REVIEW

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Physical Activity, A Polypill for Non-Communicable Diseases in Modern era: a Scoping Review

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SUMMARY

Background. Regular physical activity is widely acknowledged for health benefits however the uptake of PA is low due to lack of awareness.

Objectives. The objectives of the present scoping review are: 1) to consolidate the evidence claiming the effectiveness of physical activity interventions on the chronic disease risk; 2) to explore the difference in clinical benefits and strategies to promote physical activity across various age groups.

Methods. We searched for systematic reviews and meta-analytical studies on five databases (EMBASE, Scopus, Web of Science and Ovid Medline) and pertinent literature on mapping the association between physical activity and chronic disease risk was summarized.

Results. From 41 systematic reviews included for review, physical activity interventions were found to be effective in combating chronic diseases including diabetes, cancer, cardiometabolic, kidney disease, neurovascular and musculoskeletal disorders. Putative physiological underpinnings for the potential therapeutic effects of physical activity are regulation of hormones, vascular integrity, neuromotor and immune regulation. Majority of the reviews (n = 12, 29%) explored the effects of supervised exercise training and cardiometabolic risk, however long-term compliance questioned. Strategies to promote physical activity should be based on socio-ecological models (individual, interpersonal, institutional and national policy level). School and workplace based physical activity may be crucial in prevention of chronic disease risk.

Conclusions. Promoting physical activity is a key preventive measure and therapeutic intervention for combating chronic disease risk across different age groups and populations. However, potential culturally adaptable strategies to promote physical activity in the community are still lacking.

KEY WORDS

Physical activity; chronic disease risk; cardiovascular; sustainable community; life on land.

INTRODUCTION

Due to computerization, urbanization and uberization, household chores, manual labor and active commute time have significantly abridged in the global population (1, 2). Movement behaviors including sedentary behavior ("any waking behavior such as reclined sitting or lying with an energy expenditure of 1.5 metabolic equivalent task (MET) or less"), physical inactivity (inability to meet the global recommendations of 150 minutes of moderate – vigorous intensity physical activity) and inadequate sleep are identified as independent risk factors for the several chronic disease risk factors such as obesity, hypertension and cardiometabolic disease (3, 4). To reap potential health benefits, the World Health Organization urges individuals should participate in at least 150 minutes of moderate-intensity exercise or 75 minutes of vigorous exercise per week, along with muscular strengthening exercises at least twice a week (5). Despite knowing the potential health benefits and existence of the national guidelines, only a fraction of global population reaches the recommended activity guidelines while substantial proportion remains inactive and sedentary falling prey to the chronic disease risk (6-8).

As World Health Organization states "every movement count", physical activity of any intensity, frequency and duration is now linked with favorable health benefits such as reduced hyperglycemia, hyperlipidemia, hyperinsulinemia, hypertension, regulation of body mass and inflammatory markers leading to reduced cardiometabolic disease and cancer risk in adults and elderly (9, 10). Further preserved muscle, bone mass and neuromotor control leads to reduced risk of falls and osteoporotic fractures in retirement life (11, 12). Optimally dosed physical activity is found to be linked with optimized neurohumoral control such as cortisol and endorphins which regulate mood and vigor, proving to be an important antidote to stress, anxiety and depression commonly evident in modern world (13). Though the vast health benefits of physical activity are often discussed at the scientific community level, its public utilization and compliance are often poor at the individual level (14). The potential reasons for the poor utilization at the community level are lack of awareness to the health benefits and strategies to comply to attain the optimum physical activity level (14).

In this scoping review, we aimed to collate the available evidence that 1) explored association between physical activity and chronic disease risk; 2) age, physical activity and potential health benefits difference; 3) strategies to optimize physical activity levels to attain the potential health benefits.

METHODS

The present scoping review is reported as per the guidelines of Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) (15).

Eligibility criteria

As the present review aimed to explore and narratively explain the physical activity effects on the chronic disease and risk factors, we have included the systematic review and metanalysis which explored 1) any physical activity component (aerobic, strength, flexibility or other complementary lifestyle strategies such as Yoga or Tai-Chi); 2) any of the chronic disease and comorbidities (cancer, diabetes, obesity, stroke, polycystic ovarian syndrome, dementia, Alzheimer's, hypertension, cardiac/ coronary artery diseases, arthritis and neuromuscular diseases). If the review has explored only the prevalence, strategies to promote physical activity rather than the effectiveness in prevention of chronic disease risk as outcome, the review was excluded.

Information sources

We administered search in four databases: Experta Medica Database (EMBASE), Ovid MEDLINE, Scopus and Web of science from their inception until 6th June 2023. The MeSH terms were used as per the population (adults, children, elderly), intervention (physical activity, sedentary behavior) and outcome (chronic disease risk, inflammation, cancer, glycemic levels, insulin, atherosclerosis, diabetes, obesity, musculoskeletal disorders, stroke).

Search criteria

We performed a concept mapping based on Population, Intervention, Comparison and Outcomes (PICOT) format. Medical subheadings were identified under population ("adults", "elderly", "older adults", "children", "adolescents"), interventions ("physical activity", "exercise", "strength training", "aerobic exercise"), comparison (sham or placebo controlled), outcomes ("cardiometabolic", "cardiac failure", "diabetes", hypertension", hyperlipidemia", "hyperinsulinemia", "cancer", "neoplasm", "coronary artery disease", "obesity", "overweight", "polycystic ovarian disease", "Alzheimer's", "dementia", "mental health", "stroke", "kidney disease", "dialysis") and design (systematic review and meta-analysis). The identified MeSH terms were administered in the advance search boxes of the above-mentioned peer reviewed databases with appropriate combination of the Boolean operators 'AND' 'OR, 'NOT'. The backward citation search was also administered for the potential reviews to be included. All the searches in the databases were administered by the primary author (BC). The search strategy will be made available upon request to the corresponding author.

Selection of sources of evidence

The citations retrieved through the search from peer review journal databases were downloaded as .ris format and uploaded in the online endnote application (https://www.myendnoteweb.com/EndNoteWeb.html). All the citations were retrieved in a single folder and duplicates were removed. After the removal of duplicates, two independent reviewers (BC and MR) performed the title and abstract screening based on the eligibility criteria determined priori. The eligible reviews for in-depth analysis were then downloaded, assessed the review findings and charted for the present scoping review.

Data items and charting process

The following data were retrieved from the included systematic reviews and consolidated for the present review: author, year, type of the review, participants (age, clinical population, risk factor), review of observational or interventional studies, measures of physical activity, dose quantified, chronic disease risk outcomes (serological biomarkers, anthropometrics, physical, social and mental wellbeing

outcomes and mortality) and key findings. The data were presented in a tabular column and necessary data were extracted from the review findings for discussing the data. The results are presented in three forms: 1) search findings/evidence summary; 2) potential therapeutic physiological mechanisms and dose of physical activity to combat the chronic disease risk; 3) physical activity benefits according to age variations; and 4) strategies to promote physical activity based on age variations.

RESULTS

Of 17,186 studies initially retrieved, the majority was irrelevant to the present review. **Figure 1** depicts the screening and inclusion of the reviews in the scoping review. After title, abstract and full text screening, 41 systematic reviews and metanalysis were found appropriate for the extraction and charting of data (16-56). Strategies to improve PA, not specifically assessed chronic metabolic disease risk were the primary reasons for exclusion.

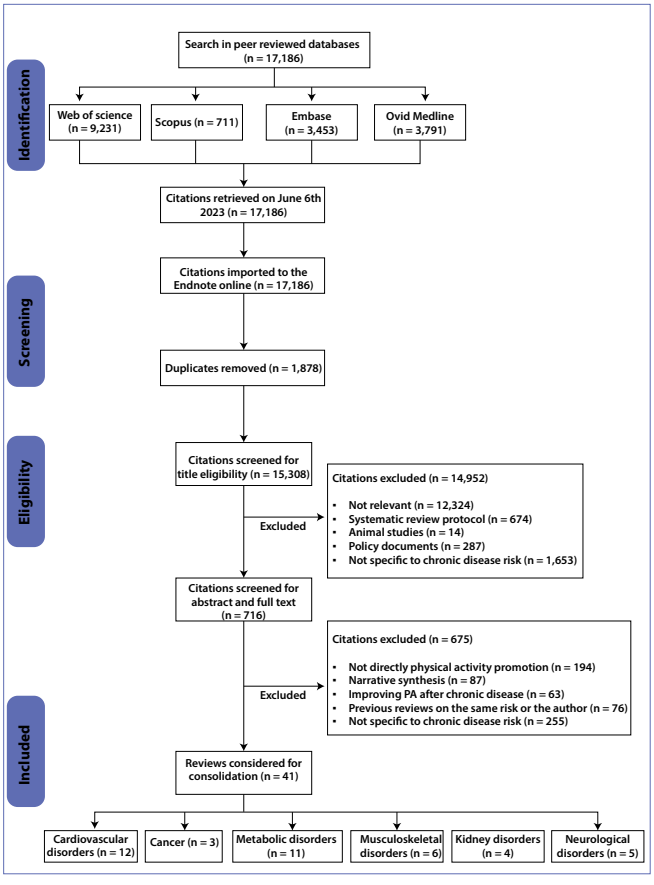


Figure 1. Screening and inclusion of the studies for the scoping review.

Domains of PA studied

During 16 hours of typical wake time, individuals engage in variety of movement behaviors not limited to activity of daily living, transport, occupation related activities and playing games or screen time. These can be broadly classified into four broad domains: 1) activities of daily living (cleaning, bathing, washroom activities) = 1-2 hours; 2) commute time (active or passive transport) = typically spending 0.5 – 1 hours; 3) occupational related PA (stationary or sitting behavior, chopping, pushing, pulling, carrying heavy loads) = typically spending 8-9 hours/day and leisure time PA (participating organized sport, gardening, group activities and screen time) = typically spending 2-3 hours/day (**figure 2**) (57, 58).

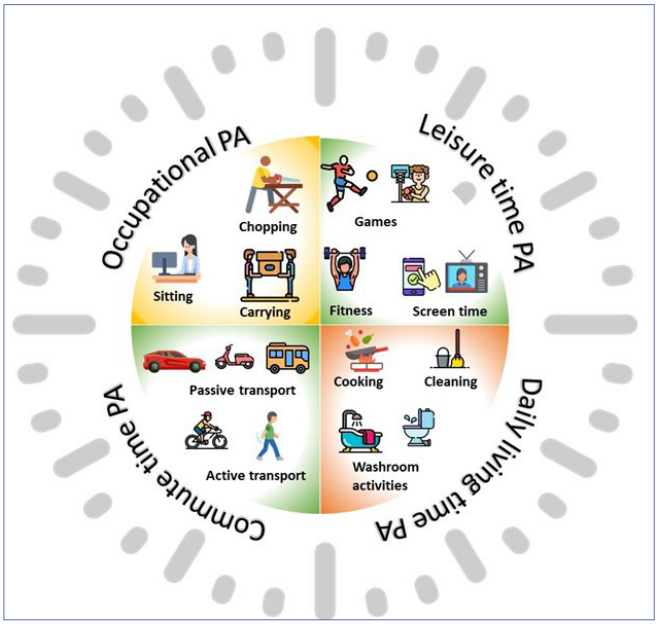


Figure 2. Domains of physical activity most of the people used to spent during the wakening hours other than their bedtime.

Contemporary evidence has evaluated the domains and its association with the cardiometabolic disease risk factors. **Table I** explains the characteristics of the studies that explored the efficacy of the PA interventions or their association with the chronic disease risk.

Summary of the findings

Of 41 systematic reviews analyzed, physical activity is identified to be an independent protective factor against the chronic disease risk. Majority of the reviews were conducted on cardiovascular disease (CVD) risk (n = 12, 29%) while few analyzed metabolic disorders such

Table I. Characteristics of the included reviews and key findings.

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Cardiovascular disorders								
Hypertension								
Correia *et al.*, 2023 (14)	To review the current evidence on the strength training on hypertension	December 2020	Fourteen studies of RCTs	253 participants, (aged 60 -68 years)	Strength training	Intensity: 50-60% 1RM 40%MHR Borg RPE 11-13 8-48 weeks 8-10 weeks minimum	75% hypertensives and antihypertensives	decreaseSBP (MD = -9.52 [95% CI – 12.89 to – 6.14, p<0.00001) decreaseDBP (MD = -5.19 [95% CI – 7.98 to – 2.39, p=0.003)
Dassanayake *et al.*, 2022 (15)	To assess the effectiveness of PA on ambulatory BP in RHT	January 6, 2021	Systematic review of four studies	178 participants (55-65 years)	Aerobic ex training Land and water based	8-16 weeks 3 times a week	Resistant hypertension	decreaseSBP -9.88 mmHg/ DBP -6.24 mmHg Aerobic ex SBP -12.06, DBP -8.19 mmHg
Pescatello *et al.*, 2019 (16)	To update the evidence on relation between physical activity and blood pressure	February 2018	Umbrella review of 17 meta-analyses and one systematic review	594,129 adults ≥18 yr. From 15 meta-analysis exploring physically inactive	Leisure time physical activity. However, the methodology of PA studied not detailed	1-7 days (3 days/ week common) 30-60 min/day 4-5 months Both aerobic and resistance Handgrip (30-50%MVC, 4 contractions held for 2 min), min 4 weeks	Hypertension (with normal, prehypertension and hypertensives)	Inverse relation between PA and incident hypertension in normal BP adults decreaseCVD risk in hypertensive adults decreaseBP in at risk, pre-hypertensive and hypertensive adults Response varies with the resting BP with pre-hypertensives response better Every 10 METh/week, the BP risk decrease 6%
Saco-Ledo *et al.*, 2020 (17)	To assess the effectiveness of PA on ambulatory BP and association with CVD mortality	April 1, 2020	Fifteen studies of RCTs	910 participants (aged 45-70 years)	Aerobic continuous or interval training Resistance or isometric training	8-24 weeks 3-5 times a week 30-36 minutes/day Intensity: Aerobic (40-60%MHR, AT), RT (30% MVC, 50-60% 1RM)	Hypertension or medicated for hypertension	decreaseSBP -5.4 mmHg/ DBP -3.0 mmHg Nighttime ambulatory BP decreaseSBP -4.7 mmHg/ DBP -3.1 mmHg Exercise benefits more who are medicated than untreated Aerobic exercise as an adjunct rather resistance or combined is better
Teixeira *et al.*, 2023 (18)	To find out the evidence of intermittent high intensity exercise on pre and established hypertension	July 2021	Twenty-seven studies	946 participants (18 HIIT and 9 RT)	High intensity interval training and recreational team sports	80% HRmax or 70% VO2max 6-48 week (median 12 weeks)	pre-hypertension or hypertension	decreaseSBP -3.29 mmHg/ DBP -2.62 mmHg decreaseoffice SBP -7.13 mmHg/ DBP -5.81 mmHg in hypertensive RTS - decreaseoffice SBP -4.18 mmHg/ DBP -4.04 mmHg in pre-hypertensive Musculoskeletal injuries were the reason for dropout

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Coronary artery diseases								
Dibben *et al.*, 2023 (19)	To update the existing Cochrane review consolidating the effectiveness on exercise-based CR on mortality and quality of life	September 2020	85 RCTs involving (n = 23 430) 12-month follow-up	23,430 participants from 85 studies 16/22 new trials from LMIC Median age – 56 Males only (25%)	>6 months follow-up Typically, aerobic Center based (47%)	F(1-2 sessions/week), I (50-90% HRmax, 50-95% VO2 max, RPE 11-16) D (20-90min),	Post MI, post vascularisation, angina	18%decrease fatal or non-fatal MI. 23%decrease hospitalisation decrease total incurring cost increase mental/ physical component scores No difference in risk of overall mortality of CABG
Du *et al.*, 2021 (20)	To compare HIIT with moderate intensity continuous training for CVD risk in CAD patients	December 2020	Twenty five studies (n = 1272)	1,272 participants (HIIT 621, MICT 651) dropout - HIIT (0% to 38%) and MICT (0% to 28%).	Intervention comparing HIIT *vs* MICT treadmill running and cycling	Frequency (2-3 days/week), duration (20-90min), period (4 – 16 weeks) Intensity: HIIT (*e.g.*, ≥85% VO2 peak or ≥85% HRR or ≥90% HRM or equivalent) MICT (50–75% VO2peak or 50–75% HRR or 50–80% HRM or equivalent)	CVD risk, quality of life in CAD patients with or without compromised left ventricular ejection fraction	Both HIIT (4.52 mil/kg/min) and MICT increase (2.36 mil/kg/min) VO2peak Both HIIT and MICT increase anaerobic threshold and peak power HIIT decrease SBP (3.61 mmHg) No significant difference in EF, HR rest, HR peak
Kaihara *et al.*, 2022 (21)	To assess the active tracker based PA on CVD risk, VO2, adverse CVD outcomes and quality of life after CAD	October 2020	Eleven RCTs	1,356 participants (11 RCTs) All from upper income countries 63-88% males	Smartphone, pedometer, accelerometer Virtual meeting, text messaging 24 weeks	Not reported	VO2max, major adverse cardiovascular events, LDL-C	significantly increase peak VO2 (MD 1.54) and decrease MACE (RR 0.51) No significant differences in LDL-C and quality of life
Yang *et al.*, 2017 (22)	To assess the effects of PA based CR after percutaneous interventions in patients with CAD	January 2016	Six RCTs (exercise n = 341, control n = 341)	682 participants from six RCTs	Exercise, Yoga, Taiichi, walking, climbing stairs	Frequency (3-14 sessions/ week), Intensity (not reported) Duration (not reported),	Mortality, MI and CABG after percutaneous interventions	Significantlyincrease angina (OR=0.41), increase total exercise time and exercise tolerance Not significantly decreaserisk cardiac deaths (OR = 0.32) or MI recurrence (OR = 0.31), reported PCI (0.67)
Cardiac failure								
Aune *et al.*, 2021 (23)	To clarify the association between the PA, CRF and risk of heart failure	January 14th 2020	Thirty six (29 cohort studies)	329,768 participants (29 cohort)	Total PA, Occupational PA, commuting and leisure activity Total PA index, Physical fitness	Intensity (moderate, vigorous) Duration and frequency quantified accordingly All based on questionnaires	Risk of heart failure	decreaserisk with total PA (RR 0.77) decreaserisk with LTPA (RR 0.77) Risk decrease above threshold 25–30 MET-hours per day High occupational PA increase risk than low OPA
Cardiovascular mortality and morbidities								
AbuElkhair *et al.*, 2023 (24)	To find the effective PA on atrial fibrillation	October 11, 2021	12 (11 RCTs, 1 singled group)	857 participants (56 – 71 years)	Aerobic (n = 4), other forms (Qigong)	3-6 months	Atrial fibrillation	increasegeneral health and vitality Yoga resulted in decrease body pain and emotional domain No significant difference in the quality of life VO_2 max increase at 12th week but not evident in 6th months
Gonzalez-Jaramillo *et al.*, 2022 (25)	To determine the association between PA and CVD mortality	March 31, 2021.	9 prospective cohort	33,576 participants with follow-up of 15.7 years	PA through questionnaires reporting at least least 2-point PA trajectories	Not a interventional study	CVD mortality	compared to inactive, all-cause mortality was 50% decrease in active 45% decrease who increase activity 20% decrease who decrease activity

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Cancer								
Friedenreich *et al.*, 2020 (26)	To assess the association between pre-diagnosis and post-diagnosis PA on mortality in cancer survivors	November 1, 2018	136 studies	Millions of participants (Breast, colorectal, renal)	Weekly physical activity volumes assessed through self-reported questionnaires and accelerometers	domain of PA (total, recreational and/or leisure time, transportation, occupational, household) Quantified METmin/week	Mortality, survival of cancer survivors	High PA decrease cancer specific mortality (HR = 0.82) decrease greater in breast and colorectal cancer High PA decrease CVD mortality Inverse dose response relation between PA and cancer related mortality
McTiernan *et al.*, 2019 (27)	To review and update evidence on PA on prevention of cancer and survival	February 2018	umbrella review on 18 systematic reviews	Millions (however not reported)	Not discussed	Not discussed	Cancer – breast, colorectal, endometrial, lung	Strong evidence on decrease risk of bladder, breast, colon, endometrial, oesophageal, renal and gastric cancer decrease in risk ratio of 10 – 20%
Takemura *et al.*, 2021 (28)	To evaluate and synthesise the effects of post diagnosis PA on mortality in cancer survivors	3rd February 2021	Fourteen studies for qualitative and 11 for meta-analysis	3,011 participants 53.8 to 68.5 years advanced cancer by stage (IIIB/IV) Lung, colorectal, multiple sites and breast cancer	Home based aerobic and strengthening exercises Mostly quantified by self-rated questionnaires	Intensity: Home based strengthening (not specified) Frequency: 2-3 times/week Duration: 30-60 minutes/ day, 6 – 18 weeks	Survival outcomes of cancer survivors	High PA was not associated with decrease mortality risk Non-randomised trials – significant association (hazard ratio = -0.25) Randomised trials – no association (hazard ratio = 0.08)
Chronic metabolic disorders								
Obesity								
van Baak *et al.*, 2021 (29)	To examine the effectiveness of PA interventions on physical fitness in obese population	December 2019	Eighty-eight citations (66 articles for meta-analyses, n = 3964)	3,964 participants >18 years, >25 BMI 20-75 years, 26.4 – 37.2 kg/m^2	Different training types (aerobic, resistance, combined) Supervised, partially and not supervised 2-70 weeks (median 12 weeks)	Intensity: 50% VO2 Duration: 12 weeks Frequency: 2-3 times/week	Aerobic capacity and muscle strength in overweight, obese	Aerobic ex increase VO2 (MD 4.08 ml/kg/min) Resistance ex increase VO2 (MD 4.52 ml/kg/min) Aerobic > RT in VO2 (-1.40 ml/kg/min) No difference between aerobic and combined aerobic training No difference in muscle strength after ex. intervention Resistance ex increase strength (MD 4.52 ml/kg/min)
Boyer *et al.*, 2023 (30)	To assess the effects of resistance exercise training on insulin resistance in overweight and obese individuals	Not reported	Twenty-seven studies with 402 individual data points	3,402 participants 25-70 years old Predominately male population	Any form of resistance training Supervised, partially and not supervised	Volume: 45 – 80% 1RM, 8-10 reps/set, 2-3 sets/ exercise, 8 exercise/session Duration: 32 weeks Frequency: 2-3 times/week	Fasting insulin and Insulin resistance in obese participants	significant decrease fasting insulin (– 1.03) and HOMA-IR (– 1.05) Males showed greater reduction than females participation in RT significantly reduced IR.
Purgato *et al.*, 2023 (31)	To consolidate the evidence of PA interventions on psychosocial outcomes in overweight, obese children	May 6, 2022	Umbrella review of 18 systematic reviews (112 studies)	21,232 children Included ADHD, CP, respiratory disorders, neuromotor impairment and obese	PA or sport interventions Heterogenous PA intervention (stretching, aerobic, Yoga) Home/ institution based	Volume: 45 – 80% 1RM, 8-10 reps/set, 2-3 sets/ exercise, 8 exercise/session Duration: 32 weeks Frequency: 2-3 times/week	Stress anxiety and depression of the general and special children	PA interventions decrease psychosocial risk Weak association between PA and psychosocial outcomes Effect size small to medium (0.013 – 0.34) PA interventions beneficial to a spectrum of psychosocial outcomes,

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Polycystic ovarian syndrome								
Patten *et al.*, 2020 (32)	To review the efficacy of exercise training on PCOS	May 2019	20 studies systematic review, 19 studies-metanalysis	18-45 premenopausal Diagnosed PCOS BMI = 26.1 to 38.3 kg/m^2 Sample size ranged from 5 - 62	Supervised or unsupervised > 2 weeks Moderate intensity (>55% HRmax or >40% VO2peak) or above	Intensity: moderate, vigorous and high Duration: 30-90 min per session for 8 to 26 weeks Frequency: 2 to 5 sessions per week	PCOS based on Rotterdam and NIH criteria	65% supervised trials (n =13/20) 70% administered aerobic alone increase VO2, glucose tolerance, HDL decrease HOMA-IR, fasting insulin Regulates hormonal markers and reproductive health Vigorous and moderate improved in VO2 by 24% and 18% compared to control while BMI and WC showed only trivial change
Woodward *et al.*, 2019 (33)	To define exercise types that benefit cardiometabolic risk in PCOS	Not Reported	3 studies for quantitative analysis	231 participants (117 intervention and 114 controls) 17-124 participants	Supervised > 2 weeks Moderate intensity (>55% HRmax or >40% VO2peak	Intensity: moderate, vigorous and high Duration: 30 - 45 min, 12-16 weeks Frequency: 3 to 5 sessions per week	PCOS based on Rotterdam and NIH criteria HDL, VLDL, HOMA-IR, WC, WHR Sex hormones (testosterone	High selection bias Significant decrease observed for TC, FBS, WC, WHR, SBP, CRP and DBP Significant increase observed for sex hormone binding globulin
Breyley-Smith *et al.*, 2022 (34)	To determine the effects of exercise on CVD in PCOS women	December 2021	19 studies qualitative and 18 studies quantitative	613 participants (19 studies) 24-32 years Majority inactive	Supervised > 4 weeks Aerobic, resistance or combination of two. Yoga, Pilates excluded	Aerobic (70 – 90% HRmax, 60-70% VO2 max, HIIT4x4, 30-60 min/ session, 2 sessions/week, 8-50 weeks) RT (75%1RM, 3 sets of 10 Reps, 3 sessions/ weeks, 10 weeks)	CRF (VO2), HDL, VLDL, FBS, TG, HOMA-IR, WC, SBP, DBP	No significant differences in CVD risk increase VO2 (WMD 3.85 ml/kg/ min), WC (-1.48cm) SBP increase (WMD -1.88mmHg), and HOMA-IR (-0.17) and FBS (0.08)
Dos Santos *et al.*, 2020 (35)	To synthesise evidence on the effects of different types of exercise on reproductive functions and body composition of PCOS	November 15, 2019	10 citations for qualitative and 8 citations for quantitative analysis	513 participants (10 RCTs) 13-224	Aerobic *vs* control (n = 4) Combined *vs* control (n=2) High intensity aerobic *vs* strengthening (n =1)	Intensity: 60-70%MHR/VO2 max Duration: 25-60 min/ session, 12-16 weeks	PCOS based on Rotterdam and NIH criteria Outcomes: Menstrual cycle, hormones, ovulation rate and fertility)	Little to no effect of exercise on luteinising and follicular stimulating hormones No effect on testosterone and free androgens Aerobic exercise decreaseBMI (SMD = −0.35)
Diabetes								
Rietz *et al.*, 2022 (36)	To summarise the protective effects of physical activity on diabetes complications	July 6, 2021.	Thirty-one studies	Millions of participants who had CVD and diabetes related morbidity and mortality	PA quantified by compendium of PA Dose quantified as METhr/week	Cycling, LTPA, MVPA, total PA and walking Converted to METhr/week	Diabetes-related complications (CVD mortality, stroke, foot ulcers and amputations),	High PA decrease 16% CVD risk High PA decrease 11% CHD risk 10METhr/week decreaseCVD risk, cerebrovascular event, retinopathy and neuropathy
Aune *et al.*, 2015 (37)	To review the evidence that explored the association between PA and risk of T2DM	2nd March 2015	78 cohort (84 publication)	104,908 (14 cohorts)-total PA 1,820,188 (55 cohorts)-leisure time PA 272,599 (8 cohort) – vigorous 184067 (5 cohort) – moderate PA 107269 (3 cohort) – light intensity	Total PA Light intensity and MVPA based on Ainsworth classification Leisure time extracted from studies	Dose calculated based on HUNT (45 min/ session), frequencies/ week and converted to METhrs/week- (Ainsworth classification), Moderate (<5.5MET) and vigorous (>5.5MET)	Diabetes (based on self-report, physician-diagnosed, record linkage, diabetes diagnosis based on medication use)	Highly active *vs* low active RR decrease 0.65 total PA, RR decrease 0.74 leisure PA, RR decrease 0.61 vigorous PA, RR decrease 0.68 moderate PA, RR decrease 0.66 low intensity PA, RR decrease 0.85 total PA Steeper reductions with low activity than high activity 300 minutes (5 – 7 hrs) of leisure, MVPA, walking or resistance reduce risk

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Amin *et al.*, 2023 (38)	To determine the effect of PA on metabolic markers in T2DM patients	August 2022	26 articles	3,336 participants (ranged from 20-794 participants)	Intensity, frequency and duration of PA (aerobic, resistance or alternate) 3-month follow-up	aerobics, resistance, and combined (aerobics plus resistance) Dose - Not reported	Metabolic syndrome markers (BP, TG, HDL, FBS and WC) in patients with T2DM	Aerobic ex decreaseWC (-0.34 cm) No significant differences in BP, TG, HDL, FBS Resistance ex observed lower trends in BP, WC but not statistically significant Low heterogeneity was seen
Wahid *et al.*, 2016 (39)	To review the evidence explored the association between PA and CVD in diabetes	March 2014	36 studies	3,439,874 participants and 179 393 events, average follow-up period of 12.3 years	Self-reported PA Time, frequency, duration and intensity was estimated	PA exposure was converted to METhr/day PA compendium Light intensity (2.5-4.5), moderate (4.5-6.5) and vigorous (> 6.5)	CVD mortality, T2DM, Heart failure incidence, CHD incidence	Meeting PA goal decrease CVD mortality by 23%, CVD incidence by 17%, T2DM by 26% CVD decrease (RR = 0.83), CHD mortality decrease (RR = 0.80), T2DM (0.74) increase11 METHrs/day
Chronic musculoskeletal disorders								
Osteoporosis								
Pinheiro *et al.*, 2020 (40)	To investigate the association between the PA and the osteoporosis risk in elderly	July 2020	59 studies (36 included from world health organisation guidelines)	2,943 elderly people with frailty, osteopenia, hip #, tennis athletes who are at risk for osteoporosis	92.5% (n=37/40) studies compared PA *vs* control	Aerobic: Frequency (3times/week), Intensity (65-90% HR_{peak}), Time (30-60 min/session) RT: F (3times/week), I (40-80%1RM), T (3sets of 16 reps, 30-60 min/session) 12 months (3-144)	Old individuals not having the diagnosis of osteoporosis at the initial stage BMD	Aerobic: significant but relatively small overall effect of exercise on osteoporosis prevention Femoral spine BMD (SES = 0.09) Lumbar spine BMD (SES = 0.17) Resistance training, balance and functional ex were not significant for BMD
Zouhal *et al.*, 2021 (41)	To evaluate the efficacy of PA on bone health in obese individuals	December 2019	10 studies	263 participants of 8 countries	Aerobic, resistance and combined training with dose specified Training duration at least 12 (8 – 48) weeks	Aerobic: F (not specified), I (60-75%VO2max), T (30-60 min/session) RT: F (3times/week), I (50-75%6RM), T (3sets, 10-15reps, 30-60 min/session)	Osteoporosis (BMD)	Trial impact on BMD (SMD 0.13) Aerobic ex significant (SMD 0.27) Non-significant resistance (SMD 0.11) Non-significant combined (SMD 0.03) PA increase BMD in obese
Low backpain								
Alzahrani *et al.*, 2019 (42)	To investigate the association between domain specific PA and the low backpain	March 2017	35 studies for quantitative and 24 quantitative analysis	106,776 (35 studies) 95796 (24 studies)	Intensity graded based on the compendium of PA Self-administered questionnaires (n = 33) 2 studies accelerometers	Weekly dose calculated based on frequency, intensity and duration in week TPA (n = 7), LTPA (n = 9)	Risk of developing low back pain	High-level PA not associated with LBP medium level LTPA decrease LBP (RR=0.90) Inverse association between physical activity and LBP No evidence on dose response
Shiri *et al.*, 2018 (43)	To review the evidence exploring the benefit of exercise in preventing LBP	June 2017	16 trials	4,310 participants from 13 RCTs and 3 RCTs	Strengthening, stretching, spinal mobility exercises 2-24 months	Combination of stretching, strengthening, aerobic was sought Not reported dose	Prevalence of LBP, new episode during follow-up	Exercise decreaseLBP by 33% (RR 0.67%) Effects not differed with short term ex (<9 months) Strengthening exercise and stretching ex (RR0.5) Strengthening exercise and aerobic ex (RR0.7)

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Osteo/rheumatoid arthritis								
Ye *et al.*, 2022 (44)	To evaluate the effectiveness and safety of aerobic exercise for rheumatoid arthritis	January 2022	13 RCTs	967 RA participants	Aerobic (bicycle riding, treadmill walk, jog, run)	Not reported or quantified	Disability, severity and functional capacity of rheumatoid arthritis	Disability index decrease in intervention than control (MD = -0.25) Disease activity score decrease in intervention than control (MD = -0.55) Long term aerobic ex decrease CRP (-2.28) and pain (-0.46) and increase VO2 (2.41), STS (1.6), but not ESR
Sasaki *et al.*, 2022 (45)	To investigate the effectiveness of PA on pain in OA patients	April 30, 2022	20 studies (7 exercise, 8 educational and 5 combined)	1,355 participants (n = 7),	Land or aquatic based ex aerobic exercise, strengthening, stretching, mind-body exercise and combined interventions	Aerobic Intensity: 40-60% HRmax, RPE – 13-15 Frequency:2-3 times/week Duration: 6-16 weeks Mode: walking cycling, home exercise Resistance Volume: 2-4 sets, 8-12 reps, 60-70%1RM	PA and pain in osteo/rheumatoid arthritis	Pain decrease in intervention than control (SMD = -0.25) Pain decrease in intervention than control (SMD = -0.25) Long term aerobic ex decrease CRP (-2.28) and pain (-0.46) and increase VO2 (2.41), STS (1.6), but not ESR
Chronic kidney diseases								
Seidu *et al.*, 2023 (46)	To review the evidence exploring the effectiveness of PA in reducing CKD risk	May 2, 2022	12 observational cohort studies	1,281,727 participants	Maximum *vs* minimal amount of PA	Heterogenous (moderate *vs* low, any *vs* never, regular *vs* irregular, 150 min/week *vs* no	66217 CKD events risk	Most physically active has lower risk (RR = 0.91) than least active High heterogeneity most physically active groups were associated with a 9% lowered risk of CKD compared to least physically active.
Villanego *et al.*, 2020 (47)	To review the evidence of physical activity on patients with CKD	Until 2018 (not reported date)	21 studies	927 patients (n=21) Glomerulopathies, DM, nephroangiosclerosis and polycystic kidney disease	Aerobic or resistance training (mostly supervised)	Aerobic Frequency: 3-6 times / week Intensity: 40-60% VO2 max, RPE – 11-15 Duration:45-50 min/day Resistance Volume: 2-4 sets, 8-12 reps, 80%1RM	Kidney disease progression (CKD, VO2max)	No differences in GFR Significant favourable effects on VO2 (SMD 2.5), functional capacity (SMD 56.6), upper limb strength (SMD 6.8) and haemoglobin (SMD 0.3) increase quality of life
Yamamoto *et al.*, 2021 (48)	To elucidate the efficacy of aerobic exercise in patients with CKD	July 30, 2019	15 trials	622 patients (n = 15) 11-111 participants 75% trials BMI>30.0 kg/m^2	80% aerobic alone while 20% combined	Not reported	Cardiometabolic and renal outcomes in CKD	aerobic exercise decreaseBMI (SMD, -0.19) Aerobic exercise increase Vo2peak (0.54) no significant difference in HbA1c, TC, HDLC, LDLC, GFR, and UP decreaseage, decreaseBMI, no diabetes - increase Vo2peak
Zhang *et al.*, 2022) (49)	To investigate the effects of exercise on health outcomes in CKD	March 9, 2021	Umbrella review of 31 systematic reviews	314 CKD patients (106 – 874)	Predominately aerobic, few resistance combined Few intradialytic approach	Not reported	CVD risk, CRF, muscle strength and endurance, dialysis adequacy and symptoms in CKD patients	Small effect on BPdecrease (SMD 0.2 – 0.43) 89% of the studies showed favourable effects on CRF Moderate positive effects on muscle strength Muscle endurance (sit-stand test, walk capacity) increase Positive impact on body composition Beneficial effect on symptoms and dialysis adequacy

Author (year)	Objective	Search updated	Total no of studies	Participants	Physical activity studied	Dose	Chronic disease risk assessed	Key findings
Chronic neurological disorders								
Stroke								
Ada *et al.*, 2006 (50)	To find the efficacy of resistance training following stroke	January 2005	21 trials investigating weak and very weak stroke patients	Age 50 to 70.5 years; (Acute: 2 weeks - 4.5 months, and chronic 2 to 8 years	Electrical stimulation, biofeedback and muscle re-education	4–8 weeks, 5–7 days /week, for 45–150 minutes per day	Acute and chronic stroke subjects	In acute, interventions increase 0.33 (95% CI 0.12 to 0.78, p = 0.01) In chronic, increase strength by 0.18 SD (95% CI –0.22 to 0.58, p = 0.38). Strength training increase strength in acute phase but failed in chronic stage increase strength without increasing spasticity
Adamson *et al.*, 2015 (51)	To review the effect of PA on depressive symptoms in stroke	May 2014	26 trials (23 meta-analysed)	1,324 patients with 7 neurological disorders	Aerobic exercise, resistance training, balance training, yoga or its combination	Varied greatly in frequency, intensity and duration (4 weeks to 12 months.) Frequency: once/ week to daily	Depressive symptoms in neurological disorders	PA decreasedepression symptoms (0.28) Overall effect 0.38 who met PA guidelines In multiple sclerosis, effects are larger (0.36)
Field *et al.*, 2013 (52)	To determine the levels and predictors of PA after stroke	July 2012	Twenty-six studies (11 meta-analysis)	1,105 stroke patients (n =26) Age = 52.8 yrs to 72.6 yrs Stroke (3-8 years)	80% of studies (pedometer/ accelerometer) Six self-reported	Step count (pedometers) Heart rate monitors Not reported dose directly	PA levels after stroke	estimate of 4355.2 steps/day after stroke EE = 155 – 321 Kcal/day Active less than 20% of the day increase habitual walking speed (MD 0.07m/s) and increase walking endurance (MD 39.2m).
Alzheimer's and dementia								
Iso-Markku *et al.*, 2022 (53)	To examine whether the PA is a protective factor for all-cause dementia, Alzheimer and vascular dementia	19-26 October 2021	58 articles (420114 participants)	257,983 (All cause dementia) 128,261 (Alzheimer's) and 33 870 (vascular dementia) Follow-up of 20 years	Single bouts, retrospectively reported PA, leisure time / work related PA	Dosage not reported Met PA guidelines/ not met PA guidelines	Incidence of vascular and all cause dementia, Alzheimer's	PA decreaseall cause dementia (RR 0.80) PA decreaseAlzheimer's (RR 0.86) PA decreasevascular dementia (RR 0.79) Dose response ex showed linear spline and quadratic trends
Stephen *et al.*, 2017 (54)	To systematically evaluate the association between PA and the risk of Alzheimer's	June 2015	24 longitudinal observational studies	176 to 5,698 participants	Leisure time and household PA Frequency, Intensity and duration were quantified >6 years follow-up	Dose quantified on basis of frequency, intensity and duration. Few studies on compendium of PA	Alzheimer's risk	PA decreaseAlzheimer's (hazard ratio 0.82) ≈80% assessed PA using questionnaires Only 25% had good follow-up LTPA inverse relationship with the PA Occupational/ commuting PA not associated

ADHD: attention deficit hypersensitivity disorder, AT: anaerobic threshold, BMD- bone mineral density, BMI: body mass index, BP: blood pressure, CABG: coronary artery bypass graft, CHD: coronary artery disease, CKD: chronic kidney disease, CI: confidence interval, CRF: cardiorespiratory fitness, CRP: C reactive protein, CVD: cardiovascular disk, D: duration, DBP: diastolic blood pressure, ESR: erythrocyte sedimentation rate, F: frequency, FBS: fasting blood sugar, GFR: glomerular filtration rate, HbA1C: glycated haemoglobin, HDL: high density lipoprotein, HIIT: high intensity interval training, HOMA-IR: homeostatic model assessment for insulin resistance, HR: heart rate, HRR: heart rate reserve, I: intensity, LBP: low back pain, LDL-C: low density lipoproteins cholesterol, LTPA: leisure time physical activity, MACE: major adverse cardiovascular events, MD: mean difference, MET: metabolic equivalent, MHR: maximal heart rate, MI: myocardial infarction, MICT: moderate intensity continuous training, MVC: maximal voluntary contraction, MVPA: moderate-vigorous physical activity, OA: osteoarthritis, ORR: odds ratio, PA: physical activity, PCOS -polycystic ovarian syndrome, RCT: randomised controlled trial, RHT: resistant hypertension, RM: repetition maximum, RPE: rate of perceived exertion, RR: risk ratio, RT: resistance training, SBP - Systolic blood pressure, SMD: standardised mean differences, STS: sit to stand, T2DM: type II diabetes mellitus, TC: total cholesterol, TG: triglycerides, TPA: total physical activity, UP: urea protein, VO2max: maximal oxygen consumption, WC: waist circumference, WHR: waist hip ratio, WMD: weighted mean difference.

as diabetes and obesity (n = 11, 28%), musculoskeletal disorders (n = 6, 14.63%), neurological disorders (n = 5, 12.20%), kidney disorders (4, 9.76%) and cancer survivors (n = 3, 7.3%). Few of the systematic reviews have analyzed millions of participants (28, 29, 34, 48, 55). With the above data, potentially favorable effects were observed for blood pressure, CVD risk and mortality, cardiorespiratory fitness, cancer mortality and risk (colorectal, breast and lung), insulin resistance and diabetes complications. Further physical activity was found to influence neurohormonal regulation, leading to favorable psychological outcomes and musculoskeletal outcomes such as backpain and bone mass in later life period (42, 53, 56). Differing doses of physical activity influences the chronic disease risk in unique way. Most favorable responses were observed for moderate to vigorous physical activity while the favorable effects on chronic disease risk with low physical activity is still accumulating. While high leisure time physical activity was found favorable in prevention of chronic disease, high occupational physical activity was found to be detrimental to cardiometabolic health (59). Leisure time physical activity of any volume and supervised exercise training of optimally dosed found to have protective effects on cardiometabolic, neuromuscular and bone health while reducing cancer risk and hospitalization (60).

Movement behaviors and chronic disease

Modern community dwelling adults spent their substantial proportion of their day in sedentary (9-11 hrs.) and only a fraction of their typical day is spent in moderate/vigorous physical activity (0.3-0.5 hrs.) (61). Further only fraction of global population meets the national recommendations on weekly dose of MVPA (150 minutes per week) (62). This increased sedentary behavior and reduced MVPA is linked independently to hyperglycemia, insulin resistance, hypertension, poor lipid oxidation, reduced energy expenditure, predominance to glucose metabolism shift from fat metabolism, poor metabolic flexibility, increased inflammatory and poor immune response, bone mineral density loss and increased body mass eventually leading to chronic disease risk (diabetes, cancer, obesity, hypertension, atherosclerosis, cardiovascular diseases, osteoporosis and neuromuscular diseases). **Figure 3** depicts physical activity and its influence on various physiological factors leading to chronic disease risk. The inner circle represents the domains of physical activity and time duration spent in each domain on a typical workday. The middle circle represents the putative physiological factors linking the domains of physical activity (inner circle) and chronic diseases (outer circle).

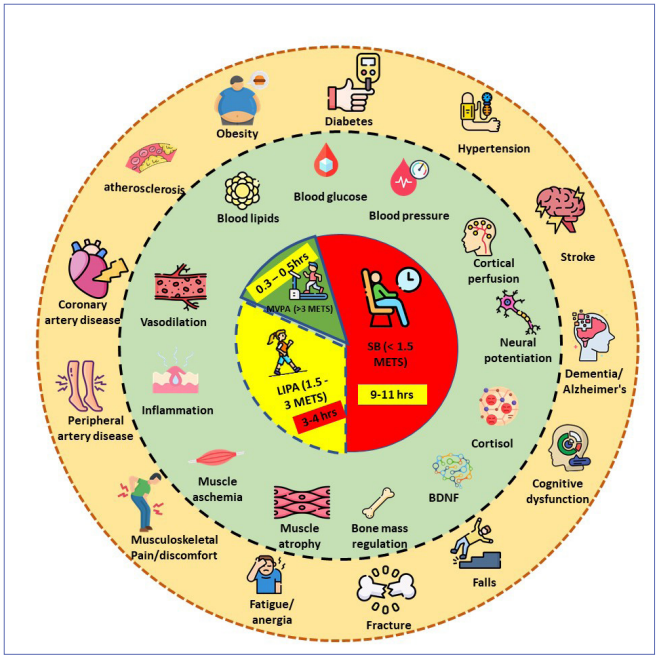


Figure 3. Physical activity and its influence on various physiological factors leading to chronic disease risk. Inner circle represents the domains of physical activity and time duration spent in each domain in a typical workday. The middle circle represents the putative physiological factors linking the domains of physical activity (inner circle) and chronic diseases (outer circle).

Therapeutic effects of physical activity in chronic diseases

Hypertension

The prevalence of hypertension (defined as raised blood pressure with systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg) is estimated to be 1.28 billion adults aged 30-79 years (63). Though one of the global targets of WHO is to reduce hypertension by 33% by 2030, it seems nearly impossible to achieve the target as 2/3rd of the global hypertensives live in low-middle income countries where access to optimized medical management and dietary counselling are fairly implausible (64). However, physical activity is still credible as a viable lifestyle measure for individuals from low-middle income countries.

Physiology behind the therapeutic effects of PA

Physical activity combats hypertension through local and central pathways such as enhanced endothelial functions (regulation of endothelin dependent vasodilator function, production of nitric oxide synthetase through improved shear stress), angiogenesis through vascular endothelial

growth factor production, reduced systemic vascular resistance, regulating autonomic stability (lowered sympathetic nervous system activity) and enhanced baroreceptor sensitivity (65). Further optimized physical activity exerts check on the aldosterone and angiotensin production there by regulating blood pressure and vascular protection. Also, physical activity enhances fatty acid metabolism, regulates the fat deposition in arteries and atherosclerosis thereby enhancing pulsatile stretch and vascular compliance in the long term. Nevertheless, physical activity also controls oxidants and inflammation there by reducing the chance of arterial stiffness (66).

PA recommendations and efficacy

Aerobic activity: exercising larger muscle Aerobic exercise impro (-3.84 mm Hg [95%CI -4.97 to -2.72 mm Hg] and -2.58 mm Hg [CI -3.35 to -1.81 mm Hg], respectively (67)). Walking, jogging or swimming for 30 to 45 minutes daily, at least 5 days a week totaling a weekly dose of 150 minutes of moderate-vigorous physical activity for 12-15 weeks for any improvement in blood pressure to be seen. The recommended aerobic intensity is 50-80% heart rate reserve, 60-70% of VO_2 max or age predicted maximal heart rate for observing minimal change in blood pressure (68).

Resistance training activity: larger muscles of upper (pectoral, latissimus, rhomboids and deltoid) and lower body (hamstrings, quadriceps, gastrocnemius and soleus) to be trained using weight or resistance training machines for 10-15 reps per set, 2-5 sets per session, frequency 3 sessions per week, minimal 8 weeks using intensity of 30-40% one-repetition maximum for upper body and 50-60% 1 RM for lower body is recommended (68).

Yoga: a systematic review on seventeen studies showed that Yoga had a modest but significant effect on SBP (-4.17 [95%CI 6.35, 1.99]) and DBP (95%CI 3.62 [4.92, 1.60]) (69).

Taiichi/Qigong: Tai Chi encourages individuals to focus on slow and graceful motions similar to fluid, encompassing balance, core stability, flexibility and graceful limb movements. 3 to 4 movements per session, single session per day, 60 minutes a day, twice a week for at least 12 weeks (70, 71).

Coronary artery diseases

Coronary artery disease is the single most risk factor for global mortality and loss of disability adjusted years (72). Compromised coronary blood flow leads to several complications not limited to acute coronary syndrome, myocardial ischemia and infarction leading to stroke and other fatal events. Physical inactivity and sedentary behavior are identified to be the independent risk factors for chronic heart diseases (73). Physical activity of any intensity is now confirmed to have favorable effects on coronary perfusion and myocardial oxygen viability and longevity (74).

Physiological benefits

Physical activity offers protective and therapeutic benefits to coronary artery diseases (74). Physical activity when optimally dosed, acts at endothelial level to increase expression and phosphorylation of the endothelial isoform of nitric oxide (NO) synthase, which produces a more effective radical scavenger system (75). Further physical activity rejuvenates endothelium by increasing circulating progenitor cells, neointima formation and angiogenesis, which promotes the growth of pre-existing coronary vessels (76). Increased vascular NO production, decreased reactive oxygen species production, regeneration of the epithelium through stimulation of endogenous progenitor cells, and myocardial expression of vascular growth factors (which in turn promote NO production in the heart). Significant evidence exists to claim the holistic benefits of physical activity such as improved aerobic capacity, muscular strength, reduced blood pressure, tobacco cessation, increased glucose tolerance and glucose sensitivity, regulates blood lipid profile and inflammatory cascade further arresting the progression of disease and improvement in functional capacity and quality of life (77). Yogic postures regulate vagal stimulation and parasympathetic stimulation, thereby improving inflammatory and heart rate profiles, glucose and lipid profiles, perceived stress, regulate sympathetic-adrenal and pituitary hypothalamic axis and inhibits oxidative stress eventually leading to reduced myocardial oxidative stress and improved endothelial function (78).

Dose recommendations

Aerobic activity: intensity (50-90% HRmax, 50-95% VO_2 max, RPE 11-16), frequency 2-5 sessions per week for 8-12 weeks and duration (20-90 min) (22). In case of any peripheral vascular claudication, critical walking speed and pain threshold to be determined and prescribed accordingly.

Resistance training activity: intensity: 50 to 80% of 1RM, 8-12 reps/sets, 2-3 sets, 1 min rest between sets, 2-4 large muscles a day, duration: 4-8 weeks, frequency: 2-5 times/week (79). Evidence cautions against Valsalva maneuver during heavy resistance exercise (< 85% 1RM) for small muscles contraction due to increased arterial stiffness and after load demanding undue myocardial oxygenation (79).

Yoga: Hatha Yoga includes stretching exercises and physical postures (Asanas), breath control (Pranayama) and concentration techniques (Meditation). Dearth of evidence to quantify the yogic posture interventions for coronary artery diseases.

Cancer

Accumulation of genetic mutations due to exposure to dietary and environmental factors such as ultraviolet radiation, viruses and tobacco eventually impairing immune functions and leading to cancers (80). Lifestyle factors such as physical activity play a crucial role in prevention and therapeutic management of cancer and morbidities.

Physiology behind the therapeutic effects

Physical activity in the form of structured exercise program is viewed as an adjunct strategy for manipulation of immune function and inflammation through moderating inflammation-immune axis thereby emerging as a viable and robust treatment for few cancers including lung, prostate, colorectal and breast cancers (81). Physical activity found to influence inflammatory cytokine (interleukin, tumor necrosis factor), regulate metabolic hormones (insulin, leptin, cortisol), optimize lipid profile and improve innate immunity (T cells, natural killer cells) and neutrophil surveillance (81). Further exercise inhibits muscle atrophy, bone loss, tissue damage associated with radiotherapy and maintains the muscle mass, thereby reducing cancer related muscle fatigue and anergia (82).

Evidence behind PA and recommendations of the dose

Aerobic activity: prolonged activity of larger muscles such as swimming, cycling, walking and cycling are found to be efficacious in prevention and therapy of cancer and its comorbidities. With intensity of 50-75% VO_2 max or 60-85% MHR or RPE – 11-16, frequency of 3-5 sessions/week and duration of 30-45 minutes/session, 6-18 weeks, aerobic activity is found to favorably thwart risk of cancer or its complication.

Resistance training activity: upper quarter (pectoral, latissimus, rhomboids and deltoid) and lower quarter (hamstrings, quadriceps, gastrocnemius and soleus) of the body to be trained using dumbbells and elastic tubes (80). With volume of 50 – 80% one RM, 8-10 reps/set, 3-6 muscles, weekly 2-3 times would seem to mitigate the muscle and bone loss with cancer therapy.

Flexibility: post radiotherapy fibrositis or post-surgical flaps induce soft tissue stiffness and flexibility exercises for upper and lower body play a major role in combating soft tissue stiffness induced by radiation and post-surgical musculoskeletal fitness and excisions (83). Stretching pectoral and neck muscles for at least 30 seconds in the pain free range after musculocutaneous flap reconstruction. Hamstring and quadriceps stretch twice a day at least 3 days a week improved the workability of the cancer survivors.

Caution during physical activity with cancer survivors

The available literature is for prevention and therapeutic management of early cancer while advanced cancer is still limited (84). Further the overdose of exercise volume on the muscle damage and the inflammatory cascade is at infancy. The exercise professional should monitor for exercise tolerance and dose to be titrated based on fatigue and sleep issues that are common with cancer therapies. Further appropriate clearance for moderate- vigorous training is recommended for those who have cardiac morbidities along with primary cancer and post flap reconstructions (83).

Obesity

Obesity is defined as having a body mass index (BMI) of 30 kg/m^2 or greater, with excessive accumulation of fat in the adipose tissues or dysregulated energy metabolism due to imbalance in leptin and ghrelin (85). Reduced prevalence and incidence of obesity are crucial since it increases susceptibility of a person's risk of cancer, stroke, metabolic disease, heart failure, and other cardiovascular problems. It is hypothesized that obesity-related chronic low-grade inflammation is linked to unfavorable cardio-metabolic side effects. Even though short-term inflammation is useful for triggering an immunological response, inflammation that is chronically increased wears down the immune system and promotes immune dysfunction leading to cardiometabolic and cancer risk (86).

Physiology behind therapeutic effects

Moderate-vigorous intensity exercise increases lipolysis, increased insulin sensitivity, restoration of glycogen deposition, increased oxidative phosphorylation and protein turnover (87). Recently low-intensity PA is found to be equally effective in lipolysis and cardioprotective in obese population (88). Local reductions in adipose tissue, decreased inflammation, increased vascularity, reduced fibrosis, smaller adipocyte size, enhanced insulin sensitivity, increased stress responsiveness, and reduced resting lipolysis are key protective mechanisms against obesity. Additional mechanisms that may mitigate obesity risk include improved metabolic flexibility, enhanced mitochondrial function, reduced ectopic lipid deposition, and increased glycogen storage in peripheral muscles (89).

Recommendations of PA for obesity

Aerobic activity: Intensity: 70-90% HRmax, 60-70% VO_2 max, 30-60 min/session, 2 sessions/week, 8-12 weeks. Aquatic exercises are suggested to offload the joints and improve the aerobic capacity. Cycling is a commonly administered mode of training for partial weightbearing.

Strengthening activity: volume: 45-80% 1RM, 8-10 reps/set, 2-3 sets/exercise, 8 exercise/session, duration: 32 weeks and frequency: 2-3 times/week (32, 33).

Type 2 diabetes mellitus (T2DM)

Globally, 537 million adults aged 20 to 79 (10.5%) are affected by diabetes, a group of metabolic disorders characterized by chronic elevation of blood sugar levels due to defects in insulin secretion (T1DM) or insulin action (T2DM) (90). T2DM leads to CVD, stroke, blindness, retinopathy, neuropathy, nephropathy, amputation leading to fatal events of death (91).

Physiology behind therapeutic effects

Physical activity improves the glucose uptake through two physiological mechanisms (91): 1) contraction signaling pathway – acute aerobic or resistance exercise improves the lean body mass either size or the number improving the storage and uptake of glucose independent of insulin. Muscle contractions improve GLUT4 translocation and non-insulin dependent glucose uptake and storage in muscle (92); (2) insulin mediated pathway – physical activity improves insulin sensitivity, which is a potent stimulator of glucose uptake in muscles. Aerobic exercise improves whole-body insulin sensitivity, glycogen synthesis activity and GLUT4 protein expression (91). Further physical activity improves storage of lipids in muscle and fat oxidation, which are speculated to be crucial factors for improved insulin sensitivity and action. Further exercise is found to reduce visceral fat mass and hepatic triglyceride and mitigate the cardiometabolic risk associated with the T2DM (93). Further improved hemoglobin and kidney functions leading to improved quality of life with reduced incidence of diabetes related co-morbidities are observed with the appropriately dosed exercise training (91).

Physical activity dose recommendations

Aerobic exercise: frequency: 3-5 times/week, mode: treadmill, cycling, intensity: 50-80% VO_2 max of 60-85% HRmax, continuous, duration: 30-40 minutes. High intensity interval training is often claimed to have superior benefits for insulin sensitivity however, risks of cardiovascular and musculoskeletal injury could not be excluded.

Resistance exercise: 4-6 large muscles, upper quarter, core and lower quarter, 50-70% of 1RM or 60-90% of 8RM, 8-12 reps/set, 2-3 sets/session, twice a week for 8-12 weeks

Balance exercise: as neuropathy is associated with T2DM with compromised proprioception, balance exercise is advocated (94). Sit to stand, single leg stands with closed or open eyes with/ without foam twice a week are recommended for T2DM patients.

Yoga: yoga is speculated to improve diabetes and complication through psycho-neuro endocrine and immune mechanisms (95). Breathing practices and standing, prone yoga postures for 20-30 minutes, 4-6 days a week, for 3-6 months have found to favorable effects of insulin, HbA1 and postprandial hyperglycemia (95).

Caution with exercise

Before any moderate to vigorous exercise test or training, the exercise professional shall ensure high caution in undermining cardiovascular diseases, microvascular and autonomic neuropathies (93). Exercise of vigorous intensity should be avoided or postponed for several hours immediately after a full dose of fast acting insulin was administered (96). Individuals with peripheral neuropathy who have any unhealed or acute foot ulcers may still be unable to engage in MVPA (93). Referral to physicians may be necessary if the patient shows symptoms of exertional dyspnea as silent myocardial ischemia is rarely seen, however cannot be ruled out during high intensity exercises.

Osteoarthritis and rheumatoid arthritis

Osteoarthritis and rheumatoid arthritis are the clinical and pathological outcome of various conditions that cause synovial joints to fail structurally and functionally due to articular cartilage loss and erosion, subchondral bone changes, meniscal degeneration, synovial inflammation, and osteophytes, which are growths of bone and cartilage (97, 98). Rheumatoid arthritis, an autoimmune disease, higher in female characterized by pain and swelling around the joints leading to mobility limitation and reduced quality of life (99). Physical activity is found to be an imperative measure to improve mobility and strength while long term exercise is found to control inflammatory cascade and disease progression in arthritis patients.

Physiology behind the therapeutic effects

Physical activity is found to improve weight loss and muscle strength thereby improving the load distribution to the weight bearing joints and prevention of the cartilage damage and inflammatory cascade (100). Further, physical activity is found to improve or maintain joint range of movement, thus improving activities of daily living and functional limitation (101, 102). In patients with osteoarthritis, isometric and lower quarter closed kinematic chain exercises found to strengthen the quadriceps, thereby supporting and offloading the joint stress (103). Aquatic exercises are speculated to relax the stiffened joint, ease the pain through neurohormonal and pain gate closure mechanisms and enhance neuromotor control of the lower limbs, however the evidence is still emerging (104, 105).

Recommendations of the dose
Aerobic exercise: intensity: 40-60% HRmax, RPE – 13-15, frequency: 2-3 times/week, duration: 6 -16 weeks, mode: supervised or unsupervised walking cycling. To be cautious with treadmill, during weight bearing activities and wear appropriate footwear not causing undue load stress in rocker bottom foot or limb length differences (105).
Resistance exercise: 4-6 large muscles, upper quarter, core and lower quarter, 50-70% of 1RM or 60-90% of 8 RM, 8-12 reps/set, 2-3 sets/session, twice a week for 8-12 weeks. Free body weight exercises are recommended as to offload the inflamed joints.
Flexibility: hamstring and quadriceps stretch in a pain free range, 10-20 seconds stretch, 3 stretches/session, 2-3 times a week are recommended for osteoarthritis. However, pain free stretches to smaller joints are advised for rheumatoid arthritis patients (106). Emerging evidence claims yoga postures could improve flexibility in arthritis patients.
Balance exercise: challenges to postural stability, limits of stability, weight shifts manually using perturbation/wobble/roller boards or electronic balance training systems are encouraged (107). The balance exercises should be advocated for 60 minutes/session, once a week for 12 weeks to attain a minimal balance improvement in arthritis patients.

Chronic kidney diseases

Though low prevalence (4.83-4.98%), chronic kidney diseases ("characterized by low glomerular filtration rate and albuminuria for at least 90 days") are emerging as leading cause of mortality and challenges present health care systems and global economy (108, 109). The primary risk factors for CKD are diabetes, hypertension and physical inactivity. The beneficial effects of physical activity on incidence and disease progression in CKD is emerging.

Physiology behind the therapeutic effects
Physical activity, when appropriately dosed and combined with low protein diet is found to improve glomerular filtration rate and delay the albuminuria onset eventually leading to delay the progress of kidney diseases (110). Moderate intensity exercise is found to reduce the blood pressure and hyperglycemic levels which are linked with higher arterial stress, stiffness and viscosity posing risk to renal tubular damage (111). Further physical activity is found to delay the muscle damage and atrophy associated with therapeutic options for kidney diseases (steroids and dialysis) by regulating muscle lipid-glucose metabolism and fiber switchover (112). Nevertheless, chronic exercise is found to be linked with lower inflammatory immune profile, osteoclastic activity, reduced angiotensin and cardiac remodeling (113). Thus, exercise is found to improve cardiorespiratory fitness, psychological, social health and overall quality of life

Recommendations of the dose
Aerobic exercise: endurance exercises (walking, running, cycling) at RPE 13-15 (somewhat hard) with a duration of at least 60 minutes per day (interspersed throughout the day in 5-10 minutes bout. While the recommended duration is 12-24 months, emerging evidence points out at least 24 months is needed for attaining metabolic benefits (113).
Resistance exercise: 4-10 exercises, 2 large muscles/day, upper quarter, core and lower quarter, 55-65% 1RM or 65 -85% of 8RM or RPE 13-17 (somewhat very hard), 8-12 reps/set, 2-3 sets/session, twice a week for 8-12 weeks (51, 114). Aquatic exercises (40-50% VO_2 peak, 30 minutes, twice weekly, 32 weeks) are found to be safe endurance exercise as it abates vasoconstrictive and orthostatic problems associated with the land-based exercises (115).
Balance exercise: static and dynamic balance exercises (standing with feet together or one leg, balance board, walking toe to heel), 10 reps/set, 2-3 sets, 3 times/week with a duration of 90 minutes, 8-12 weeks could significantly improve balance and renal outputs in CKD patients (51, 114).
Yoga: asanas (supine, sitting and standing postures) – 15-20 min, breathing exercises (10-15 min), imagery and mindfulness for 5-10 minutes, with a total duration of 30-40 minutes, 5 days a week, 3-6 months has found to improve renal functions (serum creatinine, potassium, sodium and urea) and quality of life scores in CKD patients (116).
Caution with physical activity in CKD patients: Heavy weight bearing activities should be gradually dosed in CKD patients as osteoclastic activity and lower bone mineral density are commonly observed due to steroid intake and dialysis. High impact jumps and hops should be avoided. Water intake should be moderated as water loss is common with intense exercise and both low and high blood volume with more water intake taxes renal load. In CKD patients undergoing dialysis with indwelling catheters, strenuous resistance exercise of limbs should be avoided as undulating stress on catheters and resulting vascular dehiscence becomes unavoidable. Further, appropriate physician's medical advice should be sought before maximal exercise testing and training in CKD with other cardiovascular comorbidities.

Stroke

Stroke, a disorder characterized by disrupting the blood supply to the brain either ischemic or hemorrhagic conditions, is a leading cause of morbidity and mortality globally (117). GBD 2019 study claims a significant increase in absolute number of incident strokes by 17% from 1990-2019

with an estimated global prevalence of 101.5 million people (118). Sedentary behavior and physical inactivity are identified as independent risk factors of stroke by increasing risk of hyperglycemia, hyperlipidemia and undulant stress to the endothelium eventually leading to atherosclerosis and arterial stiffness (119). Strokes can be recurrent based on the presence of underlying risk factors causing paralysis, residual disability and early death (120)

Physiology behind the therapeutic effects: Optimally dosed physical activity is found to enhance cardiovascular functions: peak oxygen consumption, optimize central blood volume and flow, autonomic functions including resting heart rate, peak left ventricular ejection fraction, and overall exercise capacity which in turn reduce the chance of recurring stroke (121, 122). Further neuromotor training is found to improve balance, gait, and strength through enhancing neuromuscular control and spasticity reduction thus enhancing functional mobility, independence and quality of life in stroke patients (123). Nevertheless, engaging in health enhancing physical activity is perceived to improve mood, reduce post-stroke depression there by improving mental health and leading active social life (124). Physical activity increases confidence in functional mobility and independence eventually reduces the care giver burden.

Recommendations of the dose

Aerobic exercise: exercise that activates large muscle (body supported treadmill walking, one leg or arm cycling or seated stepper) at 40-60% heart rate reserve or RPE 12-14 (somewhat hard) with the duration of at least 20 minutes per day for at least 8 weeks and 3 sessions/week (125). At least bouts of 5 minutes should be accumulated though "any movement count" works with stroke survivors.

Resistance exercise: 2-3 exercises, one large muscles/day, both affected and non-affected side, 50% 10 RM to 70-80%1RM, 8-10 reps/set, 2-3 sets/session, 60-90 minutes/session, twice a week for 8-12 weeks (126).

Balance exercise: 2-3 sessions/week, 45-60 minutes/session, standing balance, sit-stand tasks, challenging with eyes closed and unstable surfaces, using various fundamental postures, 10 reps/set, 2-3 sets per day interspersed during day (127).

Yoga: Ancient Yogic exercises in the form of asanas, breathing control and meditation are found to improve the functional ability and mental health in post stroke survivors. Asanas – 30-40 min, pranayama 10-12 minutes, meditation 20-30 minutes with a total of 60 minutes/session, twice weekly and 8-12 weeks (128).

Tai-Chi: Tai-Chi was found to significantly improve the activities of daily living, upper limb functions, balance and walking ability among stroke survivors (129). Taiichi of moderate intensity (4.5 METS) for 45-60 minutes/session, twice weekly for 4-52 weeks is recommended (130).

Precautions/pre-screening while considering exercise for stroke survivors.

While beginning exercise, the level of disability and verbal or non-communication should be assessed. Access to basic and advanced life support in the exercise facility should be considered.

Alzheimer's and dementia

Characterized by the extracellular deposition of senile plaques of amyloid and tau protein neurofibrillary tangles, Alzheimer's disease is a fourth leading cause of death in elderly following cancer, CVD and cerebrovascular diseases (131). Increased oxidative metabolism and dysregulation of mitochondrial calcium affects hypothalamus and cortical atrophy eventually leading to dementia (132). Sedentary behavior and physical inactivity perpetuate the dysregulation of oxidative stress and mitochondrial metabolism, increase tau, amyloid protein deposition eventually leading to neuroinflammation, cortical atrophy and dementia (133). Physical activity remains crucial in regulating the pathophysiology of dementia and Alzheimer's disease.

Physiology behind physical activity in Alzheimer's and dementia

Physical activity is speculated to improve cognitive and mental health through improved cortical circulation, regulates the oxidative metabolism and neuroproteins (tau and amyloid) release thereby slow down the neurodegeneration and cortical atrophy (133). Physical activity is speculated to improve the pathophysiology through certain molecular pathways including modulation of immune and inflammatory mediators, improving cerebral vascular endothelial functions, reducing nerve cell apoptosis and regulating synaptic plasticity. These therapeutic physiological pathways preserve the cerebral volume, neurovascular integrity and brain perfusion leading to improved neuromotor coordination and reduction of symptoms of senile dementia (134). Nevertheless, engaging in moderate-vigorous physical activity is found to be a remedy for the hallucinations, delusions and non-cognitive symptoms of dementia (135).

Recommendations of the dose

Aerobic exercise: mode of walking, jogging, cycling, swimming with an intensity of 50-80% of HRR, 30 minutes/day, 3-5 days/week, 8-18 weeks for minimal change to observe.

Resistance exercise: 65-75% 1RM or 80-90% MVC or 50-100% of body mass, 8-10 reps/set, 3 sets 5/6 exercises for 6-12 months (136).

Yoga: 30-60 minutes, 1-3 times/week, 10-12 weeks of posture, asanas, relaxation, meditation and chanting for mild cognitive impairment (137). Dose to be titrated based on the cognitive involvement in the dementia or the Alzheimer's disease.
Tai-Chi: Qigong, Chuan Yang, sun style or Mah-Jong styles 20-40 minutes, 2-3 times/week for 15 -20 weeks were found to improve working memory and executive functions (138).

Age difference in physical activity spectrum and potential clinical benefits
Contemporary evidence claims the inverse association between age and physical activity (139). The physical activity spectrum ranges from sedentary behavior (< 1.5 METS) to vigorous activity (> 6 METS) (58). While children have shown to increase MVPA, the activity dose found to decline with age with significant proportion of the aged population reduces consistently the recommended weekly dose of MVPA (7, 140). **Figure 4** depicts the physical activity spectrum across ages and the clinical benefits across each age.
The clinical benefits offered by meeting the recommended physical activity are undebatable. In children, academic achievement, social image, protection from the early cardiometabolic disease risk, obesity and mental health are few of the benefits worth mentioning (141). While optimized fundamental movement skills and efficient neuromotor development are evident with adequate PA, the long-term PA seemed to be crucial for sporting skills and long-term habit formation in children (142). In adults, the protective and therapeutic effects of PA on cardiometabolic disease, cancer and mental health disorders are well known (10). Further physical activity is found to improve cognitive functions, workability and sickness presenteeism at workplaces (143). In the elderly population, PA is imperative in prevention of the chronic disease risk including diabetes, coronary artery diseases, obesity and cancers (144). Further reduced fall risk, sarcopenia and osteoporosis is associated with the long-term compliance to PA (145). Flexibility and coordination exercises may improve social life integrity and longevity in the elderly population. Further optimized physical activity is proposed to improve the physical, mental and social well-being of elderly population there by enjoying life to the fullest and thereby reducing the caregiver stress and burnt out.

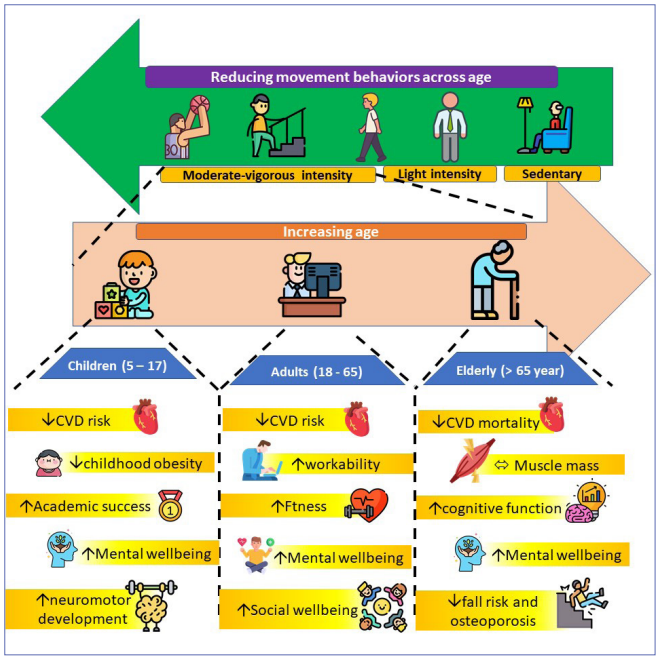


Figure 4. Movement spectrum and physical activity behaviors across the age and benefits of moderate- vigorous physical activity.

DISCUSSION

Physical activity on chronic disease

Our review has consolidated the existing evidence that have explored the potential physiological benefits associated with the physical activity and the recommended dose for attaining the potential benefits (146). Primary physiological benefits gained from the optimally dosed physical activity are:

1. improved glycemic, insulin control and lipid oxidation (diabetes and atherogenesis);
2. regulate energy expenditure, hormonal control and body composition (obesity, polycystic ovarian and other endocrine disorders);
3. higher vascular dynamics (flow, velocity and shear stress), local dilator action (nitric oxide, angiotensin control) and angiogenesis (hypertension, coronary artery disease and kidney diseases);
4. enhanced immune and inflammatory cascade regulation (cancer and immune disorders, cardiovascular diseases);
5. improved brain metabolism, perfusion, synaptic plasticity and neuromotor control (stroke, dementia, Alzheimer's);
6. delay muscle atrophy and enhanced muscle metabolism and storage (ageing related sarcopenia, diabetes);
7. improved bone and muscle strength, prevents loss (sarcopenia, arthritis);
8. reduced oxidative stress and ageing process (biological aging and vascular disorders).

These above physiological processes during and after supervised and unsupervised physical activity are claimed to curb the early chronic disease risk.

Barriers to physical activity

Despite known physiological benefits and available global recommendations on physical activity, only a fraction of global population reach the recommended weekly dose of physical activity (6, 147). Time deficiency, lack of resources (gym, equipment, expertise), fear of injury and fall, comfortable of being inactive, social factors (fear of criminal activity and assault in public spaces, high traffic density, air pollution), environmental factors (lack of parks or pathways and monsoon) and organizational policies (recess breaks, transportation, work prioritization) are few of the observed barriers for the effective physical activity promotion and implementation (148, 149). Further cultural barriers (women participation in sports and games, promotion of physical activity at churches and festivals) and policies on using escalators, elevators, stairs and using public transports are worth mentioning barriers (150). Emerging evidence also claims the effective use of blue and green spaces of the town and efficient town planning promoting physical activity are few facilitators for physical activity.

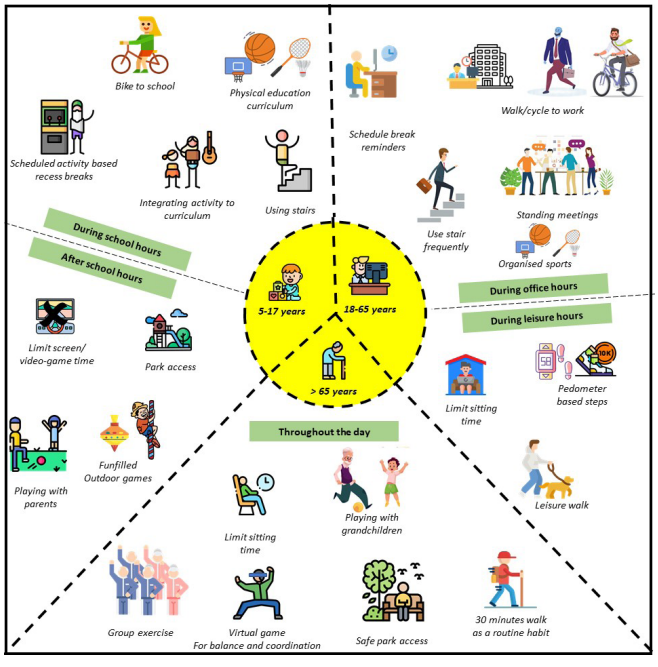


Figure 5. Strategies to promote physical activity at different age levels.

Strategies to promote physical activity in the community

Several strategies have been adopted to promote physical activity in the community based on the differing age group. **Figure 5** depicts the various strategies to promote physical activity and reduce sedentary behavior in the community.

Children and adolescents (5-17 years)

As habit formation starts at an early age, physical activity promotion should start at an early childhood. School based physical activity promotion is crucial as children spend 2/3rd of their wake hours in school. Whole school PA programs (recess breaks, integrating physical activity into curriculum, fun based physical education classes besides skill-based training) are a few strategies to be advocated which have found to yield fruitful results (151, 152). Further walk or cycle to school behaviors and engaging after school hour gardening, household and leisure time gardening are few promising strategies to enhance physical behaviors and mental health outside school hours (153). Parental role in promoting physical activity during outside school hours is undebatable. Parental physical activity, engaging in family games, leisure time activities and travel behaviors are other strategies to improve physical activity after school hours (154).

Adults (18-65 years)

In adults, physical activity can be promoted in three domains: 1) household – cooking, cleaning, activities of daily living (bathing, grooming). Minimizing electronic gadgets may improve physical activity however the level of household activity depending on disability; 2) occupational physical activity – as majority of population spends 2/3rd of wake hours in office, workplace becomes ideal in promotion of physical activity. The office workers should limit their sedentary work through individual behavior change (pomodoro techniques, wearable use, lunch break walks), environmental restructuring (sit stand workstations, treadmill desks, avoiding elevators, using stairs), organizational policies (standing meetings, elevator/escalator switch off days, roof top gardening) are few worth mentioning strategies. Blue collars should limit the load of the work carrying, pulling, pushing, mechanization and enhancing physical fitness may reduce the risk of cardiometabolic risk as physical activity paradox exists; 3) leisure time activity – limiting screen time, engage in family based outdoor games, gardening, organized games are some strategies to enhance meaningful physical activity throughout the day in adults.

Elderly (> 65 years)

In elderly, sedentary behavior and physical activity are more common and now identified as independent factors for cardiovascular and musculoskeletal risks. Limiting sedentary time (screen time) and improving physical activity (community gyms, self-help group for PA promotion, enjoyable organized and adaptive games), environmental access (safe park and lighted walkways) are a few promising strategies adapted throughout the world for improving physical activity. However appropriate preparticipation screening, optimized medical management and structured PA program allowed by the underlying disability (155).

CONCLUSIONS

Physical activity is a polypill, acting on several pathophysiological processes to reverse, manage and prevent chronic disease risk. Physical activity uptake is low in public due to regional and cultural variations including resource management. Physical activity could be easily integrated in everyday life, addressing several domains of everyday life. Efficient communication and designing culturally adaptive, feasible and fun filled physical activity interventions for the public is urgent need of the hour.

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DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

BC: conceptualization, administration, articles analysis, writing – review & editing. MR: writing – original draft.

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

REFERENCES

1. Costa TG, de Oliveira VN, Santos DAT, et al. The burden of prolonged sedentary behavior imposed by uberization. Sports Med Health Sci. 2023;5(2):159-63. doi: 10.1016/j.smhs.2023.02.005.
2. Saidj M, Menai M, Charreire H, Weber C, et al. Descriptive study of sedentary behaviours in 35,444 French working adults: cross-sectional findings from the ACTI-Cités study. BMC Public Health. 2015;15(1):379. doi: 10.1186/s12889-015-1711-8.
3. González K, Fuentes J, Márquez JL. Physical Inactivity, Sedentary Behavior and Chronic Diseases. Korean J Fam Med. 2017;38(3):111-5. doi: 10.4082/kjfm.2017.38.3.111.
4. Christofoletti M, Del Duca GF, da Silva KS, Meneghini V, Malta DC. Physical inactivity, television time and chronic diseases in Brazilian adults and older adults. Health Promot Int. 2020;35(2):352-61. doi: 10.1093/heapro/daz031.
5. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020;54(24):1451-62. doi: 10.1136/bjsports-2020-102955.
6. Guthold R, Stevens GA, Riley LM, Bull FC. Global trends in insufficient physical activity among adolescents: a pooled analysis of 298 population-based surveys with 1·6 million participants. Lancet Child Adolesc Health. 2020;4(1):23-35. doi: 10.1016/S2352-4642(19)30323-2.
7. Zongpa TC, Chandrasekaran B, Arumugam A. Effectiveness of A Smartphone Directed Physical Activity Program on Cardiometabolic Disease Risk in Desk-Based Office Employees - A Pragmatic, Two-Arm, Parallel, Cluster Randomised Trial. Muscles Ligaments Tendons J. 2020;10(4):713-23. doi: 10.32098/mltj.04.2020.19.
8. Tulasiram B, Chandrasekaran B. Are Smartphones Better in Guiding Physical Activity Among Sedentary Young Adults? A Randomised Controlled Trial. Muscles Ligaments Tendons J. 2021;11(1):83-91. doi: 10.32098/mltj.01.2021.10.
9. Eckel RH, Bornfeldt KE, Goldberg IJ. Cardiovascular disease in diabetes, beyond glucose. Cell Metab. 2021;33(8):1519-45. doi: 10.1016/j.cmet.2021.07.001.
10. Booth FW, Gordon SE, Carlson CJ, Hamilton MT. Waging war on modern chronic diseases: primary prevention through exercise biology. J Appl Physiol (1985). 2000;88(2):774-87. doi: 10.1152/jappl.2000.88.2.774.
11. Russo CR. The effects of exercise on bone. Basic concepts and implications for the prevention of fractures. Clin Cases Miner Bone Metab. 2009;6(3):223-8.
12. Smith PJ, Potter GG, McLaren ME, Blumenthal JA. Impact of aerobic exercise on neurobehavioral outcomes. Ment Health Phys Act. 2013;6(3):139-53. doi: 10.1016/j.mhpa.2013.06.008.
13. Basso JC, Suzuki WA. The Effects of Acute Exercise on Mood, Cognition, Neurophysiology, and Neurochemical Pathways: A Review. Brain Plast. 2017;2(2):127-52. doi: 10.3233/BPL-160040.

14. Collado-Mateo D, Lavín-Pérez AM, Peñacoba C, et al. Key Factors Associated with Adherence to Physical Exercise in Patients with Chronic Diseases and Older Adults: An Umbrella Review. Int J Environ Res Public Health. 2021;18(4):2023. doi: 10.3390/ijerph18042023.
15. Tricco AC, Lillie E, Zarin W, O'Brien KK, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-73. Epub 20180904. doi: 10.7326/M18-0850.
16. Correia RR, Veras ASC, Tebar WR, Rufino JC, Batista VRG, Teixeira GR. Strength training for arterial hypertension treatment: a systematic review and meta-analysis of randomized clinical trials. Scientific Rep. 2023;13(1):201. doi: 10.1038/s41598-022-26583-3.
17. Dassanayake S, Sole G, Wilkins G, Gray E, Skinner M. Effectiveness of Physical Activity and Exercise on Ambulatory Blood Pressure in Adults with Resistant Hypertension: A Systematic Review and Meta-Analysis. High blood pressure & cardiovascular prevention : the official journal of the Italian Society of Hypertension. 2022;29(3):275-86. doi: 10.1007/s40292-022-00517-6.
18. Pescatello LS, Buchner DM, Jakicic JM, et al. Physical Activity to Prevent and Treat Hypertension: A Systematic Review. Med Sci Sports Exerc. 2019;51(6):1314-23. doi: 10.1249/MSS.0000000000001943.
19. Saco-Ledo G, Valenzuela PL, Ruiz-Hurtado G, Ruilope LM, Lucia A. Exercise Reduces Ambulatory Blood Pressure in Patients With Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 2020;9(24):e018487. doi: 10.1161/JAHA.120.018487.
20. Teixeira JMM, Motta-Santos D, Milanovic Z, Pereira RL, Krustrup P, Póvoas S. Intermittent high-intensity exercise for pre- to established hypertension: A systematic review and meta-analysis. Scand J Med Sci Sports. 2023;33(4):364-81. doi: 10.1111/sms.14299.
21. Dibben GO, Faulkner J, Oldridge N, et al. Exercise-based cardiac rehabilitation for coronary heart disease: a meta-analysis. Eur Heart J. 2023;44(6):452-69. doi: 10.1093/eurheartj/ehac747.
22. Du L, Zhang X, Chen K, Ren X, Chen S, He Q. Effect of High-Intensity Interval Training on Physical Health in Coronary Artery Disease Patients: A Meta-Analysis of Randomized Controlled Trials. J Cardiovasc Dev Dis. 2021;8(11):158. doi: 10.3390/jcdd8110158.
23. Kaihara T, Intan-Goey V, Scherrenberg M, Falter M, Frederix I, Dendale P. Impact of activity trackers on secondary prevention in patients with coronary artery disease: a systematic review and meta-analysis. Eur J Prev Cardiol. 2022;29(7):1047-56. doi: 10.1093/eurjpc/zwab146.
24. Yang X, Li Y, Ren X, et al. Effects of exercise-based cardiac rehabilitation in patients after percutaneous coronary intervention: A meta-analysis of randomized controlled trials. Sci Rep. 2017;7:44789. doi: 10.1038/srep44789.
25. Aune D, Schlesinger S, Leitzmann MF, et al. Physical activity and the risk of heart failure: a systematic review and dose-response meta-analysis of prospective studies. Eur J Epidemiol. 2021;36(4):367-81. doi: 10.1007/s10654-020-00693-6.
26. AbuElkhair A, Boidin M, Buckley BJR, et al. Effects of different exercise types on quality of life for patients with atrial fibrillation: a systematic review and meta-analysis. J Cardiovasc Med (Hagerstown). 2023;24(2):87-95. doi: 10.2459/JCM.0000000000001386.
27. Gonzalez-Jaramillo N, Wilhelm M, Arango-Rivas AM, et al. Systematic Review of Physical Activity Trajectories and Mortality in Patients With Coronary Artery Disease. J Am Coll Cardiol. 2022;79(17):1690-700. doi: 10.1016/j.jacc.2022.02.036.
28. Friedenreich CM, Stone CR, Cheung WY, Hayes SC. Physical Activity and Mortality in Cancer Survivors: A Systematic Review and Meta-Analysis. JNCI cancer spectrum. 2020;4(1):pkz080. doi: 10.1093/jncics/pkz080.
29. McTiernan A, Friedenreich CM, Katzmarzyk PT, et al. Physical Activity in Cancer Prevention and Survival: A Systematic Review. Med Sci Sports Exerc. 2019;51(6):1252-61. doi: 10.1249/MSS.0000000000001937.
30. Takemura N, Chan SL, Smith R, Cheung DST, Lin CC. The effects of physical activity on overall survival among advanced cancer patients: a systematic review and meta-analysis. BMC Cancer. 2021;21(1):242. doi: 10.1186/s12885-021-07988-1.
31. van Baak MA, Pramono A, Battista F, et al. Effect of different types of regular exercise on physical fitness in adults with overweight or obesity: Systematic review and meta-analyses. Obes Rev. 2021;22 Suppl 4(Suppl 4):e13239. doi: 10.1111/obr.13239.
32. Boyer W, Toth L, Brenton M, Augé R, Churilla J, Fitzhugh E. The role of resistance training in influencing insulin resistance among adults living with obesity/overweight without diabetes: A systematic review and meta-analysis. Obes Res Clin Pract. 2023;17(4):279-287. doi: 10.1016/j.orcp.2023.06.002.
33. Purgato M, Cadorin C, Prina E, et al. Umbrella Systematic Review and Meta-analysis: Physical Activity as an Effective Therapeutic Strategy for Improving Psychosocial Outcomes in Children and Adolescents. J Am Acad Child Adolesc Psychiatry. 2024;(63(2):172-183. doi: 10.1016/j.jaac.2023.04.017.
34. Patten RK, Boyle RA, Moholdt T, et al. Exercise Interventions in Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. Front Physiol. 2020;11:606. doi: 10.3389/fphys.2020.00606.
35. Woodward A, Broom D, Harrop D, et al. The effects of physical exercise on cardiometabolic outcomes in women with polycystic ovary syndrome not taking the oral contraceptive pill: a systematic review and meta-analysis. J Diabetes Metab Disord. 2019;18(2):597-612. doi: 10.1007/s40200-019-00425-y.
36. Breyley-Smith A, Mousa A, Teede HJ, Johnson NA, Sabag A. The Effect of Exercise on Cardiometabolic Risk Factors in Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. Int J Env Res Pub Health. 2022;19(3):1386. doi: 10.3390/ijerph19031386.
37. Dos Santos IK, Ashe MC, Cobucci RN, Soares GM, de Oliveira Maranhão TM, Dantas PMS. The effect of exercise as an intervention for women with polycystic ovary syndrome: A systematic review and meta-analysis. Medicine (Baltimore). 2020;99(16):e19644. doi: 10.1097/MD.0000000000019644.
38. Rietz M, Lehr A, Mino E, et al. Physical Activity and Risk of Major Diabetes-Related Complications in Individuals With Diabetes: A Systematic Review and Meta-Analysis of Observational Studies. Diabetes Care. 2022;45(12):3101-11. doi: 10.2337/dc22-0886.
39. Aune D, Norat T, Leitzmann M, Tonstad S, Vatten LJ. Physical activity and the risk of type 2 diabetes: a systematic review and

dose-response meta-analysis. Eur J Epidemiol. 2015;30(7):529-42. doi: 10.1007/s10654-015-0056-z.
40. Amin M, Kerr D, Atiase Y, Aldwikat RK, Driscoll A. Effect of Physical Activity on Metabolic Syndrome Markers in Adults with Type 2 Diabetes: A Systematic Review and Meta-Analysis. Sports (Basel). 2023;11(5):101. doi: 10.3390/sports11050101.
41. Wahid A, Manek N, Nichols M, et al. Quantifying the Association Between Physical Activity and Cardiovascular Disease and Diabetes: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2016;5(9):e002495. doi: 10.1161/JAHA.115.002495.
42. Pinheiro MB, Oliveira J, Bauman A, Fairhall N, Kwok W, Sherrington C. Evidence on physical activity and osteoporosis prevention for people aged 65+ years: a systematic review to inform the WHO guidelines on physical activity and sedentary behaviour. Int J Behav Nutr Phys Act. 2020;17(1):150. doi: 10.1186/s12966-020-01040-4.
43. Zouhal H, Berro AJ, Kazwini S, et al. Effects of Exercise Training on Bone Health Parameters in Individuals With Obesity: A Systematic Review and Meta-Analysis. Front Physiol. 2021;12:807110. doi: 10.3389/fphys.2021.807110.
44. Alzahrani H, Mackey M, Stamatakis E, Zadro JR, Shirley D. The association between physical activity and low back pain: a systematic review and meta-analysis of observational studies. Sci Rep. 2019;9(1):8244. doi: 10.1038/s41598-019-44664-8.
45. Shiri R, Coggon D, Falah-Hassani K. Exercise for the Prevention of Low Back Pain: Systematic Review and Meta-Analysis of Controlled Trials. Am J Epidemiol. 2018;187(5):1093-101. doi: 10.1093/aje/kwx337.
46. Ye H, Weng H, Xu Y, Wang L, Wang Q, Xu G. Effectiveness and safety of aerobic exercise for rheumatoid arthritis: a systematic review and meta-analysis of randomized controlled trials. BMC Sports Sci Med Rehabil. 2022;14(1):17. doi: 10.1186/s13102-022-00408-2.
47. Sasaki R, Honda Y, Oga S, et al. Effect of exercise and/or educational interventions on physical activity and pain in patients with hip/knee osteoarthritis: A systematic review with meta-analysis. PLoS One. 2022;17(11):e0275591. doi: 10.1371/journal.pone.0275591.
48. Seidu S, Abdool M, Almaqhawi A, et al. Physical activity and risk of chronic kidney disease: systematic review and meta-analysis of 12 cohort studies involving 1,281,727 participants. Eur J Epidemiol. 2023;38(3):267-80. doi: 10.1007/s10654-022-00961-7.
49. Villanego F, Naranjo J, Vigara LA, et al. Impact of physical exercise in patients with chronic kidney disease: Sistematic review and meta-analysis. Nefrologia (Engl Ed). 2020;40(3):237-52. doi: 10.1016/j.nefro.2020.01.002.
50. Yamamoto R, Ito T, Nagasawa Y, et al. Efficacy of aerobic exercise on the cardiometabolic and renal outcomes in patients with chronic kidney disease: a systematic review of randomized controlled trials. J Nephrol. 2021;34(1):155-64. doi: 10.1007/s40620-020-00865-3.
51. Zhang F, Bai Y, Zhao X, et al. Therapeutic effects of exercise interventions for patients with chronic kidney disease: an umbrella review of systematic reviews and meta-analyses. BMJ Open. 2022;12(9):e054887. doi: 10.1136/bmjopen-2021-054887.
52. Ada L, Dorsch S, Canning CG. Strengthening interventions increase strength and improve activity after stroke: a systematic review. Aust J Physiother. 2006;52(4):241-8. doi: 10.1016/s0004-9514(06)70003-4.
53. Adamson BC, Ensari I, Motl RW. Effect of Exercise on Depressive Symptoms in Adults With Neurologic Disorders: A Systematic Review and Meta-Analysis. Arch Phys Med Rehabil. 2015;96(7):1329-38. doi: 10.1016/j.apmr.2015.01.005.
54. Field MJ, Gebruers N, Shanmuga Sundaram T, Nicholson S, Mead G. Physical Activity after Stroke: A Systematic Review and Meta-Analysis. ISRN Stroke. 2013;2013:464176. doi: 10.1155/2013/464176.
55. Iso-Markku P, Kujala UM, Knittle K, Polet J, Vuoksimaa E, Waller K. Physical activity as a protective factor for dementia and Alzheimer's disease: systematic review, meta-analysis and quality assessment of cohort and case-control studies. Br J Sports Med. 2022;56(12):701-9. doi: 10.1136/bjsports-2021-104981.
56. Stephen R, Hongisto K, Solomon A, Lönnroos E. Physical Activity and Alzheimer's Disease: A Systematic Review. J Gerontol A Biol Sci Med Sci. 2017;72(6):733-9. doi: 10.1093/gerona/glw251.
57. Liu ML, Chang CH, Hsueh MC, Hu YJ, Liao Y. Occupational, Transport, Leisure-Time, and Overall Sedentary Behaviors and Their Associations with the Risk of Cardiovascular Disease among High-Tech Company Employees. Int J Environ Res Public Health. 2020;17(10). Epub 20200512. doi: 10.3390/ijerph17103353.
58. Thivel D, Tremblay A, Genin PM, Panahi S, Rivière D, Duclos M. Physical Activity, Inactivity, and Sedentary Behaviors: Definitions and Implications in Occupational Health. Front Public Health. 2018;6:288. doi: 10.3389/fpubh.2018.00288.
59. Cillekens B, Huysmans MA, Holtermann A, et al. Physical activity at work may not be health enhancing. A systematic review with meta-analysis on the association between occupational physical activity and cardiovascular disease mortality covering 23 studies with 655 892 participants. Scand J Work Environ Health. 2022;48(2):86-98. doi: 10.5271/sjweh.3993.
60. Brown JC, Winters-Stone K, Lee A, Schmitz KH. Cancer, physical activity, and exercise. Compr Physiol. 2012;2(4):2775-809. doi: 10.1002/cphy.c120005.
61. Saint-Maurice PF, Berrigan D, Whitfield GP, et al. Amount, Type, and Timing of Domain-Specific Moderate to Vigorous Physical Activity Among US Adults. J Phys Act Health. 2021;18(S1):S114-S22. doi: 10.1123/jpah.2021-0174.
62. White DA, Willis EA, Ptomey LT, Gorczyca AM, Donnelly JE. Weekly Frequency of Meeting the Physical Activity Guidelines and Cardiometabolic Health in Children and Adolescents. Med Sci Sports Exerc. 2022;54(1):106-12. doi: 10.1249/MSS.0000000000002767.
63. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. Nat Rev Cardiol. 2021;18(11):785-802. doi: 10.1038/s41569-021-00559-8.
64. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016;134(6):441-50. doi: 10.1161/CIRCULATIONAHA.115.018912.
65. Thijssen DH, Rongen GA, Smits P, Hopman MT. Physical (in) activity and endothelium-derived constricting factors: overlooked adaptations. J Physiol. 2008;586(2):319-24. doi: 10.1113/jphysiol.2007.145698.

66. Thompson PD. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease. Arterioscler Thromb Vasc Biol. 2003;23(8):1319-21. doi: 10.1161/01.ATV.0000087143.33998.F2.
67. Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med. 2002;136(7):493-503. doi: 10.7326/0003-4819-136-7-200204020-00006.
68. Ghadieh AS, Saab B. Evidence for exercise training in the management of hypertension in adults. Can Fam Physician. 2015;61(3):233-9.
69. Hagins M, States R, Selfe T, Innes K. Effectiveness of yoga for hypertension: systematic review and meta-analysis. Evid Based Complement Alternat Med. 2013;2013:649836. doi: 10.1155/2013/649836.
70. Li X, Gao Y, Wu M, et al. Effect of Tai Chi versus aerobic exercise on blood pressure in prehypertension patients (TCOBPP): a study protocol for a 12-month single-blind randomized controlled trial. Trials. 2022;23(1):1001. doi: 10.1186/s13063-022-06840-6.
71. Liu D, Yi L, Sheng M, Wang G, Zou Y. The Efficacy of Tai Chi and Qigong Exercises on Blood Pressure and Blood Levels of Nitric Oxide and Endothelin-1 in Patients with Essential Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Evid Based Complement Alternat Med. 2020;2020:3267971. doi: 10.1155/2020/3267971.
72. Ralapanawa U, Sivakanesan R. Epidemiology and the Magnitude of Coronary Artery Disease and Acute Coronary Syndrome: A Narrative Review. J Epidemiol Glob Health. 2021;11(2):169-77. doi: 10.2991/jegh.k.201217.001.
73. Elagizi A, Kachur S, Carbone S, Lavie CJ, Blair SN. A Review of Obesity, Physical Activity, and Cardiovascular Disease. Curr Obes Rep. 2020;9(4):571-81. doi: 10.1007/s13679-020-00403-z.
74. Winzer EB, Woitek F, Linke A. Physical Activity in the Prevention and Treatment of Coronary Artery Disease. J Am Heart Assoc. 2018;7(4): e007725. doi: 10.1161/JAHA.117.007725.
75. Hambrecht R, Adams V, Erbs S, et al. Regular physical activity improves endothelial function in patients with coronary artery disease by increasing phosphorylation of endothelial nitric oxide synthase. Circulation. 2003;107(25):3152-8. doi: 10.1161/01.CIR.0000074229.93804.5C.
76. Laufs U, Werner N, Link A, et al. Physical training increases endothelial progenitor cells, inhibits neointima formation, and enhances angiogenesis. Circulation. 2004;109(2):220-6. doi: 10.1161/01.CIR.0000109141.48980.37.
77. Nystoriak MA, Bhatnagar A. Cardiovascular Effects and Benefits of Exercise. Front Cardiovasc Med. 2018;5:135. doi: 10.3389/fcvm.2018.00135.
78. Srihari Sharma KN, Choudhary NR, Subramanya P. Evidence Base of Yoga Studies on Cardiovascular Health: A Bibliometric Analysis. Int J Yoga. 2019;12(2):162-71. doi: 10.4103/ijoy.IJOY_6_18.
79. Fan YX, Yu ML, Li JE, et al. Efficacy and Safety of Resistance Training for Coronary Heart Disease Rehabilitation: A Systematic Review of Randomized Controlled Trials. Front Cardiovasc Med. 2021;8:754794. doi: 10.3389/fcvm.2021.754794.
80. Sprod LK. Considerations for Training Cancer Survivors. Strength Cond J. 2009;31(1):39-47. doi: 10.1519/SSC.0b013e318195a259.
81. Koelwyn GJ, Wennerberg E, Demaria S, Jones LW. Exercise in Regulation of Inflammation-Immune Axis Function in Cancer Initiation and Progression. Oncology (Williston Park). 2015;29(12):908-20, 922.
82. Koeppel M, Körbi C, Winkels RM, Schmitz KH, Wiskemann J. Relationship Between Cancer Related Fatigue, Physical Activity Related Health Competence, and Leisure Time Physical Activity in Cancer Patients and Survivors. Front Sports Act Living. 2021;3:687365. doi: 10.3389/fspor.2021.687365.
83. Alabaster K, Homsy C, Puyana S, et al. Exercise after Breast Reconstruction Surgery: Evaluating Current Trends and Practices of U.S. Plastic Surgeons. Plast Reconstr Surg Glob Open. 2021;9(10):e3857. doi: 10.1097/GOX.0000000000003857.
84. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Med Sci Sports Exerc. 2019;51(11):2375-90. doi: 10.1249/MSS.0000000000002116.
85. Lin X, Li H. Obesity: Epidemiology, Pathophysiology, and Therapeutics. Front Endocrinol (Lausanne). 2021;12:706978. doi: 10.3389/fendo.2021.706978.
86. Kawai T, Autieri MV, Scalia R. Adipose tissue inflammation and metabolic dysfunction in obesity. Am J Physiol Cell Physiol. 2021;320(3):C375-C91. doi: 10.1152/ajpcell.00379.2020.
87. Muscella A, Stefàno E, Lunetti P, Capobianco L, Marsigliante S. The Regulation of Fat Metabolism During Aerobic Exercise. Biomolecules. 2020;10(12):1699. doi: 10.3390/biom10121699.
88. Al-Rashed F, Alghaith A, Azim R, et al. Increasing the Duration of Light Physical Activity Ameliorates Insulin Resistance Syndrome in Metabolically Healthy Obese Adults. Cells. 2020;9(5):1189. doi: 10.3390/cells9051189.
89. Kolnes KJ, Petersen MH, Lien-Iversen T, Højlund K, Jensen J. Effect of Exercise Training on Fat Loss-Energetic Perspectives and the Role of Improved Adipose Tissue Function and Body Fat Distribution. Front Physiol. 2021;12:737709. doi: 10.3389/fphys.2021.737709.
90. Kumar A, Gangwar R, Ahmad Zargar A, Kumar R, Sharma A. Prevalence of diabetes in India: A review of IDF Diabetes Atlas 10th edition. Curr Diabetes Rev. 2024;20(1):e130423215752. doi: 10.2174/1573399819666230413094200.
91. Stanford KI, Goodyear LJ. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ. 2014;38(4):308-14. doi: 10.1152/advan.00080.2014.
92. Cortright RN, Dohm GL. Mechanisms by which insulin and muscle contraction stimulate glucose transport. Can J Appl Physiol. 1997;22(6):519-30. doi: 10.1139/h97-033.
93. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care. 2010;33(12):e147-67. doi: 10.2337/dc10-9990.
94. Mohamed AA, Jan YK. Effect of Adding Proprioceptive Exercise to Balance Training in Older Adults with Diabetes: A Systematic Review. Curr Diabetes Rev. 2020;16(4):327-39. doi: 10.2174/1573399815666190712200147.
95. Raveendran AV, Deshpandae A, Joshi SR. Therapeutic Role of Yoga in Type 2 Diabetes. Endocrinol Metab (Seoul). 2018;33(3):307-17. doi: 10.3803/EnM.2018.33.3.307.

96. Younk LM, Mikeladze M, Tate D, Davis SN. Exercise-related hypoglycemia in diabetes mellitus. Expert Rev Endocrinol Metab. 2011;6(1):93-108. doi: 10.1586/eem.10.78.
97. Loeser RF, Goldring SR, Scanzello CR, Goldring MB. Osteoarthritis: a disease of the joint as an organ. Arthritis Rheum. 2012;64(6):1697-707. doi: 10.1002/art.34453.
98. Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Bone Res. 2018;6:15. doi: 10.1038/s41413-018-0016-9.
99. Mohammed A, Alshamarri T, Adeyeye T, Lazariu V, McNutt LA, Carpenter DO. A comparison of risk factors for osteo- and rheumatoid arthritis using NHANES data. Prev Med Rep. 2020;20:101242. doi: 10.1016/j.pmedr.2020.101242.
100. Zeng CY, Zhang ZR, Tang ZM, Hua FZ. Benefits and Mechanisms of Exercise Training for Knee Osteoarthritis. Front Physiol. 2021;12:794062. doi: 10.3389/fphys.2021.794062.
101. Migliorini F, Marsilio E, Oliva F, Hildebrand F, Maffulli N. Elderly Runners and Osteoarthritis: A Systematic Review. Sports Med Arthrosc Rev. 2022;30(2):92-6. doi: 10.1097/JSA.0000000000000347.
102. Migliorini F, Marsilio E, Torsiello E, Pintore A, Oliva F, Maffulli N. Osteoarthritis in Athletes Versus Nonathletes: A Systematic Review. Sports Med Arthrosc Rev. 2022;30(2):78-86.
103. Anwer S, Alghadir A. Effect of isometric quadriceps exercise on muscle strength, pain, and function in patients with knee osteoarthritis: a randomized controlled study. J Phys Ther Sci. 2014;26(5):745-8. doi: 10.1589/jpts.26.745.
104. Hall J, Swinkels A, Briddon J, McCabe CS. Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials. Arch Phys Med Rehabil. 2008;89(5):873-83. doi: 10.1016/j.apmr.2007.09.054.
105. Migliorini F, Vecchio G, Pintore A, Oliva F, Maffulli N. The Influence of Athletes' Age in the Onset of Osteoarthritis: A Systematic Review. Sports Med Arthrosc Rev. 2022;30(2):97-101. doi: 10.1097/JSA.0000000000000345. P
106. Migliorini F, Pintore A, Torsiello E, Oliva F, Spiezia F, Maffulli N. Intensive Physical Activity Increases the Risk of Knee and Hip Arthroplasty: A Systematic Review. Sports Med Arthrosc Rev. 2022;30(2):111-6. doi: 10.1097/JSA.0000000000000340.
107. Pirayeh N, Kazemi K, Rahimi F, Mostafaee N, Shaterzadeh-Yazdi MJ. The Effect of Balance Training on Functional Outcomes in Patients with Knee Osteoarthritis: A Systematic Review. Med J Islam Repub Iran. 2022;36:107. doi: 10.47176/mjiri.36.107.
108. Kampmann JD, Heaf JG, Mogensen CB, Mickley H, Wolff DL, Brandt F. Prevalence and incidence of chronic kidney disease stage 3–5 – results from KidDiCo. BMC Nephrology. 2023;24(1):17. doi: 10.1186/s12882-023-03056-x.
109. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl (2011). 2022;12(1):7-11. doi: 10.1016/j.kisu.2021.11.003.
110. Mallamaci F, Pisano A, Tripepi G. Physical activity in chronic kidney disease and the EXerCise Introduction To Enhance trial. Nephrol Dial Transplant. 2020;35(Suppl 2):ii18-ii22. doi: 10.1093/ndt/gfaa012.
111. Wang Z, do Carmo JM, Aberdein N, et al. Synergistic Interaction of Hypertension and Diabetes in Promoting Kidney Injury and the Role of Endoplasmic Reticulum Stress. Hypertension. 2017;69(5):879-91. doi: 10.1161/HYPERTENSIONAHA.116.08560.
112. Cheng TC, Huang SH, Kao CL, Hsu PC. Muscle Wasting in Chronic Kidney Disease: Mechanism and Clinical Implications-A Narrative Review. Int J Mol Sci. 2022;23(11):6047. doi: 10.3390/ijms23116047.
113. Bishop NC, Burton JO, Graham-Brown MPM, Stensel DJ, Viana JL, Watson EL. Exercise and chronic kidney disease: potential mechanisms underlying the physiological benefits. Nat Rev Nephrol. 2023;19(4):244-56. doi: 10.1038/s41581-022-00675-9.
114. Hellberg M, Höglund P, Svensson P, Clyne N. Randomized Controlled Trial of Exercise in CKD-The RENEXC Study. Kidney Int Rep. 2019;4(7):963-76. doi: 10.1016/j.ekir.2019.04.001.
115. Pechter Ü, Raag M, Ots-Rosenberg M. Regular aquatic exercise for chronic kidney disease patients: a 10-year follow-up study. Int J Rehabil Res. 2014;37(3):251-5. doi: 10.1097/MRR.0000000000000063..
116. Pandey RK, Arya TV, Kumar A, Yadav A. Effects of 6 months yoga program on renal functions and quality of life in patients suffering from chronic kidney disease. Int J Yoga. 2017;10(1):3-8. doi: 10.4103/0973-6131.186158.
117. Kuriakose D, Xiao Z. Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. Int J Mol Sci. 2020;21(20):7609. doi: 10.3390/ijms21207609.
118. Collaborators GS. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol. 2021;20(10):795-820. doi: 10.1016/S1474-4422(21)00252-0.
119. Willey JZ, Moon YP, Sacco RL, et al. Physical inactivity is a strong risk factor for stroke in the oldest old: Findings from a multi-ethnic population (the Northern Manhattan Study). Int J Stroke. 2017;12(2):197-200. doi: 10.1177/1747493016676614.
120. Donkor ES. Stroke in the 21. Stroke Res Treat. 2018;2018:3238165. doi: 10.1155/2018/3238165.
121. Carrick-Ranson G, Hastings JL, Bhella PS, et al. The effect of lifelong exercise dose on cardiovascular function during exercise. J Appl Physiol (1985). 2014;116(7):736-45. doi: 10.1152/japplphysiol.00342.2013.
122. LaMonte MJ, Eaton CB. Physical Activity in the Treatment and Prevention of Heart Failure: An Update. Curr Sports Med Rep. 2021;20(8):410-7. doi: 10.1249/JSR.0000000000000869.
123. Eng JJ, Tang PF. Gait training strategies to optimize walking ability in people with stroke: a synthesis of the evidence. Expert Rev Neurother. 2007;7(10):1417-36. doi: 10.1586/14737175.7.10.1417.
124. Zhang W, Liu Y, Yu J, et al. Exercise interventions for post-stroke depression: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2021;100(8):e24945. doi: 10.1097/MD.0000000000024945.
125. MacKay-Lyons M, Billinger SA, Eng JJ, et al. Aerobic Exercise Recommendations to Optimize Best Practices in Care After Stroke: AEROBICS 2019 Update. Phys Ther. 2020;100(1):149-56. doi: 10.1093/ptj/pzz153.
126. Veldema J, Jansen P. Resistance training in stroke rehabilitation: systematic review and meta-analysis. Clin Rehabil. 2020;34(9):1173-97. doi: 10.1177/0269215520932964.
127. Lubetzky-Vilnai A, Kartin D. The effect of balance training on balance performance in individuals poststroke: a systematic review. J Neurol Phys Ther. 2010;34(3):127-37. doi: 10.1097/NPT.0b013e3181ef764d.

128. Lawrence M, Celestino Junior FT, Matozinho HH, Govan L, Booth J, Beecher J. Yoga for stroke rehabilitation. Cochrane Database Syst Rev. 2017;12(12):CD011483. doi: 10.1002/14651858.CD011483.pub2.
129. Lyu D, Lyu X, Zhang Y, et al. Tai Chi for Stroke Rehabilitation: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Front Physiol. 2018;9:983. doi: 10.3389/fphys.2018.00983.
130. Chen ML, Wotiz SB, Banks SM, Connors SA, Shi Y. Dose-Response Association of Tai Chi and Cognition among Community-Dwelling Older Adults: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2021;18(6):3179. doi: 10.3390/ijerph18063179.
131. Yan S, Fu W, Wang C, et al. Association between sedentary behavior and the risk of dementia: a systematic review and meta-analysis. Transl Psychiatry. 2020;10(1):112. doi: 10.1038/s41398-020-0799-5.
132. Jurcău MC, Andronie-Cioara FL, Jurcău A, et al. The Link between Oxidative Stress, Mitochondrial Dysfunction and Neuroinflammation in the Pathophysiology of Alzheimer's Disease: Therapeutic Implications and Future Perspectives. Antioxidants (Basel). 2022;11(11):2167. doi: 10.3390/antiox11112167.
133. López-Ortiz S, Pinto-Fraga J, Valenzuela PL, et al. Physical Exercise and Alzheimer's Disease: Effects on Pathophysiological Molecular Pathways of the Disease. Int J Mol Sci. 2021;22(6):2897. doi: 10.3390/ijms22062897.
134. Mahalakshmi B, Maurya N, Lee SD, Bharath Kumar V. Possible Neuroprotective Mechanisms of Physical Exercise in Neurodegeneration. Int J Mol Sci. 2020;21(16):5895. doi: 10.3390/ijms21165895.
135. Wang S, Liu HY, Cheng YC, Su CH. Exercise Dosage in Reducing the Risk of Dementia Development: Mode, Duration, and Intensity-A Narrative Review. Int J Environ Res Public Health. 2021;18(24):13331. doi: 10.3390/ijerph182413331.
136. Azevedo CV, Hashiguchi D, Campos HC, et al. The effects of resistance exercise on cognitive function, amyloidogenesis, and neuroinflammation in Alzheimer's disease. Front Neurosci. 2023;17:1131214. doi: 10.3389/fnins.2023.1131214.
137. Brenes GA, Sohl S, Wells RE, Befus D, Campos CL, Danhauer SC. The Effects of Yoga on Patients with Mild Cognitive Impairment and Dementia: A Scoping Review. Am J Geriatr Psychiatry. 2019;27(2):188-97. doi: 10.1016/j.jagp.2018.10.013.
138. Lim KH, Pysklywec A, Plante M, Demers L. The effectiveness of Tai Chi for short-term cognitive function improvement in the early stages of dementia in the elderly: a systematic literature review. Clin Interv Aging. 2019;14:827-39. doi: 10.2147/CIA.S202055.
139. Westerterp KR. Changes in physical activity over the lifespan: impact on body composition and sarcopenic obesity. Obes Rev. 2018;19 Suppl 1:8-13. doi: 10.1111/obr.12781.
140. Farooq A, Martin A, Janssen X, et al. Longitudinal changes in moderate-to-vigorous-intensity physical activity in children and adolescents: A systematic review and meta-analysis. Obes Rev. 2020;21(1):e12953. doi: 10.1111/obr.12953.
141. Gao J, Lu Y, Gokulnath P, Vulugundam G, et al. Benefits of Physical Activity on Cardiometabolic Diseases in Obese Children and Adolescents. J Transl Int Med. 2022;10(3):236-45. doi: 10.2478/jtim-2022-0041.
142. Wick K, Leeger-Aschmann CS, Monn ND, et al. Interventions to Promote Fundamental Movement Skills in Childcare and Kindergarten: A Systematic Review and Meta-Analysis. Sports Med. 2017;47(10):2045-68. doi: 10.1007/s40279-017-0723-1.
143. Lahti J, Laaksonen M, Lahelma E, Rahkonen O. The impact of physical activity on sickness absence. Scand J Med Sci Sports. 2010;20(2):191-9. doi: 10.1111/j.1600-0838.2009.00886.x.
144. Dempsey PC, Aadland E, Strain T, et al. Physical activity intensity profiles associated with cardiometabolic risk in middle-aged to older men and women. Prev Med. 2022;156:106977. doi: 10.1016/j.ypmed.2022.106977.
145. van Gameren M, Hoogendijk EO, van Schoor NM, et al. Physical activity as a risk or protective factor for falls and fall-related fractures in non-frail and frail older adults: a longitudinal study. BMC Geriatr. 2022;22(1):695. doi: 10.1186/s12877-022-03383-y.
146. Correia RR, Veras ASC, Tebar WR, Rufino JC, Batista VRG, Teixeira GR. Strength training for arterial hypertension treatment: a systematic review and meta-analysis of randomized clinical trials. Sci Rep. 2023;13(1):201. doi: 10.1038/s41598-022-26583-3.
147. Guthold R, Stevens GA, Riley LM, Bull FC. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1·9 million participants. Lancet Glob Health. 2018;6(10):e1077-e86. doi: 10.1016/S2214-109X(18)30357-7.
148. Bennett GG, McNeill LH, Wolin KY, Duncan DT, Puleo E, Emmons KM. Safe to walk? Neighborhood safety and physical activity among public housing residents. PLoS Med. 2007;4(10):1599-606. doi: 10.1371/journal.pmed.0040306.
149. Stubbs B, Patchay S, Soundy A, Schofield P. The avoidance of activities due to fear of falling contributes to sedentary behavior among community-dwelling older adults with chronic musculoskeletal pain: a multisite observational study. Pain Med. 2014;15(11):1861-71. doi: 10.1111/pme.12570.
150. Koh YS, Asharani PV, Devi F, et al. A cross-sectional study on the perceived barriers to physical activity and their associations with domain-specific physical activity and sedentary behaviour. BMC Public Health. 2022;22(1):1051. doi: 10.1186/s12889-022-13431-2.
151. Pate RR, Davis MG, Robinson TN, et al. Promoting physical activity in children and youth: a leadership role for schools: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism (Physical Activity Committee) in collaboration with the Councils on Cardiovascular Disease in the Young and Cardiovascular Nursing. Circulation. 2006;114(11):1214-24. doi: 10.1161/CIRCULATIONAHA.106.177052.
152. Papadopoulos N, Mantilla A, Bussey K, et al. Understanding the Benefits of Brief Classroom-Based Physical Activity Interventions on Primary School-Aged Children's Enjoyment and Subjective Wellbeing: A Systematic Review. J Sch Health. 2022;92(9):916-32. doi: 10.1111/josh.13196.
153. Howie LD, Lukacs SL, Pastor PN, Reuben CA, Mendola P. Participation in activities outside of school hours in relation to problem behavior and social skills in middle childhood. J Sch Health. 2010;80(3):119-25. doi: 10.1111/j.1746-1561.2009.00475.x.
154. Soubhi H, Potvin L, Paradis G. Family process and parent's leisure time physical activity. Am J Health Behav. 2004;28(3):218-30. doi: 10.5993/ajhb.28.3.3.
155. Taylor J, Walsh S, Kwok W, et al. A scoping review of physical activity interventions for older adults. Int J Behav Nutr Phys Act. 2021;18(1):82. doi: 10.1186/s12966-021-01140-9.