been answered correctly. I confirm that the participant has not been forced into giving consent, and consent has been given freely and voluntarily.

Name of researcher: ____

Place: _______________ Date: _______________ Signature: ____

Statement by the parent/legal guardian

I have read the letter of information of the study or it has been read to me in a language that I understand. I had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I know the purpose, objectives and procedures, risk and benefits of the study. I understand that I can withdraw my child from the study at any time without further consequences. I have also an additional letter of information that I can keep for future reference.

Name of schoolchild: ____

Name of parent/legal guardian: ____

Place: _______________ Date: _______________ Signature: ____

If participant is **illiterate**

I have witnessed the accurate reading of the consent form to the potential participant and the individual had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness: ____

Place: _____________ Date: _____________ Signature: _______________________________________

Thumb print of participant:

____

Study doctor or responsible nurse of the study

The purpose, objectives and procedures of the study has been accurately outlined and enough information was given including the potential benefits and risks to the parent/legal guardian of the potential participant.

Name of the doctor / nurse: ____

Place: _____________ Date: _____________ Signature: _______________________________________

------------------------------------ Thank you very much for your invested time! -------------------------------------

23 October 2014

Die impak van siektedruk en omgewingspesifieke intervensies op skoolkinders se kardio-vaskulêre liggaamlike fiksheid en psigososiale gesondheid in Port Elizabeth, Suid-Afrika

INGELIGTE TOESTEMMINGSVORM

Projektitel: Die impak van siektedruk en omgewingspesifieke intervensies op skoolkinders se kardio-respiratoriese liggaamlike fiksheid en psigososiale gesondheid in Port Elizabeth, Suid-Afrika

Verklaring deur die navorser/persoon wat die toestemming verkry

Ek het die doel, doelstellings en prosedures van die studie akkuraat aangedui en genoeg inligting aan die ouer/wettige voog van die potensiële deelnemer gegee, insluitend die potensiële voordele en risiko's.

Ek bevestig dat die ouer/wettige voog van deelnemer Mnr/Me: ______________________________________

Skoolnr.:____________________Telefoonnr.:__________________________ 'n geleentheid gegee is om vrae te vra en dat alle vrae korrek beantwoord is. Ek bevestig dat die deelnemer nie geforseer is om toestemming te gee nie, en dat toestemming vryelik en vrywillig gegee is.

Naam van die navorser: ____

Plek: _________________ Datum: _______________ Handtekening:_________________________________

Verklaring deur die ouer/wettige voog

Ek het die inligtingsbrief van die studie gelees of dit is aan my voorgelees in 'n taal wat ek verstaan. Ek het die geleentheid gehad om vrae te vra daaroor en enige vrae wat ek gevra het, is tot my bevrediging beantwoord. Ek ken die doel, doelstellings en prosedures, risiko's en voordele van die studie. Ek verstaan dat ek my kind op enige stadium kan onttrek aan die studie sonder enige gevolge. Ek het ook 'n addisionele inligtingsbiref vir toekomstige gebruik.

Naam van skoolkind: ____

Naam van ouer/wettige voog: ____

Plek: __________ Datum: _________________ Handtekening: ______________________________________

Indien die deelnemer **ongeletterd** is

Ek het die akkurate lees van die toestemmingsvorm vir die potensiële deelnemer aanskou en die persoon het die geleentheid gehad om vrae te vra. Ek bevestig dat die persoon vrywillig toestemming gegee het.

Naam van getuie: ____

Plek: ____________________ Datum: ___________________ Handtekening: _________________________

Duimafdruk van deelnemer:

____

Verklaring deur die ouer/wettige voog

Die doel, doelstellings en prosedures van die studie is akkuraat aangedui en genoeg inligting is gegee, insluitend die potensiële voordele en risiko's vir die ouer/wettige voog van die potensiële deelnemer.

Naam van die dokter / verpleegster: ____

Plek: _____________ Datum: _________________________ Handtekening: _________________________

------------------------------------Baie dankie vir die tyd wat u spandeer het! ----------------------------------

29 October 2014

Igalelo lezifo kunye neenkqubo zokungenelela ezikhethekileyo empilweni yomzimba nobume-bengqondo babantwana besikolo kumandla waseBhayi eMzantsi Afrika

IFOMU ENIKEZELA IMVUME YOMZALI

Isihloko sophando: Igalelo lezifo kunye neenkqubo zokungenelela ezikhethekileyo empilweni yomzimba nobume-bengqondo babantwana besikolo kumandla waseBhayi eMzantsi Afrika

Isteyitmente esuka kumphandi/kumngeneleli

Ndiye ndashwankathela konke okubalulekile ngolu phando-nzulu ngukuchanekileyo, ndizibandakanyile iinjongo zolu phando, kwaye nenkqubo yolu phando njengoko luzokuqhubeka. Ndizifakile zonke iinkcukacha ezibandakanya okunokuthi kuzuzwe xa kugqitywe olu phando, nabo nobungozi kwaba bangenelayo kunye nabazali babo.
Ndiyaqinisekisa ukuba umzali okanye umngcini womntwana/abantwana Mnu./Nkszn: ___________________
Inombolo yemfono-mfono yesikolo.:______ Inombolo yemfono-mfono: _______________________________
uye walinikwa ithuba lokubuza imibuzo kwaye yonke imibuzo yakhe iphendulekile ngokunyanisekileyo.
Ndiyaqinisekisa ukuba umngeneli akakhange agxagxanyiswe ukuba avume ukungenelela olu phando- nzulu engafuni, imvume uyinikezele ngentliziyo ekhululekileyo.

Igama lomphandi : ____

Indawo: _______________ Umhla: _______________ Isandla: ____

Isteyitmente esuka kumzali/umgcini womntana

Ndiyifundile incwadi equlatha inkcazelo ngolu phando-nzulu okanye ndiyifundelwe incwadi eneenkcukacha ngophando-nzulu ngolwimi endiliqondayo. Ndibe nalo ithuba lokubuza imibuzo ngalo kwaye yonke imibuzo yam iphendulekile ndade ndaxola. Ndiyazazi iinjongo zolu phando, ndiyabuqonda ubungozi obuqulathwe lolu phando kwaye ndiyazazi nenzuzo eziza kuphuma kolo phando-nzulu. Ndiyaqonda ukuba ndingamshenxisa naninina ndithanda umntwana wam kulo phando-nzulu kungekho zipheno ziza kuza ngakum. Ndinayo incwadi eneenkcukacha endizigcinele yona xa ndifuna ukufunda kuxa elizayo.

Igama lomntana wesikolo: ____

Igama lomzali/ Lowo umgcinileyo: ____

Indawo: _______________ Umhla: _______________ Isandla: ____

Ukuba abo bathatha inxaxheba abakwazi ukubhala nokufunda:

Ndibe lingqina maxa kufundwa incwadi ebuza ukuba umgeneleli uyavuma na ukuba yinxalenye yolu phando-nzulu, kwaye lo ungenelelayo ube nalo ithuba lokubuza imibuzo. Ndiyaqinisekisa ukuba umgeneleli uyinikezele imvume ngentliziyo ekhululekileyo.

Igama lengqina: ____

Indawo: _______________ Umhla: _______________ Isandla: ____

Ubhontsi walowo uthatha inxaxheba: ____

Ugqirha wophando okanye umongikazi obandakanyekayo kuphando

Konke okubalulekileyo ngolu phando-nzulu kushwankathelwe ngokuqinisekileyo, zibandakanyiwe iinjongo zolu phando, kwaye nenkqubo yolu phando njengoko luzokuqhubeka. Zifakiwe zonke iinkcukacha ezibandakanya okunokuthi kuzuzwe xa kugqitywe kolu phando-nzulu, nobungozi kwaba bangenelayo kunye nabazali babo.

Igama logqirha/ Umongikazi: ____

Indawo: ______________ Umhla: ______________ Isandla: ______________________________________

------------------------------------ Umbulelo ongazenzisiyo ngexesha osiboleke lona! ---------------------------------

12.2 Clinical examination sheet

CLINICAL EXAMINATION – INDIVIDUAL SHEET FOR MONITORING

Test date (dd/mm): ________/________/2016

ID: ☐ ☐ ☐ ☐ ☐

First name: ____________________ Last name: _____________________________

Gender: ❑ Female ❑ Male

DONE BY INVESTIGATOR:

- Did you have something to eat at home this morning before school? ❑ yes ❑ no
- How many meals did you eat yesterday? __________
- Did you go to bed hungry last night? ❑ yes ❑ no
- Do you feel hungry after meals because the meals are too small? ❑ yes ❑ no

FUNCTIONAL SIGNS:

Fever	❑ yes ❑ no	Vertigo	❑ yes ❑ no
Nervousness	❑ yes ❑ no	Cough	❑ yes ❑ no
Headache	❑ yes ❑ no	Constipation	❑ yes ❑ no
Nausea	❑ yes ❑ no	Itching	❑ yes ❑ no
Vomiting	❑ yes ❑ no	Blood in the stool	❑ yes ❑ no
Diarrhea	❑ yes ❑ no	Problems with breathing	❑ yes ❑ no
Belly ache	❑ yes ❑ no	Allergy	❑ yes ❑ no

- Menarche (to ask girls) ❑ yes ❑ no
  Starting date __________/__________ (mm/yyyy)

- Taking medication (last week): ❑ yes ❑ no
- If "yes", please specify the name or description of medication.
  Against worms:____

  Others: ____

5 November 2014

DONE BY NURSE / DOCTOR:

- Temperature: ___________ °C
- Results of the blood pressure measurement:

  Pulse______________bpm Blood pressure__________________ mmHg

- Result of the hemoglobin (Hb) test using HemoCue® Hb 301 system:

  ____________ g / L

- Results of the blood glucose (HbA1c) test using Alere Afinion AS 100 Analyzer:

  ____________ % HbA1c

  ____________ mmol/mol HbA1c

  ____________ estimated average glucose (eAG)

CONCLUSION:

Included ____________________________

Excluded (pattern) ____________________________

Name of the nurse / doctor in block letters: __________________________________

Signature of the nurse / doctor: ____

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SCHWEIZERISCHER NATIONALFONDS
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Institut Tropical et de Santé Publique Suisse

DSBG UNIVERSITY OF BASEL

SSAJRP

5 November 2014

12.3 Physical fitness score sheet

<table>
<tr><th colspan="6">PARTICIPANT EVALUATION FORM – FITNESS SCORE</th></tr>
<tr><th colspan="6">BIOGRAPHICAL INFORMATION</th></tr>
<tr><td>ID</td><td>☐ ☐ ☐ ☐ ☐</td><td>TEST DATE</td><td colspan="3">(dd / mm) : _____/_____/ 2016</td></tr>
<tr><td>NAME</td><td></td><td>SURNAME</td><td colspan="3"></td></tr>
<tr><td>BIRTHDAY</td><td colspan="5">(dd / mm / yyyy): _____/_____/20____</td></tr>
<tr><th colspan="6">PHYSICAL FITNESS COMPONENTS</th></tr>
<tr><th colspan="6">ANTHROPOMETRY</th></tr>
<tr><td>HEIGHT (cm)</td><td></td><td>WEIGHT (kg)</td><td colspan="3"></td></tr>
<tr><td>SKINFOLDS (mm)</td><td>TRIAL 1</td><td>TRIAL 2</td><td colspan="3">TRIAL 3</td></tr>
<tr><td>TRICEPS</td><td></td><td></td><td colspan="3"></td></tr>
<tr><td>SUBSCAPULAR</td><td></td><td></td><td colspan="3"></td></tr>
<tr><th colspan="6">PHYSICAL FITNESS TESTS</th></tr>
<tr><td colspan="3"></td><td colspan="2">TRIAL 1</td><td>TRIAL 2</td></tr>
<tr><td>Station 1</td><td>Flexibility</td><td>Sit & Reach (cm)</td><td colspan="2"></td><td></td></tr>
<tr><td colspan="3">CIRCLE DOMINANT HAND</td><td>TRIAL 1</td><td>TRIAL 2</td><td>TRIAL 3</td></tr>
<tr><td rowspan="2">Station 2</td><td rowspan="2">Upper body strength</td><td>Grip strength (kg) — Right hand</td><td></td><td></td><td></td></tr>
<tr><td>Left hand</td><td></td><td></td><td></td></tr>
<tr><td colspan="3"></td><td colspan="2">TRIAL 1</td><td>TRIAL 2</td></tr>
<tr><td>Station 3</td><td>Lower body strength</td><td>Standing Broad Jump (cm)</td><td colspan="2"></td><td></td></tr>
<tr><td>Station 4</td><td>Coordination & speed</td><td>Jump Sideward</td><td colspan="2"></td><td></td></tr>
<tr><td rowspan="2">Station 5</td><td rowspan="2">Cardiorespiratory fitness</td><td rowspan="2">20m Shuttle Run Test (20m SRT)</td><td colspan="2">Start Number</td><td></td></tr>
<tr><td colspan="2">Laps</td><td></td></tr>
</table>

12.4 Main questionnaire of the DASH study

Survey on the impact of disease burden on schoolchildren's physical fitness and psychosocial health in Port Elizabeth, South Africa

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Questionnaire

SSAJRP-project

Version 7, 27 January 2015

Hello,

How are you? How do you feel? This is what we would like ***you*** to tell us and is the reason why we are doing this questionnaire with you. We are not looking for right or wrong answers. We simply want you to write the response that tells us your feelings.

Please read every question carefully. Whatever answer comes to your mind that best reflects your feelings, choose the box that fits that answer best and tick (□) it. The entire test takes about 2 hours. After 1 hour, you have earned a 15 minute break.

Remember:

- This is not a test.
- There is no mark, and there are no wrong answers.
- Please answer all the questions, as honestly and accurately as you can.
- It is important that you answer all the questions.
- Make sure we can see your marks clearly.
- You do not have to show your answers to anybody.
- All answers remain secret.
- Neither your teacher nor the school principal gets to see the answers.
- Please only tick one box (☐) when answering the questions.
- If you have ticked something wrong, then cross out the field and mark the right place.
- If something is unclear, you can ask one of the investigators of course.

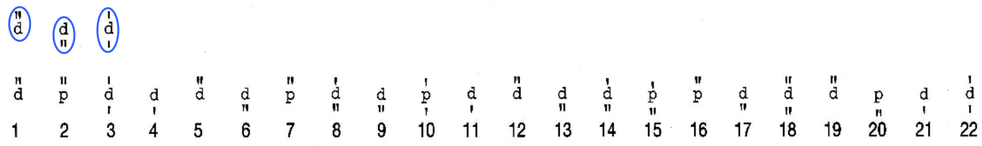
When you are done, please give the questionnaire directly to the investigator. Thank you!

Port Elizabeth and Basel, January 2015; the SSAJRP-team

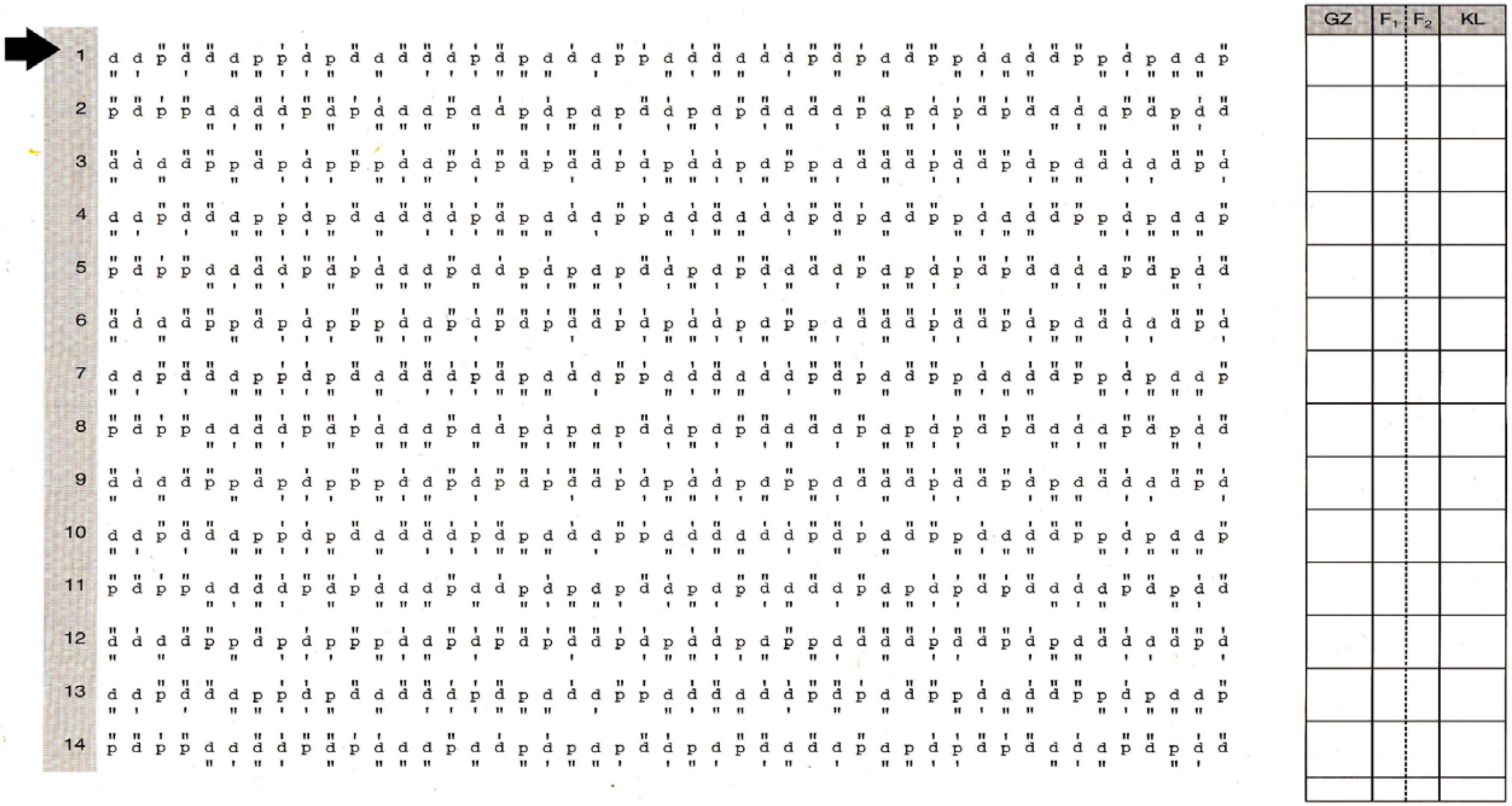
PART A
The d2 Test of Attention

At the beginning, we want to determine how well each of you ***can focus*** on a specific task (by means of the so-called d2 test). See the standard instructions for children which will be illustrated on the blackboard. The test sheet as you see below will be handed out to you prior to the execution of the test. The pure test execution time is 4 minutes and 40 seconds, the total time including instruction is about **8 minutes**.

Example:



Exercise line:



PART B
SOCIO-ECONOMIC AND DEMOGRAPHIC PROFILE

1. ID-Number (filled out by the researcher): ☐☐☐☐☐

2. First name: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

3. Surname: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

4. Age: ☐☐ **(in completed years)**

5. Grade: ☐☐

6. Surname of the teacher: ☐☐☐☐☐☐☐☐☐☐☐☐

7. Ethnic group/race: ☐ Black ☐ Indian ☐ Coloured ☐ White

☐ Mixed: _____________ & ______________

8. Home language: ☐ Xhosa ☐ Afrikaans ☐ English ☐ Other: _______________

9. Asset ownership: Do you have at home…

a.	**… a washing machine for clothes?**	☐Yes	☐No
b.	**… a fridge?**	☐Yes	☐No
c.	**… a freezer for food?**	☐Yes	☐No
d.	**… radios?**	☐Yes, how many: ________	☐No
e.	**… a land line phone / house phone?**	☐Yes	☐No
f.	**… a television?**	☐Yes, how many: ________	☐No
g.	**Do your parents have a cell phone?**	☐Yes, how many: ________	☐No
h.	**Does your family have a car?**	☐Yes, how many: ________	☐No
i.	**Does your family have a computer?**	☐Yes, how many: ________	☐No

Housing questions:

10. Do you live in a …

a. Shack in informal settlement ☐
b. Backyard shack/room ☐
c. Privately built house ☐
d. RDP house ☐
e. Council house ☐
f. Other, specify: ☐ ☐☐☐☐☐☐☐☐☐☐☐

11. How is your house made?

a. Zinc ☐
b. Bricks ☐
c. Wood ☐
d. Other, specify: ☐ | | | | | | | | | | | | |

12. How many bedrooms does your house have? | | |

13. Do you have a bathroom inside your house? ☐Yes ☐No

14. Do you have a toilet inside your house? ☐Yes ☐No

15. What type of toilet does your house have?

a. Flush toilet ☐
b. Pit toilet ☐
c. Bucket ☐
d. Communal toilet ☐

16. How does your family get water?

a. Taps inside house ☐
b. Tap in the yard ☐
c. Water tank ☐
d. Communal tap/tap shared with other families ☐

17. Does your house have electricity? ☐Yes ☐No

18. How does your family cook food? With …

a. Electricity ☐
b. Gas ☐
c. Paraffin stove ☐
d. Fire ☐

Family questions:

19. How many other people live in your house with you? | | |

20. Who looks after you for the most of the time?

a. Mother and father ☐
b. Mother only ☐
c. Father only ☐
d. Grandparents ☐
e. Brothers or sisters ☐
f. Other adults / guardians ☐

21. Who in your house has a job?

a. Both parents / guardians ☐
b. One parent or guardian ☐
c. None is employed ☐

22. Does any person in your house get a government grant? ☐Yes ☐No ☐ Don't know

PART C
BRIEF SELF-CONTROL SCALE (SCS)

Please choose the answer that best describes how you typically are.

	Never	Seldom	Sometimes	Often	Always
23. I am lazy.	☐	☐	☐	☐	☐
24. I say things that are strange and out of place.	☐	☐	☐	☐	☐
25. I do certain things that are bad for me, if they are fun.	☐	☐	☐	☐	☐
26. I refuse things that are bad for me.	☐	☐	☐	☐	☐
27. I am lacking self-discipline.	☐	☐	☐	☐	☐
28. I can’t stop myself from doing something, even if I know it is wrong.	☐	☐	☐	☐	☐

PART D
SCHOOL BURNOUT INVENTORY (SBI)

Please choose the answer that best describes your situation at school. Think about the last week…

	Never	Seldom	Sometimes	Often	Always
29. I feel overstressed by my schoolwork.	☐	☐	☐	☐	☐
30. I feel a lack of motivation in my schoolwork.	☐	☐	☐	☐	☐
31. I think of giving up in my schoolwork.	☐	☐	☐	☐	☐
32. I feel that my schoolwork is weak.	☐	☐	☐	☐	☐
33. I sleep badly because of a matter related to my schoolwork.	☐	☐	☐	☐	☐
34. I feel that I am losing interest in my schoolwork.	☐	☐	☐	☐	☐
35. I am wondering whether my schoolwork has any meaning.	☐	☐	☐	☐	☐
36. I brood over matters related to my schoolwork a lot during my free time.	☐	☐	☐	☐	☐
37. I am not able to achieve so well in my school work.	☐	☐	☐	☐	☐
38. I learn things quickly in most school subjects.	☐	☐	☐	☐	☐

PART E
KIDSCREEN-27: Health Questionnaire for Children and Young People

Think about the last week…

39. In general, how would you say your health is?

a. Excellent ☐
b. Very good ☐
c. Good ☐
d. Fair ☐
e. Poor ☐

	Never	Seldom	Some-times	Often	Always
40. Have you physically felt fit and well?	☐	☐	☐	☐	☐
41. Have you been physically active (e. g. running, playing)?	☐	☐	☐	☐	☐
42. Have you been able to run well?	☐	☐	☐	☐	☐
43. Have you felt full of energy?	☐	☐	☐	☐	☐
44. Has your life been enjoyable?	☐	☐	☐	☐	☐
45. Have you been in a good mood?	☐	☐	☐	☐	☐
46. Have you had fun?	☐	☐	☐	☐	☐
47. Have you felt sad?	☐	☐	☐	☐	☐
48. Have you felt so bad that you didn’t want to do anything?	☐	☐	☐	☐	☐
49. Have you felt lonely?	☐	☐	☐	☐	☐
50. Have you been happy with the way you are?	☐	☐	☐	☐	☐
51. Have you had enough time for yourself?	☐	☐	☐	☐	☐
52. Have you been able to do the things that you want to do in your free time?	☐	☐	☐	☐	☐

	Never	Seldom	Some-times	Often	Always
53. Have your parent(s)/guardian(s) paid enough attention to you?	☐	☐	☐	☐	☐
54. Have your parent(s)/guardian(s) treated you fairly?	☐	☐	☐	☐	☐
55. Have you been able to talk to your parent(s)/guardian(s) when you wanted to?	☐	☐	☐	☐	☐
56. Have you had enough money to do the same things as your friends?	☐	☐	☐	☐	☐
57. Have you had enough money for your needs?	☐	☐	☐	☐	☐
58. Have you spent time with your friends?	☐	☐	☐	☐	☐
59. Have you had fun with your friends?	☐	☐	☐	☐	☐
60. Have you and your friends helped each other?	☐	☐	☐	☐	☐
61. Have you been able to rely on your friends?	☐	☐	☐	☐	☐
62. Have you been happy at school?	☐	☐	☐	☐	☐
63. Have you got on well at school?	☐	☐	☐	☐	☐
64. Have you been able to pay attention?	☐	☐	☐	☐	☐
65. Have you got along well with your teachers?	☐	☐	☐	☐	☐

PART F
Health Behaviours in School Age Children Survey

Physical activity can be done in sports, school activities, playing with friends or walking to school.

66. Over the past 7 days (1 week), on how many days were you physically active for a total of at least 60 minutes (1 hour) per day?

0 days	☐	4 days	☐
1 day	☐	5 days	☐
2 days	☐	6 days	☐
3 days	☐	7 days	☐

67. OUTSIDE SCHOOL HOURS: How OFTEN do you usually exercise in your free time so much that you get out of breath or sweat?

a. Every day ☐
b. 4 to 6 times a week ☐
c. 2 to 3 times a week ☐
d. Once a week ☐
e. Once a month ☐
f. Less than once a month ☐
g. Never ☐

68. How long does it usually take you to travel to school from your home?

a. Less than 5 minutes ☐
b. 5-15 minutes ☐
c. 15-30 minutes ☐
d. 30 minutes to 1 hour ☐
e. More than 1 hour ☐

69. On a typical day is the MAIN part of your trip TO school made by…? (Please circle one only)

a. Walking ☐
b. Bicycle ☐
c. Bus or train ☐
d. Car, taxi or motorbike ☐
e. Other means ☐

70. On a typical day is the MAIN part of your trip FROM school made by…? (Please circle one only)

a. Walking ☐
b. Bicycle ☐
c. Bus or train ☐
d. Car, taxi or motorbike ☐
e. Other means ☐

71. First and last name of the investigator: ______________________ ______________________

72. Date of evaluation:

				2	**0**		