The association between healthy habits and healthy minds in today's youth

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Abbreviation

Disability adjusted life years	DALYs
Dynamic time warping	DTW
Generalized resistance resources – resistance deficits	GRR-RDs
Moderate-to-vigorous physical activity	MVPA
Non-communicable disease	NCD
Physical activity	PA
Physical inactivity	PI
Quality of life	QoL
Salutogenic model of health	SMH
Sedentary behavior	SB
Self-efficacy	SE
Sense of coherence	SOC
Sustainable development goals	SDGs
Swiss children's Objectively measured PHYsical Activity	SOPHYA
World Health Organization	WHO

Summary

The thesis is based on the Antonovsky's salutogenenesis theory, which suggests that the human experience is shaped by the opportunities. These opportunities can take the form of social capital (SC), which includes network capital (community network, personal network, and social contagion), and social cohesion (structural SC and cognitive SC). This is in addition to self-efficacy (SE), which is a construct of Bandura's social cognitive theory. SE reflects the individual's belief in having the ability to control events and the skills to achieve the individual's goals and expectations. Both SC and SE contribute to the development of the individual's sense of coherence's (SOC) constructs (comprehensibility, manageability, and meaningfulness). SOC contributes to the individual's mental and physical health through its ability to mobilize resources for overcoming stressors and challenges and ensuring positive health habits and overall well-being and health. In line with this, the analysis of "Health" is mainly based on the broadly accepted and used World Health Organization's (WHO) definition of "Health" as "a state of complete physical, mental, and social well-being and not merely the absence of disease", but with taking into account both the notion of "Health" as being subjective experience and its dependence on the individual's ability to adapt to reach positive health and enjoy life to its full potential.

This theoretical framework has been applied to two different contexts; first, in Switzerland, which is unique for being a high-income, multilinguistic and multicultural country. Second, in Palestine, which is a low income country characterized of having youthful society, which is highly collective.

In Switzerland, the theoretical framework was applied to assess the cross-sectional and prospective association of quality of life (QoL) as health outcome with accelerometer-derived physical activity (PA) as health-related behavior. In order to address this overall aim, we utilized longitudinal data from the Swiss Children's Objectively measured PHYsical Activity (SOPHYA) cohort (2013-2019). The study targeted all youth living in Switzerland and aged between 6 to 16 years old. Both PA, which was assessed using Actigraph accelerometer device, and QoL, which was assessed using the KINDL® questionnaire, were measured twice over a follow-up period of 5 years. The overall aim was addressed through conducting two main studies.

In the first study titled "Cross-sectional but not prospective association of accelerometry-derived physical activity with quality of life in children and adolescents", the main objective was to investigate associations between moderate-to-vigorous physical activity (MVPA) and QoL with focus on the longitudinal aspects. The rational of targeting this objective is related to the fact that MVPA is an established PA indicator and considered the foundation of WHO's recommendations on PA for children and adolescents. For the analysis of the primary endpoint of the study, the overall and domain-specific (Physical well-being, Emotional well-being, Self-esteem, Social well-being, Family connection and Functioning at school) scores of QoL on a scale of 0-100 were measured with higher scores representing a better QoL. The main

predictor of the study was measured based on accelerometer data averaged over a week, which was used to derive the mean hours per day spent in exercising MVPA by the participant. In order to address the first main objective, we asked three questions; 1) Is MVPA associated cross-sectionally with overall QoL and its specific dimensions? In order to answer this question, we built a cross-sectional model in which we regressed QoL on MVPA using data from both baseline and follow-up by applying linear mixed model (Model 1). 2) To what extend are these associations driven by the between-subject or within-subject variability in MVPA? To address this question, we built a model similar to model 1, but we portioned MVPA into between subject MVPA, which is the average of the subject's MVPA over two time points, and within-subject MVPA, which is the deviation of each subject's MVPA as measured at that point from the individual's mean (Model 2). 3) Does MVPA measured at baseline predict the overall QoL and its specific dimensions five years later? This question was answered by building a model in which we regressed QoL at follow-up on MVPA at baseline while adjusting for QoL at baseline using linear regression model (Model 3). In regards to the main findings of the study; the study included 352 participants with average age of 10 years at baseline and 15 years at follow-up. Both MVPA and the overall QoL decreased with the aging of children and adolescents. The results of the repeated cross-sectional analysis of the adjusted association between mean MVPA and QoL revealed the positive association of MVPA with the overall QoL ($p = 0.023$) and physical well-being ($p = 0.002$). A positive association of the between-subject MVPA with the overall QoL ($p = 0.030$), physical well-being ($p = 0.017$) and social well-being ($p = 0.028$) was observed. The within-subject MVPA was positively associated with physical well-being ($p = 0.039$) and functioning at school ($p = 0.013$). In contrast, the study did not provide evidence for a predictive association of MVPA at baseline with QoL or its specific dimensions five years later after adjusting for the participant's baseline characteristics, including baseline QoL.

In the second study titled "Weekend physical activity profiles and their relationship with quality of life: the SOPHYA cohort of Swiss children and adolescents", the main objective of the study was to explore weekend PA profiles and their relationship with QoL. In this study, the focus was on the overall PA profiles without being confined to specific established PA indicators such as MVPA and sedentary behavior (SB) and on weekend days as opposed to week days. Children's and adolescent's movement pattern is of high variability, non-structured and consists of short and frequent bursts of vigorous PA. Defining PA by only established PA indicators does not capture the entire heterogeneity of PA in children and adolescents. Accelerometer data contains additional information on specific PA-patterns and we were interested in studying whether they would associated with QoL as health endpoint beyond the QoL association with conventional PA indicators. Moreover, shedding light on PA during weekends creates a window of opportunity for interventions to promote PA in the family environment and during leisure time. To address the main objective, we first identified clusters of device-based PA during weekend days among children and adolescents from the SOPHYA cohort. This was completed by applying the dynamic time warping (DTW). Based on the distance matrix, which was obtained by the DTW, we applied the elbow and

silhouette methods to determine the optimal number of clusters. The elbow plot suggested a decrease in the within-cluster dissimilarity when moving from 1 to 2 clusters, but also when moving from 2 to 4 clusters. The silhouette method suggested that PA profiles are best described using 2 clusters model, but the 4 clusters model scored high as well. Therefore, we conducted parallel analyses with k=4 (main text) and k=2 (online supplement). With respect to the 4 clusters model, the study identified clusters of youth with different PA behavioral patterns (high activity cluster, medium activity cluster, low activity cluster and inactive cluster). The "high activity" cluster participants, compared to other clusters, scored highest in the mean counts per epoch (mean [SD]: high activity: 284.0 [61.0]; medium activity: 205.0 [29.6]; low activity: 148.0 [19.3]; inactive: 90.9 [21.1] counts; $p < 0.001$). The "high activity" cluster also scored highest in the average hours spent in MVPA. The "inactive" cluster participants scored highest in the average sedentary time (mean [SD]: high activity: 6.3 [1.4]; medium activity: 6.6 [1.3]; low activity: 7.2 [1.3]; inactive: 8.5 [1.5] hr/day; $p<0.001$). The higher activity cluster participants were on average younger (mean [SD]: high activity: 10.2 [2.3]; medium activity: 9.7 [2.1]; low activity: 10.2 [2.1]; inactive: 12.4 [2.4] years; $p<0.001$) with an overrepresentation of the male gender (percentages of boys in the "high activity", "medium activity", "low activity" and "inactive" clusters were 66.7%, 60.8%, 48.9%, and 39.5%, respectively; $p<0.001$). After identifying clusters of PA profiles, we assessed the cross-sectional and predictive association of the newly identified clusters of PA profiles with QoL with and without adjustment for conventional PA metrics. Participants in the "high activity" cluster exhibited on average 5.4 (95%CI: 1.2 to 9.6) higher social well-being scores than participants assigned to the "inactive" cluster ($p = 0.012$). This association persisted only after adjustment for SB ($p = 0.030$). There was no evidence for a predictive association of cluster membership at baseline with QoL or its dimensions at follow-up when adjusting for the baseline QoL or its dimensions, irrespective of adjustment for established PA metrics.

In Palestine, the theoretical framework was applied to plan a study to explore the role of SC, SE and social contagion in shaping lifestyle and mental health among students representing the future healthcare workface in Palestine. The study protocol was designed to identify future targeted interventions that could be implemented to address the high prevalence of non-communicable diseases and the presence of gap in the treatment and diagnosis of mental health problems in Palestine. Therefore, the study protocol targeted second and third-year students enrolled in the faculty of medicine and health of An-Najah National University in Nablus, Palestine. The protocol describes a digital prospective cohort with baseline and two follow-ups online surveys. The study protocol was published in BMJ Open (Darkhawaja R et al. BMJ Open 2022 Jan 19; 12(1):e049033) reflecting the novelty of the study. The launching of the study's survey coincided with the outbreak of the COVID-19 pandemic. As a result, the response rate in the baseline survey was very low (<10%), and the study implementation was postponed to after the completion of the thesis.

As final conclusion, the thesis confirmed existing evidence that device-measured MVPA and QoL is positively associated in youth living in Switzerland, at least cross-sectional. We were not able to identify novel PA clusters for weekend activity that were independently of conventional indicators associated with QoL. But the fact that the thesis provided evidence for the parallel decline of both PA and QoL with aging, suggests that health-in-all-policy and interventions to promote both, PA and QoL in age-specific manner are important. Future longitudinal studies on the relationship between PA and QoL in youth should employ shorter follow-up times and collect several longitudinal measurements of every participant to improve understanding of the sustainable benefit of PA promotion on QoL. The findings on PA and QoL in Swiss youth point to the relevance of implementing the developed study protocol for Palestinian youth to promote culturally adapted PA promotion interventions in the future.

Chapter 1: Introduction

In order to understand the assumptions and values, which have been made to address "Health" in the thesis, the definition of the concept of "Health", which is adopted, and why it is chosen among other definitions, should be addressed (1). Also, the chosen definition of the "Health" concept determines the health promotion patterns and the recommendations that are being suggested to improve the health and the health care system (2). Our analysis of "Health" is mainly based on the broadly accepted and used definition of "Health" as "a state of complete physical, mental, and social well-being and not merely the absence of disease", which is part of the 1948 Constitution of the World Health Organization (WHO) (3), but with taking into account other suggestions for modified contemporary definition of "Health". The WHO's definition of "Health" is revolutionary; it has led to visualizing "Health" through a different lens to include the individual's physical, mental and social well-being as a whole beyond the dualistic health-disease pathological approach. In line with that, it implies that "Health" should not be analyzed in isolation of the context of interest because "Health" is shaped by structural social and environmental determinants (4). The popularity of the definition is acknowledged, but also the several critics of the definition. The definition has been criticized for addressing "Health" as [a state of complete …]. This is because it means the attainment of complete well-being should be the goal of any health promotion and prevention initiative. This is very ambitious target as we live in world with limited availability of and accessibility to resource (5). Additionally, the world is going through demographic and epidemiological transitions as the aging population and the prevalence of non-communicable diseases (NCDs) are increasing. Thus, the state of complete well-being "Health" becomes unattainable and this definition is not practical and cannot be fully operationalized (5, 6). The definition is also critiqued for being highly subjective and its interpretation is influenced by cultural beliefs and can be manipulated to promote local political and cultural ideologies (7). These critics have been followed by proposals to modify the WHO's definition; Card suggests to define "Health" as "the experience of physical and psychological well-being. Good health and poor health do not occur as a dichotomy, but as a continuum. The absence of disease or disability is neither sufficient nor necessary to produce a state of good health" (5). While Krahn and her colleagues has proposed to define "Health" as "the dynamic balance of physical, mental, social, and existential well-being in adapting to conditions of life and the environment" (6). Lastly, Huber suggests to define "Health" as "the ability to adapt and self-manage in the face of social, physical, and emotional challenges" (8). All these proposals seem to reiterate the notion that contemporary definition of "Health" should be based on the holistic approach of integrating both the physical and psychological well-being aspects of "Health". Moreover, it should be based on the assumption that "Health" is reflection of the individual's subjective experience of well-being and the ability to enjoy life to its full potential and not merely on the absence or presence of a disease or disability (9). The last is emphasized by Antonovsky's theory, which is based on the assumption that the individual is always in an entropy position of ease/dis-ease continuum and on "generalized resistance resources – resistance deficits (GRR-RDs) continuum. And the individual's sense of coherence

(SOC) determine the individual's ability to link the generalized resistance resources to stressors and health in order to overcome stressors and challenges in a way to ensure positive health that includes well-being (10).

1.1. Health outcomes

1.1.1. Non-communicable Diseases

According to the WHO, NCDs have been defined by two major characteristics; first, NCDs cannot be transmitted. Second, it stays over long period of time and progress overtime (11). The NCDs are grouped into four main categories, which are cardiovascular diseases (heart attacks and strokes), cancer, chronic respiratory diseases (chronic obstructive pulmonary disease, asthma), and diabetes (11).

The current trend indicates that there is increase in the prevalence of cardiovascular diseases, cancers, chronic respiratory diseases and diabetes worldwide (11). The Eastern Mediterranean Region (12) and Arab countries (13) exhibit similar tends. One of the factors that has contributed to this epidemiological transition is the advancement in medical technologies, which led to the control of communicable diseases and increased the prevalence of the aging population and NCDs, which are known to develop over a prolonged period of time (14-16). Globally, NCDs are considered major contributor to morbidity and mortality. If left unmanaged, NCDs can lead to disability (17); the contribution of NCDs to the total global disability-adjusted life years (DALYs) has increased from 43.2% in 1990 to 63.8% in 2019 (18). Also, NCDs contribute to 74% of the total deaths annually with cardiovascular diseases are ranked the first contributor to the total deaths followed by cancer (11). In addition to this, it has been projected for the total annual number of deaths from NCDs to reach 55 million by 2030 (19). Besides its contribution to morbidity and mortality, NCDs have negative impact on the economy as it leads to increase in the health expenditures for its treatment and decrease productivity (17, 20).

The high burden of NCDs exists in both, low-and middle-income countries and high-income countries. Both Palestine and Switzerland are affected by it. According to the Palestinian Ministry of Health, NCDs are considered the leading cause of total death with cardiovascular diseases ranked the first contributor followed by cancer for the year 2021 (21). In Switzerland, quarter of the population are diagnosed with NCDs, which are considered the main cause of mortality (22). Despite the fact that both low-and middle-income countries and high-income countries share similar tends, the burden of NCDs is unequally distributed between them; the proportion of mortality due to NCDs is higher in high-income countries compared to low- and middle-income countries, while the later scores higher in the absolute number of mortality from NCDs (23). This is because the risk of premature death from NCDs is double in low-and middle-income countries, which accounts for 85% of premature adult deaths (24-26). The unequal distribution of the burden of NCDs exacerbates the situation in low-and middle-income countries for two reasons; first, infectious diseases are becoming treatable and chronic leaving these countries to face double

burdens of infectious and NCDs (17, 27-30). Second, there is limited resources for financing NCDs' treatments in these countries, which limit the accessibility to services for the treatment of NCDs (25, 26).

The complexity of NCDs is not only related to the fact that it has long period of latency (31), but also NCDs are associated with multiple risk factors (13, 17, 32-36). There are both individual and structural determinates of NCDs; the individual risk factors can be biological as a result of personal medical history, family history (37), age and gender (37, 38). Also, it can be behavioral and cognitive risk factors such as tobacco use, alcohol consumption, physical inactivity, unhealthy diet, low self-esteem and impulsivity (13, 17, 32-37). Globally, behavioral risk factors accounted for 45% of total deaths in 2017 (18). These risk behaviors are usually associated with physiological parameter risk factors such as high systolic blood pressure, high fasting plasma glucose, high body-mass index, and high LDL cholesterol (39). These behavioral risk factors contribute to the increase in NCDs in both low-and middle-income countries and high-income countries; for example, Palestine is becoming a country characterized by high consumption of fat-rich foods and calories and sedentary lifestyles (12, 13, 40). Also, 31.3% of the Palestinian population who are 18 years or older reported that they have smoked one or more type of tobacco products including manufactured cigarettes, hand-rolled cigarettes, cigars, and water-pipes in 2021 (41). While in Switzerland, dietary risks and tobacco smoking are considered major risk factors for NCDs (34). And there are individual sociodemographic characteristics factors associated with NCDs including marital status, residential status, refugee status (38), socio-economic status (37, 42), being exposed to adverse life events and social exclusion (37). In regards to structural determinants of NCDs, it includes both physical and psychosocial components; the former includes poor housing, proximity to food stores selling processed foods, unavailability of sidewalks, limited availability of public parks, urbanization (17, 43), air pollution (44), exposure to chemicals such as lead (45) and exposure to carcinogens (46). While the later includes poverty, lack of safety, and social norms of behavior (17, 43). The psychosocial determinants of NCDs in Palestine are distinctive; they are characterized by conflict, the economic hardship, unemployment, family conflict, lack of public spaces for recreation and leisure, and lack of sustainable facilities for physical activities, which increase the stress and ultimately their risk of developing NCDs (32). The distinction between the individual risk factors and the structural determinants of NCDs are not absolutely exclusive; the adoption of dietary risk factors, tobacco use, alcohol consumption and physical inactivity are not absolutely attributed to personal choices, but also shaped by structural system factors such as national policies on taxes, advertising and ethics of marketing, by the built environment and the urbanization patterns (17).

The United Nations have conducted several initiatives to control NCDs. In 2000, the United Nations set the Millennium Development Goals to be achieved by 2015, in which it has focused on issues related to poverty, education, gender equity, child mortality and combating infectious diseases. While the control of NCDs have been given limited attention (47). Then, in September 2011, the United Nations held its first

High-Level Summit on NCD, which led to the development of the UN Political Declaration on prevention and control of NCDs (48). And as a succession to this summit, the 65th World Health Assembly was held and adopted the resolution, which aims at 25% reduction in the premature mortality from NCDs by 2025 as global target (49). Following this, in 2015, the United Nations have adopted the sustainable development goals (SDGs) to be achieved by 2030; one third reduction of the probability of dying between 30 years and 70 years of age from NCDs (cancer, cardiovascular diseases, chronic respiratory diseases and diabetes) by 2030 has been set as important target (50).

The complex interrelated factors, which contribute to the development of NCDs, implies that any attempt for the primary prevention of NCDs would require the collaboration between different sectors and agencies (17). This includes the importance of the urban planning to take into account the health implications that goes beyond the conduction of health impact assessment (51). Research studies have provided evidence for the implementation of primary prevention measures to be the most cost effective approach for controlling NCDs (52, 53). This includes but not limited to the control of tobacco use and salt reduction (25, 26, 54). Given the fact that NCDs have long latency period, the utilization of primary prevention measures can extend the control of NCDs to the future generations (17). Despite this, there are several countries, which lag behind in its attempt to implement primary prevention measures to control NCDs; for example, Switzerland lags behind in primary prevention with regard to control tobacco use, alcohol consumption and dietary risk factors in comparison to other countries of comparable financial resources (17).

1.1.2. Mental Health

Mental health is considered important since it shapes the human's ability to think, interact with others, earn a living and enjoy life both individually and collectively (55). Conceptualizing mental health has evolved over time. Recently, the WHO has suggested mental health to be defined as [… "more than the absence of mental disorders. Mental health is a state of well-being in which an individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and is able to make a contribution to his or her community"]. Based on this definition, mental health has both subjective and objective components (56). Thus, mental health disorders include wide range of conditions including feeling of fear, anxiety, depression, sadness, despair, lack of safety and psychosocial disabilities (57, 58). Also, it is always important to consider both objective and subjective aspects of mental health because this will facilitate the identification of the contextual and the cultural differences in the understanding of mental health in different countries such as those with long-term conflict (59). The contextual effect on mental health should not be limited to the diagnosis of mental health disorders, but it should be extended to its treatment (60). In Switzerland, despite it's high income level, mental health problems have been increasing among the young over the past years, in part COVID-19 related (61). In Palestine, the sense of injustice in the light of the politically challenging situation and everyday living conditions implies defining mental

health disorders among the Palestinians should be beyond the diagnosis of psychiatric medical conditions to include the "invisible wounds inside" against them (59). Moreover, it is important for these wounds to be healed because they are usually continue to be embedded in their memories at the long term and can be developed into disease in the future (58).

There are several factors, which have contributed to the increase in the mental health disorders worldwide; the demographic transition has been associated with the increase in the prevalence of age related mental disorders such as dementia (62).

Mental health disorders have adverse implications in terms of morbidity and mortality. It is considered major contributor to disability; the proportion of the DALYs that have attributed to mental health disorders have increased from 3.1% in 1990 to 4.9% in 2019 (63). Add to this, depression, which is common mental health disorder, is considered the second leading cause of disability (19) and is expected to become the main cause of disability globally (64).

Despite the known negative outcomes associated with mental disorders, its prevention, treatment and control have not been addressed to its full potential (65). In the Global South, resource allocation for mental disorders is sparse partially due to it being stigmatized (66). For example, in Palestine, mental health care services remain weak; according to the Palestinian Ministry of Health Annual Report for 2021, at the primary healthcare level, there are 16 specialized psychiatric and community health clinics in West Bank and 6 in Gaza Strip (21). While at the secondary healthcare level, there is one psychiatric hospital in Bethlehem, which is in the south of the West Bank (67). Historically, the major contributor to the development of mental health care services in Palestine has been the Palestinian NGOs and the UNRWA. The provision of mental health services by the Palestinian NGOs and the UNRWA contributed to the decrease in the gap in the mental healthcare system, but the sustainability of this improvement it depends on sustainable funds (68).

1.1.3. Mental Health Disorders and Non-communicable Diseases

Research studies suggest bidirectional relationship between mental health disorders and NCDs (69-73). For example, there is evidence for depression to be independent risk factor for several cardiovascular diseases (74). And those who are diagnosed with NCDs are more likely to develop mental health disorders compared with the general population (75). This bidirectional relationship is the result of the intersection between mental health disorders and NCDs in many aspects; both mental health disorders and NCDs are chronic diseases, which entails that they last over long period of time and require continuous management that can last over the life-course (37). Additionally they share common risk factors (76, 77) including biological (e.g. personal medical history, family history, age, and gender) (37), and behavioral risk factors (e.g. tobacco smoking, alcohol consumption, physical inactivity, dietary risks, obesity, hypertension and hyperglycemia) (78-90). Given this, the co-occurrence of mental disorders with NCDs tends to be

inevitable and evident by several research studies especially among the "big four" NCDs and common mental disorders (91, 92); studies have provided evidence for the co-occurrence of type 2 diabetes with depression (37, 93-95), schizophrenia, and bipolar disorder (94). Similar findings have been reported for the co-occurrence of each of cardiovascular diseases (37, 96-99), chronic obstructive pulmonary diseases (37, 100), cancers (37, 100, 101) and asthma (37, 100) with depression, and anxiety. The co-occurrence of otherwise deteriorated psychological well-being with NCDs exacerbate the abnormalities associated with the later (102). Moreover, there is high probability of either the delay (103) or the miss diagnosis of NCDs when it co-occurs with mental health disorders (104, 105). Also, the management and treatment of NCDs are challenging in the presence of mental health disorder as the patient with mental health disorder is less likely to adhere to treatment plans (80, 106-108). In line with that, those who are diagnosed with NCDs are less likely to be screened for mental health disorders (109).

Given the bidirectional relationship (69-71), the shared common risk factors (37, 76-90) and the co-occurrence of NCDs and mental health disorders (37, 91-101), impose several questions on the most effective and efficient approaches to treat mental health disorders and NCDs. Despite the growing evidence for the shared behavioral risk factors between NCDs and mental disorders (37, 76-87, 89), the realization of the urgency of integrating primary prevention approaches through targeting behavioral modifiable risk factors for the control of mental health disorders have been limited compared with the several initiatives that have been implemented for the primary prevention of NCDs (110). This is despite the fact that the effectiveness of targeting behavioral modifiable risk factors in the treatment of mental health disorders is evidence-based (111). Also, there have been several suggestions to consider mental health disorders as part of NCDs (65, 112). In fact recently, WHO has recognized mental health as one of the major NCDs (24).The call for the inclusion of mental health disorders as part of NCDs have been made in parallel with the importance of developing holistic approach for the management of NCDs and mental health disorders simultaneously. This has been supported by several studies, which provided evidence for the effectiveness of the management of NCDs and mental health disorders together (113, 114).The proposed approaches for the integration of NCDs with mental health disorders share in common main features despite the differences in the terminologies used to describe each approach; there is consent on the importance of integrating the management of NCDs and mental health disorders at both the primary and secondary health care levels (66, 73, 90, 106). This is through the collaboration between primary care providers and community health workers with specialized physicians (73, 106).

1.1.4. Quality of life

In 1964, the concept of quality of life (QoL) has been first introduced by the U.S.A President Lyndon Johnson in his notion on the progress on social goals when he said "social goals cannot be measured by the size of our bank balance. They can only be measured by the quality of the lives our people lead". And he said "the great society is concerned not with how much, but with how good – not with the quantity of

goods, but with the quality of their lives" (115). QoL has different philosophical, political and health related implications (116). Overtime, it has become major indicator for the development and evaluation of different sectors. Scholars from various disciplines have defined and measured QoL by applying different social, economic and subjective indicators (117). Environmentalists have addressed QoL based on physical and biological environmental conditions. While economists have analyzed QoL in relation to objective indicators such as the Gross National Product. And for sociologists and psychologists, human needs and its fulfillment were central aspects in their assessment of QoL (118, 119). Moreover, QoL has emerged as fundamental objective in the agendas of many countries (120).

At the end of the 20th century, research focus has been tailored to understand the concept of QoL in relation to health (121).This is in part due to the recent development in the medical field, which has led to increase in the longevity of individuals including those with chronic diseases as oppose to terminal illness such as the longevity of people who suffer from life threating conditions of cancer and cystic fibrosis (122). Also, the WHO's definition of health as "a state of complete physical, mental, and social well-being and not merely the absence of disease" has challenged the way by which the individual's health should be perceived and evaluated (3). Thus, conventional health indicators such as mortality and morbidity defined by symptoms, laboratory tests, clinical observations and survival rate have become insufficient to assess the efficiency and effectiveness of the health care system (122, 123). Instead, there has been call for developing treatment plans that guarantee the personal development of the individual including his or her coping mechanisms to adapt to different life circumstances (124) such as treatments for cancer (125) and hypertension (126). Based on these accounts, QoL has been considered important indicator of health outcome to complement other conventional health indicators (127-129).

There is not unified definition for the QoL concept as health outcome because of the variation in the theoretical and conceptual accounts of the relation between QoL and health (130, 131). And its definition depends on the demographic, social, economic, cultural, political and geographical context in which QoL is being assessed (132). Based on the WHO, QoL is defined as "an individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (133). WHO's definition of QoL tends to emphasis the multidimensional and the socio-cultural understanding aspects of the QoL (132). While health-related quality of life is specific term, which sheds the light on the aspects of health directly linked to QoL; Bullinger defined health-related quality of life as "the impact of perceived health on an individual's ability to live a fulfilling life" (134). Nordenfelt has presented his account on the relation between QoL and health based on the want-equilibrium theory of happiness. He has defined happiness as "the equilibrium between the individual's wants and the belief that these wants are satisfied". While he has defined health as "the abilities of the individual to achieve vital goals, which leads to happiness". Furthermore, he has concluded health to be a major contributor to happiness. And happiness to be equivalent to QoL (130).

There has been mutual consent to consider QoL as multi-dimensional concept, which encompasses several dimensions of the individual's life. The most common dimensions, which have been used to define the concept of QoL are; personal well-being, health, education and learning, social relations, nature and environment, housing, shelter and accommodation, civic engagement, participation and rights, safety, security and crime, business and economy, and community (132). Also, QoL has been considered positive construct, which should address well-being in order to resonates with WHO's definition of health "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (3, 135, 136). In reference to the last account, several critiques have been made on the relationship between QoL and well-being; well-being has been suggested to be related to the individual's mental and emotional state including level of happiness and fulfilment. While QoL is considered broader concept, which addresses life improvement, autonomy and the achievement of one's goals (132). There are serval studies, which provided evidence for the positive correlation between QoL, happiness and subjective well-being (137). In line with this, QoL measurement has been used as a proxy for the measurement of well-being (138). Also, there are scholars who suggest the need for comprehensive concept that integrate indicators from both the QoL and well-being concepts. This is because, as combined, both concepts provide better explanation for the variation in the general QoL compared to the application of either of the two concepts, separately (139). One of the important aspects of QoL as health outcome is its reflection of the individual's subjective perception of his or her health and the personal and contextual determinates of his or her health that cannot be captured by other conventional health indicators (140-142). Scholars have debated whether to consider QoL as subjective or objective construct; for some of them, QoL is exclusively subjective construct because it is reflection of the individual's perception of their lives (132, 135, 143). For the concept of QoL to be subjective, self-report on QoL is better than proxy reporting (135). The more traditional scholars have considered QoL to be objective construct and can be assessed based on both economic and social objective indicators in isolation of the individual's perception (132, 144). While others have concluded QoL to be comprehensive construct, which can only be measured by assessing both subjective and objective indicators (145, 146).

Given the fact that there is not any instrument, which covers the wide range of QoL aspects, it has been suggested for any methodology to measure QoL should include the specification of the levels and kinds of QoL of interest. Following that careful analysis should be made to identify the dimensions and its interrelationships to be assessed. Finally, indicators, which reflect these dimensions, should be identified (147). QoL measurement has been conducted by applying several research designs and using different instruments in order to suit different purposes, populations and settings (135). For example, in Palestine, the lack of political freedom and self-determination have been reported to be important aspect of the Palestinians' QoL. This is because these factors determine the ability of people to exercise democracy and engage on political decision-making (148). The instruments, which have been used to measure QoL, are

either generic or specific QoL assessment instruments. The majority of the research studies have used generic instrument. These instruments take the form of questionnaires, which are either self-administrated or conducted through interviews with the targeted individuals (149). There is preference for using generic QoL instruments because it can it covers a wide range of QoL's aspects and it can applied among both healthy and diseased populations (150). While most of the studies on QoL as health outcome have been addressed in relation to the chronic NCDs including cardiovascular disease, hypertension, diabetes, dyslipidemia and obesity (149). Systematic reviews indicate that most studies on QoL have succeeded on identifying the dimensions of QoL being assessed and provide justification for the selection of the instrument. On the other hand, these studies have conceptual and methodological limitations as most of them don't provide precise operational definition of QoL and don't distinguish between QoL and health-related quality of life (144, 151). The variation in the instruments, the methodologies and the administrating method of the questionnaires, which have been used to assess QoL, limit the ability to compare studies on QoL between different groups (149).

Historically, research studies of QoL among adults have been more common than among children and adolescents (152). QoL research in children and adolescents has only started in the 1980s (153, 154). The assessment of QoL among children and adolescents as health outcome has become paramount for several reasons; based on the data from 2022, approximately 32% of the population worldwide are under the age of 20 years (155). In reference to the United Nation's Convention on the Rights of the Child, children have the right to express their own perspective in matters related to them such as their perception of their own health defined by QoL measurement (156). Moreover, there is evidence for the clustering of psychosomatic symptoms, which are attributed to psychosocial stress, such as headache, abdominal pain, loss of appetite and back pain, among children and adolescents (157, 158). Also, there is increase in the prevalence of chronic conditions (159, 160) and psychosocial disorders (161) among them. Similar to QoL research in adults, QoL research in children has evolved over time; initially, in the 1980s, the focus was on the development of the theoretical concept of QoL in children. While in the early 90s, the construction and development of QoL measures for children have emerged. And it is only in the beginning of 1995 when the application of QoL measures for children and adolescents has started to be applied in clinical and epidemiological studies (153, 154). In the assessment of QoL as health outcome among children, it has been recommended to decide on a unified operational generic QoL definition, which include domains applicable to all children and adolescents and assessed by both subjective and objective indicators (152). Also, the rapid development in the physical, mental and social aspects during childhood should be taken in consideration (122, 162). Furthermore, in comparison to adults, depending on their development age, children and adolescents might value certain life domains more than others (163). For example, children and adolescents seems to consider the role of the family, friends and school as important components of quality of life (164). Additionally, the instrument to be used should consider the development stage of the child, it should be easily applicable and appropriate to the cultural context of the child (123, 136).

One of the major challenges in the assessment of QoL among children and adolescents is the ability of children to report about their perceived health has been debatable (165). Given the importance of capturing the individual's subjective perception of his or her health through the assessment of QoL, there has been a support for the self-repot of QoL by children and adolescents as oppose to proxy reporting for capturing children's and adolescents' perception of their health (122). This is become evident as there is not agreement between the self-report of quality by children and adolescents with the proxy reporting of their parents (166-169). Also, research has provided evidence for the ability of children to self-report about their health (170). In order to attain accurate self-reporting on QoL by children and adolescents, it is important to choose age appropriate instrument (123, 136).

The instruments, which have been developed to measure QoL among children include the Child Health Questionnaire (171), KINDL-R (172), the KIDSCREEN Questionnaire (173), and the Inventory for Measuring Quality of Life in Children and Adolescents (174). The KINDL-R is instrument for measuring the QoL among healthy children and adolescents. Despite the fact that it has been developed in German, it has been translated into 22 languages (175). The increase popularity of assessing QoL among children and adolescents using the generic KINDL-R questionnaire is related to the fact that first, it has different versions adapted to the age of the children and adolescents. Second, it has two versions, one is appropriate for the self-report version, while the other is for the proxy reporting by the parents. Third, the questionnaire exhibits good psychometric properties including high reliability. Fourth, there is standardized values based on studies, which was conducted in Germany, which is essential for comparison matters (176-180).

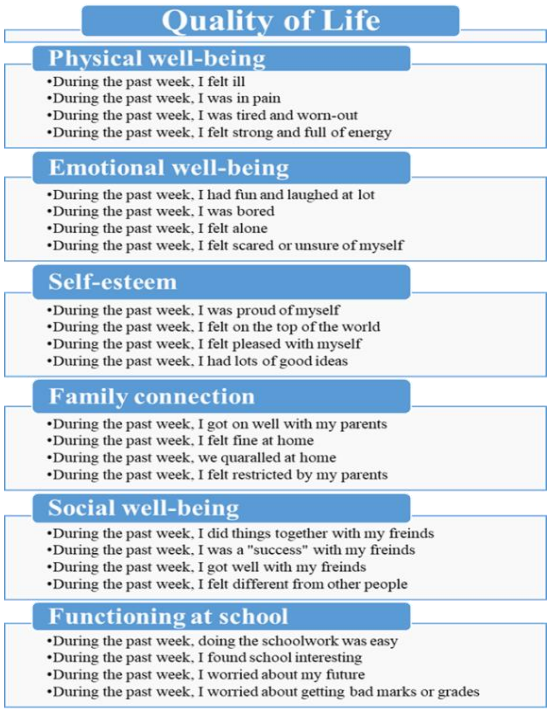

Figure 1. Quality of life and its dimensions based on the KINDL-R questionnaire

1.2. Health related behaviors

1.2.1. Physical activity: one of the big four health-related behaviors

Physical activity (PA) is defined as "all bodily actions produced by the contraction of the skeletal muscle that increase energy expenditure above basal level" (181). PA is categorized into two main domains, which are leisure-time PA and occupational PA (182). The characterization of PA involves identifying its three dimensions; intensity, duration and frequency (183). There are differences in the movement pattern between children, adolescents and adults and some of these difference are attributed to biological predisposition. Children and adolescents are more active than adults because they predominantly acquire knowledge through movement to stimulate the central nervous system. Adults attain these information through other methods such as reading (184). Also, children's and adolescents' movement pattern is of high variability, non-structured and consists of short and frequent bursts of moderate to vigorous activity (185, 186). These differences contributes to the challenges associated with the measurement of PA among children and adolescents. This requires special considerations to be taken into account in the assessment of their PA.

The measurement of PA has been performed by applying either objective or subjective methods. Both methods have advantages and limitations; the subjective method involves the use of self-report on activity logs, diaries and questionnaires (187-189). The advantages of using self-report methods are; self-report method is of low cost, it is easily applicable (189-191), it is acceptable among the different population groups (189), it permits the tracking of PA based on chronological order (190), and it captures the type and the context of PA being performed (190, 191). These advantages make it feasible for self-report methods to be used in large population studies (192). Nonetheless, several research studies have provided evidence for inability of children and adolescents to provide accurate recall for the quantity and the time of the PA being performed (193-195). Also, children and adolescents might not have the accurate understanding of what is meant by "PA" (196). These limitations increase the probability of recall bias in the measurement of PA among children and adolescents by applying self-report methods (192). The recall bias can be detected at both the reporting of the duration and intensity of PA being performed (197). Due to these limitations, instruments based on self-report for measuring PA among children and adolescents have validity level, which ranges from being poor to acceptable with children reporting poorer validity than adolescent youth (198-200). The proxy-reporting on PA of children and adolescents by their parents or teachers can minimize the recall bias, but it should be carefully applied for the effective measurement of PA in large epidemiological studies (191). In regards to objective methods for measuring PA, direct observation methods, heart rate monitors, pedometers and accelerometers are methods for measuring PA among children and adolescents objectively (186). PA can be assessed through the direct observation of a person at home or school for specific period of time and recoding the rate of the child's activity level. Measurement of PA through direct observation comes with the opportunity of identifying factors

associated with the PA being performed such as the environmental conditions, the presence of equipment and among other factors (188, 190). Examples of direction observation systems for measuring PA include the System for Observing Play and Leisure Activity in Youth (SOPLAY) (201) and the Observational System for Recording Physical Activity in Children (OSRAC) (202). Direct observation measurement of PA among children and adolescents is of high validity and reliability (203), but it can be expensive because it requires rigorous labor (190). Accelerometers, pedometers and heart rate monitors are common wearable activity tracker for the objective measurement of PA (204). The heart rate monitor has been used to assess the PA in children and adolescents because there is linear relationship between heart rate and energy expenditure (188, 204). The heart rate is confounded by several variables such as age, body size and proportion of muscle mass. Also, the heart rate is not synchronized well with the change in the movement at high and low-intensity levels of PA. These challenges associated with the use of the heart rate monitor can increase the PA measurement error due to the differences in the individual characteristics between children and adolescents and the nature of their movement pattern characterized by long periods in light and sedentary activities (191, 204). The pedometer is known to be cost-effective tool for measuring PA in children and adolescents (188, 190), but it only measures the relative volume of PA and it does not provide information on the frequency, intensity or duration of PA (190). While the accelerometer is considered the most popular wearable activity tracker for measuring PA objectively in epidemiological studies (205-208). The accelerometer can measure the frequency, intensity and duration of PA over time (209). It functions through detecting the acceleration of the body's movement. Then, it digitizes the acceleration signal and converts it to "activity count". The activity counts over specific time interval, which is called "epoch", are summed. And the sum of the activity counts can be used to derive different PA measurements (191). In the assessment of PA among children and adolescents, it is recommended to use short epoch length to attain accurate measurement (210). The accelerometer has been recommended to be used for measuring PA among children and adolescents because it is of small size, lightweight and robust design (191, 209). In line with this, measurement of PA among children and adolescents using the accelerometer has proven to be accurate and valid (211). There are two types of accelerometers; the triaxial accelerometer, which capture the acceleration from all three axes and incorporate them into a single overall vector magnitude. While the uniaxial accelerometer detects acceleration only from one axis, which is mainly the vertical access to measure PA (191, 212, 213). The limitation of using the accelerometer is its inability to provide comprehensive information about the type (e.g. cycling, weight lifting) or the purpose of the activity being performed (214). Also, it does not detect whether the person is carrying any weight while performing PA (215). The accurate assessment of PA is not guaranteed only by choosing the appropriate method for measuring PA, but it also depends on the study design being applied; there are several studies on physical activity among children and adolescents, which fail to specify the type of physical activity being measured at both the data collection and reporting levels (216). This is considered gap in the understanding of PA as there are several domains of PA including leisure-time PA, gardening and yardwork, household chores, transport and occupational PA (217). Moreover, defining the level of PA being measured is essential

because different levels of PA are predicted by different factors; for example, low intensity PA through walking is predicted by environmental factors (218). While structured sport vigorous PA is best explained by family support (219). This gap in knowledge contributes to the inconsistency on the findings of studies on the correlates of PA (220) and the outcomes of PA interventions (221) among children and adolescents. The assessment of PA is usually applied through cross-sectional and longitudinal studies; the limitations of cross-sectional studies are it's restrict estimation of the change in PA'S effect based on population mean confounders (222) and it overlooks its time-specific and context-specific effect (223). While longitudinal studies are more advantageous because it considers each individual as specific – context. Additionally, both cross-sectional and predictive associations can be derived from it if utilized to its full potential (224).

Research on PA suggests that all levels of PA including light PA (225), all intensities and mode of PA (226) and whether it is structured or non-structured PA (227) have favorable outcomes on health regardless of the individual's health status (228) and age (229). The variation of the positive health outcomes associated with PA can be explained by the PA's dose-effect (226, 230-232) and the differences of the level, intensity and mode of PA being assessed (233). This have been supported by both observational and randomized controlled studies (232, 234). The statistical inference in these studies is based on either cross-sectional association across one time point (231, 235) or longitudinal association (231). PA influences the development and health during childhood, adolescence and throughout life (236). Even modest amount of PA of 30 minutes per day can have health benefits among children and adolescents, but also dose-response relations between PA and health benefits still exists (232). The positive contribution of PA on children and adolescents is on both the biological and psycho-social health; the positive effects of PA can be detected along the biomarkers at the microlevel; there is evidence for the positive contribution of PA on the serum lipid profile (230, 232, 237), the cholesterol profile (226, 232, 238) and the insulin level (226) of children and adolescences. Also, studies suggest the beneficial effect of PA on the development of the musculoskeletal and cardiovascular systems of children and adolescents (239). This is in addition to its contribution to bone development (226, 232). Discussions on the role of PA on the primary and secondary prevention of NCDs have emerged in the literature several years ago (240-243), such as its favorable outcomes on obesity (225, 240, 244), type 2 diabetes mellitus (240, 244-246), and hypertension (240, 244). NCDs evolve over a long period of time since it requires long incubation periods before development (247). While NCDs tend to manifest in adulthood, adult disease is determined by childhood and adolescence as exposure to risk factors during these periods of development accumulate and are carried throughout the life course (19, 248-254). Recently, studies have focused on the role of health-related behaviors including PA, among children and adolescents, in controlling non-communicable diseases; this has included the risk profiles for coronary heart disease (255). The results of the study, which was conducted among adolescents who are between 10 to 15 years old, suggested PA to be the strongest predictor for favorable lipid profile among them compared with other health-related behaviors (256). Obesity among children and adolescents is another example, which has been suggested to be risk factor

for NCDs such as cardiovascular diseases, hypertension, and cancer (257-261). This has been supported by the evidence of the tracking of childhood obesity into adulthood (262, 263). In return, there is evidence for the role of PA in the control of obesity (232); in cross-sectional study among children who are between 8 to 11 years old in Sweden, there was evidence for the positive correlation between the percentage of body fat and physical inactivity (264). Similar finding was reported among children who were part of the Avon Longitudinal Study of Parents and Children (265). In regards to the positive association of PA with mental health and well-being; at the development level, PA is strong determinant of cognitive functioning in children and adolescents (266). PA is also associated with the control of several age related mental disorders at different stages of life from childhood, mid-life and late life including dementia (245, 267-271), Alzheimer (245, 268, 272) and brain aging (267, 268). Similarly, it has positive contribution in the control of depression (232, 273-275), anxiety, and psychological distress (226, 273). The role of PA is not confined to the prevention of "ill-health" through the reduction of diseases and its risk factors. Instead, it extends to its benefit for the promotion of good health. Thus, it fits with the WHO's definition of health as tool for the promotion of health (276, 277). To cite the benefits of PA in the promotion of good health; PA is positively associated with the general QoL (226, 231, 277-279), the psychological well-being (226, 234, 277, 278), social support and peers, school environment (226, 234, 278), autonomy and parent relations (278) as specific dimensions of QoL. Along with that, there is evidence for its positive association with life satisfaction (280), self-perception, self-esteem (281) resilience, emotional intelligence, and psychological distress (282). Given the overall contribution of PA on health and well-being, it is considered a determinant factor of mortality rate among the general and diseased populations (225, 240). Based on the data on PA and the relative risks of all-cause mortality for 168 counties for period 2001 and 2016, it has been suggested that PA can avert 15% of premature mortality, which is equivalent to around 4 million deaths annually (283). Additionally, PA has positive economic implications because it is associated with lower utilization of impatient admissions, visits to the emergency room and medical and prescribed drug (246). Along with this, PA contributes to increase in productivity through savings in sick allowance (284). At the broader perspective, the promotion of PA can contribute to the achievement of the third SDG, which is "Good health and well-being" (285). Since PA can contribute to the prevention and treatment of NCDs, it can contribute to the achievement of reducing one third premature mortality from NCDs target, which is part of the third SDG (286). As a result of this, PA has been integrated as a vital sign in the clinical settings (287).

As global leader in the promotion of public health, WHO launched in 2010 the first population-based public health guidelines for children, adolescents, adults and older adults in which it has recommended children and adolescents to accumulate at least 60 minutes per day of moderate-to-vigorous physical activity (MVPA). Also, children and adolescents are recommended based on the guideline to perform vigorous PA, which is important for muscle and bone development, at least three days per week (288). Following this, WHO has launched in 2013 the Global Action Plan for the Prevention and Control of

NCDs 2013-2020. The action plan aims at advocating member states to develop strategies based on multi-sectoral collaboration in order to achieve the plan's targets by 2025. Because the plan has focused on the control of risk factors associated with NCDs, it has included the target for 10% relative reduction in the prevalence of insufficient PA. In order to contribute to the achievement of the target on PA, the plan reiterated the importance of member states to adopt and implement national guidelines on PA (19). Upon the request of member states for the WHO to provide update on the guidance to increase PA, the WHO has launched the global action plan on physical activity 2018 – 2030 in 2017. By taking 2016 as baseline, the major target of the plan has set to 15% relative reduction in the global prevalence of PA in adolescents by 2030. This is to be achieved by applying strategic plan for the creation of active societies, environments, people and systems (286). Then in 2020, the WHO has replaced the 2010 guideline on PA with the guideline on PA and sedentary behavior. This is considered the most recent guideline on PA by the WHO with the added value of integrating recommendation on sedentary behavior and recommendation for pregnant and postpartum women, people with chronic conditions and people with disability (289). This is compared with older guideline on PA(288). The guideline recommends children and adolescents (5-17 years old) to accumulate at least 60 minutes per day of MVPA. Also, children and adolescents are recommended to perform vigorous PA for muscle and bone development at least three days per week. These recommendations are also applied to children and adolescents with disability (289). In the past, guidelines to promote PA among children and adolescents were consistent with PA guideline for adults and based on studies conducted among adults (290, 291). Over time, several governments and policy makers have developed robust evidence-based PA guidelines to promote PA among children and adolescents (292). The United States (239, 293, 294), the United Kingdom, Canada and Australia (291, 295) were among the first countries to develop PA guidelines for children and adolescents.

Despite the existence of guidelines on PA, there is evidence for the high percentage of people, who are not sufficiently active at the global level (296). And low percentage of children and adolescents are meeting the WHO recommendations on PA (297-303). In 2016, it has been reported that 81% of adolescents don't meet the WHO recommendation for PA for the year 2010 (297). This declining trend on the prevalence on PA has been observed in both developed and developing countries; in Switzerland, the prevalence of physical inactivity among adolescents aged between 11-17 years old has been reported to be 83% among males and 89% among females for the year 2022 (304).

The determinants of adherence to PA among children and adolescents are; individual characteristics such as age (305-307), gender (306-308), BMI (305, 306), and sports club participation (308). And school related characteristics (305, 307), culturally rooted characteristics (309), parental age, maternal BMI and education (306), parent's perception of the neighborhood (308, 310), parent's support (311, 312) and physically active parent (308, 313).

Physical inactivity (PI) is defined as "an insufficient physical activity level to meet present physical activity recommendations"(314). It is considered a major behavioral risk factor for total morbidity and mortality (315, 316). In regards to its contribution to morbidity, PI increases the risk of developing cardiovascular diseases (18, 315, 316), cancers, diabetes (18, 316), chronic respiratory diseases, hypertension, obesity, and poor mental health (18). Also, PI contributes to DALYs; in 2013, PI was reported to be responsible for around 13 million DALYs globally (317). PI and its contribution to the total morbidity and mortality has increased between 2010 and 2019 (18). The increase in PI is greatly attributed to the changes in people's everyday activities such as the mechanization of jobs (318, 319), the increase in the mechanical transportation (318, 320-323) and the sedentary leisure activities (318, 324). Thus, PI can be burden on the economy through its direct cost on the health care system services and its contribution to lost productivity (19). PI accounts for 1-3% of the national health care costs excluding the costs associated with mental health and musculoskeletal conditions (286). In 2013, PI has costed the health care system around 54 billion in international dollar worldwide (317).

Sedentary behavior (SB) is defined as "any waking behavior characterized by an energy expenditure ≤ 1.5 metabolic equivalents (METs), while in a sitting or reclining posture" (325). SB has negative effect on the health independent of the level of PA. This effect includes the increase in the risk for all-cause mortality and cardiovascular diseases mortality (324). In children and adolescents long periods of screen time and television viewing have been suggested to be associated with higher level of clustered cardiometabolic risk factors and lower physical fitness and self-esteem (326). Also, based on meta-analysis study, the negative effect of SB among children and adolescents extends to mental health because it increase the risk of depression (327). Given the negative impact of SB on health independent of physical activity, recent guidelines has included recommendations for the reduction of SB (289, 328, 329).

1.2.2. Social contagion: Transmissibility of health behaviors and mental health

In epidemiology and social science, there is interest on detecting social connections (ties) between members of group to identify network capital. Members of the group are called "egos" and individuals connected to the egos are its "alters". There are three types of relationship arise from network capital; first, ego-perceived friendship in which ego identifies alter as friend. Second, alter-perceived friendship in which alter identifies ego as friend. Third, mutual friendship in which both the ego and alter perceive themselves as friends (330, 331).

Identifying network topology is not the core interest of epidemiological and social science studies, but it is the potential clustering of particular behavior within the network (331). Epidemiological and social science studies have provided evidence for the clustering of behaviors within social networks such as smoking and obesity (330, 331). Several hypothesis emerged to explain the reason of behavioral clustering

within social networks; based on the "homophily" hypothesis, individuals are more likely to be connected with others who are similar to them (330, 331). This form of clustering can be detected through simultaneous observation (332). Others have suggested that clustering of behaviors emerge due to the exposure of the connected pair to unobserved confounding factor, which contributes to the shared behavior between them (331). While the social contagion theory suggests the spread of behaviors from one person to another within social network through induction (331, 333), which usually occurs over time (332). The induction of behaviors from person to person within social network occurs either through social or physiological mechanisms; induction through social mechanism takes place when a person is influenced to adopt specific behavior by simply being in contact with others who experience the same behavior. While induction through physiological mechanism happens because certain areas of the brain might be triggered by observing certain behaviors in others to exercise similar behavior (330). The spread of behaviors within social network is not confined to health behaviors (330, 334), but it extends to the contagion of aspects of mental health such as happiness and depression across network capital (335). There are differences in the association of behavior between pair of ego and alter based on the directionality of the relationship with the strongest effect occurs between mutual friends. This is followed by ego-perceived friendship and lastly the alter-perceived friendship. This provides stronger evidence in favor of the clustering of the behavior being due to social contagion as oppose to being caused by the existence of other confounding factor (331).

1.3. General resistances resources

1.3.1. Social capital

Social capital (SC) is divided into two components; network capital and social cohesion (336). Network capital includes community networks and personal networks (336, 337). While social cohesion includes structural SC and cognitive SC (336, 338, 339). SC is both individual and group attribute. It is applicable at different settings; it can be addressed within families, in the workplace and within large geographic areas (340). SC is considered a protective factor against mortality (340).To be specific, there is evidence for the positive association between network capital (338-341), and cognitive SC (trust and reciprocal social exchanges) (338-340, 342-345) with both physical and mental health. It might be argued that the socioeconomic status and the health status of the individual determine his/her ability to build SC; nonetheless, interventions based on helping individuals who suffer from mental disorder to improve their SC led to improvement in their mental health status (346, 347).While encouraging the development of social networks between people especially in place such as schools and public parks will lead to the development of political support to eradicate forms of disadvantaged socioeconomic status such as poverty (348). There are several proposed mechanisms for the association between SC and health; first, SC encourages adopting certain health-related behaviors through norms and attitudes (338, 349, 350). This is supported by the evidence for the association between network capital and lifestyle factors such as obesity, tobacco use, diet and physical activity (330, 351-353). Second, SC can contribute to the development of

the individual's self-esteem, sense of obligation, and reciprocal relations, which facilitates the ability of individuals to access information, and social and material assets (338, 349, 350). These resources associated with SC act as a catalyst for individuals and communities to overcome challenges, which is then reflected through health outcomes (354). Third, it has been hypothesized that SOC can act as a mediator factor between SC and health outcomes (335).

1.3.2. Self-efficacy

The concept of self-efficacy (SE) is a construct of Bandura's social cognitive theory (355). It is defined as the individual's belief in having control over events and the skills required to plan, manage and steer situations towards the individual's goals and expectations. This is through controlling his/her motivations, behaviors and feelings (355, 356). SE is not confined to the ability to change behavior, but it extends to the belief on the ability to accomplish social changes to overcome the structural determinants of health (357). There are several forms of SE; general SE is the belief in the ability to overcome a wide spectrum of obstacles and challenges to implement broad range of activities (358). And task SE is the belief in the ability to execute specific task or behavior (355, 358). While coping SE is the belief in the ability to have control over difficulties either through preventing or coping with them in order to perform certain behavior or task (355). SE is not a static personal characteristic instead it is continuously developing (355). SE is developed through four psychological processes; first, cognitive process, which is the ability to evaluate one's own capabilities, skills and resources. This is in addition to setting goals and strategies to accomplish them. Second, motivational process, which is based on three components; "attribution", "values of expected outcomes", and "clarity and value of goals". Third, affective process, which is based on the person's perception of coping abilities. In turn, this perception has effect on the individual's ability to control stress and anxiety. Fourth, selection process is the ability of people to select the physical and social environment, which permit maximum attainment of goals and personal development (355).

There is evidence for the association between SE and health-related behaviors such as exercising, cardiorespiratory fitness, weight loss, oral health, and alcohol consumption (356, 359). And its association with mental health; SE is negatively associated with depression (356, 358) and anxiety (358). While it is positively associated with well-being, quality of life (356), resilience against dangerous and stressful situations and protect against trauma (360).

1.3.3. Sense of coherence

Aaron Antonovsky has developed the salutogenesis model of health (SMH) to address the question on the origins (genesis) of health (salute) beyond the identification of pathological risk factors associated with the disease (10, 334). He has based the salutogenesis model on four main elements, which are "stressors", " (GRRs-RDs)", "SOC", and "health" (10). Based on Antonovsky's theory, humans live in changing environment characterized by entropy and continuous exposure to stressors (10, 356). At any point in

time, each individual has a position on the "GRRs-RDs" continuum; being closer to the GRRs pole implies an increased availability of resources. While being at the far end of RDs pole implies limited availability or lack of resources (10). There are internal resources within the individual (334, 356) and external resources belonging to the larger community (334, 356) or the environment (356). Resources can take a wide range of forms; there are physical and material resources (356). Also, there are cognitive resources such as knowledge, intelligence (356) and personal characteristics (10, 356). And there is the form of emotional resources such as values, attitudes (356) and individual social support relationships (10, 356). Resource accessibility influences the individual's life experiences, which shape the individual's SOC. High resources accessibility allow the individual to experience "consistency" in life, which contributes to the development of the "comprehensibility" aspect of SOC. And the "load balance" between resources and demands forms the "manageability" aspect of the individual's SOC. Lastly, the access to resources facilitates the individual's ability to experience "decision making" and develop the "meaningfulness" aspect of SOC (10, 334). In relation to this, intervention strategies, which focus on empowerment of people to identify appropriate generalized resistance resources to face life stressors, are effective for strengthening SOC (361). Overall, SOC allows the individual to perceive life events as being coherent, make cognitive sense, logical, and predictable (Comprehensibility). Also, having SOC contributes to the individual's ability to balance between available resources and life demands (Manageability). And the individual's ability to draw emotions with life events and express devotion and commitment to them (Meaningfulness) (356). SOC is the key link between GRRs, stressors and health through its ability to mobilize resources effectively in order to overcome stressors and challenges in a way to ensure positive health (10, 334, 335). Antonovsky considers "well-being" a wider concept, which "health" is one of its components (10). Also, he opposes the pathological model's dichotomization of health into "sick vs. well"; he has defined "health" as ease/dis-ease continuum in which the individual has the potential of being positioned anywhere within the continuum (10, 334, 356). And he/she moves in the direction of ease through SOC (10, 334).

There are areas of convergence between SE and SOC; the development of the individual's SE (mastery experience, vicarious experience, and social persuasion psychological factors) contributes to the development of his/her SOC's constructs (comprehensibility, manageability, and meaningfulness) (359). To be specific, efficient cognitive skills through SE lead to envision the world as being coherent. Actions based on SE can contribute to manageability of several life's demands. Also, individual with SE has the ability to become emotionally resistant and thus can live meaningful life (356). Moreover, SE is considered one of the general resistance resources (335). And the two constructs develop over the human life span and associated with different aspects of health including psychological, physical and social health (356). Thus, the two constructs can be addressed in the implementation of health promotion strategies; studies have provided evidence for the positive association between the enhancement of cancer survivors' SE and their adherence to healthy eating habits (362) and the enhancement of the SE of patients with heart failure and the improvement in their PA (363). Another online intervention study among web-health users

concluded that the improvement of the individual's SE and social support is considered intermediate factor for the promotion of PA and nutritional behavioral changes among the individual (364). Additionally, the results of cluster-randomized trial among primary school children suggested that the enhancement of the children's SOC has contributed to the increase in their oral-health-related quality of life (365).

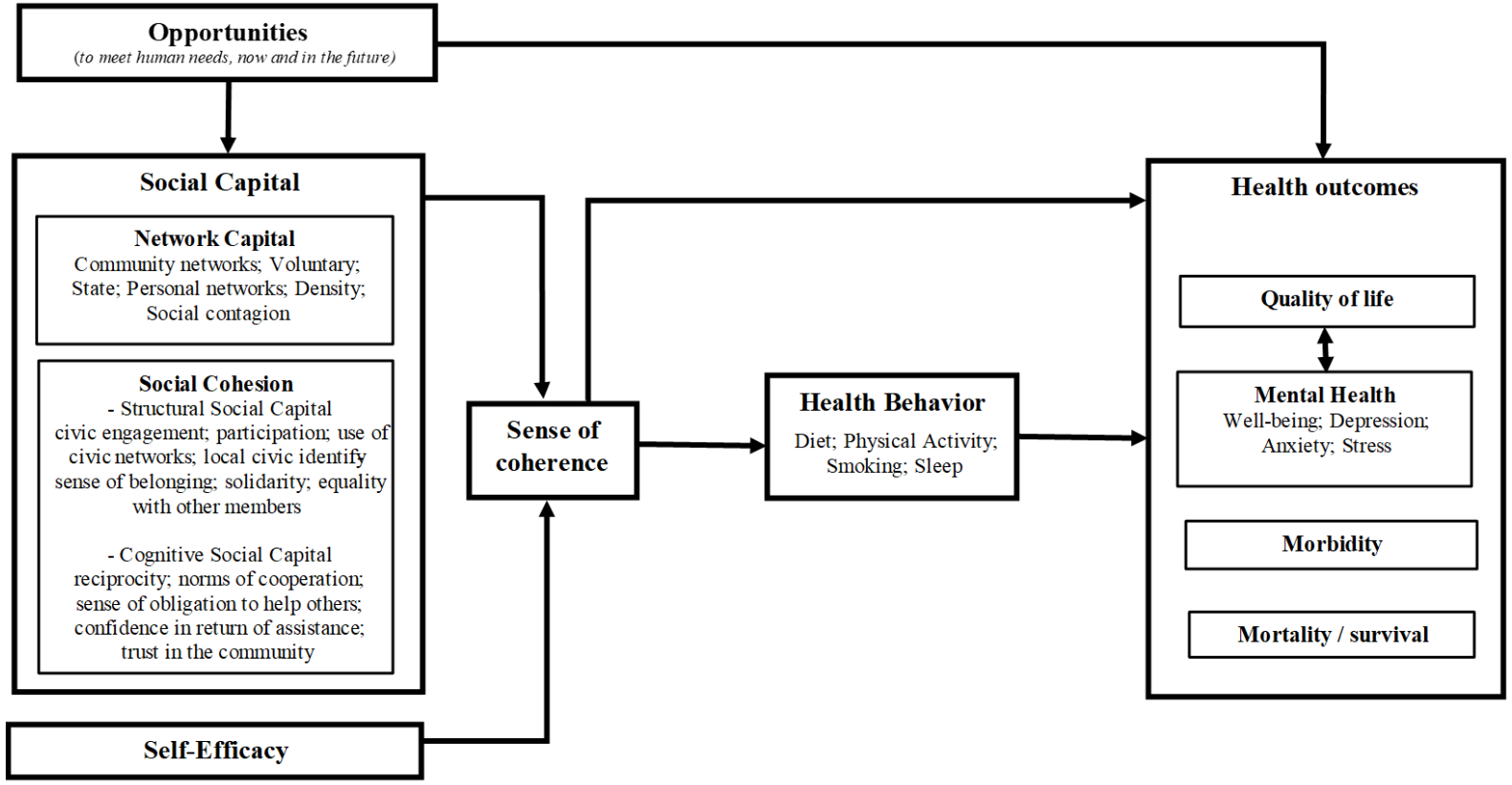

Figure 2. Conceptual framework of the thesis

Chapter 2: Aims and hypothesis of the thesis

Health promotion is important for enhancing the individual's well-being (366). It is even more critical to promote healthy behavior among children and adolescents as health-related behaviors during childhood and adolescence persists into adulthood (367-369). This is because tracking of unhealthy behaviors from childhood into adulthood implies that there is increase in the risk of developing NCDs later in life (370). While investments in the promotion of healthy behavior during childhood ensure the healthy upbringing of the individual throughout the lifespan (371).

Against this background, the current PhD thesis aims at shedding light on the association between healthy habits and minds in today's youth. It has two broad perspectives in two different contexts.

First, it explores the relation between PA and QoL in children and adolescents in Switzerland. Switzerland has population size of around 8.7 million. Children and adolescents, who are less than 20 years old, accounted for approximately 20% of the total population and those who are 65 years or older accounted for approximately 19% of the total population in 2021 (372). The growth rate of the population for the same year has been reported to be 0.8% (19) and the life expectancy at birth has been reported to be the among the highest in the world with 81.6 years for men and 85.7 years for women (373). This high life expectancy has contributed to the evolvement of Switzerland as aging society (373). One of the distinctive features of Switzerland is being "quardilinguaistic" state with four official national languages, which are French, German, Italian and Romansch (374). As in other high income countries, in Switzerland 90% of the deaths are due to (NCDs) (304). The increase in the prevalence of NCDs in Switzerland is caused by several factors including the increase in the prevalence of major NCDs risk factors such as access to and high consumption of alcohol, tobacco, and an imbalance in calorie intake and physical activity resulting in quite high rates of overweight and obesity (304, 375, 376). Moreover, the burden of mental health problems in the general population is quite high, with depression the most common mental disorder especially among those who are between 15-24 years old (373). In the light of Switzerland's high level of access to nature and places for physical activity and sports, PA can be considered a window of opportunity for health promotion and promotion of QoL. We benefited from objectively and longitudinally measured PA and repeated assessment of QoL in the Swiss children's Objectively measured PHYsical Activity (SOPHYA) cohort study to investigate the relation between device-based PA and QoL.

To be specific, the following objectives and questions have been addressed:

1. **Cross-sectional but not prospective association of accelerometry-derived physical activity with quality of life in children and adolescents**

   1.1. Is MVPA associated cross-sectionally with the overall QoL and the specific dimensions of QoL?

1.2. To what extent are these associations driven by the between-subject or within-subject variability in MVPA?

1.3. Does MVPA measured at baseline predict the overall QoL or/and the specific dimensions of QoL five years later independent of baseline participants' characteristics?

2. Weekend physical activity profiles and their relationship with quality of life: the SOPHYA cohort of Swiss children and adolescents

2.1. To identify clusters of accelerometer-derived PA profiles during weekend days among children and adolescents from the SOPHYA cohort.

2.2. To assess their cross-sectional and predictive association with overall QoL and its dimensions.

2.3. To investigate whether QoL associations with newly identified clusters persist upon adjustment for established PA indicators.

Second, the thesis developed a study protocol for the identification of novel interventions to promote healthy behaviors and mental health among youth from Palestine. The country is inhabited by 5.4 million citizens distributed between the West Bank and Gaza Strip with population growth rate of 2.4%. The Palestinian society is a youthful society. Those who are under the age of 15 years old accounted for 37.6% of the total population for the year 2022 (377). Moreover, it is collective society, which is mainly shaped by the strong affiliation to the extended family (378) and strong sense of within group cohesion (379). Thus, aspects of SC are very important (380). Thus, we aimed at investigating health promotion approaches in Palestine through exploring the relevance of SC and social contagion in shaping the health-related behaviors and mental health among youth in Palestine. We developed a study protocol, which was not yet implemented due to Covid-19 pandemic.

To be specific, the following objectives and questions have been addressed:

3. Exploring the role of social capital, self-efficacy and social contagion in shaping lifestyle and mental health among students representing the future healthcare workforce in Palestine: social cohort study protocol

3.1. To assess the frequency, distribution and clustering of self-perceived health, health-related behaviors, obesity and mental health among students.

3.2. To assess the distribution of SC, SE and SOC among students.

3.3. To estimate the association between SC, SE and SOC with the longitudinal course of self-perceived health, health-related behaviors, obesity and mental health among students.

3.4. To uncover and quantify the suspected social contagion of health-related behaviors, obesity and mental health among students.

3.5. To identify modifying and mediating factors in the association of SC and SE with the level and longitudinal course of self-perceived health, health-related behaviors, obesity and mental health among students.

Chapter 3: Original work (published or accepted for publication)

Article I: Cross-sectional but not prospective association of accelerometry-derived physical activity with quality of life in children and adolescents

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Abstract

Objectives

This study aims to quantify the cross-sectional and prospective associations between quality of life (QoL) and moderate-to-vigorous physical activity (MVPA).

Methods

It was based on the Swiss children's Objectively measured PHYsical Activity cohort. The primary endpoint is the overall QoL score and its six dimensions. The main predictor is the average time spent in MVPA per day. Linear mixed effects and linear regression models respectively were used to investigate the cross-sectional and prospective associations between MVPA and QoL.

Results

There were 352 participants in the study with complete data from baseline (2013-2015) and follow-up (2019). MVPA was positively associated with overall QoL and physical well-being ($p = 0.023$ and 0.002 respectively). The between-subject MVPA was positively associated with the overall QoL, physical and social well-being ($p = 0.030$, 0.017 and 0.028 respectively). Within-subject MVPA was positively associated with physical well-being and functioning at school ($p = 0.039$ and 0.013 respectively). Baseline MVPA was not associated with QoL five years later.

Conclusion

Future longitudinal studies should employ shorter follow-up times and repeat measurements to shed light on the direction of the PA and QoL association.

Keywords: Moderate-to-vigorous physical activity, Quality of life, Longitudinal data, Linear mixed-effects model, linear regression model

Introduction

In Switzerland, children and adolescents under 20 years account for approximately 20% of the population (372). Children are a vulnerable group, thus the protection of their rights to adequate well-being is deemed to be important (156). Understanding children's (381) and adolescents' (382) physical and mental health and their determinants is fundamental to their healthy upbringing. Investment into promoting their health and well-being can contribute to the achievement of several public health agendas (383).

Assessment of children's and adolescents' health should resonate with the comprehensive definition of health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (3). Quality of life (QoL), which is defined as "the individual's physical health, psychological state, level of independence, social relationships, personal beliefs and his/her relationships to salient features of the environment" (384), has been suggested to be a critical indicator of health (385). QoL is ideally measured on the basis of subjectively reported broad indicators not restricted to, medical well-being indicators. It is important to assess its distribution in general population samples and not only in subgroups with a specific disease (156). The KINDL® questionnaire proved to be a reliable and valid instrument for assessing QoL in different subdomains among children and adolescents (177, 179, 386, 387). It assesses the overall QoL and its six specific dimensions: physical well-being, emotional well-being, self-esteem, family connection, social well-being and functioning at school (180).

Moderate-to-vigorous physical activity (MVPA) is a strong predictor for different health aspects in children and adolescents (388). Accordingly, the World Health Organization (WHO) recommends that children and adolescents aged 5 to 17 years maintain an average of one hour per day in MVPA (389). Yet, before the COVID-19 pandemic, it was estimated that 81% of 11-17-year-old students globally were not sufficiently active (297). Similar trends were reported among children. This is of particular concern as both PA (390) and, to a much smaller extent, QoL (391) decrease with the aging of children.

A recent review summarized the evidence on the PA and QoL/well-being association in the general population and across the life course (392). Among youth aged 5-18, a higher level of physical activity (PA) and less sedentary time was associated with higher QoL and well-being perception, confirming results from an earlier review (231). The variety of instruments for assessing QoL and the differences in PA type considered complicate firm conclusions based on the evidence available. Most youth studies conducted to date were cross-sectional or the follow-up period in cohort and intervention studies was limited. No population-based cohort studies report on the PA-QoL association in the young measured PA with the help of accelerometry (231, 392).

The first meta-analysis of the effects of PA interventions on health-related quality of life (HRQoL) in healthy children and adolescents found PA to improve HRQoL overall and in several domains (393). The

authors concluded that considering a) the limited number of studies (N=17) and b) the large heterogeneity of the interventions there is insufficient evidence on the type and duration of PA intervention needed to benefit HRQoL in children and adolescents.

The current study benefits from accelerometry-derived PA and QoL assessment with the validated KINDL® questionnaire measured twice over a follow-up period of 5 years in the population-based Swiss children's Objectively measured PHYsical Activity (SOPHYA) cohort study. The study's overall objective was to investigate associations between accelerometry-derived MVPA, given the specific WHO recommendations for this PA indicator, and QoL, with a focus on the longitudinal aspects. The following specific main research questions were addressed: 1) Is MVPA associated cross-sectionally with the overall QoL and the specific dimensions of QoL? 2) To what extent are these associations driven by the between-subject or within-subject variability in MVPA? 3) Does MVPA measured at baseline predict the overall QoL or/and the specific dimensions of QoL five years later independent of baseline participants' characteristics?

Methods

Study design and population

The present study was conducted among children and adolescents participating in the baseline assessment of the SOPHYA cohort (SOPHYA1) between December 2013 and June 2015 (313). All youth who are registered as residents in Switzerland and born between 1998 and 2007 were eligible. The Federal Statistical Office drew random samples from this sampling frame stratified by sex, year of birth, and language (German; French; Italian). The recruitment and the participation rate in SOPHYA1 were described before (313). In short, the participation rate among 2032 families who could be contacted for an accelerometer measurement and answered the SOPHYA1 baseline interview, participation was 64.4%. Valid accelerometer measurements accompanied by a self-administrated questionnaire during the measurement week were obtained from 1,320 youth aged 6 to 16 years. (**Figure 1**).

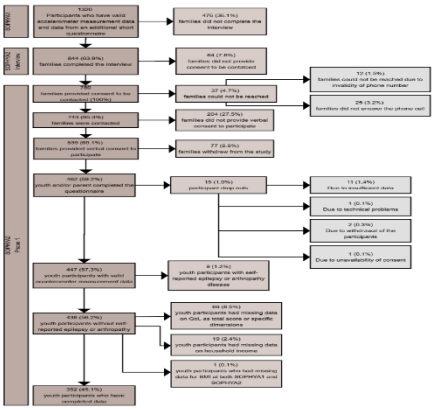

Figure 1. Flow diagram of study population (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013 – 2019)

For the assessment of the predictive association of MVPA at baseline, QoL data obtained at the follow-up assessment in 2019 (SOPHYA2 accelerometry) was considered as outcome. SOPHYA2 was based on the 1,320 SOPHYA1 baseline accelerometry participants who provided proxy-reported (parents) information on socio-demographic characteristics, weight, height, and QoL. Of these participants, 844 could be re-contacted by phone in 2019 and 780 provided consent for a follow-up accelerometer measurement. Among them, 447 participants finally had valid accelerometer measurements and self-reported socio-demographic characteristics, weight, height, and QoL (**Figure 1**).

In SOPHYA1, a parent gave written informed consent (IC) for their children's participation. Adolescents aged 12 years or older filled in an additional IC form. In SOPHYA2, for participants younger than 14 years written IC was provided by a parent as proxy; for participants aged between 14 and 18 years, both parental and an own written IC was provided; for youth above 18 years only own written IC was given.

Data collection

Since participants were spread across Switzerland, contact with them was exclusively remote by phone and by mail. The regional SOPHYA-study partners (German-speaking region: Swiss Tropical and Public Health Institute in Basel; French-speaking regions: University of Lausanne; Italian-speaking regions: Università della Svizzera Italiana) coordinated participant assessment.

1. Telephone interview

At baseline and follow-up as a first SOPHYA assessment, computer-assisted telephone interviews in the respective language region (German; French; Italian) were conducted by a professional field research institute (LINK institute, Lucerne, Switzerland) either directly with children 11 years or older or with one parent as proxy for children aged 10 years or younger (394). Interview data collected included sociodemographic characteristics (sex, nationality, and household income).

2. Accelerometer measurement

At SOPHYA1 and SOPHYA2, families were given oral instructions on accelerometer use through a phone call. Accelerometer along with written instructions were subsequently mailed to the participants, together with a pre-paid postage box to return the devices to the investigators after completion of the measurements. The participants mainly wore either Actigraph accelerometer model GT3X (exclusively used in SOPHYA2) and a few wore GT1M in SOPHYA1 (out of 1320 participants; 49 wore GT1M and 1271 wore GT3X), (ActiGraph, Pensacola, Florida, USA), both producing comparable output (395). Only the vertical axis was used when the accelerometer data was analyzed regardless of the type of the accelerometer being used. The accelerometers were tied to the right hip with an elastic band for seven consecutive days. The device was not worn during water activities or sleep. The device was set without

filtering and in 15-s epoch mode in order to detect shorter bursts of MVPA, which are typical for children (396). ActiLife 6.2 software (ActiGraph, Pensacola, Florida, USA) was used to initialize the device before wearing and, downloading and processing the data. Any period of 60 or more minutes of consecutive zero counts was considered non-wearing time. A day was considered valid if it contained at least 10 or 8 hours of wear time on weekdays or weekend days, respectively. Valid accelerometry consisted of at least 3 valid weekdays and one weekend day. To define children's time spent in MVPA, the age-dependent cut-offs of Freedson (397) with a threshold of 4 metabolic equivalents were used (398).

3. Paper-based survey

At SOPHYA1 and SOPHYA2, families who had agreed to participate in the accelerometry sub-study received an additional paper-based survey to answer questions on the child's age when the accelerometer measurements took place, sport behavior of the children during the measured week, their weight, their height and any diagnosis of chronic disease. Additionally, the survey included the validated KINDL® questionnaire (178) for assessing children's QoL. The questionnaire was administered in the three language areas in Switzerland using the official translation of the questionnaire (Romansh-speaking people filled in the German questionnaire). Validated questionnaire versions tailored to different age groups are available for self-assessment and as a parent-proxy tool (180). In SOPHYA1, the questionnaire was exclusively answered by a parent. At follow-up in SOPHYA2, questionnaires were answered additionally by the participants themselves given their higher age.

Measures

1. Primary endpoint: QoL

The validated KINDL® QoL questionnaire consists of 24 items, each answered on a five-point ordinal Likert scale ranging from "never" = (5) to "always" = (1). Each item belongs to one of the six QoL dimensions (four items per dimension): physical well-being, emotional well-being, self-esteem, family connection, social well-being and functioning at school. The QoL dimensions are scored separately as the sum of the scores of 4 items, ranging from 4 to 20. The domain-specific scores are subsequently transformed to a scale from 0 to 100. The overall QoL score is calculated based on the mean value of all answered items. Higher scores represent a higher QoL. If missing values occurred and affected less than 70% of the answers contributing to a dimension or the total score, the algorithm proposed by the authors of the KINDL® questionnaire was used to replace these missing data (175). The exclusion of participants affected only 2.0% in SOPHYA1 and 2.3% in SOPHYA2 (399).

2. Main predictors: Mean of MVPA in hour per day

Accelerometer data averaged over a week was used to derive the participant's mean hours per day spent in exercising MVPA. To account for different numbers of valid weekdays and weekend days and to reflect that potential differences in MVPA between weekdays and weekend were considered when estimating

average MVPA spend per day in the light of missing weekdays or weekend days, respectively, mean MVPA over the week was calculated as follows: (Average MVPA spent per day for weekdays * 5) + (Average MVPA spent per day for weekend days * 2)] / 7. MVPA was defined by age-related cut points with a threshold for moderate activity of 4 MET (397, 398).

3. Confounders

- **Sociodemographic characteristics**

  Telephone interview was used to collect information on the participant's sex (male, female), nationality (Swiss, foreign nationality, Swiss dual citizen), language region (German, French, Italian) and household income (less or equal to 6,000 CHF, 6001 to 9,000 CHF, 9,001 and more CHF, no information provided). Age (years) at the time of measurement was assessed by subtracting the date of birth from the date of measurement recorded by the paper-based survey during the measurement week.

- **Body Mass Index (BMI)**

  Based on the paper-based survey, the participants self-reported their height and weight. BMI was calculated based on the following equation: Weight (kg)/ height^2(m^2)

  For sensitivity, analysis, BMI-for-age percentiles were calculated.

- **Health status**

  In their responses to the paper-based survey, participants self-reported the following chronic disease diagnoses: asthma, hay fever, allergy, atopic dermatitis, diabetes mellitus, chronic enteritis, hypertension, epilepsy, arthropathy and attention deficit hyperactivity disorder. They also self-reported the presence of any other chronic disease not specifically included in the above-mentioned list. Self-reported diagnosis of at least one chronic disease was defined as having had at least one chronic disease.

- **Use of the accelerometer**

  The season of the wear time was assigned based on the month of accelerometer measurement (Spring: March-May; Summer: June-August; Autumn: September-November; Winter: December-February).

Statistical analysis

Participants included in the analysis were required to have complete data from both time points for the overall QoL and its specific dimensions (physical well-being, emotional well-being, self-esteem, family connection, social well-being, and functioning at school), MVPA, BMI and for the selected covariates (sex, age, household income, language region, nationality, self-reported diagnosis of chronic disease, and season of measurement). If the BMI of the participant was missing at one-time point only, it was imputed by regressing it on the BMI value available from the other time point while adjusting for age, sex, and time

interval between the two time points (See result section). Participants self-reporting epilepsy or arthropathy were excluded from the study, because of their strong potential influence on both, PA and QoL (400, 401).

The flow diagram of the study population is presented in **Figure 1**.

Potential selection bias was assessed by comparing baseline characteristics of all SOPHYA1 participants with those retained for the current study using chi-squared tests and student's t-tests (**Table S1**).

Descriptive statistics (n, %, mean, SD) of the study population, QoL and its specific dimensions, and of MVPA, BMI and covariates were calculated for the total study sample, and for SOPHYA1 and SOPHYA2 separately (**Table 1**).

The selection of the covariates as potential confounders was done a priori. We adjusted all models for age, sex, household income, language region, nationality, self-reported diagnosis with a chronic disease and season of measurement.

We assessed whether MVPA is cross-sectional or longitudinally associated with QoL and its specific dimensions by regressing QoL on MVPA while adjusting for the above-mentioned covariates. The following models were sequentially applied.

First, in **Model 1** (Table 2) we assessed whether MVPA is associated cross-sectionally with QoL. We considered data from both time points (SOPHYA1 and SOPHYA2). We used a linear mixed model that included a subject-specific random intercept.

Second, in **Model 2** (Table 3) we assessed the relationship of between- and within-subject variation in MVPA with the variation in QoL. The between-subject MVPA value for each participant was defined as their individual mean, which is the average of their MVPA over the two time points. The participant's within-subject MVPA value at each time point was defined as the deviation of MVPA as measured at that point from the participant's individual mean. We included both the between- and within-subject MVPS instead of MVPA in linear mixed models mirroring model 1. This modelling approach is described in more detail in (402).

Third, in **Model 3** (Table 4) we assessed whether MVPA measured at baseline predicted QoL after five years of follow-up. QoL scores at follow-up were regressed on MVPA at baseline in the context of a linear regression model adjusting for covariates as described above and in addition for the respective QoL scores at baseline.

Fourth, a secondary analysis (Supplementary Tables 2-4), models 1-3 described above were re-fitted with an additional adjustment for BMI to assess the independence of the studies associations from the participants' BMI.

The association size in **Models 1-3** represented by the regression coefficient is reflecting the change in QoL (sub)-score for an increase in MVPA by an average of 1 hour / day during the measurement week.

As sensitivity analyses, models 1 to 3 were repeated a) using QoL at follow-up derived from parental-proxy questionnaire instead of youth self-report at follow-up, and b) using BMI_for_age percentiles instead of BMI for additional adjustment. As the sample sizes for parental-proxy derived QoL (N = 302) and percentiles (N = 341) were only available from a smaller follow-up sample, the sensitivity analyses were conducted on these smaller samples.

All analyses were performed in R version 4.1.3.

Results

The final sample consisted of 352 children and adolescents (**Figure 1**). Of the 447 SOPHYA1 and SOPHYA2 accelerometry participants, 66 (8.5%) participants were not included in the final analysis because they did not have valid QoL score (overall or specific dimension). Additionally, 19 (2.4%) participants were dropped because they did not have valid data on household income. BMI at baseline or follow-up was imputed for 28 participants (11 participants did not have valid BMI at SOPHYA1 and 17 participants did not have valid BMI at SOPHYA2). One participant (1; 0.1%) was excluded for not having valid BMI information from either time point. Participants who self-reported a diagnosis with epilepsy 2 (0.3%) or arthropathy 7 (0.9%) at either SOPHYA1 or SOPHYA2 were also excluded from this study analysis.

Potential selection bias was assessed by comparing baseline characteristics of all SOPHYA1 accelerometry participants with those retained for the current study using chi-squared tests and student's t-test. Comparison of baseline characteristics between participants not included versus those who are included in this current analysis is presented in **Table S1**. Participants included in this analysis exhibited a lower BMI at baseline (mean [SD]: 16.8 [2.4] vs. 17.7 [2.9], $p < 0.0001$), higher MVPA levels (mean [SD]: 1.4 [0.6] vs. 1.2 [0.6], $p < 0.0001$) and better overall QoL (mean [SD]: 82.3 [7.7] vs. 80.2 [9], $p < 0.0001$), better physical well-being (mean [SD]: 84.9 [12.6] vs. 83.2 [14.6], $p = 0.041$), self-esteem (mean [SD]: 77.3 [12.4] vs. 74.6 [14.9], $p = 0.001$) and functioning at school (mean [SD]: 82.9 [14.2] vs. 78.4 [15.5], $p < 0.0001$).

Table 1 describes the study sample. The final sample consisted of 52.8% females and 47.2% males. The average ages of the participants at SOPHYA1 and SOPHYA2 were (mean [SD]: 10.3 [2.4] years) and (mean [SD]: 15.1 [2.6] years), respectively. Mean MVPA decreased from (mean [SD]: 1.4 [0.6] hr/day) at SOPHYA1 to (mean [SD]: 0.8 [0.4] hr/day) at SOPHYA2. In regards to the QoL, the average score of the overall QoL decreased from (mean [SD]: 82.3 [7.7]) at SOPHYA1 to (mean [SD]: 74.2 [9.9]) at

SOPHYA2. Of the specific QoL dimensions, self-esteem exhibited the lowest score at both time points and decreased from (mean [SD]: 77.3 [12.4]) to (mean [SD]: 60.9 [17.3]) over five years of follow-up. Males and females were comparable on all characteristics except for the mean of MVPA and the mean of QoL score. Males had significantly higher MVPA (mean [SD]: 1.6 [0.7] vs. 1.3 [0.5], $p < 0.0001$) at SOPHYA1 and (mean [SD]: 0.9 [0.4] vs. 0.7 [0.3]), $p < 0.0001$) at SOPHYA2. Overall QoL was lower in females (mean [SD]: 73.1 [10.1] vs. 75.4 [9.5], $p = 0.026$) at SOPHYA2 only.

Table 1. Characteristics of study participants at baseline (SOPHYA1; 2013) and follow-up (SOPHYA2; 2019) (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013 – 2019)

N =352		
	SOPHYA 1	**SOPHYA 2**
	Mean (SD) / N (%)	**Mean (SD) / N (%)**
Socio-demographic		
Age	10.3 (2.4)	15.1 (2.6)
Sex		
- *Male*	166 (47.2%)	
- *Female*	186 (52.8%)	
Household income[1]		
- *≤ 6,000 CHF*	66 (18.8%)	
- *6,001 to 9,000 CHF*	115 (32.7%)	
- *9,000 and more CHF*	158 (44.9%)	
- *Not willing to provide information*[2]	13 (3.7%)	
Language region[1]		
- *German*	245 (69.6%)	
- *French*	74 (21.0%)	
- *Italian*	33 (9.4%)	
Nationality[1]		
- *Swiss*	245 (69.6%)	
- *Foreign nationality*	33 (9.4%)	
- *Swiss dual citizen (Swiss and foreign nationality)*	74 (21.0%)	
Health status		
BMI kg/m^2	16.8 (2.4)	19.8 (3.1)
Self-reported diagnosis with at least one chronic disease		
- *Did not have any of the chronic diseases*	254 (72.2%)	232 (65.9%)
- *Had at least one chronic disease*	98 (27.8%)	120 (34.1%)
Physical activity		
Season of measurement		
- *Spring*	85 (24.1%)	104 (29.5%)
- *Summer*	54 (15.3%)	73 (20.7%)
- *Autumn*	92 (26.1%)	127 (36.1%)
- *Winter*	121 (34.4%)	48 (13.6%)
Weartime hour/day	13.2 (0.9)	13.9 (1.1)
MVPA Mean hour/day	1.4 (0.6)	0.8 (0.4)
Quality of life[3]		
- *Overall QoL*	82.3 (7.7)	74.2 (9.9)
- *Physical well-being*	84.9 (12.6)	74.2 (14.9)
- *Emotional well-being*	87 (10.6)	79.7 (13.0)
- *Self-esteem*	77.3 (12.4)	60.9 (17.3)
- *Family connection*	82.5 (12.0)	86.3 (14.1)
- *Social well-being*	79.2 (11.2)	74.3 (14.0)
- *Functioning at school*	82.9 (14.2)	69.6 (17.6)

[1] The information for both time points stems from baseline assessment
[2] Participant answered the question, but chose to abstain from declaring the range of the household income
[3] Obtained from KINDL® questionnaire

Cross-sectional associations

The results of cross-sectional analysis of data obtained from the same children at baseline and follow-up on the adjusted association between mean MVPA and QoL are shown in **Table 2**. Mean MVPA was positively associated with the overall QoL and with physical well-being ($p = 0.023$ and 0.002 respectively). A one-hour increase in MVPA per day was associated with a 2.0 (95%CI: 0.3, 3.7) points and 4.2 (95%CI: 1.6, 6.8) points increase in the overall QoL and physical well-being score, respectively. Positive, but statistically non-significant associations were also observed for social well-being and functioning at school ($p = 0.053$ and 0.086 respectively) with an effect size of 2.4 (95%CI: 0.002, 4.9) points and 2.6 (95%CI: -0.4, 5.6) points, respectively per each one hour increase in MVPA. No associations were observed with other dimensions of QoL ($p = 0.151$).

The between-subject MVPA value, reflecting the cross-sectional association, was positively associated with the overall QoL, physical and social well-being ($p = 0.030$, 0.017 and 0.028 respectively). For every one hour increase in the between-subject MVPA value, there was a 2.6 (95%CI: 0.3, 4.9) points, 4.3 (95%CI: 0.8, 7.7) points and 3.8 (95%CI: 0.5, 7.2) points increase in the overall QoL, the physical well-being, and the social well-being, respectively. The within-subject MVPA value, reflecting the longitudinal association, was positively associated with the physical well-being and functioning at school ($p = 0.039$ and 0.013 respectively), with effect sizes of 4.2 (95%CI: 0.2, 8.2) points and 5.6 (95%CI: 1.2, 10.1) points increase in physical well-being and functioning at school scores, respectively, for every one hour increase in the within-subject MVPA. See **Table 3**.

The results presented in **Table 2** and **Table 3** did not materially change upon additional adjustment for BMI (**Table S2** and **Table S3**).

Table 2. Repeated adjusted[1] cross-sectional association of mean moderate- to-vigorous physical activity with quality of life (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013 – 2019)

Model 1[2]			
MVPA			
Primary endpoint[3]	Coefficient[4]	95% CI	P-value
Overall QoL	2.0	(0.3 to 3.7)	0.023
Physical well-being	4.2	(1.6 to 6.8)	0.002
Emotional well-being	1.7	(-0.6 to 4.0)	0.151
Self-esteem	1.4	(-1.4 to 4.4)	0.335
Family connection	-0.6	(-3.0 to 1.9)	0.660
Social well-being	2.4	(0.002 to 4.9)	0.053
Functioning at school	2.6	(-0.4 to 5.6)	0.086

[1] Adjusted for age, sex, household income, language region, nationality, diagnosis with a chronic disease, and season of measurement

[2] Moderate- to-vigorous physical activity at the respective time point

[3] Obtained from KINDL® questionnaire

[4] Coefficient is reflecting the change in score associated with an average 1-hour increase in moderate- to-vigorous physical activity during the accelerometry measurement week

Table 3. Repeated adjusted[1] cross-sectional association of between-and within-subject moderate- to-vigorous physical activity values with quality of life (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013 – 2019)

Model 2[2]						
	MVPA - Between subjects			MVPA - Within subjects		
Primary endpoint[3]	Coefficient[4]	95% CI	P-value	Coefficient[5]	95% CI	P-value
Overall QoL	2.6	(0.3 to 4.9)	0.030	1.3	(-1.1 to 3.7)	0.302
Physical well-being	4.3	(0.8 to 7.7)	0.017	4.2	(0.2 to 8.2)	0.039
Emotional well-being	2.7	(-0.3 to 5.7)	0.085	0.4	(-3.0 to 3.8)	0.804
Self-esteem	3.5	(-0.4 to 7.4)	0.084	-1.0	(-5.3 to 3.3)	0.649
Family connection	1.2	(-2.3 to 4.7)	0.510	-2.3	(-5.8 to 1.2)	0.205
Social well-being	3.8	(0.5 to 7.2)	0.028	0.9	(-2.7 to 4.5)	0.623
Functioning at school	0.2	(-3.8 to 4.1)	0.938	5.6	(1.2 to 10.1)	0.013

[1] Adjusted for age, sex, household income, language region, nationality, diagnosis with a chronic disease, and season of measurement

[2] Moderate- to-vigorous physical activity included in the model as participant's mean moderate- to-vigorous physical activity over both time points (between-subject variation) and as difference from that mean at either time point (within-subject variation)

[3] Obtained from KINDL® questionnaire

[4] Coefficient is reflecting the change in score associated with an average 1-hour increase in between-subject moderate- to-vigorous physical activity during the accelerometry measurement week

[5] Coefficient is reflecting the change in score associated with an average 1-hour increase in within-subject moderate- to-vigorous physical activity during the accelerometry measurement week

Prospective associations

We did not find evidence of an association of MVPA at baseline with QoL five years later, after adjusting for the baseline characteristics, including baseline QoL (**Table 4**). Again, results were not materially altered by an additional adjustment for BMI (**Table S4**).

Table 4. Prospective adjusted[1] association of mean of moderate- to – vigorous physical activity at baseline with quality of life (overall and specific dimension scores) at follow-up (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013-2019)

Model 3			
Main predictor			
MVPA			
Primary endpoint[2]	Coefficient[3]	95% CI	P-value
Overall QoL	-0.9	(-3.5 to 1.6)	0.479
Physical well-being	-0.7	(-4.6 to 3.2)	0.730
Emotional well-being	0.1	(-3.2 to 3.5)	0.946
Self-esteem	-0.1	(-4.6 to 4.5)	0.980
Family connection	-1.0	(-4.6 to 2.7)	0.598
Social well-being	-0.1	(-3.8 to 3.6)	0.971
School functioning	-2.9	(-7.5 to 1.8)	0.226

[1] Adjusted for age, gender, household income, language region, nationality, diagnosed with a chronic disease, season of measurement, and respective quality of life score at baseline
[2] Obtained from KINDL® questionnaire
[3] Coefficient is reflecting the change in score associated with an average 1-hour increase in within-subject moderate-to-vigorous physical activity during the accelerometry measurement week

Sensitivity analyses

Replacing QoL follow-up information provided by children and adolescents themselves with QoL information provided by parental proxy did not materially alter the results reported. Replacing additional adjustment for BMI with adjustment for BMI-age percentiles did not change the conclusion.

Discussion

This study demonstrates a cross-sectional, positive association of device-based MVPA with both, overall QoL and physical well-being of Swiss children and adolescents. Partitioning of the variation in MVPA into between- and within-subject variation to differentiate between cross-sectional and longitudinal associations revealed that the latter is associated with the functioning at school dimension of QoL. As another approach to assessing longitudinal associations, baseline MVPA did not predict a better QoL in any specific dimension five years later.

The cross-sectional association between QoL and PA is in agreement with many findings of previous cross-sectional studies in children and adolescents, which were based on device-based PA, self-reported PA or sport activities and applied different QoL instruments (392, 403). Differences in observed associations with QoL specific dimensions across studies may in part be due to differences in PA assessment. This is evidenced by a cross-sectional study conducted among adolescents in Germany to compare the QoL association with self-reported PA versus device-based PA assessment. While self-reported PA was associated with almost all specific dimensions of QoL, device-based PA was mostly associated with physical well-being (403). Furthermore, sports activity and PA more generally seem to have different influences on QoL (404, 405). Observed associations in cross-sectional studies do not inform the direction of associations and are primarily based on between-subject effects. The results of PA intervention trials support positive short-term effects on children's QoL (393).

Additionally, we attempted to characterize the relationship of MVPA and QoL from two distinct longitudinal perspectives. First, employing a conventional epidemiological analysis, we did not find evidence of an effect of baseline PA on QoL at the follow-up five years later. While such an effect is plausible, our study may have lacked the statistical power to detect it. This is especially likely given the long follow-up consisting of our young participants' formative years which would have attenuated the effect size. Longitudinal evidence of the longer-term benefit of PA on QoL in children and adolescents is still rare and absent to our knowledge for accelerometry-derived MVPA. But several prospective and interventional studies reported different type of PA to be a predictor of QoL among children and adolescents (406, 407). However, PA was mostly self-reported and related to engagement in sports activities or school interventions. A few longitudinal studies with data from more than two time-points specifically investigated the bidirectional association between PA and QoL in children and adolescents using cross-lagged panel models. Jensen et al. (2014) found higher baseline QoL to predict higher PA one year later (408). Wunsch et al. (2021) found pre-pandemic HRQoL to predict higher PA during the pandemic, but only in children and not in adolescents (409). Consistent with our results, none of the two studies above found PA to predict HRQoL. In contrast, a positive predictive effect of PA on HRQoL one year later in the absence of a predictive effect of HRQoL on PA was reported for Finnish adolescents aged 11 to 15 years (410). A bidirectional predictive association was reported in French adolescents based on self-reported PA obtained in adolescents assessed over three one-year follow-ups (411).

The second perspective related deviations of participants' MVPA at either time point from their five-year mean to their QoL scores. Here, notably, we observed an association with the functioning at school domain. It is plausible that an increased PA enables a child to feel more comfortable at school, either directly or through the multitude of its physical and mental health benefits. Another possibility is that a decreased PA is a marker of a lowered school-related QoL. The associations may also be artifacts arising from complex

interplays of parallel downward trends in PA and QoL over the study period, regression to the mean, and the five-year mean of MVPA being an imprecise characterization of the child's typical behavior.

Recently a study on children applied a cross-lagged panel model to distinguish both between- and within-person variance to investigate prospective within-person effects between PA and HRQoL (412). According to this study, positive deviations from an individual's level of PA were followed by a positive deviation in the individuals' level of HRQoL at the next measurement occasion and vice versa.

The strengths of this study include its population-based design covering a whole country. It is to our knowledge the first population-based youth cohort longitudinally assessing the association of accelerometry-derived MVPA with QoL over an extended period of time. QoL was assessed with the help of the widely used and validated KINDL® instrument.

The study has several limitations. First the sample size was limited as the study was embedded into a cohort with the primary aim to study the longitudinal course of PA and its determinants. Accordingly, no sample size calculations for the current objective were conducted. Second, bias due to follow-up cannot be excluded and its direction is difficult to judge given that both, physical activity and QoL influenced follow-up participation. Third, two follow-up time points 5 years apart are not sufficient to clearly differentiate between predictor (MVPA) and outcome. The observed difference in within-subject variation in MVPA and QoL associations and predictive MVPA and QoL associations may reflect this fact.

Conclusion

The results support the positive cross-sectional association between PA and QoL among children and adolescents. Future longitudinal studies employing shorter follow-up times and repeat measurements can shed light on the direction of the PA and QoL association.

List of abbreviations

BMI: Body Mass Index
HRQoL: Health Related Quality of Life
MVPA: Moderate- to-vigorous physical activity
PA: Physical activity
QoL: Quality of life
SOPHYA: Swiss children's Objectively measured PHYsical Activity
WHO: World Health Organization

Ethics approval and consent to participate

SOPHYA1 and SOPHYA2 protocols were approved by the ethics committee of the Canton of Basel/North-Western Switzerland (147/13; EKNZ 2018-01786). The SOPHYA cohort was performed in accordance with the ethical standards delineated in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Either the participants themselves or, if minors, their parents gave written informed consent for participation in the SOPHYA1 and SOPHYA2 study.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NP-H: SOPHYA study concept; SOPHYA data collection; concept of current study; data analysis plan; drafting of manuscript.

RAMD: data analysis plan; data analysis; drafting of manuscript.

JH: SOPHYA data collection; concept of current study; drafting of manuscript.

ES: data analysis plan; data analysis; drafting of manuscript.

MK: data analysis plan; supervision of data analysis; drafting of manuscript.

AA: approval of final manuscript.

BK: SOPHYA data collection; approval of final manuscript.

SS: SOPHYA data collection; approval of final manuscript.

BB: SOPHYA study concept; SOPHYA data collection; concept of current study; approval of final manuscript.

Appendix I

Supplement Table 1. Comparison of baseline characteristics of participants with accelerometry only participants in SOPHYA1[1] with those participants in SOPHYA1 and SOPHYA2 (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013-2019)

	Children who participated only in SOPHYA1 N = 781	Children who participated in SOPHYA1 & SOPHYA2 N = 352		
Sociodemographic characteristics				
Variable	Mean (SD)	Mean (SD)	95% CI	P-value[2]
Age				
Children and adolescents (6 to 16 years old)	11.4 (2.6)	10.3 (2.4)	(-1.4 to -0.8)	< 0.001
Variable	n (%)	n (%)	x-squared	P-value[3]
Sex				
- *Female*	391 (50.1%)	186 (52.8%)	0.6	0.423
- *Male*	390 (49.9%)	166 (47.2%)		
Household income				
- *≤ 6,000 CHF*	188 (24.1%)	66 (18.8%)	7.3	0.063
- *6,001 to 9,000 CHF*	274 (35.1%)	115 (32.7%)		
- *9,000 and more CHF*	289 (37.0%)	158 (44.9%)		
- *Not willing to provide information*[4]	30 (3.8%)	13 (3.7%)		
Language region				
- *German*	547 (70.0%)	245 (69.6%)	1.7	0.431
- *French*	145 (18.6%)	74 (21.0%)		
- *Italian*	89 (11.4%)	33 (9.4%)		
Nationality				
- *Swiss*	536 (68.6%)	245 (69.6%)	0.2	0.917
- *Foreign nationality*	79 (10.1%)	33 (9.4%)		
- *Swiss dual citizen (Swiss and foreign nationality)*	166 (21.3%)	74 (21.0%)		

Health status				
Diagnosed with chronic diseases				
Astham				
- No	730 (93.5%)	326 (92.6%)	0.2	0.687
- Yes	51 (6.5%)	26 (7.4%)		
Hay fever				
- No	659 (84.4%)	309 (87.8%)	2.0	0.158
- Yes	122 (15.6%)	43 (12.2%)		
Allergy (other than hay fever)				
- No	688 (88.1%)	314 (89.2%)	0.2	0.659
- Yes	93 (11.9%)	38 (10.8%)		
Atopic dermatitis				
- No	722 (92.4%)	322 (91.5%)	0.2	0.659
- Yes	59 (7.6%)	30 (8.5%)		
Diabetes mellitus				
- No	780 (99.9%)	352 (100.0%)	<0.01	1.000
- Yes	1 (0.1%)	0 (0.0%)		
Chronic enteritis (colitis ulcerosa, morbus Crohn)				
- No	779 (99.7%)	352 (100.0%)	0.03	0.853
- Yes	2 (0.3%)	0 (0.0%)		
Hypertension				
- No	780 (99.9%)	351 (99.7%)	<0.01	1
- Yes	1 (0.1%)	1 (0.3%)		
Attention deficit hyperactivity disorder (ADHS/ADS)				
- No	757 (96.9%)	346 (98.3%)	1.3	0.259
- Yes	24 (3.1%)	6 (1.7%)		
Other specified sever chronic diseases				
- No	758 (97.1%)	343 (97.4%)	0.03	0.864
- Yes	23 (2.9%)	9 (2.6%)		
Diagnosed with at least one chronic disease				
- Did not have any of the chronic diseases	521 (66.7%)	254 (72.2%)	3.1	0.079
- Had at least one chronic disease	260 (33.3%)	98 (27.8%)		
Variable	Mean (SD)	Mean (SD)	95% CI	P-value[2]

BMI				
- *BMI kg/m²*	17.7 (2.9)	16.8 (2.4)	(-1.2 to -0.5)	< 0.001
Physical activity				
Variable	n (%)	n (%)	x-squared	P-value[3]
Season of measurement				
- *Spring*	241 (30.9%)	85 (24.1%)	5.9	0.117
- *Summer*	101 (12.9%)	54 (15.3%)		
- *Autumn*	180 (23.0%)	92 (26.1%)		
- *Winter*	259 (33.2%)	121 (34.4%)		
Variable	Mean (SD)	Mean (SD)	95% CI	P-value[2]
Mean of MVPA				
- *MVPA Mean hr/day*	1.2 (0.6)	1.4 (0.6)	(0.1 to 0.3)	< 0.001
Quality of life[5]				
- *Overall QoL*	80.2 (9.0)	82.3 (7.7)	(1.1 to 3.1)	< 0.001
- *Physical well-being*	83.2 (14.6)	84.9 (12.6)	(0.1 to 3.4)	0.041
- *Emotional well-being*	85.8 (11.5)	87.0 (10.6)	(-0.3 to 2.5)	0.122
- *Self-esteem*	74.6 (14.9)	77.3 (12.4)	(1.0 to 4.4)	0.001
- *Family connection*	81.0 (13.0)	82.5 (12)	(-0.1 to 3.0)	0.075
- *Social well-being*	78.2 (13.4)	79.2 (11.2)	(-0.5 to 2.5)	0.178
- *Functioning at school*	78.4 (15.5)	82.9 (14.2)	(2.5 to 6.3)	< 0.001

[1] The exclusion criteria, which was applied to the participants at SOPHYA2 cohort, was also applied to all SOPHYA1 participants. This is why the sample size upon which the comparison was made is less than 1320

[2] P-value from student's t-test

[3] P-value from chi-squared test

[4] Participant answered the question, but chose to abstain from declaring the range of the household income

[5] Obtained from KINDL® questionnaire

Supplement Table 2. Repeated adjusted[1] cross-sectional association of moderate- to-vigorous physical activity with quality of life, additionally adjusted for body mass index[2] (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013-2019)

Model 1[3]						
	MVPA			BMI		
Primary endpoint[4]	Coefficient[5]	95% CI	P-value	Coefficient	95% CI	P-value
Overall QoL	1.9	(0.2 to 3.6)	0.027	-0.2	(-0.5 to 0.01)	0.065
Physical well-being	4.2	(1.6 to 6.8)	0.002	-0.02	(-0.4 to 0.4)	0.924
Emotional well-being	1.6	(-0.6 to 3.9)	0.161	-0.2	(-0.5 to 0.2)	0.299
Self-esteem	1.3	(-1.5 to 4.3)	0.368	-0.5	(-1.0 to -0.1)	0.028
Family connection	-0.6	(-3.1 to 1.9)	0.616	-0.3	(-0.7 to 0.05)	0.088
Social well-being	2.4	(-0.04 to 4.9)	0.058	-0.3	(-0.7 to 0.1)	0.175
Functioning at school	2.6	(-0.4 to 5.5)	0.092	-0.2	(-0.7 to 0.3)	0.410

[1] Adjusted for age, sex, household income, language region, nationality, diagnosis with a chronic disease, season of measurement and BMI
[2] Sample size = 352
[3] MVPA included in the model as MVPA at the respective time point
[4] Obtained from KINDL® questionnaire
[5] Coefficient is reflecting the change in score associated with an average 1-hour increase in MVPA during the accelerometry measurement week

Supplement Table 3. Repeated adjusted[1] cross-sectional association of partitioned moderate- to-vigorous physical activity with quality of life, additionally adjusted for body mass index[2] (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013-2019)

Model 2[3]									
	MVPA Between subjects			MVPA Within subjects			BMI		
Primary endpoint[4]	Coefficient[5]	95% CI	P-value	Coefficient[6]	95% CI	P-value	Coefficient	95% CI	P-value
Overall QoL	2.6	(0.3 to 4.9)	0.031	1.2	(-1.2 to 3.6)	0.338	-0.3	(-0.5 to 0.01)	0.063
Physical well-being	4.3	(0.8 to 7.7)	0.017	4.2	(0.2 to 8.2)	0.040	-0.02	(-0.4 to 0.4)	0.923
Emotional well-being	2.7	(-0.3 to 5.7)	0.087	0.4	(-3.0 to 3.7)	0.836	-0.2	(-0.5 to 0.2)	0.290
Self-esteem	3.4	(-0.4 to 7.3)	0.080	-1.2	(-5.5 to 3.1)	0.590	-0.5	(-1.0 to -0.1)	0.026
Family connection	1.2	(-2.3 to 4.7)	0.522	-2.4	(-5.9 to 1.1)	0.181	-0.4	(-0.8 to 0.04)	0.083
Social well-being	3.8	(0.5 to 7.2)	0.028	0.8	(-2.8 to 4.4)	0.663	-0.3	(-0.7 to 0.1)	0.167
Functioning at school	0.1	(-3.8 to 4.1)	0.945	5.6	(1.1 to 10.0)	0.014	-0.2	(-0.6 to 0.3)	0.430

[1] Adjusted for age, sex, household income, language region, nationality, diagnosis with a chronic disease, season of measurement and BMI
[2] Sample size = 352
[3] MVPA included in the model as participant's mean MVPA over both time points (between-subject variation) and as difference from that mean or either time point (within-subject variation)
[4] Obtained from KINDL® questionnaire
[5] Coefficient is reflecting the change in score associated with an average 1-hour increase in between-subject MVPA during the accelerometry measurement week
[6] Coefficient is reflecting the change in score associated with an average 1-hour increase in within-subject MVPA during the accelerometry measurement week

Supplement Table 4. Prospective adjusted[1] association of moderate- to-vigorous physical activity at baseline with quality of life at follow-up, additionally adjusted for body mass index[2] (Swiss children's Objectively measured PHYsical Activity cohort study, Switzerland, 2013-2019)

Main predictors						
	MVPA			BMI		
Primary endpoint[3]	Coefficient[4]	95% CI	P-value	Coefficient	95% CI	P-value
Overall QoL	-0.9	(-3.5 to 1.7)	0.488	-0.1	(-0.6 to 0.4)	0.661
Physical well-being	-0.7	(-4.6 to 3.2)	0.728	0.1	(-0.6 to 0.8)	0.834
Emotional well-being	0.1	(-3.3 to 3.4)	0.961	0.2	(-0.4 to 0.8)	0.528
Self-esteem	0.03	(-4.5 to 4.6)	0.989	-0.5	(-1.3 to 0.4)	0.267
Family connection	-1.0	(-4.6 to 2.7)	0.605	-0.1	(-0.8 to 0.5)	0.693
Social well-being	-0.01	(-3.7 to 3.7)	0.994	-0.3	(-1.0 to 0.4)	0.384
Functioning at school	-2.9	(-7.5 to 1.8)	0.226	-0.003	(-0.9 to 0.9)	0.995

[1] Adjusted for age, sex, household income, language region, nationality, diagnosed with a chronic disease, season of measurement, BMI, and respective QoL score at baseline
[2] Sample size = 352
[3] Obtained from KINDL® questionnaire
[4] Coefficient is reflecting the change in score associated with an average 1-hour increase in MVPA during the accelerometry measurement week

Article II: Weekend physical activity profiles and their relationship with quality of life: the SOPHYA cohort of Swiss children and adolescents

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Abstract

Introduction

Quality of life (QoL) is an important health indicator among children and adolescents. Evidence on the effect of physical activity (PA)-related behaviors on QoL among youth remains inconsistent. Conventional accelerometer-derived PA metrics and guidelines with a focus on whole weeks may not adequately characterize QoL relevant PA behavior.

Objective

This study aims to a) identify clusters of accelerometer-derived PA profiles during weekend days among children and adolescents living in Switzerland, b) assess their cross-sectional and predictive association with overall QoL and its dimensions, and c) investigate whether the associations of QoL with the newly identified clusters persist upon adjustment for the commonly used PA metrics moderate-to-vigorous physical activity (MVPA) and time spent in sedentary behavior (SB).

Methods

The population-based Swiss children's Objectively measured PHYsical Activity (SOPHYA) cohort among children and adolescents aged 6 to 16 years was initiated at baseline in 2013. PA and QoL information were obtained twice over a five-year follow-up period. The primary endpoint is the overall QoL score and its six dimension scores obtained by KINDL® questionnaire. The primary predictor is the cluster membership of accelerometer-derived weekend PA profile. Clusters were obtained by applying the k-medoid algorithm to the distance matrix of profiles obtained by pairwise alignments of PA time series using the Dynamic Time Warping (DTW) algorithm. Secondary predictors are accelerometer-derived conventional PA metrics MVPA and SB from two combined weekend days. Linear regression models were applied to assess a) the cross-sectional association between PA cluster membership and QoL at baseline and b) the predictive association between PA cluster membership at baseline and QoL at follow-up, adjusting for baseline QoL.

Results

The study sample for deriving PA profile clusters consisted of 51.4% girls and had an average age of 10.9 [SD 2.5] years). The elbow and silhouette methods indicated that weekend PA profiles are best classified in two or four clusters. The most differentiating characteristic for the two-clusters classification ("lower activity" and "high activity"), and the four-clusters classification ("inactive", "low activity", "medium activity", and "high activity"), respectively was the participant's mean counts per 15-seconds epoch. Participants assigned to high activity clusters were younger and more often male. Neither the clustered PA profiles nor MVPA or SB were cross-sectionally or predictively associated with overall QoL. The only association of a conventional PA metrics with QoL while adjusting for cluster membership was observed between MVPA during the weekend days and social well-being with a mean score difference of 2.4 (95%CI: 0.3 to 4.5; p = 0.025).

Conclusion

The absence of strong associations of PA metrics for the weekend with QoL, except for the positive association between MVPA during the weekend days and social well-being, is in line with results from two randomized studies not showing efficacy of PA interventions on youth QoL. But because PA decreases with age, its promotion and relevance to QoL remain important research topics. Larger longitudinal study samples with more than two follow-up time points of children and adolescents are needed to derive new novel accelerometer-derived PA profiles and to associate them with QoL dimensions.

Keywords

Physical activity profiles, Clustering, Moderate-to-vigorous physical activity, Sedentary behaviour, Quality of life, Longitudinal data, Dynamic Time Warping, k-medoid, Elbow method, Silhouette method

Introduction

Quality of life (QoL) is an important health determinant and indicator, which complements other conventional health indicators such as mortality and morbidity. The World Health Organization (WHO) defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns". QoL is a subjective and multidimensional well-being construct that includes physiological, psychological, and functional aspects (133).

According to the WHO Mental Health Division, the measurement of QoL among children and adolescents should be age-appropriate, applicable independent of the health status of the targeted group, appropriate cross-culturally, and include both positive and negative aspects. There is a preference for self-reported measurement. QoL assessment should consider aspects of health, subjective well-being and social indicators (413). The KINDL® questionnaire is an accepted, valid and reliable QoL instrument for children and adolescents (177).

Few studies assessed QoL in youth in a population-representative manner. High QoL in children and adolescents is essential for a healthy transition to adulthood and for maintaining a good QoL later in life, in line with the United Nations SDG 3 of ensuring good health and improving QoL for all (172). Furthermore, the understanding of health and well-being before adulthood is relevant in itself, in line with Article 12 of the United Nation's Convention of the Rights of the Child (414).

Population-based assessment of QoL and its determinants in the young is important for evaluating the impact of existing public health programs and policies targeting children and adolescents (415). In recent years, there has been a growing focus on understanding the relationship of physical activity (PA) and sedentary behavior (SB) with the overall QoL and its dimensions among children and adolescents without chronic health conditions (231, 416), beyond the well-established evidence for the effect of PA and SB on physical health (326, 417). In these studies of children sampled from the general population, inconsistencies and the absence of associations between PA-related behaviors and QoL exist. They may in part reflect challenges in measuring, characterizing, and summarizing PA and SB as relevant for specific health and well-being endpoints.

PA related behavior is measured by applying subjective (192) and objective (205, 207) methods. PA questionnaires have the advantage of being low cost, easily applicable and having highly acceptable rate among the participants (189), but they are not valid for measuring overall PA in youth (301, 418-422). Accelerometers are the most commonly used instruments for objectively measuring PA-related behaviors (205, 206) and allow characterizing it in different dimensions (423, 424).

Dimensions of PA-related behavior include Frequency, Intensity, Time, and Type (FITT) (425). Different dimensions of PA-related behaviors have specific and in part independent health benefits (426, 427). Even low levels of PA can have health benefits (428-430). Moving from an inactive to an active state promotes health considerably (428, 431). Moreover, with regard to time, children's and adolescents' PA and SB vary between weekdays and weekend days. The young tend to be more physically active on weekdays compared to weekend days (432, 433). They are generally more likely to engage in unhealthy behaviors including SB during weekend days (434).

Many studies on PA-related behaviors and health or QoL are still questionnaire-based and focus on established PA metrics such as time in a week spent in SB or in moderate-to-vigorous physical activity (MVPA) (435). These categories also form the basis of national and international PA recommendations to date (431). Yet, they are unlikely to capture the entire health and well-being relevant heterogeneity of PA and PA-related behaviors between individuals (435). The rich data captured by activity sensors such as accelerometers contain additional information with the potential to unlock novel insights into the association of specific PA-patterns with health endpoints including QoL (436, 437). The pattern difference in the accumulation of certain PA-related behavior over time can have significant implication (438). Dynamic time warping (DTW) enabled progress in the more exhaustive utilization of sensor based time series data such as, captured by the accelerometer. It is a technique proved appropriate and unique for measuring cross-correlated differences between sensor based time series data sets from two aspects; first, the difference in time traces and second, the difference in the motion paths taken (439).

This study aimed to a) identify clusters of accelerometer-derived PA profiles during weekend days among children and adolescents from the Swiss children's Objectively measured PHYsical Activity (SOPHYA) cohort, b) assess their cross-sectional and predictive association with overall QoL and its dimensions, and c) investigate whether QoL associations with newly identified clusters persist upon adjustment for established PA indicators.

Methods

Study design and population

The present study was conducted among children and adolescents participating in the baseline assessment of the SOPHYA cohort (SOPHYA1) between November 19, 2013, and May 28, 2015 (313, 440). All youth who were registered in Switzerland and born between 1998 and 2007 were eligible. The Federal Statistical Office drew random samples from this sampling frame stratified by sex, year of birth, and language (German; French; Italian). The recruitment and the participation rate in SOPHYA1 was described before (313, 440). In short, the participation rate among 2032 families who answered to the SOPHYA1 baseline interview was 65%. Valid accelerometer measurements accompanied by self-administrated questionnaires during the measurement week were obtained from 1320 youth aged 6 to 16 years. The

SOPHYA1 baseline accelerometry formed the basis for deriving PA profiles and for the assessment of the cross-sectional association between clusters of PA profiles and QoL.

For the assessment of the predictive association of clusters of PA profiles at baseline, QoL data obtained at the follow-up assessment between January 9, 2019, and November 20, 2020 (SOPHYA2 accelerometry) was considered as outcome. SOPHYA2 was based on the 1,320 SOPHYA1 baseline accelerometry participants who provided self-administered questionnaire information on socio-demographic characteristics, weight, height, and QoL. Of these participants, 844 could be re-contacted by phone in 2019 and 780 of them provided consent to be re-contacted for a follow-up accelerometer measurement. Among them, 447 participants finally had valid accelerometer measurements as well as self-reported socio-demographic characteristics, weight, height, and QoL.

In SOPHYA1, a parent gave written informed consent (IC) for their children's participation. Adolescents aged 12 years or older filled in an additional IC form. In SOPHYA2, for participants younger than 14 years written IC was provided by a parent as proxy; for participants aged between 14 and 18 years, both parental and an own written IC was provided; for youth above 18 years only own written IC was given

Data collection

Since participants were spread across Switzerland, contact with them was exclusively remote. The regional SOPHYA-study partners (German-speaking region: Swiss Tropical and Public Health Institute in Basel; French-speaking regions: University of Lausanne; Italian-speaking regions: Università della Svizzera Italiana) coordinated participant assessment.

1. Telephone interview

At baseline and follow-up as a first SOPHYA assessment computer-assisted telephone interviews in the respective language region (German; French; Italian) were conducted with one parent as proxy for all children (SOPHYA1), and with children 15 years or older or with one parent as proxy for children aged 14 years or younger (SOPHYA2), respectively. Interview data collected included sociodemographic characteristics (sex, language region (based on the zip code), nationality, urbanicity (based on the zip code), parental education, and household income).

2. Accelerometer measurement

At baseline and follow-up, instructions were given via phone to families on how to use the accelerometer. Subsequently, an accelerometer and written instructions were mailed to the address of the participants with a pre-paid postage box to return the devices to the investigators after completion of the measurements. Most of the participants wore Actigraph accelerometer model GT3X, while few of them wore GT1M, (ActiGraph, Pensacola, Florida, USA), both producing comparable output (204,

395, 441). The device was tied to the participant's right hip with an elastic band and worn for seven consecutive days except when the participant was performing water activities or was sleeping. To ensure the detection of shorter bursts of PA, which are typical for children (396), the device was set without filtering and in 15-seconds epoch mode (measured as milli-gravity units, mg). ActiLife 6.2 software (ActiGraph, Pensacola, Florida, USA) was used to initialize the device, to download the data and to process the data. Non-wearing time was defined as any period of 60 or more minutes of consecutive zero counts.

3. Paper-based survey

At SOPHYA1 and SOPHYA2, families participating in the accelerometry sub-study received an additional paper-based survey to answer questions on the child's age when the accelerometer measurements took place, sport behavior during the measured week, their weight, their height and any diagnosis of chronic disease. Additionally, the survey included the validated KINDL® questionnaire for assessing children's QoL. The questionnaire was administered in the three language areas in Switzerland using the official translation of the questionnaire (Romansh-speaking people filled in the German questionnaire). Validated questionnaire versions tailored to different age groups are available for self-assessment and as parent-proxy tool (178, 180). In SOPHYA1, the questionnaire was filled out by a parent. At follow-up in SOPHYA2, the participants themselves completed the questionnaires given their higher age.

Statistical analysis

1. Study sample

The study samples for this current paper are described in **S1 and S2 Figs**. Based on the subsequent inclusion and exclusion criteria, the sample size for deriving clusters of PA profiles at baseline and for the cross-sectional association of PA profiles with QoL at baseline was N=926, and the sample size for the predictive association of clusters of PA profiles at baseline with QoL at follow-up was N=292.

Inclusion criteria

For deriving clusters of PA profiles on the weekend days at baseline (where the sample was much larger), and for associating clusters of PA profiles cross-sectionally in SOPHYA1 with QoL the following inclusion criteria was applied:

- Participants were restricted to those providing valid accelerometry baseline data from at least 8 hours of wear time for one Saturday and one Sunday, respectively, with both days from the same weekend. In the cases where accelerometers were worn for two consecutive weekends or more, the first weekend was chosen.
- Participants were required to have complete SOPHYA1 data for the overall QoL and its dimensions (see below for partially missing information) and for the selected covariates (age, sex,

parental education, household income, language region, nationality, urbanicity, self-reported diagnosis with at least one chronic disease and season of measurement).

Additional criteria for associating clusters of PA profile predictively with QoL at follow-up:

- Participants were additionally required to have complete data for overall QoL and its dimensions at follow-up (see below for partially missing information).

Exclusion criteria (for all analyses)

- Participants self-reporting a diagnosis of epilepsy or arthropathy at either SOPHYA1 or SOPHYA2.
- Participants with accelerometer data collected at 60-seconds epoch time.
- Participants lacking acceleration data in all three axes.

2. Measures

Primary endpoint: QoL

The validated KINDL® QoL questionnaire consists of 24 items, each answered on a five-point ordinal Likert scale ranging from "never" (=5) to "always" (=1). Each item belongs to one of the six QoL dimensions (four items per dimension): physical well-being, emotional well-being, self-esteem, family connection, social well-being and functioning at school. The QoL dimensions are scored separately as the sum of the scores of 4 items, ranging from 4 to 20. The domain specific scores are subsequently transformed to a scale from 0 to 100. The overall QoL score is calculated based on the mean value of all answered items (https://www.kindl.org/english/analysis/). Higher scores represent a higher QoL. If missing values occurred and affected less than 70% of the answers contributing to a dimension or the total score, the algorithm proposed by the authors of the KINDL® questionnaire was used to replace these missing data (175). If more than 70% of the answers were missing, the score of the respective participant was excluded from the analysis. Based on this, the exclusion criteria affected 2% of the participants in SOPHYA1 and less than 1% participants in SOPHYA2 (399).

Main predictors

a. Primary predictor: PA profile cluster membership

Every participant was assigned to a cluster based on their accelerometer-recorded weekend PA profile (See section **"Statistical analysis steps: In a second step"** for details), and the cluster membership indicator variables were used as the main explanatory variables in the subsequent statistical analyses.

b. Secondary predictors: Established physical activity metrics

- Average MVPA in hours per day during the weekend

  The average MVPA in hours per day during the weekend was derived by ActiLife 6.2, which is based on the age-dependent cut-offs of Freedson (397) with a threshold of four metabolic equivalents (398).

- Average SB in hours per day during the weekend

  The average SB in hours per day during the weekend was derived by ActiLife 6.2, which is defined as an intensity of less than 100 cpm (442).

Covariates

a) Sociodemographic characteristics

Age; sex (boy, girl); language region (German, French, Italian); nationality (Swiss, foreign nationality, Swiss dual citizen); urbanicity (agglomeration, rural, urban); participation in organized sport activities (child participate in sport club at least once a week, child does not participate in a sport club at least once a week); parental education (apprenticeship, high school diploma, higher vocational training, undefined category, compulsory school, diploma school, not willing to provide information); and monthly household income (≤ 6,000 CHF, 6,001 to 9,000 CHF, 9,000 more CHF, not willing to provide information, missing).

b) Health indicator

Self-reported diagnosis of at least one chronic disease (did not have any of the chronic diseases, had at least one chronic disease).

c) Use of the accelerometer

Season of measurement (spring, summer, autumn, winter).

3. Statistical analysis steps

In a first step, we calculated descriptive statistics (n, %, mean, SD) for characterizing the study populations included in cross-sectional and predictive analyses at baseline (Table 1 and S1 Table).

In a second step, we clustered profiles of accelerometer-derived PA from two combined weekend days using the k-medoid algorithm on a distance matrix obtained by DTW (443). DTW calculates normalized pairwise dissimilarity score of time series and has previously been applied to study accelerometer data (444, 445). Using the DTW distance matrix, the k-medoid algorithm (446) finds "k" representative participants, called medoids, by minimizing the average DTW dissimilarity of all the participants' PA profiles to the nearest candidate medoid. Then, each participant is assigned to the cluster represented by the nearest medoid (447, 448). This algorithm requires choosing the number of clusters (k) in advance. We have applied the widely used elbow and the silhouette methods to select the optimal number of clusters. In the main manuscript we present the results for k=4. Supplementary materials contain analogous data for k=2. All calculations were performed in R v4.2.1 (449), using the dtw v1.23-1 (443) for the DTW algorithm and cluster v2.1.2 (446) for clustering. Calculations were performed at sciCORE (http://scicore.unibas.ch/) scientific center at University of Basel.

In a third step, we described the distribution within the derived clusters of sociodemographic characteristics, health indicators including QoL, established PA metrics (Table 2 and S2 Table) and several ad-hoc PA profile summaries (Fig 3 and S4 Fig).

In a fourth step, the cross-sectional association between cluster membership and QoL scores (overall and dimensions) at baseline without (Model 1) and with adjusting for established PA metrics (Model 2: adjusting for MVPA; Model 3: adjusting for SB) was estimated with linear regression models. All models were adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, household income, parental education, self-reported diagnosis with at least one chronic disease, and season of measurement (Tables 3-5 for 4 clusters and S3-S5 Tables for 2 clusters).

In a fifth step, the predictive association between cluster membership at baseline and QoL scores (overall; dimensions) at follow-up was estimated in the same manner as in step four, with additional adjustment for QoL at baseline. The sample was restricted to participants in SOPHYA2 accelerometry (S6-S11 Tables for 4 clusters and for 2 clusters).

Results

Characteristics of the study participants

Baseline characteristics of the study population are summarized in **Table 1**. The SOPHYA1 study sample for the deriving the clusters of PA profiles and for assessing the cross-sectional QoL association consisted of 926 children and adolescents (48.6% boys, 51.4% girls). The average age of the participants was (mean [SD]: 10.9 [2.5] years). The majority of the participants were of Swiss nationality (68.7%) from the German-speaking region (71.3%) reflecting Swiss demographics. The average overall QoL score was (mean [SD]: 81.1 [8.3] points). Of the specific QoL dimensions, self-esteem had the lowest score (mean [SD]: 75.7 [13.7] points), while emotional well-being exhibited the largest score (mean [SD]: 86.4 [10.7] points). The mean of time spent in MVPA and in SB were (mean [SD]: 1.1 [0.7] hr/day) and (mean [SD]: 7.6 [1.6] hr/day), respectively.

Table 1. Characteristics of study participants at baseline (SOPHYA1; 2013) assessment

N=926	
Sociodemographic characteristics	**Mean (SD) / N (%)**
Age	10.9 (2.5)
Sex	
- *Boy*	450.0 (48.6%)
- *Girl*	476.0 (51.4%)
Language region	
- *German*	660.0 (71.3%)
- *French*	174.0 (18.8%)
- *Italian*	92.0 (9.9%)
Nationality	
- *Swiss*	636.0 (68.7%)
- *Foreign nationality*	95.0 (10.3%)
- *Swiss dual citizen (Swiss and foreign nationality)*	195.0 (21.1%)
Urbanicity	
- *Agglomeration*	438.0 (47.3%)
- *Rural*	305.0 (32.9%)
- *Urban*	183.0 (19.8%)
Parental education[1]	
- *Apprenticeship*	409.0 (44.2%)
- *High school diploma*	214.0 (23.1%)
- *Higher vocational training*	168.0 (18.1%)
- *Undefined category*	84.0 (9.1%)
- *Compulsory school*	34.0 (3.7%)
- *Diploma school*	16.0 (1.7%)
- *Not willing to provide information*	1.0 (0.1%)
Household income	
- *≤ 6,000 CHF*	195.0 (21.1%)
- *6,001 to 9,000 CHF*	299.0 (32.3%)
- *9,000 and more CHF*	334.0 (36.1%)
- *Not willing to provide information*	31.0 (3.3%)
- *Missing*	67.0 (7.2%)
Health indicators	**Mean (SD) / n (%)**
Self-reported diagnosis with at least one chronic disease[2]	
- *Did not have any of the chronic diseases*	636.0 (68.7%)
- *Had at least one chronic disease*	290.0 (31.3%)
Quality of life	
- *Overall QoL*	81.1 (8.3)
- *Physical well-being*	84.3 (12.9)
- *Emotional well-being*	86.4 (10.7)
- *Self-esteem*	75.7 (13.7)
- *Family connection*	81.6 (12.5)
- *Social well-being*	78.3 (12.5)
- *Functioning at school*	80.4 (14.7)
Use of the accelerometer	**Mean (SD) / n (%)**
Season of measurement	

- *Spring*	269.0 (29.0%)
- *Summer*	128.0 (13.8%)
- *Autumn*	222.0 (24%)
- *Winter*	307.0 (33.2%)
Conventional physical activity measures during the weekend	**Mean (SD)**
Sedentary Behavior during weekend days[3]	
- *Average time in sedentary behavior (hours/day)*	7.6 (1.6)
Moderate to Vigorous Physical Activity during weekend days[4]	
- *Average time in moderate to vigorous physical activity (hours/day)*	1.1 (0.7)
Mean counts per epoch on weekend days[5]	143.9 (58.6)

[1] Highest parental education
[2] The participant self-reported at least one of the following chronic diseases: asthma, hay fever, allergy, atopic dermatitis, diabetes mellitus, chronic enteritis, hypertension, epilepsy, and arthropathy and attention deficit hyperactivity disorder. Or any other chronic disease not specifically included in the mentioned list
[3] Derived by ActiLife 6.2, which is defined as an intensity of less than 100 cpm
[4] Derived by ActiLife 6.2, which is based on the age-dependent cut-offs of Freedson with a threshold of four metabolic equivalents
[5] Average of the total physical activity counts based on the vector magnitude axis

Baseline characteristics comparing participants included versus not included in the predictive association analysis are presented in **S1 Table**. The sample size for assessing the predictive associations was 292. Youth participating at follow-up tended to be younger and more active and to have higher QoL scores at baseline.

Clusters of PA profiles

The elbow and the silhouette methods were applied to determine the optimal number of clusters k (**Fig 1**). The elbow plot (**Fig 1a**) points to a substantial reduction in the within-cluster dis-similarity when moving from one to two and then, more noticeably, three to four clusters. The silhouette plot (**Fig 1b**) suggests that PA profiles are best described with two clusters, but the four-cluster model scores highly as well. Therefore, we conducted parallel analyses with k=4 (main text) and k=2 (**Online Supplement**).

The four clusters differed markedly in the participants' overall level of PA as measured by mean counts per 15-seconds epoch (**Figs 2 and 3**). Accordingly, they were labeled as "inactive", "low activity", "medium activity", and "high activity" clusters. We calculated additional summaries of the count time series to identify qualitative differences between clusters beyond average activity levels. These metrics were: autocorrelation at lag-1 (15 seconds) and lag-2 (30 seconds) (correlation between values that are 15 seconds and 30 seconds apart, respectively); coefficient of variation (standard deviation of epoch counts divided by the mean); approximate intensity gradient (slope of linear regression of log counts on log number of epochs with that number of counts) (450); the time periods with second and third highest spectral density (the highest always corresponding to 24h due to the diurnal cycle); the longest number of consecutive epochs with non-zero and with zero counts; and the proportion of zero-count epochs). The

distribution of these summaries in each cluster visualized in **Fig 3** differ notably between clusters for the autocorrelation, intensity gradient and proportion of zero-count epochs.

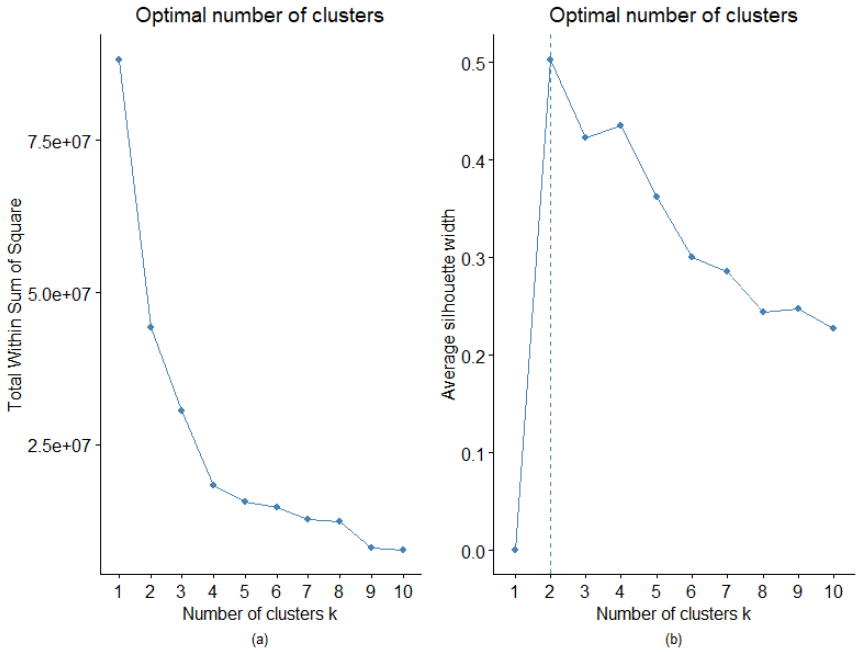

Figure 1. Number of physical activity profile clusters using (a) Elbow and (b) Silhouette methods

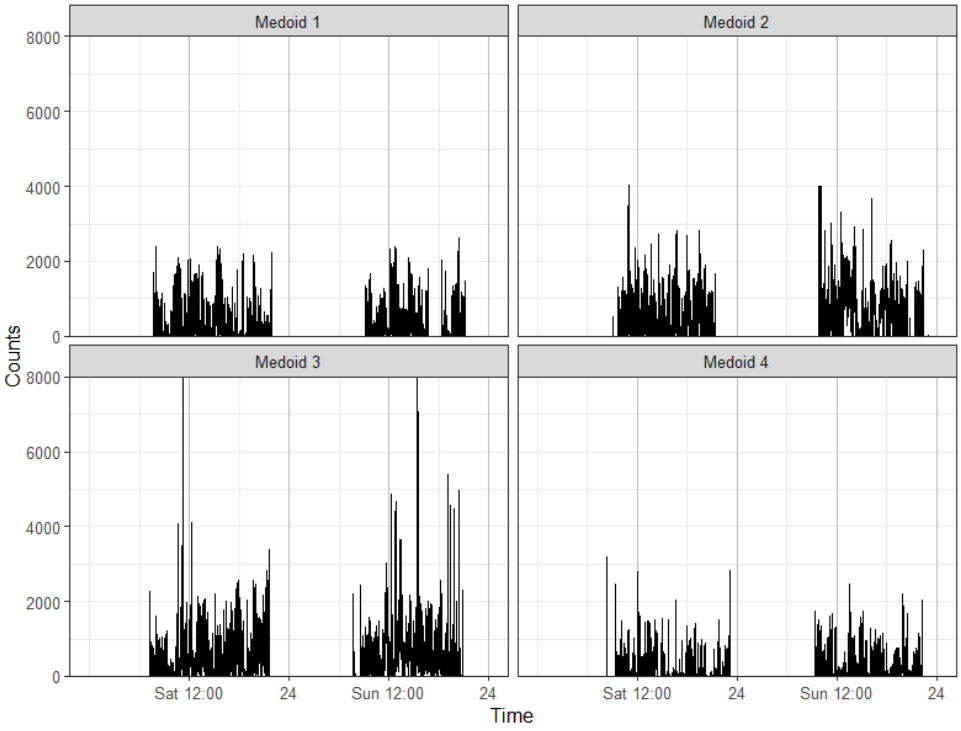

Figure 2. Physical activity pattern (counts in 15-seconds epoch) of the clusters' four medoids (participants)

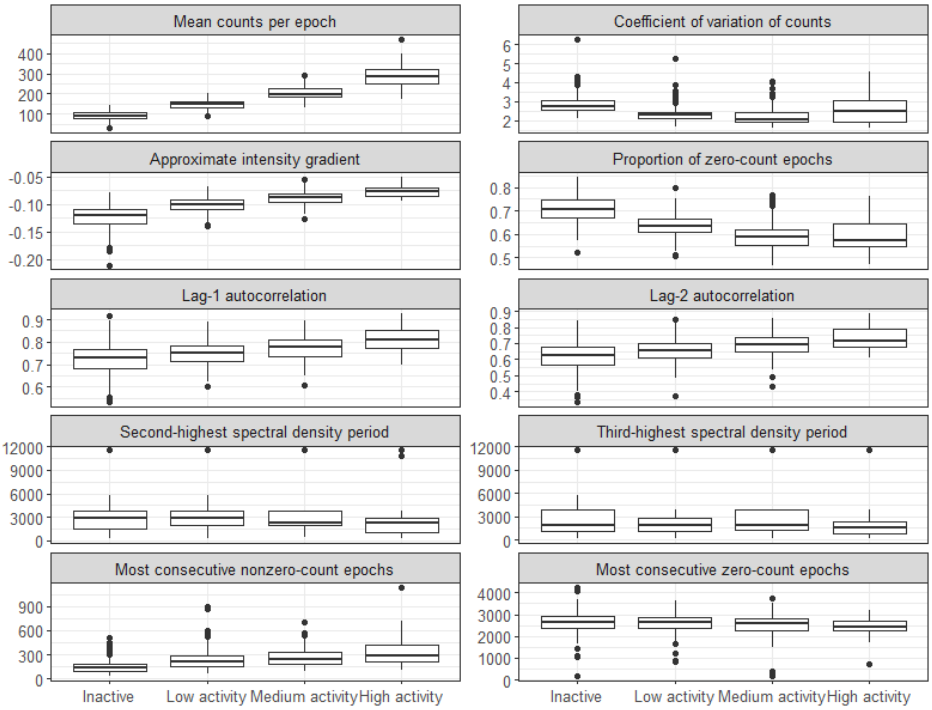

Figure 3. Distributions of summaries of physical activity patterns per cluster

Distribution of participant characteristics according to clusters of PA profiles

The distribution of sociodemographic characteristics, health indicators, including QoL, accelerometry use, and conventional PA metrics between clusters of PA profiles are presented in **Table 2**. The "high activity" cluster participants, compared to the other clusters, scored higher in the mean counts per epoch (mean [SD]: high activity: 284.0 [61.0]; medium activity: 205.0 [29.6]; low activity: 148.0 [19.3]; inactive: 90.9 [21.1] counts; p <0.001). Average sedentary time was highest in the "inactive" cluster (mean [SD]: high activity: 6.3 [1.4]; medium activity: 6.6 [1.3]; low activity: 7.2 [1.3]; inactive: 8.5 [1.5] hr/day; p<0.001) and average hours spent in MVPA was highest in the "high activity" cluster's participants (mean [SD]: high activity: 2.4 [0.9]; medium activity: 1.8 [0.6]; low activity: 1.2 [0.4]; inactive: 0.6 [0.3] hr/day; p<0.001). The higher activity cluster participants were on average younger (mean [SD]: high activity: 10.2 [2.3]; medium activity: 9.7 [2.1]; low activity: 10.2 [2.1]; inactive: 12.4 [2.4] years; p<0.001) and with an overrepresentation of the male gender (p<0.001) with the percentages of boys in the "high activity", "medium activity", "low activity" and "inactive" clusters 66.7%, 60.8%, 48.9%, and 39.5%, respectively. There was a tendency for QoL overall and its dimensions to go from being highest in the "high activity" cluster to lowest in the "inactive" cluster's participants. This reached statistical significance for overall QoL (p<0.001), physical well-being (p<0.001) and functioning at school (p<0.001).

Table 2. Characteristics of study participants at baseline (SOPHYA; 2013), by cluster of physical activity profile

N = 926					
	High activity n = 39 (4.2%)	Medium activity n = 209 (22.6%)	Low activity n = 313 (33.8%)	Inactive n = 365 (39.4%)	P-value
Variable	Mean (SD)/ n (%)	Mean (SD)/ n (%)	Mean (SD)/ n (%)	Mean (SD)/ n (%)	
Socio-demographic characteristics					
Age	10.2 (2.3)	9.7 (2.1)	10.2 (2.1)	12.4 (2.4)	<0.001[1]
Sex					
- *Boy*	26.0 (66.7%)	127.0 (60.8%)	153.0 (48.9%)	144.0 (39.5%)	<0.001[2]
- *Girl*	13.0 (33.3%)	82.0 (39.2%)	160.0 (51.1%)	221.0 (60.5%)	
Language region					
- *German*	29.0 (74.4%)	155.0 (74.2%)	230.0 (73.5%)	246.0 (67.4%)	0.202[3]
- *French*	9.0 (23.1%)	34.0 (16.3%)	58.0 (18.5%)	73.0 (20.0%)	
- *Italian*	1.0 (2.6%)	20.0 (9.6%)	25.0 (8.0%)	46.0 (12.6%)	
Nationality					
- *Swiss*	27.0 (69.2%)	148.0 (70.8%)	218.0 (69.6%)	243.0 (66.6%)	0.442[3]
- *Foreign nationality*	3.0 (7.7%)	19.0 (9.1%)	39.0 (12.5%)	34.0 (9.3%)	
- *Swiss dual citizen (Swiss and foreign nationality)*	9.0 (23.1%)	42.0 (20.1%)	56.0 (17.9%)	88.0 (24.1%)	
Urbanicity					
- *Agglomeration*	14.0 (35.9%)	86.0 (41.1%)	143.0 (45.7%)	195.0 (53.4%)	0.442[3]
- *Rural*	13.0 (33.3%)	79.0 (37.8%)	105.0 (33.5%)	108.0 (29.6%)	
- *Urban*	12.0 (30.8%)	44.0 (21.1%)	65.0 (20.8%)	62.0 (17.0%)	
Parental education					
- *Apprenticeship*	17.0 (43.6%)	89.0 (42.6%)	134.0 (42.8%)	169.0 (46.3%)	0.603[3]
- *High school diploma*	11.0 (28.2%)	45.0 (21.5%)	66.0 (21.1%)	92.0 (25.2%)	
- *Higher vocational training*	8.0 (20.5%)	39.0 (18.7%)	59.0 (18.8%)	62.0 (17.0%)	
- *Undefined category*	2.0 (5.1%)	27.0 (12.9%)	33.0 (10.5%)	22.0 (6.0%)	
- *Compulsory school*	1.0 (2.6%)	6.0 (2.9%)	14.0 (4.5%)	13.0 (3.6%)	
- *Diploma school*	0.0 (0.0%)	3.0 (1.4%)	6.0 (1.9%)	7.0 (1.9%)	

- *Not willing to provide information*	0.0 (0.0%)	0.0 (0.0%)	1.0 (0.3%)	0.0 (0.0%)	
Household income					
- *≤ 6,000 CHF*	8.0 (20.5%)	36.0 (17.2)	62.0 (19.8%)	89.0 (24.4%)	0.164[3]
- *6,001 to 9,000 CHF*	14.0 (35.9%)	62.0 (29.7%)	98.0 (31.3%)	125.0 (34.2%)	
- *9,000 and more CHF*	14.0 (35.9%)	83.0 (39.7%)	126.0 (40.3%)	111.0 (30.4%)	
- *Not willing to provide information*	1.0 (2.6%)	10.0 (4.8%)	11.0 (3.5%)	9.0 (2.5%)	
- *Missing*	2.0 (5.1%)	18.0 (8.6%)	16.0 (5.1%)	31.0 (8.5%)	
Health indicators					
Self-reported diagnosis with at least one chronic disease					
- *Did not have any of the chronic diseases*	30.0 (76.9%)	155.0 (74.2%)	211.0 (67.4%)	240.0 (65.8%)	0.123[3]
- *Had at least one chronic disease*	9.0 (23.1%)	54.0 (25.8%)	102.0 (32.6%)	125.0 (34.2%)	
Quality of life					
- *Overall QoL*	83.2 (6.6)	82.6 (7.5)	81.6 (8.3)	79.6 (8.7)	<0.001[1]
- *Physical well-being*	85.7 (10.6)	88.1 (10.3)	84.9 (13.0)	81.4 (13.8)	<0.001[1]
- *Emotional well-being*	88.1 (9.2)	87.2 (9.7)	86.6 (11.2)	85.6 (11.0)	0.173[1]
- *Self-esteem*	76.3 (14.8)	76.2 (13.2)	76.4 (13.5)	74.7 (13.9)	0.089[1]
- *Family connection*	82.4 (10.7)	81.8 (11.3)	80.7 (12.9)	82.2 (13.0)	0.138[1]
- *Social well-being*	82.5 (11.7)	78.8 (11.4)	78.4 (11.6)	77.5 (13.8)	0.378[1]
- *Functioning at school*	84.0 (11.9)	83.2 (13.9)	82.7 (13.8)	76.5 (15.4)	<0.001[1]
Use of the accelerometer					
Season of measurement					
- *Spring*	13.0 (33.3%)	54.0 (25.8%)	86.0 (27.5%)	116.0 (31.8%)	<0.001[3]
- *Summer*	7.0 (17.9%)	42.0 (20.1%)	43.0 (13.7%)	36.0 (9.9%)	
- *Autumn*	15.0 (38.5%)	58.0 (27.8%)	76.0 (24.3%)	73.0 (20.0%)	
- *Winter*	4.0 (10.3%)	55.0 (26.3%)	108 (34.5%)	140.0 (38.4%)	
Conventional physical activity measures during the weekend					
Sedentary Behavior on weekend days					
- *Average time in sedentary in hours/day*	6.3 (1.4)	6.6 (1.3)	7.2 (1.3)	8.5 (1.5)	<0.001[1]
Moderate to Vigorous Physical Activity on weekend days					

- *Average time in moderate to vigorous physical activity in hours/day*	2.4 (0.9)	1.8 (0.6)	1.2 (0.4)	0.6 (0.3)	<0.001[1]
Mean counts per epoch on weekend days	284.0 (61.0)	205.0 (29.6)	148.0 (19.3)	90.9 (21.1)	<0.001[1]

[1] P-value from the analysis of variance (ANOVA)
[2] P-value from the chi-squared test
[3] P-value from Finsher's exact test

Cross-sectional association of clusters of PA profiles with QoL

The association of cluster membership with QoL was first estimated without adjustment for conventional PA metrics (**Model 1, Table 3**). No statistically significant differences between the reference "inactive" cluster and the remaining three were present, albeit a suggestion for a positive trend for increasing QoL with increasing activity was observable. The strongest trend for an increasingly positive association of more activity with QoL was observed for social well-being. Participants in the "high activity" cluster exhibited on average 5.4 (95%CI: 1.2 to 9.6) higher social well-being scores than participants assigned to the "inactive" cluster (p = 0.012). With regard to physical well-being a statistically significant association was observed for higher score in the "medium activity" cluster compared to the "inactive" cluster (p <0.001) with average increase of 4.2 (95%CI: 1.7 to 6.6) units. The coefficients for the "high activity" 2.4 (95%CI: -1.9 to 6.7) and "low activity" 2.1 (95%CI: -0.02 to 4.2) clusters were also positive but did not reach statistical significance.

Table 3. Linear adjusted[1] cross-sectional association of physical activity profile cluster membership with QoL (relative to the participants in the "inactive" cluster)

Model 1 – no adjustment for established physical activity metrics				
Primary endpoint	Main predictor	Coefficient	95% CI	P-value
Overall QoL	Low activity	0.6	(-0.7 to 1.9)	0.366
	Medium activity	1.0	(-0.5 to 2.5)	0.197
	High activity	2.0	(-0.7 to 4.7)	0.139
Physical well-being	Low activity	2.1	(-0.02 to 4.2)	0.053
	Medium activity	4.2	(1.7 to 6.6)	<0.001
	High activity	2.4	(-1.9 to 6.7)	0.276
Emotional well-being	Low activity	0.4	(-1.4 to 2.1)	0.690
	Medium activity	0.5	(-1.5 to 2.6)	0.628
	High activity	1.6	(-2.0 to 5.2)	0.379
Self-esteem	Low activity	0.7	(-1.6 to 2.9)	0.571
	Medium activity	0.1	(-2.6 to 2.7)	0.968
	High activity	-0.4	(-5.1 to 4.3)	0.865
Family connection	Low activity	-1.1	(-3.1 to 0.9)	0.291
	Medium activity	0.2	(-2.2 to 2.6)	0.858
	High activity	0.9	(-3.3 to 5.1)	0.665
Social well-being	Low activity	1.1	(-0.9 to 3.2)	0.284
	Medium activity	1.7	(-0.7 to 4.1)	0.162
	High activity	5.4	(1.2 to 9.6)	0.012
Functioning at school	Low activity	0.5	(-1.6 to 2.6)	0.636
	Medium activity	-0.6	(-3.0 to 1.9)	0.646
	High activity	2.4	(-1.9 to 6.7)	0.269

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, and season of measurement

Table 4. Linear mutually adjusted[1] cross-sectional association of physical activity profile cluster membership (relative to the participants in the inactive cluster) and MVPA (per 1h/day) with QoL

Model 2 - additionally adjusted for MVPA							
Cluster membership					MVPA		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	Low activity	0.5	(-0.9 to 1.9)	0.473	0.2	(-1.1 to 1.6)	0.744
	Medium activity	0.8	(-1.2 to 2.8)	0.443			
	High activity	1.7	(-1.7 to 5.1)	0.334			
Physical well-being	Low activity	1.7	(-0.5 to 4.0)	0.129	0.8	(-1.3 to 2.9)	0.446
	Medium activity	3.4	(0.2 to 6.6)	0.040			
	High activity	1.1	(-4.3 to 6.5)	0.695			
Emotional well-being	Low activity	0.7	(-1.2 to 2.6)	0.458	-0.9	(-2.7 to 0.9)	0.314
	Medium activity	1.4	(-1.3 to 4.1)	0.307			
	High activity	3.1	(-1.5 to 7.7)	0.190			
Self-esteem	Low activity	1.0	(-1.5 to 3.4)	0.446	-0.7	(-3.1 to 1.6)	0.525
	Medium activity	0.8	(-2.7 to 4.3)	0.657			
	High activity	0.8	(-5.2 to 6.7)	0.798			
Family connection	Low activity	-1.1	(-3.3 to 1.1)	0.327	0.0	(-2.1 to 2.1)	0.999
	Medium activity	0.2	(-2.9 to 3.3)	0.893			
	High activity	0.9	(-4.4 to 6.2)	0.733			
Social well-being	Low activity	0.2	(-2.0 to 2.4)	0.867	2.4	(0.3 to 4.5)	0.025
	Medium activity	-0.6	(-3.8 to 2.5)	0.695			
	High activity	1.7	(-3.6 to 7.0)	0.536			
Functioning at school	Low activity	0.6	(-1.6 to 2.8)	0.603	-0.2	(-2.3 to 1.9)	0.826
	Medium activity	-0.3	(-3.5 to 2.9)	0.836			
	High activity	2.8	(-2.6 to 8.2)	0.314			

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, and additionally adjusted for MVPA

Table 5. Linear mutually adjusted[1] cross-sectional association of physical activity profile cluster membership (relative to the participants in the inactive cluster) and sedentary behavior (per 1h/day) with QoL

Model 3 – additionally adjusted for sedentary behavior							
Cluster membership					Sedentary behavior		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	Low activity	0.7	(-0.6 to 2.1)	0.288	0.2	(-0.2 to 0.6)	0.388
	Medium activity	1.2	(-0.4 to 2.8)	0.137			
	High activity	2.3	(-0.4 to 5.1)	0.101			
Physical well-being	Low activity	2.2	(0.01 to 4.3)	0.049	0.1	(-0.5 to 0.8)	0.711
	Medium activity	4.3	(1.8 to 6.9)	<0.001			
	High activity	2.6	(-1.8 to 7.0)	0.252			
Emotional well-being	Low activity	0.6	(-1.2 to 2.4)	0.524	0.3	(-0.2 to 0.9)	0.237
	Medium activity	0.9	(-1.3 to 3.0)	0.416			
	High activity	2.1	(-1.6 to 5.9)	0.258			
Self-esteem	Low activity	1.1	(-1.3 to 3.4)	0.374	0.6	(-0.1 to 1.3)	0.109
	Medium activity	0.7	(-2.1 to 3.5)	0.608			
	High activity	0.5	(-4.3 to 5.3)	0.836			
Family connection	Low activity	-1.0	(-3.1 to 1.1)	0.356	0.2	(-0.5 to 0.8)	0.605
	Medium activity	0.4	(-2.1 to 2.9)	0.746			
	High activity	1.2	(-3.1 to 5.5)	0.589			
Social well-being	Low activity	0.8	(-1.3 to 3.0)	0.428	-0.4	(-1.0 to 0.2)	0.218
	Medium activity	1.2	(-1.3 to 3.8)	0.332			
	High activity	4.8	(0.4 to 9.1)	0.030			
Functioning at school	Low activity	0.7	(-1.4 to 2.8)	0.521	0.3	(-0.3 to 0.9)	0.391
	Medium activity	-0.2	(-2.8 to 2.3)	0.853			
	High activity	2.8	(-1.5 to 7.2)	0.203			

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, and additional adjusted for sedentary behavior

Predictive association

There was no evidence for an association of cluster membership at the SOPHYA1 baseline with QoL or its dimensions at SOPHYA2 when adjusting for the baseline QoL or its dimensions irrespective of adjustment for established PA metrics (**S6-S11 Tables**).

Discussion

The data driven unsupervised analysis of PA profiles derived from accelerometer measurements during the weekend identified clusters of youth with different behavioral patterns. The most discriminating PA characteristics between the profiles were the mean intensity of PA and the time spent in SB. A similar study clustered PA including SB based on accelerometer data obtained from pre-pubertal children in which three clusters of PA profiles were identified that primarily reflected intensity levels of PA and time spent in SB (451). This is in contrast to results from a similar clustering approach of objectively measured PA data obtained at 5-seconds intervals from the UK Biobank. Nine distinctly different profiles were identified, but the study used data from a whole week and from more than 90'000 adults (452).

Young age and being a boy were most prevalent in the high activity profile cluster in this current study. This is in agreement with the most robust finding of a review of studies clustering PA based on a combination of conventional PA metrics (453). It also confirms the observed objective longitudinal MVPA decline as children and adolescents grow older (390). Furthermore, a recent study among 6- and 9-year old children confirmed the overrepresentation of boys of young age in the cross-sectional and longitudinal high activity classes. It fitted cross-sectional and longitudinal latent profile analysis models to accelerometer derived proportions of time spent in MVPA and sedentary time for weekdays and weekends. Interestingly, participants assigned to high activity profiles, in which most children achieved the recommended MVPA guidelines, were more likely to be active at weekends than on weekdays. Participation in out-of-school activities contributed importantly to changes on the patterns of PA over time (454). The importance of the pre-school, weekend (432, 433), and holiday (455) activities is further reinforced by a study conducted among children between 7 and 11 years old to examine day-to-day PA variability. The MVPA levels were most stable during the pre-school segment of the day (456). While differences in PA patterns between weekend days and weekdays were previously reported for the young (308, 457), it is not known whether the observed health benefit in adults reaching activity guidelines during the weekend only (458) extends to young age.

This study did not provide evidence for cross-sectional or predictive associations of either the newly derived PA cluster profiles or the conventional metrics of PA with overall QoL among children and adolescents living in Switzerland during weekend days. Overall QoL may not be the optimal endpoint for assessing the impact of PA behavior on the QoL in youth. To date, PA-related behaviors were found to be

positively associated with children's and adolescents' psychological well-being (226, 459), social well-being (234, 460) autonomy and parents relations (278) and functioning at school (234) as dimensions of QoL. This QoL enhancement can be mediated in part by positive PA effect on the improvement of cardiorespiratory fitness (459), self-concept (407), and subjective happiness (407). There is also empirical evidence for a negative association between SB and several QoL dimensions including psychological well-being (461), social support (461), physical well-being (462), and school functioning (461) dimensions. Also in this study, some associations with QoL sub-domains were observed.

The most consistent association between PA and QoL subdomains was the observed positive association of the high activity profile cluster with the social well-being dimension, which disappeared upon MVPA, but not SB adjustment. In mutually adjusted models, MVPA was only associated with the social well-being dimension, but not any other QoL domain. PA, primarily MVPA, may therefore explain the variability of the social dimension of QoL better than the variability of other dimensions of QoL among children and adolescents. Evidence for the positive association between self-reported as well as objectively measured PA and social well-being among children and adolescents has been provided before (234, 460). Some evidence additionally points to a causal link between the two constructs. A previous two year longitudinal study with three follow-up times was conducted among adolescents in France. The bidirectional association between PA and several dimensions of health related QoL was strongest for the social well-being dimension of health related QoL (411). In Australia, another study based on longitudinal population-based data obtained at ages 12 and again five years later provided evidence for the predictive association between higher levels of PA and QoL, mainly driven by improvement in the physical and social well-being dimensions (463).

It is worth mentioning the positive association between activity profile clusters and physical well-being, which was stronger for the medium activity clusters than for the highest activity clusters. The associations were not sensitive for adjustment for MVPA or SB. This finding may suggest that low and medium PA levels provide the right balance between maintaining physical well-being and creating a healthy strain on the body. Light intensity PA was previously associated with higher health related QoL in girls (464).

While in adults, evidence from randomized trials points to causal short- and mid-term effects of conventional PA metrics on QoL (465, 466), very few randomized trials were conducted in children or adolescents, most of them in subgroups with specific health conditions such as cancer, type 1 diabetes, asthma, or mental health disorders. A seven-month, school-based cluster-randomized controlled PA intervention in 10-year old children in Norway did not find an effect on the overall QoL or its dimensions (467). A randomized controlled trial in Swiss elementary school children found little effect of a school-based PA program on QoL (468).

Strengths and limitations

The fact that the study was cohort and population-based is a major strength. This is in addition to the objective measurement of PA, which diminishes self-reporting bias in PA assessment compared to subjective PA measurement (423, 424). Given the opportunity presented by the availability of the accelerometer-recorded weekend PA data, this study applied the k-medoid algorithm to the distance matrix of profiles obtained by pairwise alignments of PA time series using the DTW algorithm to extract clusters of PA profiles. Then, it assessed the role of PA profiles in QoL, as indicator of health, beyond conventional PA metrics, which is considered main added value of this study. The assessment of QoL was based on the KINDL® questionnaire, which is reliable and valid instrument (177).

Among the main limitations of the study is the relatively small sample size, in particular for the predictive analysis of the association of PA at baseline with QoL at the follow-up. The small sample size might have precluded identification of small or poorly separated clusters that might nevertheless capture aspects of PA variability beyond MVPA and SB that are relevant to health. This could explain the broad absence of associations between PA cluster profiles and QoL in models adjusted for established conventional PA metrics. An additional limitation of the study is the parent-proxy report on children's and adolescents' QoL at baseline, which compromises the essence of QoL as the individual's subjective perception of his or her health (142). The correlation between parent-proxy versus self-report of QoL among children and adolescents has previously been reported to be poor (469). We acknowledge the bias in the predictive association between PA at baseline and QoL that may have been introduced due to loss to follow-up. Follow-up participants tended to be younger, more physically active and with better QoL. This may have led to an underestimation of any true association between PA and QoL.

Conclusion

In this first population-based study that derived among children and adolescents data driven clusters of objectively measured PA profiles on the weekend no consistent and independent associations of these clusters with overall and domain-specific QoL were observed.

Because PA decreases with age and during the transition from childhood to adolescence (389, 470), PA promotion and its relevance to QoL remain important research topics. Future research based on larger longitudinal study samples with more than two follow-up time points of children and adolescents is needed to derive novel accelerometer derived PA profiles and to associate them with QoL dimensions.

List of abbreviations

DTW: Dynamic Time Warping

MVPA: Moderate-to-vigorous physical activity

PA: Physical activity

QoL: Quality of life

SB: Sedentary behavior

SOPHYA: Swiss children's Objectively measured PHYsical Activity

WHO: World Health Organization

Ethics approval

SOPHYA1 and SOPHYA2 protocols were approved by the ethics committee of the Canton of Basel/North-Western Switzerland (147/13; EKNZ 2018-01786). The SOPHYA cohort was performed in accordance with the ethical standards delineated in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent for publication

Not applicable.

Availability of data and materials

The analyzed dataset of the current study are not publicly available due to ethical consideration and restrictions, but are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RD, MK, JH and NPH conceived the study objective and analysis plan.

RD and MK conducted the data analysis.

RD and NPH drafted the manuscript.

BBI and NPH developed the SOPHYA cohort protocol.

BBI, JH, BK, and SS were involved in collection and management of SOPHYA data.

All authors read and approved of the final main and online manuscript text, tables, figures.

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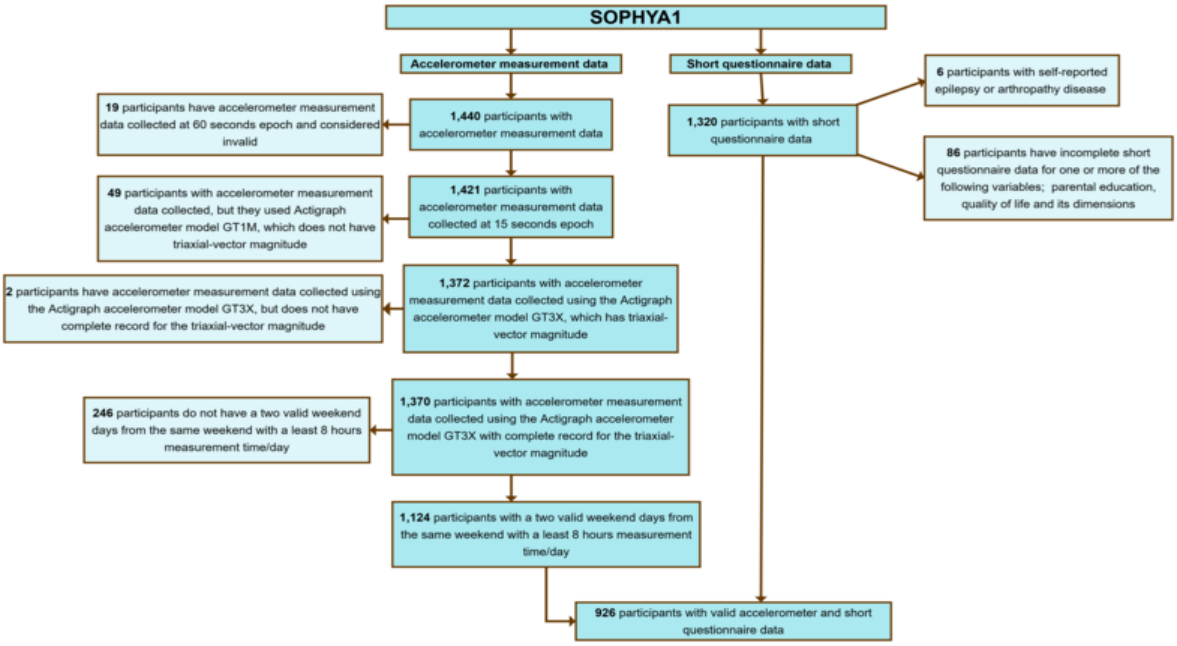
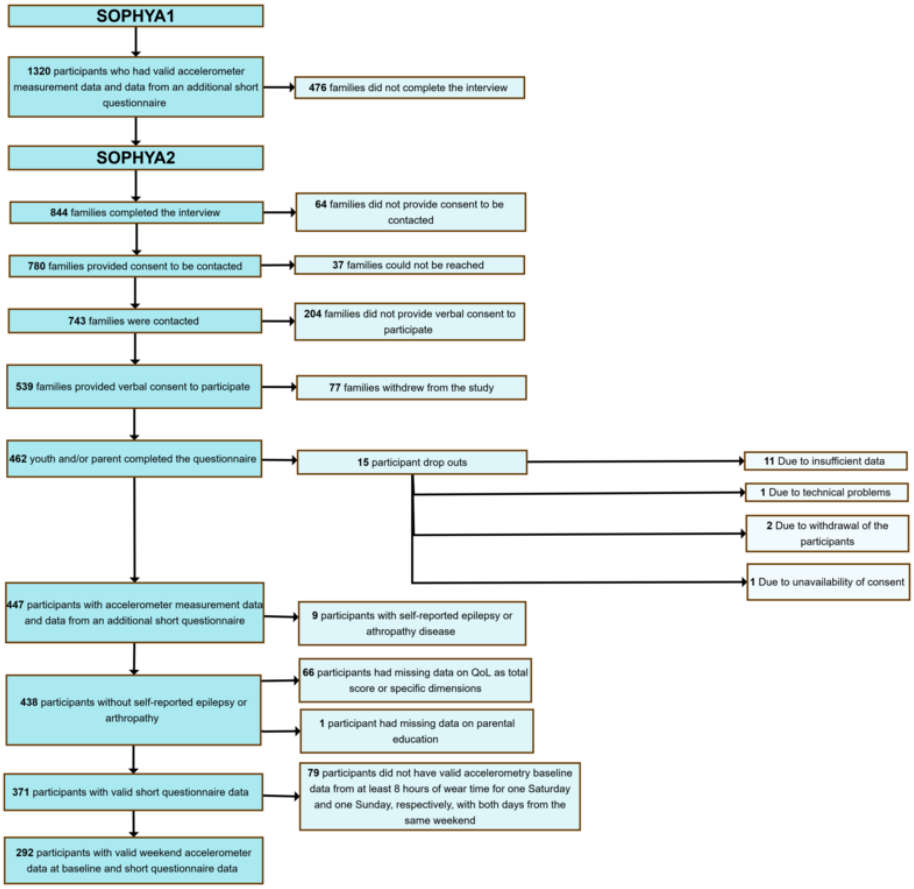
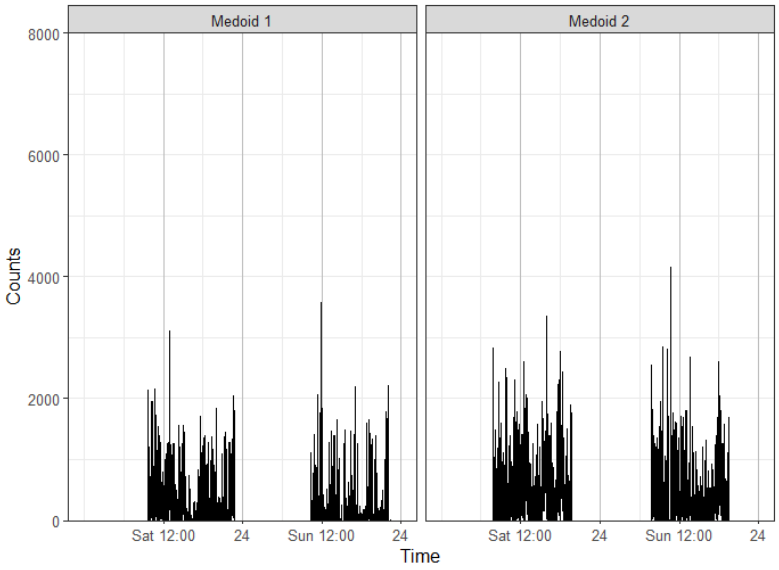
Appendix II



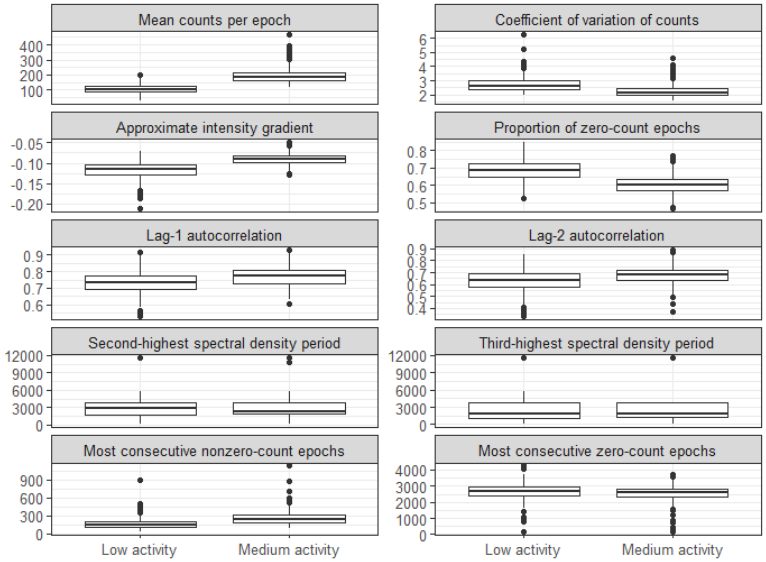
S1 Fig. Study sample for physical activity profiles' clustering and cross-sectional association with quality of life



S2 Fig. Study sample for predictive association of physical activity profiles' clustering at baseline with quality of life at follow-up



S3 Fig. Physical activity pattern (counts in 15-seconds epoch) of the clusters' two medoids (participants)



S4 Fig. Distributions of summaries of physical activity patterns per cluster

S1 Table. Baseline characteristics of participants included in the cross-sectional analysis only compared to participants included in the predictive analysis

	Children who participated only in SOPHYA1 N = 634	Children who participated in SOPHYA2 N = 292	95% CI	P-value
Variable	**Mean (SD) / N (%)**	**Mean (SD) / N (%)**		
Socio-demographic characteristics				
Age	11.3 (2.6)	10.1 (2.3)	(0.9 to 1.5)	<0.001[1]
Sex				
- *Boy*	315.0 (49.7%)	135.0 (46.2%)		0.365[2]
- *Girl*	319.0 (50.3%)	157.0 (53.8%)		
Language region				
- *German*	452.0 (71.3%)	208.0 (71.2%)		0.374[2]
- *French*	114.0 (18.0%)	60.0 (20.5%)		
- *Italian*	68.0 (10.7%)	24.0 (8.2%)		
Nationality				
- *Swiss*	435.0 (68.6%)	201.0 (68.8%)		0.749[2]
- *Foreign nationality*	68.0 (10.7%)	27.0 (9.2%)		
- *Swiss dual citizen (Swiss and foreign nationality)*	131.0 (20.7%)	64.0 (21.9%)		
Urbanicity				
- *Agglomeration*	298.0 (47.0%)	140.0 (47.9%)		0.582[2]
- *Rural*	215.0 (33.9%)	90.0 (30.8%)		
- *Urban*	121.0 (19.1%)	62.0 (21.2%)		
Parental education[3]				
- *Apprenticeship*	291.0 (45.9%)	118.0 (40.0%)		0.102[4]
- *High school diploma*	137.0 (21.6%)	77.0 (26.4%)		
- *Higher vocational training*	110.0 (17.4%)	58.0 (19.9%)		
- *Undefined category*	54.0 (8.5%)	30.0 (10.3%)		
- *Compulsory school*	29.0 (4.6%)	5.0 (1.7%)		
- *Diploma school*	12.0 (1.9%)	4.0 (1.4%)		
- *Not willing to provide information*	1.0 (0.2%)	0.0 (0.0%)		

Household income				
- *≤ 6,000 CHF*	144.0 (22.7%)	51.0 (17.5%)	0.124[1]	
- *6,001 to 9,000 CHF*	206.0 (32.5%)	93.0 (31.8%)		
- *9,000 and more CHF*	213.0 (33.6%)	121.0 (41.4%)		
- *Not willing to provide information*	21.0 (3.3%)	10.0 (3.4%)		
Health indicators				
Self-reported diagnosis with at least one chronic disease[5]				
- *Did not have any of the chronic diseases*	422.0 (66.6%)	214.0 (73.3%)	0.048[2]	
- *Had at least one chronic disease*	212.0 (33.4%)	78.0 (26.7%)		
Quality of life				
- *Overall QoL*	80.5 (8.6)	82.4 (7.6)	(-3.0 to -0.8)	<0.001[1]
- *Physical well-being*	83.9 (13.3)	85.1 (12.0)	(-3.0 to 0.5)	0.158[1]
- *Emotional well-being*	85.9 (10.9)	87.5 (10.2)	(-3.0 to -0.1)	0.037[1]
- *Self-esteem*	75.0 (14.3)	77.2 (12.1)	(-4.0 to -0.4)	0.017[1]
- *Family connection*	81.4 (12.7)	82.1 (12.1)	(-2.4 to 1.0)	0.422[1]
- *Social well-being*	77.9 (13.0)	79.1 (11.3)	(-2.8 to 0.5)	0.167[1]
- *Functioning at school*	79.0 (15.1)	83.5 (13.5)	(-6.4 to -2.5)	<0.001[1]
Use of the accelerometer				
Weartime				
- *Average scored time per day (minutes)*	801.6 (53.5)	791.9 (48.5)	(2.8 to 16.7)	0.006[1]
Season of measurement				
- *Spring*	197.0 (31.1%)	72.0 (24.7%)	0.151[2]	
- *Summer*	83.0 (13.1%)	45.0 (15.4%)		
- *Autumn*	143.0 (22.6%)	79.0 (27.1%)		
- *Winter*	211.0 (33.3%)	96.0 (32.9%)		
Conventional physical activity measures during the weekend				
Sedentary Behavior during weekend days[6]				

- *Average time in sedentary behavior (hours/day)*	7.7 (1.6)	7.3 (1.6)	(0.2 to 0.6)	<0.001[1]
Moderate to Vigorous Physical Activity during weekend days[7]				
- *Average time in moderate to vigorous physical activity (hours/day)*	1.1 (0.7)	1.3 (0.7)	(-0.3 to -0.1)	<0.001[1]

[1] P-value from student's t-test
[2] P-value from the chi-squared test
[3] Highest parental education
[4] P-value from Finsher's exact test
[5] The participant self-reported at least one of the following chronic diseases: asthma, hay fever, allergy, atopic dermatitis, diabetes mellitus, chronic enteritis, hypertension, epilepsy, arthropathy and attention deficit hyperactivity disorder. Or any other chronic disease not specifically included in the mentioned list
[6] Derived by ActiLife v6.13.3, which is defined as an intensity of less than 100 cpm
[7] Derived by ActiLife v6.13.3, which is based on the age-dependent cut-offs of Freedson with a threshold of four metabolic equivalents

S2 Table. Characteristics of study participants at baseline (SOPHYA; 2013) by cluster of physical activity profile

N = 926				
	High activity n = 396 (42.8%)	**Lower activity n = 530 (57.2%)**	**95% CI**	**P-value**
Variable	**Mean (SD)/ n (%)**	**Mean (SD)/ n (%)**		
Socio-demographic characteristics				
Age	9.7 (2.1)	11.8 (2.5)	(1.8 to 2.4)	<0.001[1]
Sex				
- *Boy*	229.0 (57.8%)	221.0 (41.7%)	<0.001[2]	
- *Girl*	167.0 (42.2%)	309.0 (58.3%)		
Language region				
- *German*	293.0 (74%)	367.0 (69.2%)	0.2862	
- *French*	67.0 (16.9%)	107.0 (20.2%)		
- *Italian*	36.0 (9.1%)	56.0 (10.6%)		
Nationality				
- *Swiss*	275.0 (69.4%)	361.0 (68.1%)	0.7622	
- *Foreign nationality*	42.0 (10.6%)	53.0 (10%)		
- *Swiss dual citizen (Swiss and foreign nationality)*	79.0 (19.9%)	116.0 (21.9%)		
Urbanicity				
- *Agglomeration*	176.0 (44.4%)	262.0 (49.4%)	0.3102	
- *Rural*	136.0 (34.3%)	169.0 (31.9%)		
- *Urban*	84.0 (21.2%)	99.0 (18.7%)		
Parental education				
- *Apprenticeship*	164.0 (41.4%)	245.0 (46.2%)	0.116[3]	
- *High school diploma*	83.0 (21.0%)	131.0 (24.7%)		
- *Higher vocational training*	82.0 (20.7%)	86.0 (16.2%)		
- *Undefined category*	44.0 (11.1%)	40.0 (7.5%)		
- *Compulsory school*	14.0 (3.5%)	20.0 (3.8%)		
- *Diploma school*	8.0 (2.0%)	8.0 (1.5%)		

- *Not willing to provide information*	1.0 (0.3%)	0.0 (0.0%)		
Household income				
- *≤ 6,000 CHF*	70.0 (17.7%)	125.0 (23.6%)	0.0512	
- *6,001 to 9,000 CHF*	121.0 (30.6%)	178.0 (33.6%)		
- *9,000 and more CHF*	159.0 (40.2%)	175.0 (33%)		
- *Not willing to provide information*	17.0 (4.3%)	14.0 (2.6%)		
- *Missing*	29.0 (7.3%)	38.0 (7.2%)		
Health indicators				
Self-reported diagnosis with at least one chronic disease				
- *Did not have any of the chronic diseases*	283.0 (71.5%)	353.0 (66.6%)	0.1322	
- *Had at least one chronic disease*	113.0 (28.5%)	177.0 (33.4%)		
Quality of life				
- *Overall QoL*	82.3 (7.3)	80.2 (8.9)	(-3.1 to -1.0)	<0.0011
- *Physical well-being*	86.7 (11.7)	82.5 (13.5)	(-5.9 to -2.6)	<0.0011
- *Emotional well-being*	87.0 (9.7)	86.0 (11.4)	(-2.4 to 0.3)	0.1441
- *Self-esteem*	76.3 (13)	75.3 (14.1)	(-2.8 to 0.7)	0.2461
- *Family connection*	81.4 (11.8)	81.7 (13)	(-1.3 to 1.9)	0.7011
- *Social well-being*	78.9 (10.9)	77.9 (13.6)	(-2.6 to 0.6)	0.2141
- *Functioning at school*	83.6 (13.4)	78.0 (15.2)	(-7.5 to -3.8)	<0.0011
Use of the accelerometer				
Weartime				
- *Average scored time per day in minutes*	795.0 (49.0)	801.0 (54.2)	(-0.3 to 13.1)	0.0611
Season of measurement				
- *Spring*	99.0 (25%)	170.0 (32.1%)	<0.0012	
- *Summer*	73.0 (18.4%)	55.0 (10.4%)		
- *Autumn*	115.0 (29.0%)	107.0 (20.0%)		
- *Winter*	109.0 (27.5%)	198.0 (37.4%)		
Conventional physical activity measures during the weekend				
Sedentary Behavior during weekend days on weekend days				
- *Average time in sedentary in hours/day*	6.7 (1.3)	8.2 (1.5)	(1.3 to1.6)	<0.0011
Moderate to Vigorous Physical Activity				

- *Average time in moderate to vigorous physical activity in hours/day*	1.7 (0.6)	0.7 (0.4)	(-1.1 to -0.9)	<0.0011
Mean counts per epoch on weekend days	196.0 (46.4)	105.0 (28.4)	(-96.6 to -86.2)	<0.0011

[1] P-value from student's t-test
[2] P-value from the chi-squared test
[3] P-value from Fisher's exact test

S3 Table. Linear adjusted[1] cross-sectional association of physical activity cluster membership (relative to the participants in the lower activity cluster) with QoL

Model 1 - no adjustment for established physical activity metrics				
Primary endpoint	**Main predictor**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	High activity	0.6	(-0.6 to 1.7)	0.338
Physical well-being	High activity	2.1	(0.2 to 3.9)	0.029
Emotional well-being	High activity	0.2	(-1.4 to 1.7)	0.824
Self-esteem	High activity	-0.1	(-2.1 to 1.9)	0.925
Family connection	High activity	0.2	(-1.6 to 2.0)	0.854
Social well-being	High activity	1.2	(-0.6 to 3.0)	0.210
Functioning at school	High activity	-0.1	(-1.9 to 1.8)	0.953

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, and season of measurement

S4 Table. Linear mutually adjusted[1] cross-sectional association of physical activity profile cluster membership (relative to the participants in the lower activity cluster) and MVPA (per 1h/day) with QoL

Model 2 – additionally adjusted for MVPA							
Cluster membership					MVPA		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	High activity	0.1	(-1.3 to 1.5)	0.895	0.6	(-0.5 to 1.8)	0.278
Physical well-being	High activity	1.0	(-1.3 to 3.3)	0.410	1.5	(-0.3 to 3.3)	0.114
Emotional well-being	High activity	0.3	(-1.6 to 2.3)	0.721	-0.2	(-1.8 to 1.3)	0.762
Self-esteem	High activity	0.4	(-2.1 to 2.9)	0.765	-0.6	(-2.6 to 1.3)	0.526
Family connection	High activity	-0.1	(-2.3 to 2.1)	0.935	0.3	(-1.4 to 2.1)	0.698
Social well-being	High activity	-0.9	(-3.2 to 1.3)	0.409	2.8	(1.0 to 4.6)	0.002
Functioning at school	High activity	-0.1	(-2.3 to 2.2)	0.939	0.05	(-1.8 to 1.9)	0.961

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, and additionally adjusted for MVPA

S5 Table. Linear mutually adjusted[1] cross-sectional association of physical activity profile cluster membership (relative to the participants in the lower activity cluster) and sedentary behavior (per 1h/day) with QoL

Model 3 – additionally adjusted for sedentary behavior							
	Cluster membership				Sedentary behavior		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	High activity	0.7	(-0.5 to 1.9)	0.285	0.1	(-0.3 to 0.5)	0.585
Physical well-being	High activity	2.0	(0.1 to 4.0)	0.038	-0.02	(-0.6 to 0.6)	0.949
Emotional well-being	High activity	0.4	(-1.2 to 2.0)	0.634	0.2	(-0.3 to 0.8)	0.339
Self-esteem	High activity	0.4	(-1.7 to 2.4)	0.739	0.5	(-0.1 to 1.2)	0.123
Family connection	High activity	0.3	(-1.6 to 2.2)	0.756	0.1	(-0.5 to 0.8)	0.625
Social well-being	High activity	0.7	(-1.2 to 2.6)	0.447	-0.5	(-1.1 to 0.11)	0.105
Functioning at school	High activity	0.1	(-1.8 to 2.1)	0.882	0.2	(-0.4 to 0.9)	0.456

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, and additionally adjusted for sedentary behavior

S6 Table. Linear adjusted[1] predictive association of physical activity profile cluster membership (relative to the participants in the inactive cluster) at baseline with QoL at follow-up

Model 1 – no additional adjustment for established physical activity metrics				
Primary endpoint	**Main predictor**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	Low activity	1.5	(-1.6 to 4.5)	0.350
	Medium activity	0.4	(-2.9 to 3.7)	0.799
	High activity	-0.3	(-6.3 to 5.7)	0.922
Physical well-being	Low activity	2.7	(-1.9 to 7.2)	0.251
	Medium activity	1.4	(-3.5 to 6.4)	0.564
	High activity	3.1	(-5.7 to 11.9)	0.486
Emotional well-being	Low activity	0.8	(-3.1 to 4.6)	0.696
	Medium activity	-0.4	(-4.6 to 3.7)	0.846

	High activity	-3.1	(-10.6 to 4.3)	0.410
Self-esteem	Low activity	2.0	(-3.3 to 7.4)	0.453
	Medium activity	1.0	(-4.8 to 6.8)	0.734
	High activity	-5.8	(-16.3 to 4.6)	0.273
Family connection	Low activity	3.1	(-1.3 to 7.5)	0.171
	Medium activity	1.5	(-3.3 to 6.2)	0.542
	High activity	4.5	(-4.1 to 13.0)	0.307
Social well-being	Low activity	-1.9	(-6.2 to 2.5)	0.402
	Medium activity	0.1	(-4.6 to 4.9)	0.957
	High activity	-0.2	(-8.8 to 8.3)	0.955
Functioning at school	Low activity	2.5	(-3.1 to 8.1)	0.384
	Medium activity	-0.1	(-6.2 to 6.0)	0.967
	High activity	0.7	(-10.3 to 11.6)	0.903

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement and respective QoL domain at baseline

S7 Table. Linear mutually adjusted[1] predictive association of physical activity profile cluster membership (relative to the participants in the inactive cluster) and MVPA (per 1h/day) at baseline with QoL at follow-up

Model 2 – additionally adjusted for MVPA							
Cluster membership					**MVPA**		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	Low activity	1.3	(-2.0 to 4.5)	0.443	0.6	(-2.2 to 3.5)	0.669
	Medium activity	-0.2	(-4.5 to 4.1)	0.938			
	High activity	-1.2	(-8.4 to 6.0)	0.751			
Physical well-being	Low activity	3.6	(-1.1 to 8.4)	0.135	-2.9	(-7.1 to 1.3)	0.176
	Medium activity	4.2	(-2.1 to 10.6)	0.192			
	High activity	7.1	(-3.4 to 17.7)	0.184			
Emotional well-being	Low activity	0.3	(-3.7 to 4.4)	0.870	1.3	(-2.3 to 4.9)	0.473
	Medium activity	-1.7	(-7.1 to 3.7)	0.543			

	High activity	-4.9	(-13.9 to 4.0)	0.279			
Self-esteem	Low activity	1.8	(-3.8 to 7.4)	0.527	0.7	(-4.3 to 5.7)	0.774
	Medium activity	0.3	(-7.2 to 7.8)	0.938			
	High activity	-6.8	(-19.4 to 5.7)	0284			
Family connection	Low activity	3.2	(-1.5 to 7.8)	0.179	-0.3	(-4.4 to 3.8)	0.901
	Medium activity	1.7	(-4.5 to 7.9)	0.584			
	High activity	4.8	(-5.5 to 15.1)	0.358			
Social well-being	Low activity	-1.9	(-6.5 to 2.7)	0.411	0.1	(-3.9 to 4.2)	0.946
	Medium activity	0.00	(-6.1 to 6.1)	0.999			
	High activity	-0.4	(-10.6 to 9.7)	0.933			
Functioning at school	Low activity	0.9	(-5.0 to 6.8)	0.759	4.8	(-0.4 to 10.0)	0.071
	Medium activity	-4.7	(-12.6 to 3.1)	0.236			
	High activity	-6.0	(-19.1 to 7.1)	0.369			

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, respective QoL domain at baseline, and additionally adjusted for MVPA

S8 Table. Linear mutually adjusted[1] predictive association of physical activity profile cluster membership (relative to the participants in the inactive cluster) and sedentary behavior (per 1 h/day) at baseline with QoL at follow-up

Model 3 - additionally adjusted for sedentary behavior							
Cluster membership					**Sedentary behavior**		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	Low activity	1.8	(-1.4 to 5.1)	0.256	0.4	(-0.5 to 1.4)	0.398
	Medium activity	1.0	(-2.6 to 4.6)	0.581			
	High activity	0.5	(-5.8 to 6.7)	0.886			
Physical well-being	Low activity	2.9	(-1.9 to 7.6)	0.239	0.2	(-1.2 to 1.6)	0.779
	Medium activity	1.7	(-3.6 to 7.0)	0.523			
	High activity	3.5	(-5.7 to 12.7)	0.456			
Emotional well-being	Low activity	1.2	(-2.8 to 5.2)	0.565	0.4	(-0.8 to 1.6)	0.479
	Medium activity	0.2	(-4.3 to 4.7)	0.933			

	High activity	-2.3	(-10.2 to 5.5)	0.556			
Self-esteem	Low activity	2.0	(-3.6 to 7.6)	0.477	0.0	(-1.7 to 1.6)	0.978
	Medium activity	1.0	(-5.3 to 7.2)	0.760			
	High activity	-5.9	(-16.8 to 5.0)	0.290			
Family connection	Low activity	3.3	(-1.3 to 7.9)	0.157	0.3	(-1.1 to 1.6)	0.711
	Medium activity	1.8	(-3.3 to 7.0)	0.482			
	High activity	4.9	(-4.0 to 13.9)	0.279			
Social well-being	Low activity	-0.3	(-4.8 to 4.2)	0.903	1.7	(0.4 to 3.1)	0.013
	Medium activity	2.4	(-2.6 to 7.5)	0.338			
	High activity	2.8	(-6.0 to 11.6)	0.535			
Functioning at school	Low activity	2.3	(-3.6 to 8.2)	0.440	-0.2	(-2.0 to 1.6)	0.829
	Medium activity	-0.4	(-7.0 to 6.2)	0.905			
	High activity	0.3	(-11.1 to 11.8)	0.956			

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, respective QoL domain at baseline, and additionally adjusted for sedentary behavior

S9 Table. Linear adjusted[1] predictive association of physical activity profile cluster membership (relative to the participants in the lower activity cluster) at baseline with QoL at follow-up

Model 1 – no adjustment for established physical activity metrics				
Primary endpoint	**Main predictor**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	High activity	0.4	(-2.2 to 3.0)	0.766
Physical well-being	High activity	1.1	(-2.7 to 4.9)	0.568
Emotional well-being	High activity	0.3	(-3.0 to 3.6)	0.854
Self-esteem	High activity	1.9	(-2.7 to 6.4)	0.420
Family connection	High activity	2.1	(-1.6 to 5.9)	0.261
Social well-being	High activity	-1.9	(-5.7 to 1.8)	0.301
Functioning at school	High activity	-0.7	(-5.5 to 4.1)	0.773

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement and respective QoL domain at baseline

S10 Table. Linear mutually adjusted[1] predictive association of physical activity profile cluster membership (relative to the participants in the lower activity cluster) and MVPA (per 1h/day) at baseline with QoL at follow-up

Model 2 – additionally adjusted for MVPA							
Cluster membership					MVPA		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	High activity	0.4	(-2.9 to 3.6)	0.826	0.0	(-2.5 to 2.6)	0.973
Physical well-being	High activity	2.8	(-1.9 to 7.6)	0.238	-2.3	(-6.0 to 1.4)	0.221
Emotional well-being	High activity	0.4	(-3.6 to 4.5)	0.825	-0.2	(-3.4 to 3.0)	0.902
Self-esteem	High activity	3.2	(-2.4 to 8.8)	0.269	-1.7	(-6.1 to 2.7)	0.440
Family connection	High activity	2.7	(-1.9 to 7.4)	0.245	-0.8	(-4.4 to 2.8)	0.665
Social well-being	High activity	-3.4	(-7.9 to 1.2)	0.145	1.9	(-1.7 to 5.6)	0.287
Functioning at school	High activity	-3.4	(-9.3 to 2.4)	0.249	3.7	(-0.9 to 8.3)	0.118

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, respective QoL domain at baseline, and additionally adjusted for MVPA

S11 Table. Linear mutually adjusted[1] predictive association of physical activity profile cluster membership (relative to the participants in the lower activity cluster) and sedentary behavior (per 1h/day) at baseline with QoL at follow-up

Model 3 – additionally adjusted for sedentary behavior							
Cluster membership					Sedentary behavior		
Primary endpoint		**Coefficient**	**95% CI**	**P-value**	**Coefficient**	**95% CI**	**P-value**
Overall QoL	High activity	0.7	(-2.0 to 3.5)	0.600	0.4	(-0.5 to 1.3)	0.427
Physical well-being	High activity	1.2	(-2.9 to 5.2)	0.567	0.0	(-1.3 to 1.4)	0.922
Emotional well-being	High activity	0.8	(-2.6 to 4.2)	0.649	0.5	(-0.6 to 1.7)	0.360
Self-esteem	High activity	2.1	(-2.7 to 6.8)	0.395	0.2	(-1.4 to 1.8)	0.787
Family connection	High activity	2.3	(-1.6 to 6.2)	0.248	0.2	(-1.1 to 1.5)	0.778
Social well-being	High activity	-0.7	(-4.6 to 3.1)	0.708	1.4	(0.1 to 2.7)	0.344
Functioning at school	High activity	-1.0	(-6.0 to 4.0)	0.701	-0.3	(-2.0 to 1.4)	0.718

[1] Adjusted for age, sex, language region, nationality, urbanicity, participation in organized sport activities, self-reported diagnosis with at least one chronic disease, household income, parental education, season of measurement, respective QoL domain at baseline, and additionally adjusted for sedentary behavior

Article III: Exploring the role of social capital, self-efficacy, and social contagion in shaping lifestyle and mental health among students representing the future health care work force in Palestine: social cohort study protocol

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Abstract

Introduction: Non-communicable diseases (NCDs) and depression form an unhealthy mix. The project focuses on potentially effective psychosocial factors shaping health-related habits and mental health. The study is conducted among health domain students. Understanding what shapes their health will determine their quality of care. The study is implemented at An-Najah National University in Palestine. In this zone of continuous conflict psychological stress is high and mental health problems are stigmatized.

Methods and analysis: Students who are enrolled in second and third year will be invited to fill in a baseline and two follow-up online questionnaires. The questionnaires will assess: health behaviors and outcomes (health-related habits, obesity and mental health), main predictors (social capital (SC), social network, self-efficacy (SE)), confounders (general and sociodemographic characteristics), and effect modifiers (sense of coherence (SOC) and family SOC). Friendships within participating students will be identified by allowing students to name their friends from a pull-down menu of all students. Descriptive statistics and scores will describe participant's characteristics. The relationship between health behavior, outcomes, and main predictors will be examined by regression and structural equation models. Clustering of health behaviors and outcomes will be assessed by permutation tests. Their spread within the network of friends will be investigated by longitudinal generalized estimating equations.

Discussion: The study will identify the prevalence of NCD related health-habits and mental health aspects in the future healthcare workforce in Palestine. It will be the first study to address the role of psychosocial factors for the targeted students. It has the potential to identify targets for promoting physical and mental health among these future professionals.

Ethics and dissemination: Ethical approval was obtained from Ethikkommission Nordwest-und Zentralschweiz (EKNZ) in Switzerland and the Institutional Review Board Committee (IRBC) in Palestine. Participation in the study is voluntary and requires informed consent. The data management

methodology ensures the confidentiality of the data. The outcomes of the study will be published as scientific papers. In addition, it will be presented in stakeholder conferences to students to An-Najah National University.

Keywords: health-related habits, mental health, psychosocial factors, social capital, sense of coherence, self-efficacy, social contagion, university students, permutation tests, generalized estimating equations.

Strengths and limitations of this study

1. As one of the rare studies to longitudinally address the role of psychosocial factors including social contagion in shaping the lifestyle and mental health among network ties of students, it may identify novel cost-effective preventive targets.
2. By focusing on health domain students in a geographical area of long-term conflict that generally promotes unhealthy habits and aggravates mental ill-health, the study offers novel insight on how to promote prevention knowledge, acceptance and skills of the future healthcare workforce.
3. The analysis of the longitudinal directional network ties and attributes of the study participants uncovers and quantifies the suspected social contagion of health-related behaviors and mental health.
4. The sample will be taken only from An-Najah National University. The results of the study will therefore not be representative of all health domain students in Palestine.
5. The study will be based on self-report tools and restricted to friendship nominations among the student network. This can lead to misclassification of characteristics, in particular those associated with some stigma including mental health symptoms.

Introduction

Background

NCDs are major contributors to morbidity and mortality worldwide (471). Globally, NCDs accounted for more than 70% of all deaths in 2017 (18). In 2019 NCDs were also the leading causes of death in Palestine. Cardiovascular diseases followed by cancer accounted for 29.9% and 15.5% of total deaths, respectively (40). Research studies reported a high prevalence of important NCD risk factors such as tobacco smoking (472), waterpipe smoking (473), alcohol drinking, use of illicit drugs (474), low adherence to healthy nutrition (38, 472, 475), and low physical activity (64, 475) among Palestinian youths. Because NCDs evolve over the course of life and because lifestyle tracks from young to old age, young Palestinians put themselves at high risk of developing NCDs later in life by adopting an unhealthy lifestyle at young age. In Palestine, there is a high prevalence of mental health problems. Poor mental health is a major driver of disability (476). Despite this, there is still a gap in the recognition, diagnosis and treatment of mental disorders in Palestine (67). Unaddressed mental care needs are an important barrier to the successful control of NCDs in low and middle income countries (477). The relationship between the most common NCDs (cardiovascular diseases and diabetes) and depression is thought to be bidirectional (478).

Alarmingly high rates of severe depression and anxiety were reported among Palestinian cardiac patients (99).

Based on Antonovsky's salutogenenesis theory, the current study focuses on the role of individuals' psychosocial factors in shaping their lifestyle and mental health. According to the theory, at any point in time, an individual has a position on the generalized resistance resources – resistance deficits (GRRs-RDs) continuum (10). Accessibility of resistance resources along the continuum allows the individual to experience "consistency" in life, to have "load balance" between resources and demands, and to "participate in decision making". In turn, these experiences allow the individual to develop a sense of coherence (SOC) (10, 334, 356). SOC development contributes to the individual's mental and physical health through its ability to effectively mobilize resources for overcoming stressors and challenges and ensuring positive health and health habits (10, 334, 479). Social capital (SC) is hypothesised to be one of the GRRs through which SOC can act as a mediator between SC and health outcomes (335). There is evidence for the positive association of network capital (338-341) and cognitive social capital (338-340, 342-345) with both, physical and mental health. In addition, there are areas of convergence between self-efficacy (SE) and SOC. SE is characterized by being consistent, by contributing to shaping outcome expectancies and behavior, and by leading to overload and underload balance. Thus, it appears to be one of the GRRs that contributes to the enhancement of SOC (356, 359). There is evidence for an association between SE and health-related behaviors (356, 359). Also, SE is positively associated with perceived good health, well-being and quality of life (356), but inversely with depression and anxiety (358).

This study is based on the assumption that SC and SE contribute to the development of SOC, which in turn influences individuals' health-related behaviors and mental health. See **Figure 1**

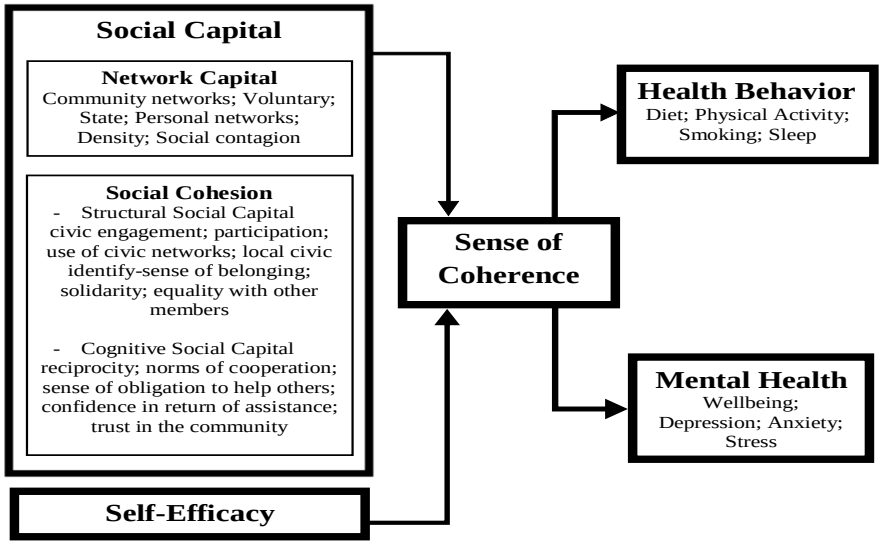


Figure 1. Conceptual framework of the study based on the Antonovsky's theory of salutogensis

Furthermore, the social contagion theory suggests that behaviors can spread from one person to another within social networks through induction (331, 333). This is evidenced by the clustering of smoking and obesity within social networks (330, 331). There is also evidence for the contagion of mental health through the spread of happiness (480) and depression (481) within social networks. Psychosocial factors and social contagion may be important and cost-effective targets for more efficient NCD prevention and mental health promotion in Palestine. The continuous conflict in this region contributes to poor health habits and to mental problems, but the later are not properly addressed due to cultural stigmatization. Healthcare professionals own health, mental health, habits and perceptions play an important role in how they provide care including preventive and mental health counselling (482, 483). It is therefore important to study health-habits and mental health as well as their psychosocial contributors in health domain students. They are the future health care workforce, but they are still at an age where habits and perceptions are more easily modified (335).

Aim

The aim of the study is to explore the role of SC, SE, SOC and social contagion in shaping lifestyle and mental health among health domain students representing the future health care work force in Palestine.

Specific objectives

The study will be conducted among students enrolled in the faculty of medicine and health sciences of An-Najah National University to:

1. Assess the frequency, distribution and clustering of self-perceived health, health-related behaviors, obesity and mental health among students.
2. Assess the distribution of SC, SE, and SOC among students.
3. Estimate the association between SC, SE, and SOC with the longitudinal course of self-perceived health, health-related behaviors, obesity and mental health among students.
4. Uncover and quantify the suspected social contagion of health-related behaviors, obesity, and mental health among students.
5. Identify modifying and mediating factors in the association of SC and SE with the level and longitudinal course of self-perceived health, health-related behaviors, obesity and mental health among students.

Methods and analysis

Study population

Inclusion criteria

The study will invite all second and third-year students enrolled in the optometry (104 students), medical imaging (110), nursing (480), pharmacy (304), medicine (331), physiotherapy (122), biomedical sciences I (739), medical laboratory (345), midwifery (29), doctor of pharmacy (122), and audiology and speech

therapy (157) programs of the faculty of medicine and health sciences of An-Najah National University, Nablus, Palestine. First-year students will be excluded from the study because friendship ties among university students are more likely to start evolving during the first academic year of enrollment and develop by the second academic year of enrollment. Also, first-year students are less likely to continue studying. Senior students (fourth, fifth and sixth- year students) are excluded because the minimum number of years required to complete programs in the faculty of medicine and health sciences is 4 years. Furthermore, inclusion of senior students harbors the risk of high attrition of the participants due to graduation from the university. The data collection will continue over the course of 1 year.

Recruitment

A promotion video will be shared with the targeted students to introduce the study and encourage them to take part in the survey. Students will obtain personal invitations for study participation by email. The email will include a personalized link to access online study information, e-consent form and questionnaires. SMS messages and emails will be sent to the students as reminders to complete the survey. After the end of the study, an event will be organized with the aim of increasing the students' understanding and awareness on aspects related to their future professional career. The study's result will form the basis for input into this event.

Study design

The study is a digital prospective cohort; it is based on online baseline survey and two follow-up surveys (first follow-up 6 months after baseline and second follow-up 12 months after baseline) surveys. The study will be conducted between 2021 and 2022.

Data collection and management

Data will be collected with a culturally sensitive online questionnaire. Questionnaires will be developed in English and will be translated to Arabic and back-translated to English. The questionnaires will be piloted among a subset of first-year students enrolled at the faculty of medicine and health sciences of An-Najah National University, Nablus, Palestine.

Data recording will be performed in the data collection tool REDCap, a secure web application for building and managing online surveys and databases. The questionnaire will be administered three times. For each of the baseline and follow-up surveys, students will be given 30 days to complete the survey, starting from the day they receive the invitation.

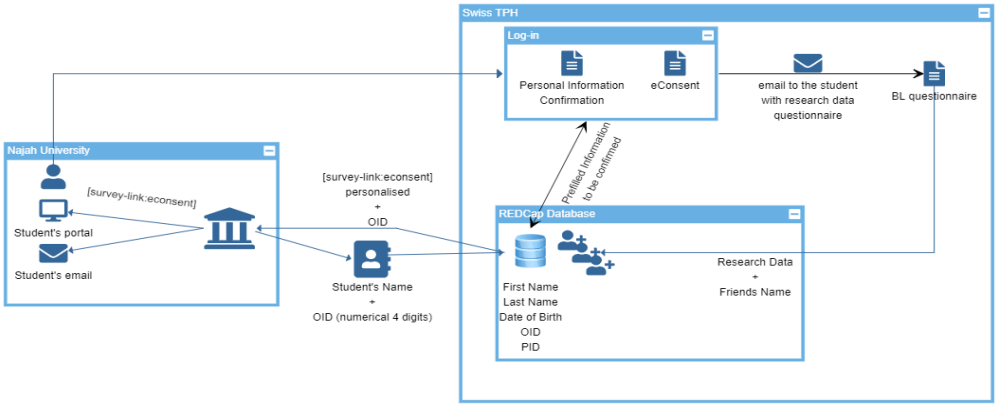
An-Najah National University will provide Swiss Tropical and Public Health Institute (Swiss TPH) with emails and names of the eligible students. An open person-identifying ID (OID) will be assigned to each student. First, a personalized link (OID as identifier for the link) will be mailed to students. Both, student's email and the student portal "Zajel" will be used for this mailing. The link will allow the students to access

and fill in the participant information sheet, the contact information sheet and the e-consent. Second, after the students provide their e-consent and confirm their personal information, they will receive an email with a personalized link for accessing online questionnaires.

The completed online research questionnaire (research data) will be stored in REDCap. To assure a high quality of the data, the records of the survey in REDCap will be checked daily by the responsible researcher. Students will be immediately reconnected to complete missing data. At the end of data collection, the research data will be pseudonymized with each student being assigned a research ID (PID). The students' personally identifying information (first name, father name, grandfather name and last name, date of birth, gender, student domain, year of the study, student ID and student email) will be stored in a separate file in REDCap, linked to OID. In addition, a link file between OID and PID will be stored separately as a file outside REDCap. The files with person identifying data and the link file will only be accessible to the principal investigator of the study (N-PH) and the chief security officer of Swiss TPH. The social network of a student (friends and colleagues) will be identified in the research database as friends' and colleagues' PIDs. After completion of the study and by December 31, 2023, any information that would identify the participant (first name, surnames, date of birth, gender, student domain, year of the study, student ID and student email) will be deleted from REDCap. The link file between OID and PID will be deleted in order to fully anonymize the research data. The anonymized research data of the study along with the e-consent forms will be stored on servers of Swiss TPH in Switzerland.

The procedure for administrating the first and second follow-up surveys will be the same as administrating the baseline survey.
Students and their personal identifying information will only be retained in the participant management file if they provided consent for study information. Only students who completed the previous survey will be targeted for the next survey. See **Figure 2** for reference.

Data collection



Data management

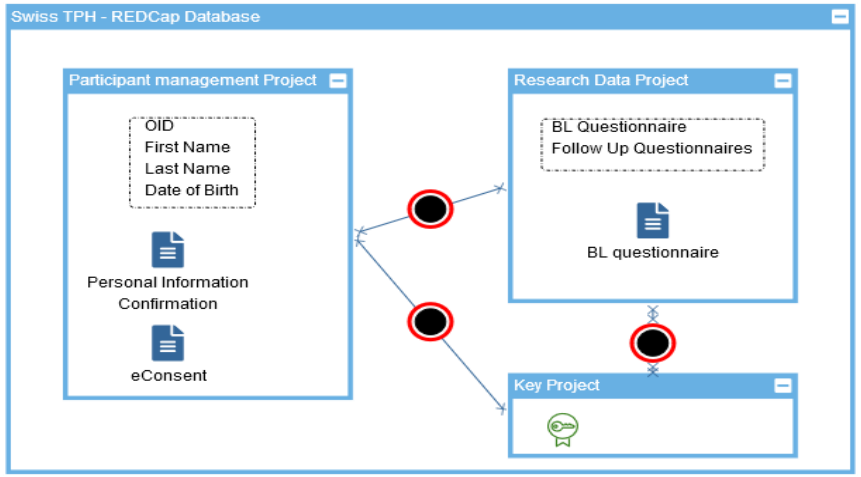


Figure 2. Data collection and management procedure. BL, baseline; OID, open person-identifying ID; PID, Pseudonymisation

Measurements

Primary endpoint

Health-related habits

Diet

1. Food intake: the intake frequency of 14 items will be measured; fruits, vegetables, dried fruits, poultry, meat, fish & seafood, instant noodles, soft drinks, sweetened juice, cake & sweets &chocolate & biscuits, chips & salty snacks, fast food, caffeinated beverages, and energy drinks. This will ensure the assessment of students' dietary intake according to the WHO dietary guidelines recommendations for the Eastern Mediterranean region (484).

2. Drinking water: the quantity and the type of drinking water will be assessed.

The food intake will be categorized into healthy and unhealthy dietary intake based on the WHO dietary guidelines recommendations for the Eastern Mediterranean region (484). One point will be given if the food frequency intake is in line with the WHO dietary guidelines recommendations for the Eastern Mediterranean region (484). See **Table 1** for more details.

A score of 6 or more total points will be considered as "healthy dietary intake", a score below 6 points as "unhealthy dietary intake".

3. Weight loss: participants will be asked if they have tried to lose weight in the past. The relation of perception of weight loss with participant's own BMI on the one hand, and with attempts to lose weight in the participant's student network will be investigated.

Table 1. WHO dietary guidelines recommendations for Eastern Mediterranean region

Item	Recommended food frequency intake
Health items	
Fruits	Several times per week, daily, or several times per day
Vegetables	
Dried fruits	Several times per week
Poultry	
Meat	
Fish & Seafood	
Water	8 cups or more per day
Unhealthy items	
Instant noodles	1-4 times a month or never
Soft drinks	
Sweetened juice	
Cake & Sweets & Chocolate & Biscuits	
Chips & Salty snacks	
Fast food	
Caffeinated beverages	
Energy drinks	

PA and sedentary behavior: physical activity in the past 7 days will be assessed with the short version of the international physical activity questionnaire (IPAQ), which will be included in the questionnaire.

Participants' physical activity (PA) will be estimated based on the frequency "days per week" and duration "hours/minutes spent" spent in three activity domains: walking, moderate PA and vigorous PA (485). Sedentary activity of the participants will be assessed separately for weekend days and weekdays. Scores will be calculated for each PA intensity level and converted into metabolic equivalent (MET) according to the IPAQ scoring protocol. Minutes per week will be converted to MET using the conversion factor 3.3 for walking, 4.0 for moderate PA and 8 for vigorous PA. The total score of PA will be categorized into low PA, moderate PA and high PA (485).

Tobacco use: the history of and the current tobacco use (cigarettes, hookah/shisha, and electronic cigarettes) among participants will be assessed in addition to the participant's attempt to quit smoking.

Sleep pattern: it will be measured with the help of the Pittsburgh Sleep Quality Index (PSQI) (486). Global PSQI score ranging from 0 to 20 will be calculated. A global score >5 = poor quality of sleep and ≤5 = good quality of sleep (486).

Obesity: the participants will be asked to measure or self-report their weight and height. According to the WHO classifications of body mass index (BMI) for adults, participants will be categorized as underweight (BMI <18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (BMI 25 – 29.9 kg/m^2) and obese (BMI ≥30 kg/m^2) (487). It will be recorded whether the reported height and weight were measured or not.

Self-perceived health: it will be evaluated by asking the participant about their experience of chronic health condition or disability.

Mental health

Well-being: most of the existing research focuses on the negative aspects of mental health including depression (335). Thus, the assessment of well-being is important to explore the relationship between the psychosocial factors (SC, SE, and SOC) and health-related habits with the positive aspect of mental health. Moreover, based on the salutogenesis theory, well-being is one component of health, which is shaped by psychosocial factors (10). Well-being will be rated by using the WHO five well-being index (488). The total score will range from 0 – 100 (≥50 = moderate to high level of well-being; <50 = ill-being).

Depression, anxiety, and stress: these are negative aspects of mental health. They will be measured by applying the depression, anxiety, and stress scale (DASS 21) (489). The DASS-21 scale assesses each of DASS based on seven items. Each item is scored on a 0-4 scale: "never = 0, sometimes = 1, often = 2, almost = 3 and always = 4". The score for each domain will be calculated by summing up the scores for the corresponding seven items and multiplying the total by 2. Then, the score will be divided into the following categories; (normal=0 – 9, mild= 10-13, moderate = 14-20, severe = 21-27, and extremely severe = 28+) for each domain.

Main predictors

Social capital: SC will be measured using the SC questionnaire developed by Yari *et al.* (490).

Social network: the social contagion of health-related behaviors, obesity and mental health will be assessed by collecting information on the close friends/colleagues of each student. An-Najah National University will provide a list of the name of all students enrolled at the faculty of medicine and health sciences. Additionally, the list will include the main sociodemographic characteristics of the students (gender, date of birth, program name, and academic year). The survey will include a drop down menu of the student list obtained from the university. The participants can mark their close friend in this list. Because the list includes all potential study participants it allows for the assessment of social contagion.

Self-efficacy: both general SE and social SE among the students will be measured based on Sherer *eta al's* scale (1982) (103).

Confounders, effect modifiers

General and sociodemographic characteristics: this section inquires about gender, age, marital status, religion, place of residence, housing facility, refugee status, household monthly income, size of household, employment status, parent's occupations, care provision for others, affiliated faculty, current academic year.

Mediators

Sense of coherence: it will be assessed based on Antonovsky's SOC scale (491). The scale consists of 13 items. Each item is scored from 1 to 7. Thus, the scale will have a maximum score of 91 and a minimum score of 13, with high scores indicating high SOC.

Family sense of coherence: it will be assessed based on Shifra Sagy's scale (492). The scale consists of 12 items. Each item is scored from 1 to 7. Thus, the scale will have a maximum score of 84 and a minimum score of 12. High scores indicate perception of better family life coherence. The scale consists of 12 items. Each item is scored from 1 to 7. Thus, the scale will have a maximum score of 84 and a minimum score of 12. High scores indicate perception of better family life coherence.

Statistical analysis

Sample size and characteristics

Assuming a 50% participation rate, we aim to achieve a sample size of n=1000, which is sufficient to estimate prevalence of any binary trait with a margin of error of at most 3.1 percentage points. We expect that 50% of the students do not exhibit healthy habits and 20% have at least moderate depression symptoms. If we dichotomised a predictor such as SC along the median, this sample would confer 85%

power to detect at the 5% significance level risk differences of 8 percentage points for depression and 10 percentage points for unhealthy lifestyle between the low and high SC groups. We anticipate having similar power to detect considerably smaller effects when analysing continuous outcomes and pooling data across survey waves. We have forgone formal power calculations for the clustering and contagion objectives because they depend critically on network topology, for which we have no prior information.

Descriptive statistics (n, %, mean) will describe participant's general and sociodemographic characteristics, as well as tobacco use, obesity and self-perceived health. Scores will describe diet, physical activity, sleep pattern, happiness, loneliness, well-being, depression, anxiety, stress, SC, social network, SE, and SOC. The longitudinal associations between primary endpoints and main predictors will be studied using mixed linear and logistic regression models Interactions terms will be included in the models to capture effect modification. Mediation will be assessed by structural equation modelling.

Non-response and attrition

We acknowledge the potential of non-respondent and attrition given the longitudinal design of the study. This can affect the generalizability of the outcomes due to selection bias and decrease the statistical power of the study (493-495). Several mitigation strategies will be applied to account for potential non-respondent and attrition among participants. First, at the recruitment level, the targeted study population was selected to maximize both participation and retention rates. The study population are second and third-years students of the faculty of medicine and health sciences of An-Najah National University, Palestine. The minimum number of years to complete any programme in the faculty of medicine and health sciences is 4 years and the tenure of data collection will be 1 year. This will avoid the possibility of loss to follow-up due to graduation and absence of any connection to the university. Second, incentives will be provided for participants with the condition of completing the baseline and two follow-up surveys. Additionally, reminders will be sent to the students through emails and text messages to increase participation rate and retention of the participants. Furthermore, a promotion video will be shared with the targeted students to introduce the study and encourage them to take part in the survey. These strategies proved to increase participation rate and maximize retention rate in cohort studies (493, 494). At the statistical analysis level, we have access to basic demographic characteristics of all the study population. This will allow us to make comparisons between participants and non-participants at baseline and to assess if there is significant differences between them. Analysis of non-respondents will help establish who will be at high risk of attrition in the future wave (494). Subsequently, strategies to increase the retention rate of such participants will be implemented (495, 496). Inverse probability weighting will be applied to ensure that the analyses are unbiased in spite of attrition (494, 497, 498).

Clustering of health behaviors and outcomes in social networks

The relationships between the study participants will be captured in a network: each participant will be represented as a node that is linked to other nodes according to the friendship information provided in the

surveys. We will distinguish between directed links, when one participant nominates another as a friend but not vice versa, and undirected links, when nomination was mutual. Thus, three types of relationships are possible between any pair of nodes ("ego" and "alter"): ego-perceived friendship, alter-perceived friendship, and mutual friendship. We will perform our analyses separately for each type. We will also be able to follow the evolution of this network across time due to the follow-up surveys.

Our statistical approach is based on that of Christakis and Fowler (331). We will use permutation tests to assess clustering of the primary outcomes in the network. Every outcome will be dichotomized. The degree of clustering will be characterized by the relative increase in the probability (i.e. risk ratio) that an ego has the dichotomous trait of interest given that an alter has it, compared to the probability that an ego has the trait given that an alter does not have it. This value computed for the observed network will be compared to that of computer-generated networks of the same topology. In the later, the trait is distributed uniformly randomly across the nodes while keeping the overall observed prevalence. If the risk ratio in the observed network is greater than in 95% or more of the synthetic networks, then the hypothesis that the observed clustering is entirely due to chance will be rejected at the 5% significance level.

Social contagion analysis

Longitudinal regression models will be used to assess the spread of health outcomes and health-related behaviors across network ties. The status of ego at first follow-up (respectively, second follow-up) will be expressed as a function of the ego status, alter status and covariates at baseline (respectively first follow-up). Thus, each node in the network (ego) will contribute as many observations as there are nodes (alters) that it is connected to. The models will be estimated using generalized estimating equations with clustering on ego to take into account multiple observations of the same participant across surveys and alters. The fitted coefficient of the alter's status at baseline will be interpreted as an estimate of the intensity of spread. In particular, we will consider an outcome or a behavior to have spread through the network if this coefficient is significantly different from 0.

Patient and public involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Discussion

In 2015, the UN Member States have adopted the target to reduce the premature mortality from NCDs by one-third by 2030 to achieve the third SDG (499). Prior to this, in 2013, the World Health Assembly adopted the WHO Global Action Plan for the Prevention and Control of NCDs 2013-2020. It aims to accomplish 25% relative reduction in overall mortality caused by major NCDs (471). Along with that WHO has recognized mental disorders as one of the major NCDs (24). Depression is expected to become

the main cause of disability globally (64). In the Global South, resource allocation for mental disorders is sparse, partly reflecting their stigmatization. The Lancet Commission on Global Mental Health and SDGs is pointing to the importance of integrating mental health services with care for NCDs (66). In Palestine, on few and insufficient reports describe the size of the NCD problem. Complete national data on the burden of NCDs does not exist (500). There is still gap in the recognition, diagnosis and treatment of mental disorders in Palestine despite their high prevalence (67, 476). For example, despite the well- known bidirectional association between depression and cardiovascular disease, none of the cardiac patients treated in the main Nablus hospitals were ever assessed for depression by their treating cardiologists (99). The youth sector in Palestine is important as it accounts for a little less than quarter of the total population (501). The health needs of young Palestinians should be addressed as a matter of urgency.

To the best of our knowledge, no study has addressed the role of SC, SE SOC and social contagion in the health and well-being of the youth in Palestine. This study will target medical and other health domain students. They are also at risk of adopting risky health and lifestyle habits, particularly in the light of the challenges they face during their tenure of study (502).

The assessment of self-perceived health, health-related behaviors, obesity and mental health is important as a way to identify health problems and modifiable risk factors (dietary risks, use of tobacco, and low physical activity) among the students. The participating students are the future health professionals. Their health behaviors and mental health will shape the health care they will provide and their impact as role models in the society (503). There is evidence for the positive association between poor well-being (504, 505) and sleep-related impairment among physicians (506) and the increase in medical errors (504-506). Also, stress among healthcare provider is associated with an increase in the odds of medical errors (507). Physicians' positive well-being is associated with patient satisfaction and quality of patient care (508). Furthermore, this study can increase their awareness of healthy habits and healthy minds. This can contribute to their perception of primary prevention as a cost effective approach to NCDs and it can promote the destigmatization of mental health problems among these future health care professionals (17). Healthcare providers are not only the most credible source of prevention and health promotion counselling, but also they have ethical obligations to provide counselling to their patients (482). There is evidence for the positive association between the healthcare provider's personal habits and their practice of counselling to patients (482). This positive association has been found in relation to a wide range of health-related and prevention practices including physical activity, smoking, nutrition, vaccination, and screening (483). This is confined not only to practicing physicians but also to medical students (482, 509) in both developed and developing countries (510). Patient's adherence to preventive and health promotion counselling is also enhanced if it is rooted in the health provider's personal experience (483).

Our study will estimate the association between SC, SE and SOC with the longitudinal course of self-perceived health, health-related behaviors, obesity and mental health among students. This will be based

on the Antonovsky's (SMH) theory. The theory resonates with the health promotion framework, which focuses on the individual's ability to control different determinants of health through their own resources, processes and outcomes in order to attain health regardless of what is offered by the healthcare system (334). Salutogenesis does not necessarily eradicate diseases such as NCDs; instead, it enhances the individual's ability to manage them well. In turn, it enhances well-being (511). Thus, the study will identify another potential target for future health intervention strategies. SE and SOC proved to be effective in the implementation of health promotion strategies because of their ability to detect, predict, and change health status (356). SE is not confined to the ability to change behavior. It extends to the belief in the ability to accomplish social changes and to overcome the structural determinants of health (357). In addition, SE contributes to the increase of the individual's resilience against dangerous and stressful situations and protects against trauma (360). This is important for Palestine, as the psychosocial determinants of NCDs are influenced by the presence of political instability (32). The daily stresses due to economic hardship, unemployment, family conflict, lack of public spaces for recreation and leisure, and lack of sustainable facilities for physical activities, all increase the stress and ultimately their impact on NCD risk (32). Interventions to promote healthy behaviors among students were positively associated with their prevention-related attitudes and counselling practices (482, 509, 512, 513). Thus, appropriate interventions can be implemented to improve the health and well-being of the students.

The proposed study has several strengths. First, by focusing on Palestine where poor health habits and mental stressors are highly prevalent due to the ongoing conflict, cost-effective interventions to strengthen primary prevention and mental health promotion are much needed. From the study on the spread of health-habits and mental health symptoms in the social network of students novel interventions can be derived.

The limitations of the study include, first, bias due to non-participation, which is of particular concern if students with few friends, poor health habits or poor mental health are not participating. This would lead to a lower appreciation of the role of psychosocial factors as determinants of healthy habits. Second, as any longitudinal study, loss to follow-up can bias the outcomes, particularly if it is differential. Third, the prevalence of factors considered less healthy/unhealthy may be underestimated if students tend to underreport them for reasons of stigma. Fourth, despite the longitudinal nature of the study, three measurement time points may not be sufficient to properly characterize the short-term fluctuation of health habits and mental health symptoms. If this fluctuation is high and not captured, it potentially inhibits the ability of the study to identify associations if present.

Ethics and dissemination

The research protocol was approved by the Ethikkommission Nordwest- und Zentralschweiz (EKNZ) (AO_2020-00047) in Switzerland and the Institutional Review Board Committee at An-Najah National University (Ref: Med Nov. 2020/32).

Participation in the study is voluntary and participants will provide written informed e-consent. The students have the right to withdraw from the study at any time.

It is important to maintain the privacy of students and the information provided due to the high sensitivity. The proposed methodology ensures the confidentiality of the data as the study will be conducted in compliance with the current version of the Declaration of Helsinki as well as all national legal and regulatory requirements. During the active phase of data collection, participants will be identified by an open ID, which links to their person-identifying data and serves as personalised link to access study information and e-consent. Research data derived from each study follow-up will be stored with a separate research ID and will not contain person-identifying information. The link file between the person-identifying information and the research ID will only be accessible to a small and well defined group of persons. After finalisation of the study following the second follow-up and by 31 December 2023, any information that would identify the participant (names, birth date, student ID) will be deleted for a fully anonymised research database.

The students who complete the survey will be rewarded with scoring points related to the student unions and non-governmental organizations (NGOs). These scoring points give the students the opportunity to participate in events and projects organised by the university such as "receiving scholarship to conduct scientific research". In addition, the names of students who complete the survey will be entered into a drawing for a chance to win a coupon. Four names will be selected.
The outcomes of the study will be published as scientific papers. In addition, it will be presented in stakeholder conferences and to students at An-Najah National University.

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Author's contribution

NP-H developed the idea for the study.
RD, MK, SM and NPH developed the study concept, the study protocol and the study objectives.
RD, AA, HA, and NPH developed the study instruments.
RD and MK developed the statistical analysis approach.
RD, TV, AA and NPH developed the data management approach and the RedCap database.
RD, AA, and NPH wrote the ethics protocol.
RD, TV, MK and NPH drafted the manuscript.
All authors read, commented, and approved the manuscript

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Competing interests

None declared.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication

Not applicable.

Provenance and peer review

Not commissioned; externally peer reviewed.

Acknowledgments

Not applicable

Availability of data and material

Data cannot be made publically available. Upon justified request to the corresponding author, data can be shared in the context of research collaboration.

Chapter 5: Synthesis of main findings

5.1. Cross-sectional but not prospective association of accelerometry-derived physical activity with quality of life in children and adolescents

The aim of this study was to assess the role of MVPA, on which many PA recommendations focused so far, in the QoL of Swiss children and adolescents. The study benefited from the objectively and longitudinally measured physical activity and repeated assessment of QoL in the SOPHYA cohort study. To be specific, the study assessed the cross-sectional association of MVPA with the overall QoL and the specific dimensions of QoL. To better clarify the directionality in the MVPA-QoL association and to assess whether MVPA has a longer-term effect two approaches were taken: the study addressed the role of the within-subject versus between-subject variability in MVPA in the cross-sectional association between MVPA and the overall QoL and its specific dimensions; and b) the study evaluated the predictive association between MVPA measured at baseline with the overall QoL and its specific dimensions five years later irrespective of the baseline participants' characteristics including MVPA at baseline.

The study sample consisted of 352 children and adolescents (52.8% females, 47.2% males). The average ages of the participants at SOPHYA1 and SOPHYA2 were (mean [SD]: 10.3 [2.4] years) and (mean [SD]: 15.1 [2.6] years), respectively. Mean MVPA decreased from (mean [SD]: 1.4 [0.6] hr/day) at SOPHYA1 to (mean [SD]: 0.8 [0.4] hr/day) at SOPHYA2. While the average score of the overall QoL score decreased from (mean [SD]: 82.3 [7.7]) at SOPHYA1 to (mean [SD]: 74.2 [9.9]) at SOPHYA2.

The results of the study provided evidence for the positive cross-sectional association of mean MVPA with the overall QoL and with physical well-being ($p = 0.023$ and 0.002 respectively). The average effect size of one-hour increase in MVPA per day on physical well-being (4.2 (95%CI: 1.6, 6.8) points) was larger than its association with the overall QoL (2.0 (95%CI: 0.3, 3.7) points). The between-subject and within-subject variability in MVPA played different roles in the repeated cross-sectional association between MVPA and the overall QoL and its dimensions. The between-subject MVPA variability, reflecting the cross-sectional association was positively associated with the overall QoL, the physical well-being and the social well-being ($p = 0.030$, 0.017 and 0.028 respectively). The effect sizes were reported to be 2.6 (95%CI: 0.3, 4.9) points, 4.3 (95%CI: 0.8, 7.7) points and 3.8 (95%CI: 0.5, 7.2) points increase in the overall QoL, the physical well-being, and the social well-being, respectively. In contrast, the within-subject MVPA variability, reflecting the longitudinal association, was associated positively with the physical well-being and functioning at school ($p = 0.039$ and 0.013 respectively) with effect sizes of 4.2 (95%CI: 0.2, 8.2) points and 5.6 (95%CI: 1.2, 10.1) points increase in physical well-being and functioning at school scores, respectively, for every one hour increase in the within-subject MVPA. In regards to the assessment of the prospective association between MVPA and QoL and its dimensions, the study did not provide any evidence of an association of MVPA at baseline with QoL five years later, after adjusting for the baseline

characteristics, including baseline QoL, in contrast to the observed within-subject MVPA associations with aspects of QoL.

5.2. Weekend physical activity profiles and their relationship with quality of life: the SOPHYA cohort of Swiss children and adolescents

The data driven unsupervised analysis of PA profiles derived from accelerometer measurements during the weekend identified clusters of youth with different behavioral patterns. The most discriminating PA characteristics between the profiles were the mean intensity of PA and the time spent in SB. Young age and being a boy were most prevalent in the high activity profile cluster in this current study.

This study did not provide evidence for cross-sectional or predictive associations of either the newly derived PA cluster profiles or the conventional metrics of PA with overall QoL among children and adolescents living in Switzerland during weekend days. Overall QoL may not be the optimal endpoint for assessing the impact of PA behavior on the QoL in youth

5.3. Exploring the role of social capital, self-efficacy and social contagion in shaping lifestyle and mental health among students representing the future healthcare workforce in Palestine: social cohort study protocol

The project titled "Social capital, social contagion, healthy minds and healthy habits in the future health care work force in the Palestine was initially planned to be implemented in Palestine as the main component of the PhD dissertation. The project was designed to address the dual disease burden of NCDs and mental disorders, which has been increasing, in Palestine (21). Furthermore, it aimed to focus on the primary prevention of NCDs (17) and mental disorders (110) as cost-effective approach to its control. The targeted population of the study was the students from the faculty of medicine and health sciences of An-Najah National University in Nablus, Palestine. They were targeted as they represent the future health work force in Palestine. The study aimed at understanding the health determinants among these students through which interventions can be applied for the control of NCDs (482, 483). Meeting the human needs through access to life opportunities such as SC (335) and SE (356, 358, 359). In addition to the role of social contagion (331, 333, 480) were aspects to be explored through the study as potential mechanisms for shaping the healthy minds and habits of these students.

As part of the PhD project, the study protocol titled "Exploring the role of SC, self-efficacy, and social contagion in shaping lifestyle, and mental health among students presenting the future health care work force in Palestine: social cohort protocol" including the questionnaires were developed. It was approved by both the Ethikkommission Nordwest- und Zentralschweiz (EKNZ) (AO_2020-00047) in Switzerland and the Institutional Review Board Committee at An-Najah National University (Ref: Med Nov. 2020/32)

in Palestine. Then, it was published in BMJ Open (Darkhawaja R et al. BMJ Open 2022 Jan 19; 12(1):e049033).

I was, along with my supervisors, eager to the successful implementation of the study protocol to its full potential and we have made every effort to achieve that. In collaboration with An-Najah University Computer Science Department, the survey was launched. The survey was implemented and administrated through REDCap, which is a secure web application for building and managing online surveys and databases, to ensure maximal consideration of privacy issues. Initially, the survey was administrated as a pilot. The survey was updated based on the students' feedback. Then, several communication approaches were implemented with the aim to maximize the student's participation. Promotion video was developed in which the aim of the study and the procedure of completing the survey were explained. The video was launched through different platforms including the student portal "Zajel" at An-Najah National University, WhatsApp groups, and Facebook groups. Approximately, 5,953 students were invited to participate in the survey. Only 451 students initiated the survey including 386 students, who completed e-consent and participated in the baseline survey. The participation rate remained low despite the fact that several zoom meetings (in person meetings were not possible due to COVID-19 pandemic) were organized with the students in order to further explain the aim of the study and the importance of the student's participation in the survey. Up to 10 emails were sent as reminder for the students to participate in the survey. Given that the participation of the students in the survey was lower than 10%, we, as PhD project team, came to the conclusion we will not attain sufficient sample size for unbiased follow-up investigation and in particular for social network analysis.

There are several hypothesis why the response rate was low; the launching of the study's survey coincided with the outbreak of the COVID-19 pandemic. To the best of our knowledge, the COVID-19 pandemic has been the major factor, which contributed to the low response rate in the survey among the participants. This could be due to the disruption of the education system at An-Najah University, which was associated with the outbreak of the COVID-19 pandemic. The disruption of the education system at An-Najah University has created conflict between the university administration and the students, which hindered the ability of the students to cooperate with the university administration in any non-curriculum activities. This hypothesis is supported by the evidence provided by scholars in Palestine on the effect of COVID-19 pandemic on the young generation; Palestinians have been suffering from economic hardship, political violence, restriction on the movement and lack of sovereignty over people and resources (514-516). The COVID-19 pandemic and the consequences of the lockdown have created double burden situation for the Palestinians as they are already suffering from challenging socio-political situation. This has had impact on the younger generation more than the older generation. This might be due to the fact that the older generation had already experienced lockdowns before in the form of curfews and political invasions especially during the first Palestinian uprising *"First Intifada"*. Also, the disturbance of the education

system by the pandemic implied a delay in the day of the students' graduation and thus securing a career and having established life (517).

Given the importance of the innovative study protocol and its applicability in different low- and middle-income contexts, other potential setting to implement the study protocol were explored. Communication was made with the dean of the College of Health Sciences at Qatar University to implement the study protocol, but we were constrained by the limited time and the funds available for the completion of the PhD thesis in a timely manner.

As the low participation rate in epidemiological studies seems to be common, several recommendations and strategies have been suggested to improve the participation on health research studies; first, increasing the awareness of the students including students within the healthcare sectors, on the importance of health research, has deemed to be important. Second, identify barriers and challenges that hinder the students from participating in health research studies (518). Future attempt to implement the project's study protocol could involve the conduction of explorative qualitative study to explore students' attitudes towards health research and identify challenges and facilitators, which determine their participation in epidemiological studies. This could contribute to the increase in the participation of the students on the survey in two ways; first, identifying challenges and facilitators of participation is important to develop evidence-based strategies for the promotion of the research study. Moreover, it ensures the engagement of the students and the implementation of the study based on participatory approach, which has proven effective for increasing the participation rate in study surveys among university students (519). The decision on whether to take part in a research study or not is usually based on evaluating the cos and pros of either decision to be made. Thus, it is essential for researchers to identify and highlight the intrinsic and extrinsic added values of the students' participation in particular research study (520). We were able to identify and communicate the importance of implementing the study protocol for the health domain students at An-Najah National University. But the further engagement of the university stakeholders, on the promotion of the study protocol and its importance, could have increased the trust of the value of participating in the study's survey by the students.

Chapter 6: General discussion and perspectives

6.1. Physical activity over the life course among children and adolescents

Our studies provided evidence for the decrease in the time spent in MVPA with the increase in age among Swiss children and adolescents. This finding corroborates the findings of many studies, which further emphasized gender as additional determinant factor for the rate of age-related decline in MVPA. The highly cited systematic review on objectively measured changes in MVPA among children and adolescents, Farooq et al., indicated that MVPA declines with age and the rate of decline is greater and

starts at an earlier age among females compared with males. While the same study concluded that the rate of decline during childhood and adolescence is comparable. Also, this review added that the rate of the age-related decline in MVPA is higher on weekend days compared with weekdays (390). The last has been reiterated on the longitudinal study, which was based on the data from the National Institute of Child Health and Human Development Study of Early Child Care and Youth Development birth cohort (521). In another longitudinal study among Slovenian adolescents, who are known to be one of the most physically active in the world, the assessment of the change in objectively measured MVPA revealed the decline in MVPA between the age of 11 and 14 years old. Similar to the findings in the previously mentioned reviews, this study indicated that the decline in MVPA with the increase in age is more pronounced in females compared with males (522). Given the evidence of gender being determinant factor in the rate of age-related decline in PA, reported by several studies, might be attributed to differences in the timing of biological maturation between females and males of the same chronological age (523). Whereas the findings of these studies are based on average changes in MVPA among groups of children and adolescents, other studies provided the unique opportunity to assess the trajectory of PA over time with integrating different PA profiles, taking into account individual trajectories and assessing other determinants of the rate of age-related decline in PA. The Gateshead Millennium Cohort Study, with 8 years of follow-up, showed that the total volume of PA starts to decline from the age of 7 years among children and adolescents. Also, the same study highlighted individual differences by indicating that individuals who exhibit high MVPA are more likely to maintain the same level of PA activity with the increase in age (524). In another study aimed at assessing the age-related decline in PA among children in their transition from elementary school to high school, the decline of both the total PA and MVPA with the increase in age has been observed. Additionally, consistent with other findings, the rate of decline was steeper among females compared with males. But gender was not the only determinant factor for the rate of decline, but it extended to include urbanicity and parent level of education (525). In another longitudinal study on objectively measured PA among children, the change over two years in three constructs of PA related behaviors, which are total volume of PA, MVPA and SB, was studied; the study added to the body of evidence of the decline of both the mean daily volume of PA and the time spent in MVPA and the increase in the time spent in SB with the increase in age. Also, the study indicated that both gender and weight status were determinant factors for the age-related change in PA and SB among children (526). In line with this, studies have suggested that musculoskeletal fitness, school environment (527), and role of the parents in terms of monitoring and encouragement (528) are additional determinant factors for the rate of age-related decline in PA. In previous longitudinal study among adolescent school students, there has been indication for the decrease in vigorous PA and increase in time spent in SB with the increase in age (529). To further support the importance of tracking both PA and SB in parallel with the increase in age, there is evidence that the decrease in PA with the increase in age is in part attributed to the replacement of PA by sedentary behavior (530, 531). The decrease of PA and increase in SB with the increase in age among children and adolescents is concerning. Nonetheless established physically active lifestyle starts to

develop at early childhood and can be tracked from youth to adulthood (532). Additionally, cardiorespiratory fitness, resistance strength and flexibility indicator associated with PA were found to be tracked from childhood to adulthood (533) and PA is known to be protective factor against obesity during adulthood (534, 535). Overall, the benefits of PA during childhood and adolescence can be tracked to adulthood as it is positively associated with healthy aging and offsetting the decline in health and functioning (536). Thus, the transition from childhood to adulthood can be viewed as window of opportunity in the promotion of PA among children and adolescents such as the promotion of active commuting (537).

6.2. Trajectory of quality of life among children and adolescents

Our studies revealed decrease in the QoL with age among Swiss children and adolescents. This finding is in line with previous cross-sectional studies, which reported differences in the QoL by age (538-540). And it has been further confirmed by longitudinal research studies indicating the decline in children's (541) and adolescents' (541-543) QoL over time. Langeland et al. (2019) conducted three years follow-up study among upper secondary school adolescents. The study indicated significant decrease in the QoL among adolescents in the transition from the first year to the third year of the upper secondary school. And it has shown that upper secondary school can be appropriate target for promoting the health and well-being of adolescents (542). Meade et al. (2015) conducted similar study among Australian high school students. The study pointed out that the social support and peers dimension of QoL decreased with age. This has been attributed to change in the perception of adolescents about QoL dimensions over time. And the study also found that the change in the QoL is gender related as females scored decline in five dimensions of QoL (physical well-being, psychological well-being, autonomy and parent relations, social support and peers, and school environment) in the transition from the second to the third time point. And additional steady decline in the psychological well-being dimension of QoL over the three time points. This might be related to a gender-specific vulnerability during adolescence (544). While those studies were based on school setting, Palacio-Vieira et al. (2008) found, during three years follow-up period of general population-based sample of children and adolescents that QoL declined with age. The study also added that the decline in the QoL was significantly steeper in females compared with males in part due to the negative effect of pubertal development on QoL, which was more pronounced among females (541). The previous studies mainly addressed the changes in the QoL over time among children and adolescents, while fewer longitudinal studies aimed at exploring the predictors associated with the change in QoL over time. In more recent longitudinal study among adolescents in Norway by Mikkelsen et al. (2022), the decline in the QoL with age, primarily with respect to the physical and psychological well-being dimensions of QoL, was further confirmed in the transition of the adolescents from the lower secondary to the upper secondary school. Also, the study found that stress, loneliness, and pain were predictive negative factors, while self-esteem and SE are positive factors of the change in the QoL over time (545).

While previous longitudinal study among representative sample of Spanish children and adolescents showed that poor mental health was associated with the greatest deterioration in the psychological well-being dimension of QoL over three years (546). Similarly, analysis from data of a German children and adolescents population-based study, authors indicated that mental health problems were associated with negative effect on the change in QoL over two years. While SE, family climate and social support were associated with positive effect on the change in QoL over the same period (547). Yet Gillison et al. (2008) concluded the stability of QoL among adolescents in the absence of health problems (548).

6.3. The contribution of physical activity to children's and adolescents' quality of life

Our studies have provided evidence for the positive cross-sectional association between the average time spent in MVPA and QoL among children and adolescents living in Switzerland. This included its positive association with the overall QoL and the physical well-being, social well-being and functioning at school as specific dimensions of QoL. Also, our results revealed that the average time spent in MVPA during the weekends is positively associated with the social well-being dimension of QoL independent of time spent in SB or the cluster membership of PA. Overall, there are limited number of studies, which addressed the association between MVPA and QoL among children and adolescents. Moreover, existing studies are mostly derived from cross-sectional studies and subjective measurement of PA (416). Nonetheless, our results are in agreement with previous studies, which provided evidence for the cross sectional association between MVPA and several aspects of QoL among children and adolescents; in the study among youth, who were between 9 to 10 years old and recruited from schools in communities of low income in the U.S.A, the cross-sectional analysis on the association between objectively measured MVPA and QoL revealed positive association between MVPA and overall QoL, physical functioning, school functioning and psychosocial dimensions of QoL. This positive association was concluded irrespective of reaching the recommended one hour per day on MVPA (549).While similar study, which was conducted among 8 to 9 years old children in Ireland, suggested that meeting the MVPA guideline has been associated with the overall QoL and its all dimensions including physical well-being, psychological well-being, parent relations and autonomy, social support and school environment. The last was limited by the subjective assessment of MVPA (550).

There are few studies, which attempted to address the mechanism by which MVPA contributes positively to the subjective well-being of children and adolescents; in a school based cross-sectional study among adolescents in China, it has been concluded that subjectively measured MVPA is positively associated with the subjective perception of adolescent's health. This relationship was mediated in part by the impact of MVPA on adolescent's social and interpersonal relationships (551). In another study among Malaysian children, who were between 9 to 11 years old, there has been evidence for the positive association of

MVPA with both the overall QoL and the psychosocial dimension of QoL, but the relation was dependent on gender and BMI (552).

Another important aspect in addressing the relation between PA and well-being is the variation in the contribution of PA to different aspects of the individual's well-being; the dose-response positive relationship between MVPA and HRQoL among Spanish adolescents, was greater than the relationship between MVPA and other aspects of self-reported health including self-rated health, health complaints, and satisfaction with life. The differences in the contribution of MVPA to health among adolescents has been attributed to several factors; MVP has different effects on the different dimensions of self-rated health. Also, it could be due to the variation in the family and social relationships between the participants, which might have contributed to the greater health benefits of MVPA on HRQoL compared with other aspects of self-rated health (553). In another study, which was conducted among elementary school-age youth, the naturally occurring profiles of MVPA and SB were found to have differentiating association with HRQoL; the "Active" profile, which was characterized by the highest time spent in MVPA, exhibited the most statistically and clinically positive association with the psychosocial dimension of HRQoL compared with the "Moderate" and "Inactive" profiles, which have higher levels of time spent in SB. This is suggestive that MVPA is the driving factor for the association between the "Active" profile and the psychosocial dimension of the HRQoL only excluding the physical dimension of the HRQoL (554).

Alberto and his colleagues has conducted the first meta-analysis study on the effect of physical activity interventions on the health-related quality of life among healthy children and adolescents; the study provided evidence for the positive contribution of both exclusive physical activity interventions and multicomponent interventions to the overall health-related quality of life and its dimension, including physical well-being, psychological well-being, autonomy, parent relation and social support and peers. This is irrespective of the type and the duration of physical intervention being implemented (393).

6.4. Challenges of public health research in Palestine

Despite the fact that the project titled "Social capital, social contagion, healthy minds and healthy habits in the future health care work force in Palestine was not completed, the piloting of the study, the launching of the study's survey and the publication of the study protocol have enhanced my knowledge and scientific thinking is various ways; I have acquired professional experience on scientific planning, study design, implementation of longitudinal survey, data analysis, and manuscript writing. Also, I have become familiar with data management tools including REDCap and how it can be used to ensure privacy and protection of the data. The publication of the study protocol has enhanced my understanding of the scholarly publication process and proved the novelty of the study. Thus, the last is an indication for the feasibility of its implementation. Also, given that the pilot of the study has been completed, it can be easily implemented in the future. It is in my best interest to implement the study protocol in the future.

I am and will always be passionate about public health including public health in Palestine. The Palestinian context played a major role for allowing me to understand the importance of public health as opposed to medicine because the healthcare system in Palestine is mainly shaped by social, political and economic determinants (68, 555-557). Thus, I will take the opportunity to address some of the challenges of implementing public health research in Palestine and propose potential solutions.

Every human being has the right to enjoy the highest attainable standard of health (558). Health data and scientific evidence are important factors contributing to the realization of the right of people to health and fundamental for achieving universal health coverage, which is the practical expression of the right to health. Health research has the potential to identify the health needs and services requirements to improve health and to determine the indicators required for monitoring the progress towards universal health coverage (559). In line with this, health research is considered a major determinant for achieving the SDGs including SDG3, which aims at "ensuring health and well-being for all"; health research is one way to provide evidence–based evaluation of the progress towards the SDGs at different levels through the production of data and approaches on sustainability measurements. Also, research is essential for defining the linkages between the SDGs, which are essential for achieving the SDGs (560).

The successful implementation of epidemiological studies in Palestine such as the "Social capital, social contagion, healthy minds and healthy habits in the future health care work force in Palestine study protocol, has the potential of contributing to the social dimension of the SDGs in Palestine. This is because the ultimate goal of the study was to develop evidence-based strategies that could contribute to the strengthening of health promotion and prevention with the primary healthcare system in Palestine. Health equity is integral part of health promotion and prevention, which in turn fundamental for the achievement of SDG3 "ensure health for all and at all ages" (561). Even though the study protocol aimed to target only future healthcare professionals in Palestine, the essence of the study could have become a reference for similar studies targeting different communities in Palestine. This is because of the high relevance of the study to the Palestinian context in general. The main added value of the study is related to the fact that the analysis of the best practices for strengthening health promotion in Palestine is addressed with the framework of the SMH, which is more advantageous than the pathogenic model of health. The later has unfortunately been predominately applied to address several gaps existed within the Palestinian healthcare system, while disregarding the importance of the salutogenic approach to health. This is because by applying the salutogenic approach to health, the study allows for the disclosure of otherwise hidden and ignored GRRs within the Palestinian society, mainly SC and SE. By identifying the GRRs within the Palestinian society, we acknowledge the power of the Palestinian society and we amplify the resources they can utilize for resistance and resilience in their attempt to face challenges and stressors. By doing so we contribute to the enhancement of their SOC. Through SOC, the Palestinian society can better have

control over and improve their health, which eventually can lead to the attainment of health equity, empowerment and well-being, which are essential aspects of the SDG3 (562).

Also, the study aimed at assessing the health-related behaviors among students at the health domains representing the future healthcare professionals in Palestine. Healthy behaviors are essential component of any attempt for strengthening health promotion and prevention. It is known that health is a prerequisite for sustainable development, but what is less acknowledged is the fact that unhealthy behaviors can undermine sustainable development. Unhealthy diet can contribute to the increase in malnutrition and increasing the risk of diet-related NCDs. While, promoting physically active society contributes to the healthy development of people of all ages and contribute to the decrease in the prevalence of coronary heart diseases and cancers. Overall, diet and PA are considered important health-related behaviors that can impact the progress towards the achievement of the SDG3 (563).

Moreover, the study protocol aimed at assessing both the negative (depression, anxiety and stress) and positive (well-being) aspects of the health domain students, which is otherwise overlooked by epidemiological research studies implemented in Palestine (67). Nonetheless, mental health is integral part of the SDGs. This is because mental health is interconnected with other essential aspects within different SDGs; eradicating poverty, which is SDG1, is essential as poverty can contribute to the increase of mental health disorders. Also, mental health is part of the comprehensive definition of health, which should be addressed along with physical and social aspects of health in order to contribute the attainment of the SDG3. Also, given the negative stigma associated with mental health disorders, people with mental disorders are one of the groups, which are increasingly discriminated and marginalized. Any public health agenda, which does not address mental health as essential aspect of health, is considered limited for its ability to contribute to the SDGs mainly SGD10, which calls for reducing inequality (564).

The production of knowledge through health research does not guarantee its positive contribution to the improvement of the healthcare system in any context. It is only through translating the knowledge derived from research into practice and through influencing health policy decision-makers that health research can contribute to the development of the healthcare system and eventually the improvement of people's health (565). Moreover, synergies should be ensured between applied health research and heath needs to overcome the 10/90 gap as it has been reported that less than 10% of the health research expenditure is channeled to target health problems affecting 90% of the world's population (566).

In Palestine, the main contributors to health research are the Ministry of Health, the Palestinian National Institute of Public Health, the Palestinian Council for Health Research, and the Scientific Research Council. Also, Palestinian universities, non-governmental organizations and national agencies contributes to the production of health research (567). Nonetheless, their role has been insufficient (568). In regards to the productivity of health research, there is evidence for the increase in the quantity of health research

in Palestine over time (569). This increase has been remarkable since 2001 (570). Despite this, health research in Palestine has been of low quality in terms of accuracy and quality of reporting (571-573). Along with this, there is mismatch between the burden of diseases and the research applied to address these diseases (574) and there is dearth of research in certain health domains such as health economics (575).

The challenges of conducting public health research in Palestine can be detected at several levels; at the organizational level, health research is not a priority in the political agenda and it is not adequately accounted for in the national budgets (576). In line with this, there is not national governance structure for health research, which is related to the absence of mutual consent on the importance of health research and its priorities. In addition to the lack of sovereignty over resources due to the political instability (567). At the operational level, the financial resources, which are available for health research, are limited and usually conditional based on the agenda of the external donor's funding (577). Also, the fact that the Palestinian healthcare system is administrated by several actors, including the public sector, the private sector, the United Nations Relief and Works Agency and the non-governmental organization sector (556), makes it challenging for any attempt to standardize data collection (578).

Given that knowledge transfer is a core aspect of health research, one of the major concerns regarding health research in Palestine is the inadequate health evidence-based practice due to the limited utilization of health research findings. This is can be attributed in part to the skepticism about the importance of evidence-based research in decision making, the absence of centralized health research system, the existence of fragile information infrastructure and the lack of channel for communication between researchers, policy-makers and health practitioners (579, 580).

6.5. Conclusion and recommendations

The conclusions and recommendations, which will be addressed, are inspired findings derived from the analysis of the SOPHYA cohort on the cross-sectional and prospective association of PA with the QoL among children and adolescents living in Switzerland. Also, it is based on the study protocol on exploring the role of SC, SE, SOC and social contagion in shaping lifestyle and mental health among health domain students representing the future healthcare workforce in Palestine.

As it has been previously mentioned, the PA dimension of the health promotion profile is the most health promotion profile dimension to worsen among medical students (581-584). Also, we have concluded that medical students' own health behaviors predict their ability to integrate health promotion and prevention in their future role as health professionals (585, 586). Also, the literature review suggests the health benefits of PA (225-229), which has been highlighted previously. In particular, PA has been well-known for its positive contribution to the primary and secondary prevention of NCDs (240-246). Also, existence

literature points to the positive contribution of PA in the control of depression (274, 275) and psychological distress (587, 588). Both conditions have been reported to be of high prevalence among medical students (589-592). Additional remarkable aspect of PA that has been mentioned previously is its role in the promotion of good health including general QoL and its specific dimensions (392, 593). Based on these findings, PA can be a window of opportunity for the enhancement of health and well-being among the medical students in Palestine. In fact, there are several intervention studies, which provided evidence for the effectiveness of PA intervention in the promotion of health and well –being among medical students in different settings; the exercise intervention, the 'MED-WELL' program, was experimented among medical students in the West of Ireland. The aim of the program was to engage students in PA as a way to promote their health and well-being and educating them how to apply exercise as medicine; the program improved to be effective in improving the well-being, and the sleep pattern among the medical students. Additionally, it had positive contribution on the loneliness level among them. The medical students perceived exercise as medicine even prior being part of 'MED-WELL' program (594). In another nonrandomized controlled study among medical students at the University of New England College of Osteopathic Medicine, three two interventions were applied among the students; the first intervention involved students participating in 30-minute CXWORX (Les Mills International LTD) group fitness classes. The second intervention is the same as the first intervention expect students exercised alone or with up to 2 additional partners regularly. While students in the control group did not engage in regular exercise. The regular group fitness classes had significant positive contribution among the medical students through decreasing the stress level and increasing the physical, mental and emotional dimensions of QoL among them (595).

Also, it has been stated that Palestine is youthful society (377) and it is going through epidemiological transition with trend of increase in the prevalence of NCDs (21). The later is further worsen by the increase in risky health behaviors among the Palestinians mainly among the youth (12, 13, 40, 41). It has been suggested that it is rather urgent to improve health promotion and prevention through strengthening primary healthcare services (596) and encourage people to have control over the improvement of their health (597). Given this, the ultimate goal of the PhD project was to assess the health and well-being of the medical students in Palestine, as they are representing the future healthcare professionals, and develop evidence-based programs and intervention strategies to promote their health and well-being, and to enhance their roles in health promotion and prevention among Palestinian patients. The evidence derived from our research is limited given the low participation rate of the targeted population on the study's survey. Nonetheless, based on the study, which was conducted among Palestinian medical students between 2018 and 2019, the prevalence of depression and anxiety was reported to be 23.1% and 46.8%, respectively. Additionally, 4.5% of the participants reported that they have suicidal thoughts (598). Furthermore, the prevalence of depression and anxiety among them has increased and their mental health has worsen during the COVID pandemic (589). This is in agreement with the result provided by the meta-

analysis studies, which estimated that approximately one-third of the medical students globally are affected by depression (590) and that medical students have higher overall prevalence of depression symptoms compared with the general population (591). Also, the current evidence suggests the high prevalence of burnout (599) and stress (592). In addition to the previously mentioned evidence for the increase risk for the deterioration of the mental health of medical students, they also at higher risk of suffering from physical health problems, such as migraine and tension-type headache (600). The currents studies are important, but it has its own limitations; the findings of these studies are not representative for the entire population of medical students in Palestine (598) and it focuses mainly on negative aspects of health (589, 598, 600). Only few studies have addressed positive aspects of health such as quality of life, but also limited to its relevance to sleepiness, (601) and emotional intelligence (602). Where the previous studies have focused on the health outcomes among medical students, several studies have been conducted to assess the health-related behaviors among medical students; the evidence suggests that medical students are at high risk of engaging on risky-health behaviors such as unhealthy diet (603), substance use (604), and insufficient PA (605). Along with this PA, which is important component of the individual's health promotion profile (606), tends to worsen among medical students (581-584); Fashafsheh conducted study among nursing students in Palestine. They used the Health Promoting Lifestyle Profile II (HPLP II), which is instrument for measuring 6 dimensions of the health-promoting behavior; health responsibility, nutrition, PA, stress management, interpersonal relations, and spiritual growth. The study suggested that the nursing student scored the lowest on the PA dimension. The authors attributed this to the Palestinian social and the cultural context, which does not promote PA as daily leisure activity. Also, sport clubs are usually privatized and can only be accessed by paying certain fee (581). In similar study, which was conducted among medical students in Egypt, the score of the PA dimension of the health promotion profile was also the lowest. It has been explained by the high demands associated with the medical curriculum, which tends to interfere with other aspects of the student's life (582). Also, PA dimension of the health promotion profile was reported to be the lowest among medical students in Turkey with last year students significantly have lower score for the PA dimension of the health promotion profile compared to first year students (583). This is of concern because the engagement in healthy behavior, including PA is protective factor against the worsening of the students' health; in a randomized control trial, which was conducted among medical students at An-Najah National University, the role of cognitive behavioral therapy program on improving well-being among the students has been examined. The model has proven to be effective for lowering the score for depression, anxiety and social functioning among the students (607). Furthermore, medical students' own health behaviors predict their ability to integrate health promotion and prevention in their future role as health professionals; this has been evident by the longitudinal study of Norwegian Medical Students and Doctors. The study consisted of two cohorts: the student cohort and the young doctors cohort. The student cohort consisted of all medical students, who were enrolled in four medical schools in Norway in 1993. While the young doctor cohort consisted of all students who graduated from all four medical faculties in Norway in 1993. The students completed baseline survey in 1993/94, then follow-up surveys

were conducted at six measurement points over a period of 20 years (1993-2014). The results of the study were derived from the two cohorts; both the participants self-reported their own engagement in PA, alcohol habit, and counselling their patients on PA and alcohol consumption. The participants' own PA level was significantly associated with the frequency of asking about PA to their patients, but the study did not provide evidence for the association between the participant's lifestyle habits with counselling on alcohol habits (585). In another study among medical students in New Zealand, leisure time PA level among the students was found to be associated with the frequency of their patient counseling practices (586). The deterioration of the mental and physical health of the medical students (581-584, 589, 598, 600-602, 606) and the fact that their lifestyle health is predictor for their health prevention and promotion role as future health professionals (585, 586), should be driving factors for the development of, otherwise limited, support services for the enhancement of medical students' health and well-being (607-609). Also, evidence-based strategies for the health promotion of medical students is still lacking due to the limited research available on best intervention strategies and intervention to promote the health and well-being of the medical students; strategies to improve the medical students' health and well-being can be addressed at two levels: system level and individual level. At the system level, current literature review suggest that introducing P/F grading system, implementing longitudinal, collaborative learning approach with peer support could contribute to the enhancement of the health and well-being among medical students. At the individual level, it has been suggested that it is important to encourage medical students to engage on hobbies and being part of social support networks. Additionally, it is essential to put in place system, which is based on top-down approach and ensure high confidentiality, to screen medical students who are at risk of mental health deterioration. Along with this medical students should have access to cognitive behavioral therapy and training in cognitive restructuring techniques (610). The last is important, but it should be coupled with the introduction of interventions with the goal of decreasing mental health stigma among medical students (611).

In light of the previous findings, the following are final conclusions and remarks:

1. The thesis confirms existing evidence that device-measured MVPA and QoL are positively associated in youth living in Switzerland.
2. The thesis does not provide evidence for the independent association of device-based PA profile clusters for the weekend with QoL.
3. As both PA and QoL declined with aging, health-in-all-policy and interventions should be tailored to promote PA and QoL in age-specific manners.
4. Future longitudinal studies on the relationship between PA and QoL in youth should employ shorter follow-up times and collect several longitudinal measurements of every participant.
5. Attempt to implement the thesis' study protocol could involve the conduction of qualitative study to identify challenges and facilitators, which determine their participation in epidemiological studies.

6. Attempt to implement the thesis' study protocol should further involve the engagement of the university stakeholders to increase the trust of the value of participating in the study.

7. Implement initiatives with the aim of the continuous assessment of the health and well-being among the health domain students representing the future healthcare workforce in Palestine. This include the design and implementation of population based cohort studies through which causal effects, predisposing and protective factors of the health and well-being among the students can be derived and thus better inform health intervention agendas. Current existing evidence are based on sub-population samples or convenient samples and limited to addressing mainly negative aspects of health among health domain students.

8. Develop programs and services to address the physical and mental health needs of the health domain students with focus on those who are at risk of physical and mental health disorders. These programs and services should be based on top-down approach, ensure high confidentiality of the information provided by the students, should be culturally sensitive and should be accessible.

9. Apply interventions with the aim of enhancing the health and well-being among health domain students. This includes, but not limited to lifestyle intervention programs on PA, healthy diet, and tobacco use.

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Profile

I'm a motivated researcher with a broad range of expertise in research skills including study design, data analysis, statistical inference, and manuscript writing. Doctor of Philosophy (PhD) candidate with focus on quantitative data analysis techniques tackling public health topics on health-related behaviors, mental health and non-communicable diseases. Experienced professional in public relations, fundraising, project management, lecturing and advocacy skills with proven record of accomplishment on health and development projects for more than 6 years.

EXPERIENCES

Doctor of Philosophy **September 2019- January 2024**
University of Basel
Swiss Tropical and Public Health Institute
Basel, Switzerland
PhD thesis: ***"The association between healthy habits and healthy minds in today's youth"***
Supervised by Prof. Dr. Nicole Probst-Hensch

- Worked on the **Swiss children's Objectively measured PHYsical Activity cohort study** through which I drew evidence on the factors related to physical activity that drive quality of life among children in Switzerland.
- Developed study protocol to explore the role of social capital, self-efficacy and social contagion in shaping lifestyle and mental health among students representing the future healthcare workforce in Palestine.

Statistics Intern **August 2023 - February 2024**
United Nations High Commissioner for Refugees
Global Data Service - Statistics and Demographics
Copenhagen, Denmark

- Supported the projects of the Data Science Team in applying statistical and data science techniques to global forced displacement and statelessness situations data to improve the understanding of population behavior and vulnerabilities.
- Supported the design, development and maintenance of data products, which help improve the understanding of forced displacement issues.
- Documented background analysis and the design of final data products.

EXPERIENCES

Research Officer **November 2017 – August 2019**
World Health Organization
The Palestinian National Institute of Public Health
Ramallah, Palestine

- Updated the main indicators of the data collected to conduct the study titled "Improving newborn health in countries exposed to political violence: an assessment of the availability, accessibility, and distribution of neonatal health services at Palestinian hospitals".
- Conducted the study's quantitative data analysis at the level of all the participating hospitals based on aggregated data. In addition to analyzing data at the hospital level and at the neonatal units level.
- Co-wrote manuscript of the study for publication.
- Wrote individual report per hospital to communicate the result of assessing the neonatal health services, the assigned level of the neonatal care of the hospital, and the recommendations to improve the neonatal health services at the hospital.
- Co-organized national conference for neonatal health service providers and policy makers to disseminate the study's results and recommendations for improving existing services and developing national guideline for effective referral system of pregnant women and neonates in Palestine.

Health Researcher – Consultant **June 2016 – October 2017**
World Health Organization
The Palestinian National Institute of Public Health
Ramallah, Palestine

- Conducted literature review to gain understanding and identify gaps on the existing research on illicit drug use as part of larger research study, which was conducted by the institute to estimate the extent of illicit drug use in Palestine.
- Analyzed, coded and categorized the qualitative research study data into themes and sub-themes, which shed light on the illicit drug use in Palestine in terms of substance use and services.

Assistant Professor (Part time) **February 2016 – December 2018**
Al-Quds Open University
Jericho, Palestine

- Planned engaging and well-structured lectures on public health, epidemiology, ethics of health professions and the management of shelter and nutrition.
- Delivered scheduled lectures for students enrolled at the health management program of the administrative and economic sciences faculty.
- Evaluated the performance of the students based on regular assignments in addition to administrating midterm and final written exams.

EXPERIENCES

Health Officer **March 2013 – October 2017**
Public Relations Department, Health Work Committees (HWC)
Ramallah, Palestine
Public Relations & Fundraising

- Co-developed the department's strategic plan with focus on fundraising targets.
- Mapped and recruited international non-governmental organizations and private companies as potential donors for the organization.
- Formulated project proposals and concept notes and pursed targeted donors to adopt them.
- Co-designed brochures, annual reports and other communication materials that are essential for promoting the organization's work.

Project management

- Managed the primary health care and development projects based on the different projects' work plans.
- Monitored and evaluated the projects and executed reports to the corresponding funding agency.
- Supervised the national and international volunteers of HWC.

Middle Eastern Advocate – Intern **March 2011 – February 2012**
Middle Eastern Program, Interval House
Long Beach, California, United States of America

- Provided advocacy and support services to Middle Eastern victims of domestic violence, linking them with appropriate social services.
- Organized initiatives to raise awareness on combating domestic violence among local organizations and communities.
- Led English as a Second Language (ESL) classes.
- Carried out office duties and handled routine correspondences.

EDUCATION

University of Basel **September 2019 – January 2024**
Swiss Tropical and Public Health Institute
Basel, Switzerland
Doctor of philosophy, Public Health / Epidemiology

Birzeit University **September 2013 – June 2015**
Institute of Community and Public Health
West Bank, Palestine
Master of Public Health

Manchester University **January 2007 – January 2011**
Indiana, United States of America
Bachelor of Science, Pre-medicine (Biology-Chemistry)

PUBLICATIONS

- **The role of non-governmental organizations in the health sector in the occupied Palestinian territory: a cross-sectional qualitative study – Abstract published in the Lancet**
  Marina Tucktuck, **Ranin Darkhawaja**, Tareq Areqat, Shatha Mansour, Rita Giacaman, Motasem Hamdan
  https://doi.org/10.1016/S0140-6736(17)32080-9
- **Cross-Sectional but Not Prospective Association of Accelerometry-Derived Physical Activity With Quality of Life in Children and Adolescents**
  Ranin Darkhawaja, Johanna Hänggi, Emmanuel Schaffner, Marek Kwiatkowski, Abdulsalam Alkaiyat, Alain Dössegger, Bengt Kayser, L. Suzanne Suggs, Bettina Bringolf-Isler, Nicole Probst-Hensch
  https://doi.org/10.3389/ijph.2024.1606737
- **Exploring the role of social capital, self-efficacy and social contagion in shaping lifestyle and mental health among students representing the future healthcare workforce in Palestine: social cohort study protocol**
  Ranin A M Darkhawaja, Marek Kwiatkowski, Thomas Vermes, Hala Allabadi, Sonja Merten, Abdulsalam Alkaiyat, Nicole Probst-Hensch
  https://bmjopen.bmj.com/content/12/1/e049033
- **Improving Newborn Health in Countries Exposed to Political Violence: An Assessment of the Availability, Accessibility, and Distribution of Neonatal Health Services at Palestinian Hospitals**
  Massad S, Tucktuck M, **Darkhawaja R**, Dalloul H, Abu Saman K, Salman R, Kafri R, Khammash H
  https://doi.org/10.2147/JMDH.S270484
- **Occupational safety precautions among nurses at four hospitals, Nablus District, Palestine**
  IA Al-Khatib, W El Ansari, TA Areqat, **RA Darkhawaja**, SH Mansour, MA Tucktuck, JI Khatib
  https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6977042/
- **Palestinian women's satisfaction with reproductive health services at the health centers of the Health Work Committees, West Bank – Abstract**
  Sahar Hassan, Hanan Abu Qtesh, **Ranin Darkhawaja**
  https://fada.birzeit.edu/handle/20.500.11889/3921