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Efficacy of the Swedish model for physical activity on prescription

Börjesson M, Arvidsson D, Blomqvist Å, Daxberg E-L, Jonsdottir I.H, Lundqvist S, Mellén A, Onerup A, Persson J, Sjögren P, Svanberg T, Jivegård L

VÄSTRA GÖTALANDSREGIONEN
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Title

Efficacy of the Swedish model for physical activity on prescription [Effekter av den svenska modellen för fysisk aktivitet på recept (FaR)]

Börjesson M[1,2,3], Arvidsson D[2], Blomqvist Å[4], Daxberg E-L[5], Jonsdottir I.H.[2,6], Lundqvist S[4,7], Mellén A[8], Onerup A[9,10], Persson J[11], Sjögren P[11], Svanberg T[5], Jivegård L[11*]

[1] Department of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg
[2] Department of Food and Nutrition and Sport Science, University of Gothenburg
[3] Sahlgrenska University Hospital/Östra; Göteborg, Sweden
[4] Närhälsan FaR- teamet Gothenburg, Region Västra Götaland
[5] Medical Library, Sahlgrenska University Hospital
[6] Institute of Stress Medicine, Region Västra Götaland
[7] Department of Health and Rehabilitation, Unit of Physiotherapy, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg
[8] Department of Clinical Pharmacology, Sahlgrenska University Hospital
[9] Department of Surgery, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg
[10] Department of Pediatrics, Sahlgrenska University Hospital
[11] HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital

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[*]Corresponding author

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Efficacy of the Swedish model for physical activity on prescription [Effektivitet av den svenska modellen för fysisk aktivitet på recept (FaR)].
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1. Abstract

Background Lack of physical activity is identified as the fourth leading risk factor for non-communicable diseases (World Health Organization. 2009). In a recent study from Gothenburg, only 30% of the middle-aged population adhered to Swedish recommendations on physical activity. There is a lack of consensus on methods to achieve increased physical activity. Methods currently used in the health care system include counselling with or without the use of Physical Activity on Prescription (PAP). The individualised Swedish PAP model differs from physical activity and exercise prescription models used in other countries.

Objective To study if physical activity on prescription, according to the Swedish PAP-model, is better than not receiving Swedish PAP when it comes to mortality, morbidity, level of physical activity, health-related quality of life (HRQoL), and aerobic capacity for adults that have been deemed to be in need of increased physical activity by a healthcare professional.

Methods During September 2017 two authors performed systematic searches in PubMed, Embase, the Cochrane Library, Amed, Cinahl and Swemed+. These authors selected studies and independently assessed the abstracts and made a first selection of full-text articles. Inclusion was finally decided in a consensus meeting with all authors. The included articles were critically appraised using checklists. Data were extracted by at least two authors and, when possible, pooled in meta-analysis.

Main results The search identified nine relevant articles: seven RCTs, one cohort study and one case series. Overall, the controlled studies had no or minor problems with directness, some problems with study limitations and some or major problems with precision. The presented results concern Swedish PAP in adult patients deemed to be in need of increased physical activity by a health care professional, in Nordic settings, compared with usual care, group sessions, or written general information on the importance of physical activity.
Critical outcomes: No studies reported mortality or morbidity data.
Health related quality of life (HRQoL) was studied in two RCTs with no or small intergroup differences. Conclusion: Swedish PAP may result in little or no difference for HRQoL (GRADE⊕⊕◯◯).
Level of physical activity was reported in seven articles derived from five RCTs and one cohort study. Significant positive effect on physical activity was seen in three RCTs and in the cohort study. Conclusion: Swedish PAP probably results in an increased level of physical activity (GRADE⊕⊕⊕◯).
Important outcomes:
Body weight and waist circumference were studied in three RCTs with no or small intergroup differences. Conclusion: Swedish PAP may result in a slight reduction in body weight and waist circumference. Glucose metabolism was studied in two RCTs with no or small intergroup differences. Conclusion: Swedish PAP may result in little or no difference in glucose metabolism. Physical function was studied with the 6-minute walk test (6-MWT) in one RCT with some problems with directness due to a population limited to patients with transient ischemic attack showing improvement at six months by Swedish PAP (+70 vs +31 m, p=0.01). Conclusion: Swedish PAP may increase 6-MWT walking distance (GRADE⊕⊕◯◯).
Blood pressure (BP) was studied in three RCTs, whereof two had major problems with directness, with no or very small intergroup differences. Conclusion: It is uncertain whether blood pressure is affected by Swedish PAP. Blood lipids were studied in one RCT with no or small intergroup differences. Conclusion: It is uncertain whether blood lipids are affected by Swedish PAP (GRADE ⊕◯◯◯). Adverse events**,** reported in four RCTs and one case series, were limited to musculo-skeletal pain in one RCT with no intergroup difference and no reported adverse events in three RCTs and one case series. Swedish PAP probably results in little or no difference in adverse events compared with no PAP (GRADE⊕⊕⊕◯).

Concluding remarks This HTA report included seven RCTs, one cohort study and one case series comparing Swedish PAP in Nordic settings with usual care, group sessions, or written general information on the importance of physical activity in adult patients deemed to be in need of increased physical activity by a healthcare professional. Mortality or morbidity data were not reported. There may be little or no difference regarding HRQoL (GRADE ⊕⊕◯◯). Swedish PAP probably improves the level of physical activity and probably results in little or no difference in adverse events compared with no PAP. Moderate certainty of evidence (GRADE⊕⊕⊕◯ for both outcomes). There may be slight reduction in body weight and waist circumference, and there may be a little or no difference in glucose metabolism whereas walking distance (6-minute-walk-test) may be slightly improved by PAP (GRADE ⊕⊕◯◯). The effects of Swedish PAP on blood pressure and blood lipids are uncertain (GRADE ⊕◯◯◯). In summary, Swedish PAP probably improves the level of physical activity but the magnitude of this improvement is poorly defined.

2. Svensk sammanfattning – Swedish summary

Bakgrund Fysisk inaktivitet är den fjärde största riskfaktorn för icke smittsamma sjukdomar (World Health Organisation, 2009). I en aktuell Göteborgsstudie visades att bara 30% av medelålders individer uppfyllde de svenska rekommendationerna för fysisk aktivitet. Det saknas samsyn i hälso- och sjukvården angående vilka metoder som ska användas för att öka fysisk aktivitet. Befintliga metoder inkluderar rådgivning med respektive utan användning av Fysisk aktivitet på Recept (FaR). Den individualiserade svenska FaR-metoden skiljer sig från fysisk aktivitets- och träningsrekommendationer som används i andra länder.
Syfte Att studera om den svenska modellen för FaR i nordiska förhållanden är bättre än att inte använda FaR vad gäller dödlighet, sjuklighet, fysisk aktivitetsnivå, hälsorelaterad livskvalitet (HRQoL) och fysisk kapacitet för vuxna som av hälso- och sjukvården bedömts vara i behov av ökad fysisk aktivitet.
Metoder Två författare genomförde i september 2017 en systematisk litteratursökning i PubMed, Embase, the Cochrane Library, Amed, Cinahl and Swemed+. Samma författare selekterade studier och granskade oberoende av varandra abstrakts och gjorde ett första urval av artiklar att läsa i fulltext. Inklusion beslutades slutligen i ett konsensusmöte med alla författare. Inkluderade artiklar granskades kritiskt med stöd av granskningsmallar. Data ur artiklarna extraherades av minst två författare och meta-analys gjordes när så var möjligt.
Resultat Nio relevanta artiklar identifierades: sju randomiserade kontrollerade studier (RCT), en kohortstudie och en fallserie. De åtta kontrollerade studierna hade generellt små eller inga problem med överförbarhet, måttliga begränsningar i studiekvalitet och måttliga eller stora problem med precision. Redovisade resultat avser den svenska modellen för FaR i nordiska förhållanden jämfört med rutinvård, gruppsessioner eller allmän skriftlig information om betydelsen av fysisk aktivitet hos vuxna som av hälso- och sjukvården bedömts behöva öka sin fysiska aktivitetsnivå.
Kritiska utfallsmått
Mortalitet och morbiditetsdata var ej studerade.
I två RCT redovisades livskvalitet med liten eller ingen skillnad mellan grupperna.
Slutsats: FaR kan ge liten eller ingen skillnad i livskvalitet (GRADE ⊕⊕◯◯).
Fysisk aktivitetsnivå studerades i sex RCT och en kohortstudie. I tre RCT och i kohortstudien sågs signifikanta positiva effekter av FaR.
Slutsats: FaR resulterar troligen i ökad fysisk aktivitetsnivå (GRADE⊕⊕⊕◯) .
Viktiga utfallsmått
Kroppsvikt och midjemått, redovisade i tre RCT, visade små eller inga skillnader mellan grupperna.
Slutsats: FaR kan minska kroppsvikt och midjemått något.
Gångsträcka under 6 minuter (6-MWT) förbättrades något av FaR efter sex månader (+70 m vs +31 m, p= 0,01) i en RCT med vissa problem med överförbarhet då bara TIA-patienter studerades.
Slutsats: FaR kan öka 6-MWT gångsträcka.
Glukos-metabolism visade i två RCT liten eller ingen skillnad mellan grupperna.
Slutsats: FaR kan resultera i liten eller ingen skillnad i glukosmetabolism (GRADE ⊕⊕◯◯).
Blodtryck (BT) redovisades i tre RCT, varav två hade stora problem med överförbarhet, med liten eller ingen skillnad mellan grupperna.
Slutsats: Det är osäkert huruvida FaR påverkar blodtrycket.
Blodfetter visade i en RCT liten eller ingen skillnad mellan grupperna.
Slutsats: Det är osäkert huruvida FaR påverkar nivån av blodfetter (GRADE ⊕◯◯◯).
Risker och bieffekter, redovisade i fyra RCT och en fallserie, bestod av muskuloskeletal värk. Samma frekvens rapporterades i båda grupperna i en RCT. Tre RCT och en fallserie fann inga bieffekter.
Slutsats: FaR resulterar troligen i liten eller ingen skillnad avseende risker och biverkningar (GRADE⊕⊕⊕◯)
Sammanfattande slutsats I denna HTA-rapport identifierades sju RCT, en kohortstudie och en fallserie där FaR i nordiska förhållanden har jämförts med rutinvård, gruppsessioner eller allmän skriftlig information avseende betydelsen av fysisk aktivitet hos vuxna som av vården bedömts vara i behov av ökad fysisk aktivitet. Dödlighets- och sjuklighetsdata var ej rapporterade.
FaR jämfört med ej FaR kan troligen öka den fysiska aktivitetsnivån och är troligen förenad med liten eller ingen skillnad i risker och biverkningar (GRADE⊕⊕⊕◯). Fysisk aktivitet på recept kan öka sex minuters-gångsträckan (6-MWT), samt leda till liten eller ingen skillnad i hälsorelaterad livskvalitet, glukosmetabolism, samt kan minska kroppsvikt och midjemått något (GRADE⊕⊕◯◯). Det är osäkert huruvida FaR påverkar blodtryck eller nivån av blodfetter (GRADE⊕◯◯◯). Sammanfattningsvis förbättrar FaR troligen den fysiska aktivitetsnivån men storleksordningen på förbättringen är dåligt definierad.

The above summaries were written by representatives from the HTA-centrum. The HTA report was approved by the Regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the Health Technology Assessment. The Swedish summary is a brief summary of the Health Technology Assessment intended for decision makers, and is ended with a concluding summary.

Christina Bergh, Professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 2018-02-28

Christina Bergh
MD, Professor

Susanne Bernhardsson
PT, PhD

Elisabeth Hansson-Olofsson
RN, PhD, Senior lecturer

Magnus Hakeberg
DDS, Professor

Lennart Jivegård
MD, Senior university lecturer

Josefine Persson
Health economist, PhD

Anders Larsson
MD, PhD

Olle Nelzén
MD, Associate professor

Christian Rylander
MD, Associate professor

Ola Samuelsson
MD, Associate professor

Max Petzold
Statistician, Professor

Henrik Sjövall
MD, Professor

Petteri Sjögren
DDS, PhD

Maria Skogby
RN, PhD

Annika Strandell
MD, Associate professor

Therese Svanberg
HTA librarian

DDS Doctor of dental surgery
MD Medical doctor
PhD Doctor of Philosophy
PT Physiotherapist
RN Registered Nurse

3. Summary of Findings

Outcomes	Study design Number of studies	Relative effect (95%CI)	Absolute effect	Certainty of evidence GRADE[1]
HRQoL	2 RCTs		1 RCT: Intergroup difference EQ-5D VAS at 6 months: 1, n.s. 1 RCT: Intergroup difference Δ SF36 MCS (range 0-100) at 6 months: 4.4, p=0.03 Δ SF36 PCS (range 0-100) at 6 months: 3.8, n.s.	Low [1] ⊕⊕◯◯
Body weight and waist circumference	3 RCTs	2 RCT, data on body weight SMD (CI95%): -0.33 (-0.62 to -0.04), p= 0.025 2 RCT, data on waist circumference SMD (CI95%) -0.20 (-0.48 to +0.09), p= 0.18	<u>1 RCT</u> Body weight (kg) I Δ 3 years: -0.8 (-2.1; 0.6) C Δ 3 years: 0.1 (-2.3; 2.6), p=0.73 WC (cm) I Δ 3 years: -1.7 (-3.2; -0.3) C Δ 3 years: -0.03 (-2.6; 2.5) p=0.97 <u>1 RCT</u> Body weight (kg) I Δ 18 months: -0.4 (-1.6; 0.7) C Δ 18 months: -0.3 (-1.2; 0.7), n.s. WC (cm) I Δ 18 months: -2.1 (-3.4; -0.8) C Δ 18 months: -2.6 (-4.0; -1.2), n.s. <u>1 RCT</u> Body weight (kg) I Δ 6 months: -1.8 (-2.8; -0.8) C Δ 6 months: -0.5 (-1.1; 0.1), p=0.023 WC (cm) I Δ 6 months: -2.3 (-3.5; -1.1) C Δ 6 months: -1.4 (-2.2; -0.6), n.s.	Low [2] ⊕⊕◯◯
Blood pressure	2 RCTs		1 RCT: SBP (mmHg) I Δ 3 years: -15.6 (-11.0; -20.2) C Δ 3 years: -9.2 (-3.8; -14.7), n.s. DBP (mmHg) I Δ 3 years: -5.5 (-3.1; -7.8) C Δ -3.0 (-7.0; 0.9), n.s. 1 RCT: SBP (mmHg) I Δ 6 months: 0.2 (-4.3; 4.7) C Δ 6 months: -4.1 (-7.5; -0.6), n.s. DBP (mmHg) I Δ 6 months: -1.0 (-3.5; 1.6) C Δ 6 months: -1.7 (-4.4; 0.9), n.s.	Very low [3] ⊕◯◯◯

Glucose metabolism	2 RCTs		1 RCT: HbA1c (mmol·mol-1) I Δ 3 years: -2.7 (-1.7; -3.6) C Δ 3 years: -2.2 (-0.9; -3.5), n.s. 1 RCT: HbA1c (% average total Hb) I Δ 6 months: -0.1 (-0.2; 0.0) C Δ 6 months: 0.2 (0.1; 0.3), p=0.001	Low [2] ⊕⊕◯◯
Blood lipids	1 RCT		1 RCT: Cholesterol (mmol·l-1) Intergroup difference in mean Δ (I-C) at 6 months: -0.4, p=0.042 Triglycerides (mmol·l^{-1}) Intergroup difference in mean Δ (I-C) at 6 months: -0.2, p=0.08 HDL (mmol·l^{-1}) Intergroup difference in mean Δ (I-C) at 6 months: 0.0, n.s. LDL (mmol·l^{-1}) Intergroup difference in mean Δ (I-C) at 6 months: -0.2, n.s.	Very low [4] ⊕◯◯◯
Level of physical activity	5 RCT (6 articles) 1 Cohort		1 RCT: PA sessions/week I Δ 6 months: +1.7 C Δ 6 months: +0.5, p=0.07 MVPA sessions/week I Δ 6 months: +1.2 C Δ 6 months: +0.2, p=0.023 1 RCT: I Δ Sedentary/low level PA: -7.2% C Δ Sedentary/low level PA: -3.8%, n.s I Δ Moderate level PA: 7.2 % C Δ Moderate level PA: 3.8%, n.s 1 RCT: Cycling >4.0 km/d, 18 months: 24.8% Cycling >4.0 km/d, 18 months: 4.6% p=0.001 1 RCT: MVPA sessions/week: I Δ 6 months: +3 C Δ 6 months: no data, p<0.001 1 RCT: MVPA minutes/day I Δ 6 months: +3 C Δ 6 months: -2, n.s. 1 RCT: Exercise min/week I Δ 6 months: +137 (0-490) C Δ 6 months: 0 (-105-240), p=0.03 1 Cohort: I patients with increased PA: 9/16 C patients with increased PA: 3/16 p=0.039	Moderate [4] ⊕⊕⊕◯

Physical function	1 RCT		6MWT Intergroup difference in mean Δ (I-C) at 6 months: 39 m, p=0.01	Low [1] ⊕⊕◯◯
Adverse events	4 RCT 1 Case-series		1 RCT 24 % musculoskeletal pain in both groups. 3 RCT and 1 Case-series: No adverse events reported	Moderate [4] ⊕⊕⊕◯

DBP = Diastolic blood pressure; EQ-5D = EuroQoL-5 Dimension Questionnaire; HbA1c = Glycated haemoglobin; MCS = Mental Component Summary; MVPA = Moderate vigorous physical activity; NS = Not significant; n.s; PA = Physical activity; PCS = Physical Component Summary; SBP = Systolic blood pressure; SF-36 = 36-Item Short Form Health Survey.

[1] Downgraded for study limitations, some indirectness, and imprecision.

[2] Downgraded for some study limitations, some inconsistency and imprecision.

[3] Downgraded for some study limitations, indirectness and imprecision.

[4] Downgraded for some study limitations and imprecision.

Certainty of evidence

High certainty ⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty ⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty ⊕⊕◯◯	Confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low certainty ⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

4. Abbreviations/Acronyms

BMI = Body mass index
C = Control
CI = Confidence interval
DBP = Diastolic blood pressure
EQ5D = EuroQoL-5 dimension questionnaire
FYSS = Physical activity in the prevention and treatment of disease (Fysisk aktivitet i sjukdomsprevention och sjukdomsbehandling)
Hb = Haemoglobin
HbA1c = Glycated haemoglobin
HDL = High density lipoproteins
HOMA-IR = Homeostatic model assessment – insulin resistance
HPH = Health-Promoting Hospitals and healthcare services
HRQoL = Health-related quality of life
HTA = Health technology assessment
I = Intervention
IFG = Impaired fasting glucose
IGT = Impaired glucose tolerance
IPAQ = International physical activity questionnaire
KVÅ = Registered treatment codes (Klassifikation av vårdåtgärder)
LDL = Low density lipoproteins
MCS = Mental Component Summary
MID = Minimal important difference
MPA = Moderate-intensity physical activity
MVPA = Moderate-vigorous physical activity
NS = Not significant
OR = Odds ratio
PA = Physical activity
PAP = Physical activity on prescription
PCS = Physical Component Summary
PICO = Patients, intervention, comparison, outcome.
RCT = Randomised controlled trial
SBP = Systolic blood pressure
SF-36 = 36-item short form survey.
VAS = Visual analogue scale
VGR = Region Västra Götaland
VPA = Vigorous-intensity physical activity
WC = Waist circumference
YFA = Professional associations promoting physical activity (Yrkesföreningar för fysisk aktivitet)
6-MWT = Six-minute walk test

5. Background

Disease/disorder of interest and its degree of severity

Lack of physical activity is a major health threat globally. According to the World Health Organization, physical inactivity is identified as the fourth leading risk factor for non-communicable diseases, and has accounted for more than 3 million premature deaths in 2004 (World Health Organization. 2009). Specifically, physical inactivity has accounted for 30% of the ischaemic heart disease burden, 27% of diabetes cases and 21-25% of the breast and colon cancer burden (World Health Organization. 2009).

Accordingly, regular physical activity may prevent diseases such as cardiovascular disease and also be used to treat established disease. For instance, there is evidence for physical activity as treatment for, e.g., atherosclerotic cardiovascular disease (Thompson et al. 2003), chronic obstructive pulmonary disease (McCarthy et al. 2015), diabetes (Colberg et al. 2016) and overweight (Donnelly et al. 2009).

Prevalence and incidence of physical inactivity

Globally, almost one third of adults are estimated not to reach public health guidelines for recommended levels of physical activity (Hallal et al. 2012). The national recommendations on physical activity for adults in Sweden include recommendations of ≥150 minutes of moderate-intensity physical activity (MPA), or alternatively, vigorous-intensity physical activity (VPA) 75 minutes per week. These recommendations have been prepared by the Swedish Professional Associations for Physical Activity and approved by the Swedish Medical Association (Yrkesföreningar för fysisk aktivitet. 2011). In a recent population-based study from Gothenburg, only 30% of the middle-aged population (50-64 years) adhered to these recommendations, while only 7% adhered to the strictest recommendations of ≥30 minutes of MVPA ≥5 days/week, in bouts of ≥10 minutes (Lindgren et al. 2016).

Present treatment – Methods for increasing physical activity

While there is a global consensus on the threat that lack of physical activity imposes on health, and that increased physical activity will have positive health effects, there is still a lack of consensus on how to achieve increased physical activity in health care. There are several available methods. Many citizens are in contact with healthcare facilities due to health problems each year, and individuals who experience health problems have a higher probability of being physically inactive. Many individuals in need of physical activity interventions may thus be reached by health care professionals (Kallings 2008b). Lifestyle interventions have become an increasing part of routine healthcare, with, e.g., smoking and alcohol counselling. In the Swedish healthcare system, several approaches to promote physical activity have been proposed and evaluated. One such approach is counselling, which is the base for physical activity promotion according to The Swedish National Board of Health and Welfare's National Guidelines for Methods of Preventing Disease (Socialstyrelsen, 2017) Counselling is defined as a dialogue between a healthcare professional and a patient, with adaptation to the individual's age, health and risk levels. According to these recommendations, counselling can be combined with the use of Physical Activity on Prescription (PAP) – a first line treatment strategy for preventive and therapeutic purposes, a pedometer that registers the number of daily steps, and/or by the use of a physical activity diary (Socialstyrelsen. 2017). Today, a majority of patients who would benefit from increased level of physical activity do not receive counselling on physical activity when they are in contact with healthcare. Many receive brief advice, at most.

The normal pathway through the health care system and current waiting time for medical assessment /treatment

Patients with insufficient physical activity are seen in inpatient as well as in outpatient health services. For patients with some diagnoses, e.g. myocardial infarction or diabetes, physical activity in the form of group exercise sessions are used. Traditionally, counselling and other interventions for physical activity are mainly used in primary healthcare, but promoting better life-style habits including increased levels of physical activity should be applied among all patients with little or no physical activities being part of their lifestyle.

Only 30% of middle-aged individuals in Gothenburg meet the current recommendations for physical activity (Lindgren et al. 2016), suggesting that 70% of the middle-aged population would need increased physical activity. Since a majority of patients in the Swedish healthcare system suffer from non-communicable diseases, whereof many are caused by lifestyle habits, an even higher proportion of patients might be physically inactive. There are no data showing how many of these individuals that receive advice on physical activity from healthcare professionals. During 2016, there were 16,000 prescriptions for physical activity (PAP) in Region Västra Götaland (VGR), corresponding to 1.2 % of all adult patients. This percentage is uncertain since patients can receive more than one PAP during one year. The corresponding rate of counselling on the levels of physical activity recommended by the Swedish National Board of Health and Welfare was 2.8 % during the same period. Promotion of physical activity has probably been carried out in more patients without being registered.

Present recommendations from medical societies or health authorities

The base for PA promotion is counselling according to The Swedish National Board of Health and Welfare's National Guidelines for Methods of Preventing Disease. Counselling can be combined with the use of physical activity on prescription (PAP), a pedometer that registers the number of daily steps, and/or a physical activity diary (Socialstyrelsen. 2017).

6. Health Technology at issue: The Swedish model for physical activity by prescription (PAP)

Swedish PAP is individually tailored for the patient. In Sweden, all licensed healthcare professionals may prescribe physical activity (Socialstyrelsen. 2017). Knowledge about the patient´s health status and the use of physical activity for prevention or treatment of diseases according to the *Physical activity in the prevention and treatment of disease* (FYSS) is required (Yrkesföreningar för fysisk aktivitet. 2016). Prescription of PAP also requires skills in the patient-centred dialogue concerning behavioural change as well as knowledge about the PAP method. The PAP treatment includes a dialogue with the patient illuminating previous experiences of physical activity, current level of physical activity and sedentary behaviour. The patient´s health status, level of motivation, self-efficacy and readiness to change physical activity behaviour are assessed and measured.

Based on this information, a target for physical activity is agreed upon. The type and dose (frequency, duration, intensity) of physical activity are discussed and a prescription is written. An adequate relative intensity of the chosen physical activity is communicated by using the Borg´s rate of perceived exertion scale (Borg 1998). Individualised, structured follow-up will then be offered to the patient by revisit and/or telephone contact. At follow-up, the PAP and possible use of a physical activity diary and pedometer are evaluated and the dose of physical activity may be revised. The health status of the patient is again checked at this time.

The individualised Swedish PAP model differs from physical activity and exercise prescription models used in other countries. A model used in several other countries is exercise referral schemes where the patient usually is recommended and included in supervised group exercise at specific exercise centres for a specified amount of time. The efficacy of exercise referral schemes has been evaluated in systematic reviews (Pavey et al. 2011, Campbell et al. 2015) showing varying results, with small to medium increases in physical activity levels. Since the exercise referral schemes differ from the Swedish PAP model in many respects, generalising the results to the Nordic setting is questionable. In this Health Technology Assessment, the Swedish PAP model as it is used in Swedish and Nordic settings was considered to include three elements: 1. Individualised counselling. 2. Individually tailored physical activity recommendation with a written prescription. 3. Structured follow-up. The follow-up may be in form of follow-up visits, telephone calls, mail or e-mail, at one or several occasions (Socialstyrelsen, 2017b)

Several publications, mainly case series, have reported the adherence to PAP prescription and factors related to the adherence, for the Swedish PAP model (Kallings et al. 2008a, Leijon et al. 2008, Kallings et al. 2009, Leijon et al. 2009, Leijon et al. 2010, Sundquist et al. 2010, Leijon et al. 2011, Sjoling et al. 2011, Lerdal et al. 2013, Rodjer and Borjesson. 2016, Lundqvist et al. 2017).

It has been debated whether there is sufficient evidence to support the use of the Swedish PAP in clinical practice (Lövtrup 2014). There have been several attempts to transform knowledge about the positive health effects of physical activity into improved lifestyle behaviour in individuals. For a long time, this was attempted mainly by means of short advice, which now is known to be ineffective in achieving lifestyle changes. Due to this, the Swedish PAP method was developed (Kallings, 2012). In the light of existing reviews on exercise-referral schemes (Pavey et al. 2011, Campbell et al. 2015) and the lack of similar systematic reviews on the Swedish PAP model, this Health Technology Assessment (HTA) was initiated. Our aim was to review the existing scientific evidence for the efficacy of the Swedish PAP model.

7. Objective

To study if physical activity on prescription, according to the Swedish PAP-model, is better than not receiving Swedish PAP when it comes to level of physical activity, mortality, morbidity, health-related quality of life (HRQoL), and physical function for adults that have been deemed to be in need of increased physical activity by a healthcare professional.

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P	Adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional
I	Physical activity on prescription (PAP) according to the Swedish model in a Nordic setting, including individual counselling, written, individualised prescription, and follow-up
C	No PAP according to the Swedish model, excluding disease/injury-specific rehabilitation
O	<u>Critical for decision making</u> Mortality Morbidity (e.g. AMI, stroke, cardiovascular events) Health related quality of life Level of physical activity <u>Important for decision-making</u> Morbidity (risk factors, i.e. Body Mass Index (BMI), waist circumference, blood pressure, fasting glucose, HbA1c/insulin resistance, cholesterol, HDL/LDL ratio) Physical function Adverse events

8. Methods

Systematic literature search (Appendix 1)

During September 2017 two authors (TS, ELD) performed systematic searches in PubMed, Embase, the Cochrane Library, Amed, Cinahl, PsycINFO and Svemed+. The websites of SBU, Folkehelseinstituttet and Sundhedsstyrelsen were also searched. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, selected studies, and independently of one another assessed the obtained abstracts and made a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to all the participants of the project group. All authors read the articles independently of one another and it was finally decided in a consensus meeting which articles should be included in the Health Technology Assessment.

Critical appraisal and certainty of evidence

The included studies and their design and patient characteristics are presented in Appendix 2. The excluded studies and the reasons for exclusion are presented in Appendix 3. The included studies, except for the case series, have been critically appraised using a checklist from the SBU for assessment of randomised controlled trials, modified by HTA-centrum and a checklist for assessment of cohort studies, also from SBU but modified by HTA-centrum. The results and the assessed quality of each article have been summarised per outcome in Appendix 4.
Data were extracted by at least two authors per outcome. When possible, data were pooled in meta-analyses in Stata 14.0 using a random effects model and presented as forest plots.
A summary result per outcome and the associated certainty of evidence are presented in a Summary-of-findings table (page 8). The certainty of evidence was defined according to the GRADE system (Atkins et al. 2004; GRADE Work group).

Ongoing research

A search in Clinicaltrials.gov (2017-12-11) using the search terms (Prescription OR Referral OR Consultation) AND (Physical activity OR Exercise) AND (Sweden OR Swedish OR Norwegian OR Norway OR Danish OR Denmark OR Finland OR Finnish OR Iceland OR Icelandic OR Nordic OR Scandinavian) identified 139 trials**.**

9. Results

Systematic literature search (Appendix 1)

The literature search identified 1,093 articles after removal of duplicates. After reading the abstracts 1,015 articles were excluded. Another 39 articles were excluded by two authors after reading the articles in full text. The remaining 39 articles were sent to all participants of the project group, and nine articles (seven RCTs, one cohort study and one case series) were finally included in the assessment (Appendix 2). The case-series was included to collect information on adverse events. Overall, the controlled studies had no or minor problems with directness, some problems with study limitations and some or major problems with precision.

Results per outcome

Outcomes, critical for decision-making

Mortality and direct morbidity

No studies reported mortality or direct morbidity data.

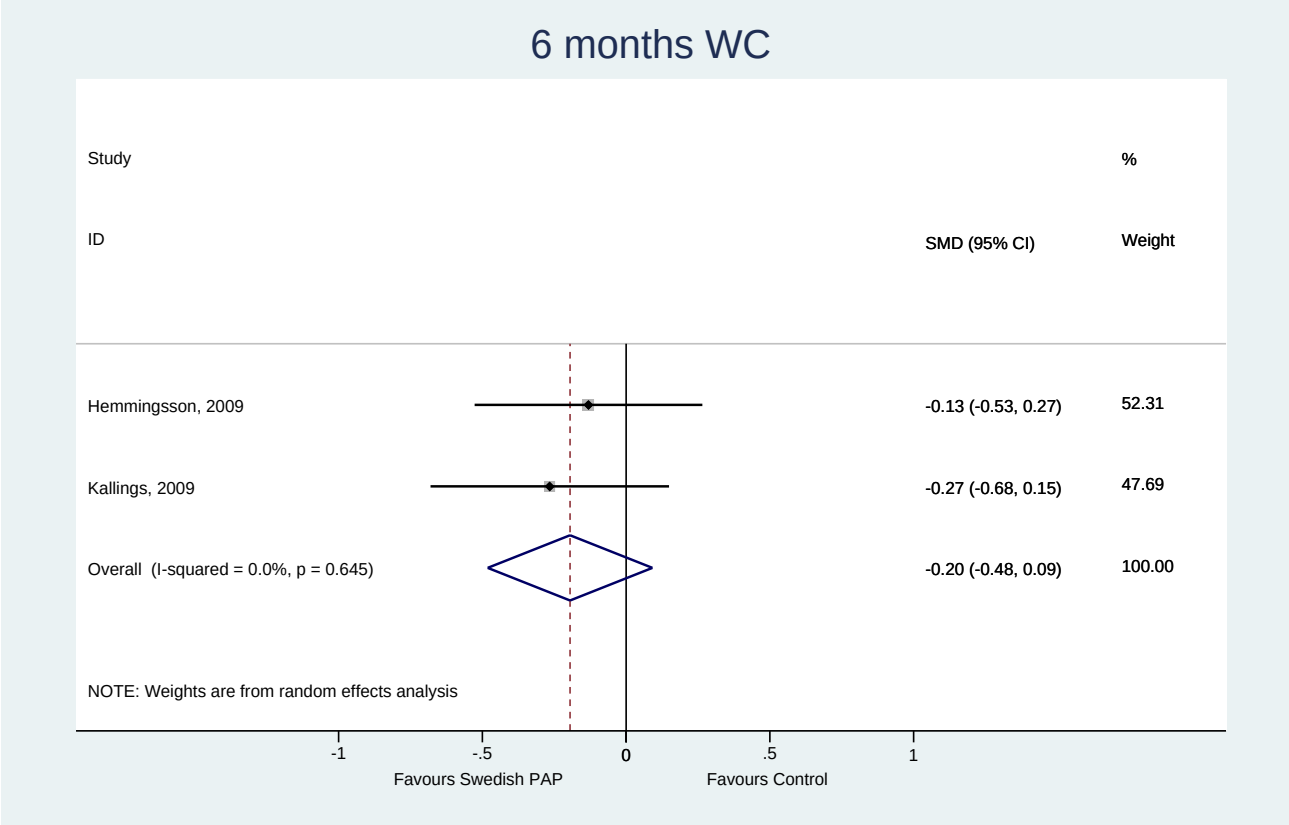
Health related quality of life (HRQoL) (Appendix 4.1)
The effect on HRQoL was studied in two RCTs comparing Swedish PAP with usual care or written general information on the importance of physical activity. Both studies had minor problems with directness and some problems with study limitations and precision.
One of the RCTs showed no significant difference on HRQoL, measured by EQ-5D VAS over six months. The other RCT showed a small but significant improvement (+4.4 for Swedish PAP versus 0.0 for control, p= 0.03) in the SF-36 mental component summary (MCS, range 0 - 100), but no significant intergroup difference in any single domain or in the physical component summary (PCS), by PAP compared with written general information.
Conclusion: Swedish PAP compared with no PAP may result in little or no difference regarding HRQoL in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Low certainty of evidence (GRADE ⊕⊕◯◯).

Level of physical activity (Appendix 4.2)
The effect on the level of physical activity was reported in seven articles that derived from five RCTs and one cohort study. The studies had no or minor problems with directness, some problems with study limitations and precision.
Several different aspects of level of physical activity were reported and with different follow-up times, ranging from three months to three years, making meta-analysis impossible. Three out of five RCTs, and the cohort study showed positive effects on level of physical activity for Swedish PAP compared with no PAP. Aittasalo et al. reported an increase from 2.3 to 3.5 MVPA sessions per week. Kallings et al. and Sjögren et al. both reported that participants more than doubled their weekly exercise time (an increase by 159 and 137 minutes/week, respectively). For full details, please see appendix 4.2.
Conclusion: Swedish PAP probably results in an increased level of physical activity compared with no PAP, in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Moderate certainty of evidence (GRADE ⊕⊕⊕◯).

Outcomes, important for decision-making

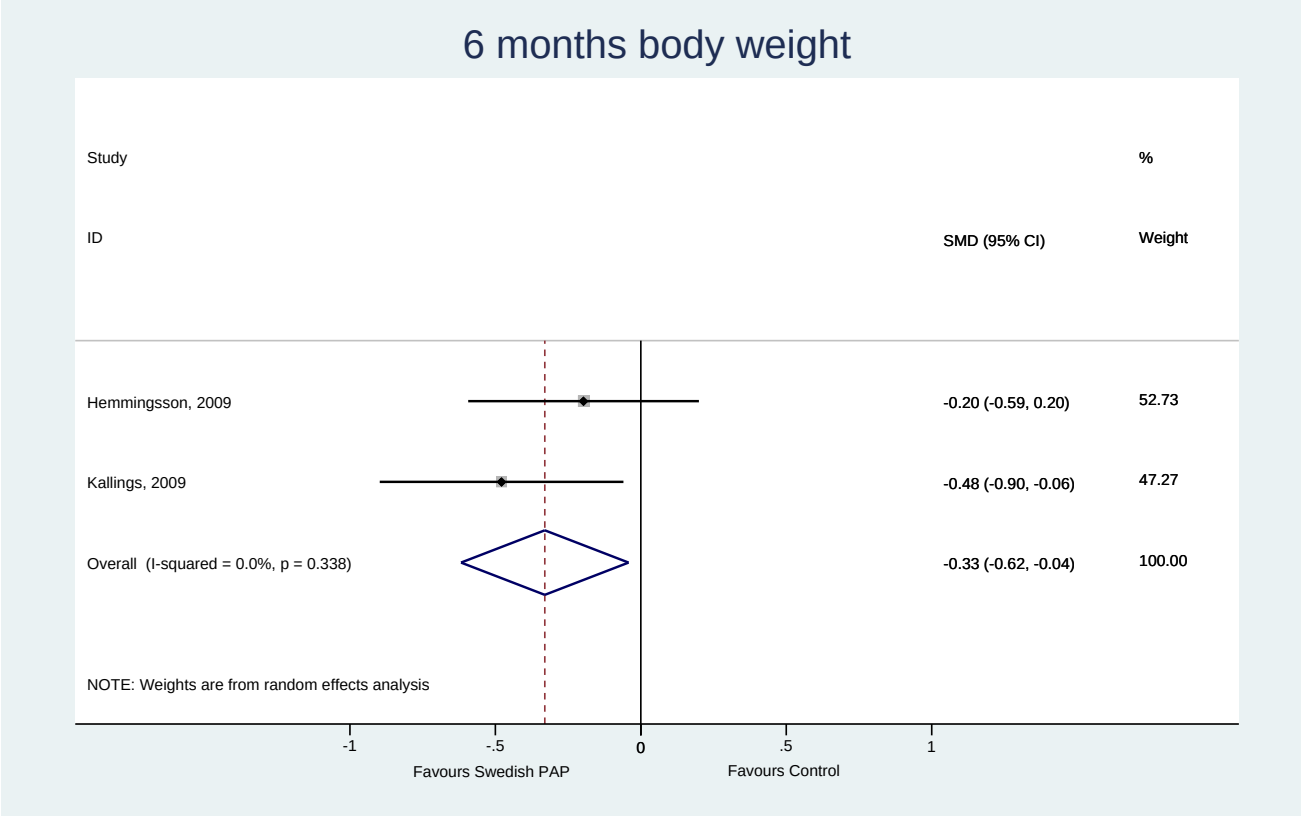
Anthropometric factors (waist circumference and body weight) (Appendix 4.3)
The effect on anthropometric factors was studied in three RCTs comparing Swedish PAP with usual care, group sessions, or written general information on the importance of physical activity. All three RCTs had no or minor problems with directness, minor problems with study limitations and some problems with precision.
None of the RCTs showed any significant effect on waist circumference (WC). Meta-analysis showed a non-significant effect of Swedish PAP on WC (SMD -0.20, 95%CI -0.48 to +0.09, p= 0.18).

Figure 1. Meta-analysis of the effects of Swedish PAP versus control on waist circumference (WC) at six months



Two RCTs showed effects of Swedish PAP on body weight at six months. There was a small but significant positive effect of Swedish PAP in one of these studies (p= 0.023). The third RCT showed a non-significant effect on body weight at three years. A meta-analysis of effects of Swedish PAP on body weight at six months based on two RCTs resulted in a pooled estimate of SMD: -0.33 (95%CI -0.62 to -0.04, p= 0.025).

Figure 2. Meta-analysis of the effects of Swedish PAP versus control on body weight (bw) at six months.



Conclusion: Swedish PAP compared with no PAP may result in a slight reduction in body weight and in WC in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Low certainty of evidence (GRADE ⊕⊕◯◯).

Blood pressure (Appendix 4.4)

The effect on blood pressure was studied in two RCTs comparing Swedish PAP with usual care or written general information on the importance of physical activity. Both RCTs had major problems with directness since the populations studied had mean systolic blood pressure of 137-143 mmHg. Both RCTs had some problems with study limitations, and some problems with precision.
None of the RCTs showed any significant effect on systolic or diastolic blood pressure.
Conclusion: It is uncertain whether blood pressure is affected by Swedish PAP compared with no PAP in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Very low certainty of evidence (GRADE ⊕◯◯◯).

Glucose metabolism (Appendix 4.5)

Effect on glucose metabolism was studied in two RCTs comparing Swedish PAP with usual care or written general information on the importance of physical activity. Both RCTs had no or minor problems with directness, minor or some study limitations and some problems with precision.
One RCT did not show any statistically significant effect on the risk for developing diabetes or on insulin resistance (HOMA-IR) or HbA1c. The other RCT showed no effect on fasting glucose, but a small positive effect on HbA1c in the Swedish PAP treatment group compared with written general information, p=0.001.
Conclusion: Swedish PAP compared with no PAP may result in little or no difference regarding glucose metabolism in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Low certainty of evidence (GRADE ⊕⊕◯◯).

Blood lipids (Appendix 4.6)
The effect on blood lipids was studied in one RCT comparing Swedish PAP with written general information on the importance of PA. The RCT had minor problems with directness, some problems with study limitations and precision.
The RCT showed no effect on triglycerides, HDL or LDL, but a positive effect on total cholesterol in the Swedish PAP treatment group (-0.3 mmol/L) compared with written general information (0.1 mmol/L), p=0.042.
Conclusion: It is uncertain whether blood lipids are affected by Swedish PAP compared with no PAP in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Very low certainty of evidence (GRADE ⊕◯◯◯).

Physical function (Appendix 4.7)
The effect on physical function was studied in one RCT, assessed with the 6-minute walk test (6-MWT). The RCT had some problems with directness due to a study population limited to patients with transient ischemic attacks. The RCT had some problems with study limitations and precision.
The RCT showed no significant effect at three months, but a significant improvement in 6-MWT walking distance at 6 months in the Swedish PAP group (+70 m) compared with usual care (+31 m), p=0.01.
Conclusion: Swedish PAP compared with no PAP may increase 6-MWT walking distance in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Low certainty of evidence (GRADE ⊕⊕◯◯).

Adverse events (Appendix 4.8)
Adverse events due to Swedish PAP were reported in four RCTs and one case series. The only detected adverse event was musculo-skeletal pain. Four of the studies reported no adverse events. In one RCT, musculoskeletal pain was reported in 24% in both groups.
Conclusion: Swedish PAP probably results in little or no difference in adverse events compared with no PAP in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional. Moderate certainty of evidence (GRADE ⊕⊕⊕◯).

10. Ethical issues

The proposed treatment and ethical values
Health care is aimed at providing the best possible treatment for and/or advice for prevention of disease, according to existing guidelines and recommendations. For this reason alone, refraining from giving lifestyle advice to patients with lifestyle-related diseases is ethically doubtful. The PAP is developed to make the patient take the necessary active part, required for any lifestyle change. In addition, barriers and facilitators for achieving lifestyle change are to be identified for each individual in the PAP dialogue. This principle is an important component of person centred care. The strong socioeconomic association to adverse lifestyle behaviour, may be counteracted by active lifestyle promotion as part of routine health care, and may thus contribute to less inequality in health care.

As a counter-argument it has been put forward that health care involvement in lifestyle behavioural change constitutes an unnecessary restriction of the patients´ integrity. Physical activity is recommended as a part of treatment for several symptoms and diagnoses in routine health care (YFA. 2016). Thus, PAP as part of routine care is congruent with ethical values in health care (Arlebrink 2016).

11. Organisational aspects

Time frame for the putative introduction of the new health technology
Swedish PAP has already been introduced into routine healthcare in Region Västra Götaland, and there are no major obstacles to increase the number of prescriptions of PAP. There are national, regional and local guidelines on how to use the Swedish PAP model. The Medical committee of Region Västra Götaland has a therapy group on Physical activity (Läkemedelskommitten i VGR) that recommends the types of physical activity that should be used for different diagnoses. These are included in the regional recommendations for treatments of common diagnoses (REKlistan. 2018) that are widely used both in primary healthcare and hospitals. More detailed information on the effect of physical activity for different diagnoses is provided in the book "FYSS 2017" (Yrkesföreningar för fysisk aktivitet, 2016). All healthcare facilities and hospitals in Region Västra Götaland are members of the national Health-Promoting Hospitals and healthcare (HPH) services network, where the use of Swedish PAP is promoted.

Present use of the technology in other hospitals in Region Västra Götaland
Swedish PAP is used to some degree in all parts of Region Västra Götaland. It is hard to achieve reliable data on the number of visits that include PAP. According to the procedure code (KVÅ) recorded, there were 79,469 healthcare visits in Region Västra Götaland in 2016 that recorded either brief advice, counselling or advanced counselling regarding physical activity. Counselling, which is the level recommended by the Swedish National Board of Health and Welfare, constituted 47% of these activities. In the same year, it was reported that 17,041 individuals were prescribed PAP, a decline by 49% from the 33,362 PAP prescriptions in 2015. This decline is likely due to the fact that economic compensation for using PAP was removed in 2016. To conclude, only 21% of the patients where physical activity advice in some form was recorded received PAP. It can be assumed that the number of patients where physical activity advice was recorded only reflects a fraction of those patients in contact with healthcare in Region Västra Götaland that are in need of increased physical activity.

Consequences of the new health technology for personnel

Consequences for other clinics or supporting functions at the hospital or in the Region Västra Götaland
A majority of the patients with diseases that can be prevented and to some extent treated with increased levels of physical activity primarily seek care in primary healthcare. A more widespread use of counselling and PAP to patients in need of increased physical activity will probably necessitate increased resources in the short term. However, given the documented primary and secondary preventive effects of physical activity (Thompson et al. 2003, World Health Organization. 2009, McCarthy et al. 2015, Piepoli et al. 2016), long-term effects may include fewer years with disease burden for the individual.

12. Economic aspects

Present costs of currently used technologies
During 2016, there were 79,469 healthcare visits when counselling concerning physical activity was provided and 17,041 visits when PAP was used in Region Västra Götaland (Table 1). For this total of 96,510 visits, the main diagnosis was endocrine, nutritional or metabolic in 24%, circulatory system in 21%, musculoskeletal system and connective tissue in 14%, and nervous system diseases in 12%.

Table 1. Health care visits of counselling concerning physical activity and physical activity on prescription (PAP) in the Region Västra Götaland.

	2015	2016
Brief advice (code DV131)	31,601	32,851
Counselling (code DV132)	37,148	37,268
Advanced counselling (code DV133)	7,959	9,350
Total	**76,708**	**79,469**
PAP (code DV200, UV101)	33,362	17,041

Data source: Healthcare consumption register VEGA, Region Västra Götaland

In this aggregated data, the total annual healthcare visits are presented. However, we do not have any information regarding the number of patients that received the counselling. If we assume that each individual received an average of two counselling occasions per person, then approximately 40,000 individuals received counselling during 2016.
In the primary care in Region Västra Götaland, the reimbursement per visit to a physician is 1 500 SEK and 600 SEK per visit to a nurse or other health care professionals. Of all the health care visits during 2016, 20% of the brief advice, 22% of the counselling and 25% of the advance counselling were to a physician. Further, 33% of PAPs were prescribed by a physician. Hence, 17,405 of these healthcare visits were to a physician at a cost of 26.1 million SEK, and 62,064 of the healthcare visits were to a nurse or other profession at a cost of 37.2 million SEK. The total cost during 2016 was thus 63.3 million SEK.

Expected costs of increasing physical activity on prescription (PAP)
It is difficult to make a fair estimation of the total change of cost for implementing Swedish PAP. With the realisation that promoting physical activity is a very important area for the healthcare systems, the cost of PAP should really be compared with counselling, which is the recommended minimum level of intervention according to the Swedish National Board of Health and Welfare (Socialstyrelsen. 2017). Since the difference between physical activity counselling and PAP mainly constitutes the time it takes to describe the individualised recommendation on a prescription, the real added cost for PAP is marginal. Thus, when estimating the expected cost of implementing Swedish PAP, there is an uncertainty whether the increase in PAP will cause more visits to the healthcare or if the increase in PAP could be expected to be included in the already existing visits to the healthcare. Hence, in this economic analysis, three scenarios will be described.

Scenario 1 – minimum costs
In the first scenario, we assume that implementing Swedish PAP could be expected to be included in the already existing visits to the healthcare. Thus, there will be no additional cost when increasing the prescriptions of physical activity.

Scenario 2 – maximum costs
In the second scenario, we assume that 70 percent of the adult population in Region Västra Götaland, i.e. 1.3 million inhabitants, that has unhealthy lifestyle would take part of any of the recommended interventions by the Swedish National Board of Health and Welfare during a five-year period. According to the Swedish National Board of Health and Welfare (Socialstyrelsen. 2017), half of the female population and one third of male population have at least one unhealthy lifestyle habit, corresponding to 440,000 males and 330,000 females, equal to 770,000 individuals in Region Västra Götaland. Thus, in this second scenario we are assuming that 70 percent of this population are possible candidates for counselling concerning physical activity. If we also assume that 10 percent of this population already have received a PAP, corresponding to an assumed population of 485,000 individuals.

If this population receive two healthcare visits, i.e. one counsel and one follow-up, whereof 23% to a physician, the annual average cost during a five-year period would be 156.4 million SEK in this scenario.

Scenario 3 – the middle way
In the third scenario, we assume a middle way between the current strategy and the maximum strategy (scenario 2), where 75% of the population in scenario 2 are possible candidates for counselling concerning physical activity and receive two health care visits, i.e. one counselling visit and one follow-up, whereof 23% to a physician. The annual average cost during a five-year period would be 117.3 million SEK in this scenario.

Total change of cost
With scenario 2, the maximum cost approach, the annual additional cost would be 93.1 million SEK compared with the current strategy. The middle way strategy (scenario 3), would lead to an additional cost of 54 million SEK (Table 2).

Table 2. Additional cost of implementing Swedish PAP in the Region Västra Götaland.

	Individuals during a five year period	Individuals per year during a five year period	Annual average cost (million SEK)	Additional cost compared with the current strategy (million SEK)
Current strategy	200,000	40,000	63.3	
Scenario 1	-	-	-	0.0
Scenario 2	485,000	97,000	156.4	93.1
Scenario 3	363,000	72,600	117.3	54.0

Possible economic savings within the health care sector
Compared with the compelling evidence base for prevention of premature death and morbidity by increased physical activity, it can be assumed that increased PAP prescription could be translated to a future reduction in healthcare consumption. However, analysing the estimated economic savings within the health care sector for implementing Swedish PAP has not been possible within the scope of this economic analysis. Physical inactivity has been estimated to have an economic burden on the health care system corresponding to international $ 53.8 billion worldwide in 2013, and be responsible for 13.4 million disability-adjusted life years (Ding et al. 2016). It has been shown that physical inactivity attributes to 1% to 2.6% of the healthcare costs in various settings (Pratt et al. 2014). According to the Public Health Agency in Swedish (Statens folkhälsoinstitut 2010), the health care cost caused by physical inactivity was 860 million SEK during 2010. These costs were based on the relative risk of developing colon and breast cancer, hypertension, cardiovascular disease, depression and anxiety, type-2 diabetes and osteoporosis. A Swedish report from 2006 (Bolin and Lindgren 2006) estimated the total healthcare cost to 750 million SEK during 2002, 0.4% of the total national healthcare cost. This economic analysis was based on the cost of developing colon and breast cancer, hypertonia, vascular diseases, ischemic heart disease, stroke, depression and anxiety, type-2 diabetes and osteoporosis. For the health care system, physical inactivity contributed to 17,800 healthcare visits and 88,600 days of inpatient care. Of the corresponding total health care costs, 34% were for inpatient care, 37% for outpatient care and 20% were for pharmaceuticals.

Possibility to adopt and use the new technology within the present budget

There may be a short-term increase in healthcare costs if PAP is more widely introduced before a reduction in healthcare resource consumption is seen.

Available economic evaluations or cost advantages/disadvantages

There are no published economic evaluations on cost effects of introducing Swedish PAP.

13. Discussion

Summary of main results

The main result from this Health Technology Assessment is that Swedish PAP probably results in an increase in the level of physical activity, compared with no PAP, in adult individuals who who have been deemed to be in need of increased physical activity by a healthcare professional (GRADE⊕⊕⊕◯). The magnitude of this increase is poorly defined. No studies on the effects on mortality and direct morbidity exist to date although the effects on risk factors for morbidity have been reported in a few studies.

Overall completeness and applicability of evidence

The effect of PAP on the level of physical activity was based on data reported from five RCTs and one cohort study. Study participants represented several of the major patient groups suitable for receiving PAP, suggesting that the results are generalisable to many patients in need of increased PA. This HTA report was restricted to the Swedish PAP model used in Nordic settings increasing the applicability of our report to Swedish healthcare settings.

Agreements and disagreements with other studies and reviews

No systematic review, evaluating Swedish PAP in Nordic settings, has been published up to now. The effects of exercise referral schemes used in other countries, have been evaluated in systematic reviews (SR) and the results from these constituted the basis for the national guidelines on promoting physical activity from the Swedish National Board of Health and Welfare (Socialstyrelsen. 2017). These SRs assessed exercise referral schemes (Pavey et al. 2011, Campbell et al. 2015). In the latest of these, it was concluded that based on evidence from eight studies with 5190 participants, there was a relatively small increase in participants that reached recommended levels of MVPA.

A majority of the studies included in our HTA report showed improvements in level of physical activity. One difference between the two mentioned models for promoting physical activity is that exercise referral schemes are more focused on referring patients to a program performed outside the healthcare system lasting typically 10-12 weeks, whereas Swedish PAP focuses on incorporating individually dosed physical activity into the lifestyle of the patient and continuing follow-up of the patient within the healthcare setting. The follow-up of the PAP is often performed in association with other planned follow-ups with the health care facility, and may be performed in person, through telephone calls, or by mail or e-mail at one or several occasions.

The clinical importance of increased levels of physical activity need to be discussed. A dose-response association between physical activity and outcome parameters such as death and cancer has been suggested (Wen et al. 2011, Holme and Anderssen 2015). Wen et al concluded that every addition of 15 minutes of daily exercise beyond the minimum amount of 15 minutes per day reduced mortality by 4%. Individuals with at least 15 minutes of daily exercise had three years higher life expectancy than inactive individuals. Holme and Anderssen found that light-intensity physical activity four hours per week was associated with a 38% reduction in all-cause mortality compared to being sedentary, while four hours per week of MPA was associated with a 53% reduction in all-cause mortality compared to being sedentary. Holme and Anderssen also found that for each added hour of physical activity per week, there was a significant increase in survival. In summary, although there is no formal definition of the minimal important difference (MID) in level of physical activity, an increase with 15 minutes per day, or 1 hour per week is likely to be clinically relevant.

Regarding physical function, there was an improved 6MWT walk distance by Swedish PAP versus control (+70 versus +31 meters, p= 0.01). The minimally clinically important difference for 6-MWT walk distance across patient groups is reported to 14 – 30.5 meters (Bohannon and Crouch. 2017).

The 2011 guidelines from the Swedish National Board of Health and Welfare on methods to prevent disease, have not been implemented uniformly in Sweden, up to now. (Socialstyrelsen. 2011). Physical Activity on Prescription is used to a varying degree in different parts of Sweden. The reasons for this variation are multiple, and include lack of resources, lack of structural support (reimbursement), and lack of prioritising and motivation (Borjesson and Jonsdottir 2016).

Implications for research

Further research is needed to quantify the effect on level of activity as well as on the long-term efficacy and the cost effectiveness of PAP. In addition, studies on morbidity and mortality are needed.

Conclusion

The results from this HTA report show that Swedish PAP probably results in an increase in level of physical activity compared with no PAP although the magnitude of the increase is poorly defined, in adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional.

Future perspective

Scientific knowledge gaps

While there is evidence for reduced morbidity and mortality with regular physical activity, well-dimensioned effectiveness studies quantifying the direct effect of PAP on morbidity in selected patient-groups would further improve the level of evidence. Further studies defining the magnitude of increased level of physical activity would be helpful.

Ongoing research

We found five studies in Clinicaltrials.gov that match the PICO, that were either recruiting patients or completed but not yet published. No studies were completed more than two years ago. The studies are presented in the table below.

Clinical trials ID	Study design	Participants	Intervention	Control	Outcome	Status
NCT02387034	RCT	Patients with osteoarthritis in hip or knee. n=140.	Swedish PAP	General advice	Level of physical activity Physical capacity HRQoL	Recruiting
NCT02131701	RCT	Individuals with a family history of type 2 diabetes. n=290.	Swedish PAP	Group exercise	Physical fitness Body composition Muscle strength	Completed 2013. No results published for these outcome measures.
NCT02493400/ NCT02493387	Cohort	Patients with atrial fibrillation. n=90.	Swedish PAP	Group exercise	Physical fitness Level of physical activity HRQoL	Recruiting

NCT02869854	RCT	Physically inactive individuals. n=90.	Swedish PAP with/without mindfulness training	Mindfulnes training	Level of physical activity Self-rated health Insomnia severity Biomarkers	Recruiting
NCT00451425	RCT	Pregnant women with BMI ≥19.9. n=430.	Swedish PAP + motivational interviewing	Usual care	Weight gain during pregnancy Weight retention Delivery complications Child birth weight	Unknown (last update 2009)

14. Participants in the project

The question was nominated by

Malin Wiklund, PhD, physiotherapist, Region Västra Götaland

Participating health care professionals

Mats Börjesson, MD, PhD, Department of food and nutrition and sport Science, University of Gothenburg
Daniel Arvidsson, MSc nutrition, PhD, Department of food and nutrition and sport Science, University of Gothenburg
Åse Blomqvist, Physiotherapist, Närhälsan FaR- teamet Gothenburg, Region Västra Götaland
Ingibjörg H. Jonsdottir, MD, PhD, Institute of Stress Medicine, Region Västra Götaland
Stefan Lundqvist, Physiotherapist, Närhälsan FaR- teamet Gothenburg, Region Västra Götaland
Anders Mellén, MD, PhD, Department of Clinical Pharmacology, Sahlgrenska University Hospital
Aron Onerup, MD, Department of Pediatrics, Sahlgrenska University Hospital

Participants from the HTA-centrum

Lennart Jivegård, MD, Senior university lecturer, HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden
Petteri Sjögren, DDS, PhD, HTA-centrum, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden
Eva-Lotte Daxberg, librarian, Sahlgrenska University Hospital, Gothenburg, Sweden
Therese Svanberg, HTA-librarian, Sahlgrenska University Hospital, Gothenburg, Sweden
Josefine Persson, PhD, Health economist, HTA-centrum of Region Västra Götaland, Gothenburg

External reviewers

Anneli Schwarz, speech therapist, Research Unit, Södra Älvsborg Hospital
Robert Eggertsen MD, PhD, professor, Department of Medicine, University of Gothenburg, Mölnlycke Primary Health Care Center, Mölnlycke, Sweden

Declaration of interest

The authors declare no conflict of interest.

Project time

HTA was accomplished during the period of 2017-08-18– 2018-02-28.
Literature searches were made in September 2017.

Appendix 1: Search strategy, study selection and references

Objective

To study if physical activity on prescription, according to the Swedish PAP-model, is better than not receiving Swedish PAP when it comes to level of physical activity, mortality, morbidity, health-related quality of life (HRQoL), and physical function for adults that have been deemed to be in need of increased physical activity by a healthcare professional.

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P	Adult individuals who have been deemed to be in need of increased physical activity by a healthcare professional
I	Physical activity on prescription (PAP) according to the Swedish model in a Nordic setting, including individual counselling, written, individualized prescription, and follow-up
C	No PAP according to the Swedish model, excluding disease/injury-specific rehabilitation
O	<u>Critical for decision making</u> Mortality Morbidity (e.g. AMI, stroke, cardiovascular events) HRQoL Level of physical activity <u>Important for decision-making</u> Morbidity (risk factors, i.e. Body Mass Index (BMI), waist circumference, blood pressure, fasting glucose, HbA1c/insulin resistance, cholesterol, HDL/LDL ratio) Physical function Adverse events

<u>Eligibility criteria:</u>

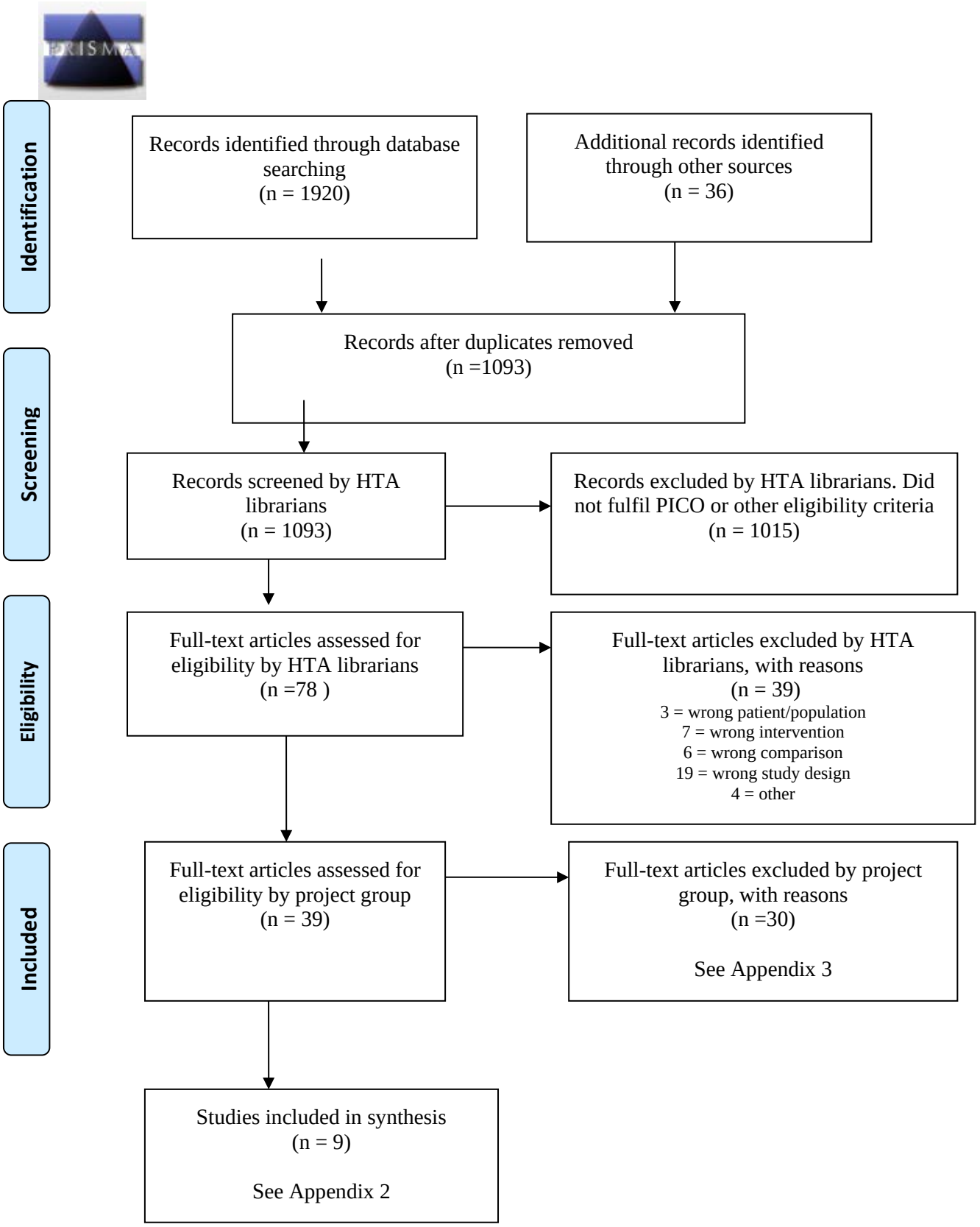
Study design:
Systematic reviews
Randomised controlled trials
Non-randomised controlled studies
Case series for complications only

Follow up ≥12 veckor
Nordic setting

Language:
English, Swedish, Danish, Norwegian

Year of publication:
1999-

Selection process – flow diagram



Search strategies

Database: PubMed
Date: 2017-09-07
No of results: 670

Search	Query	Items found
#18	**Search #11 AND #15 Filters: Publication date from 1999/01/01; Swedish; Norwegian; English; Danish**	**670**
#17	Search #11 AND #15 Filters: Publication date from 1999/01/01	673
#16	Search #11 AND #15	763
#15	Search #12 OR #14	845792
#14	Search "Scandinavian and Nordic Countries"[Mesh]	177413
#12	Search Sweden OR Swedish OR Norwegian OR Norway OR Danish OR Denmark OR Finland OR Finnish OR Iceland OR Icelandic OR Nordic OR Scandinavi*	845792
#11	Search #4 AND #10	15137
#10	Search #7 OR #9	471629
#9	Search referr*[tiab] OR prescri*[tiab]	420712
#7	Search "Referral and Consultation"[Mesh] OR "Prescriptions"[Mesh]	95212
#4	Search #2 OR #3	387229
#3	Search physically active[tiab] OR physical activit*[tiab] OR exercise*[tiab]	314267
#2	Search "Exercise"[Mesh] OR "Exercise Therapy"[Mesh]	181124

Database: Embase 1974 to 2017 September 06 (OVID SP)
Date: 2017-09-07
No of results: 782

#	Searches	Results
1	exp *exercise/	125885
2	exp *physical activity/	103420
3	kinesiotherapy/	28495
4	(physically active or physical activit$ or exercise$).ab,ti.	412589
5	1 or 2 or 3 or 4	514245
6	exp *prescription/	32699
7	patient referral/	85235
8	(referr$ or prescri$).ab,ti.	647143
9	6 or 7 or 8	693257
10	5 and 9	23551
11	(Sweden or Swedish or Norwegian or Norway or Danish or Denmark or Finland or Finnish or Iceland or Icelandic or Nordic or Scandinavi*).af.	1540299
12	exp Scandinavia/	185708
13	11 or 12	1541227
14	10 and 13	1410
15	**limit 14 to ((danish or english or norwegian or swedish) and yr="1999 -Current" and (article or conference paper or note or "review"))**	**782**

Database: The Cochrane Library
Date: 2017-09-07
No of results: 283
Cochrane reviews: 44
Other reviews: 2
Trials: 234
Technology assessments: 1
Economic evaluations: 2

ID	Search	Hits
#1	MeSH descriptor: [Exercise] explode all trees	19395
#2	MeSH descriptor: [Exercise Therapy] explode all trees	10763
#3	physically active or (physical activit*) or exercise*:ti,ab,kw (Word variations have been searched)	70924
#4	#1 or #2 or #3	73065
#5	MeSH descriptor: [Referral and Consultation] explode all trees	2279
#6	MeSH descriptor: [Prescriptions] explode all trees	919
#7	referr* or prescri*:ti,ab,kw (Word variations have been searched)	33373
#8	#5 or #6 or #7	34003
#9	#4 and #8	3496
#10	Sweden or Swedish or Norwegian or Norway or Danish or Denmark or Finland or Finnish or Iceland or Icelandic or Nordic or Scandinavi*	60546
#11	MeSH descriptor: [Scandinavian and Nordic Countries] explode all trees	5287
#12	#10 or #11	60551
#13	**#9 and #12**	**283**

Database: AMED, CINAHL, PsycINFO (EBSCOhost) (samsökning)
Date: 2017-09-07
No of results: 164 after removal of duplicates when downloaded to EndNote

#	Undran	Resultat
S6	**S3 AND S4** **Language: - english**	**164**
S5	S3 AND S4	200
S4	Sweden OR Swedish OR Norwegian OR Norway OR Danish OR Denmark OR Finland OR Finnish OR Iceland OR Icelandic OR Nordic OR Scandinavi*	199,566
S3	S1 AND S2	6,939
S2	TI (prescri* OR referr*) OR AB (prescri* OR referr*)	161,380
S1	TI (exercise* OR "physically active" OR (physical N1 activit*)) OR AB (exercise* OR "physically active" OR (physical N1 activit*))	149,381

Database: Svemed+
Date: 2017-09-07
No of results: 21

Nr	Sökträng	Antal träffar
1	fysisk aktivitet	2369
4	FYSS	3
5	PAP OR FAR OR recept OR ordination	419
6	#1 AND #5	19
7	**#4 OR #6**	**21**

The web-sites of SBU, Folkehelseinstituttet och Sundhedsstyrelsen were visited 2017-09-15. Three documents of potential relevance to the question was found.

Reference lists
A comprehensive review of reference lists brought 36 new records

Reference lists

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Project: Physical activity on prescription

Appendix 2 – Characteristics of included studies

Author, Year, Country	Study Design	Study Duration (years)	Participant characteristics	Study Groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Aittasalo, 2006 Finland	RCT	2003 (1 year)	Primary health care patients with inadequate level of physical activity.	I = PAP C2 = Usual care	203	47	24	Frequency total PA (IPAQ) Duration total PA (IPAQ) Frequency MVPA (IPAQ) Duration MVPA (IPAQ)
Hellgren, 2016 Sweden	RCT	3 years	Individuals with impaired glucose tolerance or impaired fasting glucose.	I1 = PAP + pedometer + cost-free glucose monitoring I2 = I1 + supervised group sessions (8 during 12 months) + reminder every 3 months C = Usual care	96	63	42	Development of diabetes HOMA-IR HbA1c Waist circumference Systolic blood pressure Diastolic blood pressure Body weight PA (four-level scale)
Hemmingsson, 2009 Sweden	RCT	2005-2008 (4 years)	Healthy, working volunteers with abdominal obesity.	I = PAP focus on cycling & walking + bicycle + pedometer C = Group sessions focused on walking + pedometer	120	48	0	Cycling (measured in I, self-assessed in C) Steps (pedometer) Body weight Waist circumference
Kallings, 2009 Sweden	RCT	2005-2007 (3 years)	Healthy but insufficiently physically active individuals with overweight and abdominal obesity.	I = PAP C = Written general information	101	68	43	Frequency MVPA (diary) Duration MVPA (diary) Steps (pedometer) Body weight BMI Waist circumference Total body fat (BIA) Systolic blood pressure Diastolic blood pressure Glucose HbA1c Cholesterol Triglycerides HDL LDL
Morén, 2016 Sweden	RCT	2010-2014 (4 years)	Patients with a diagnosis of an acute TIA.	I = PAP C = Usual care	88	71	47	Duration MVPA (accelerometer) Steps (accelerometer) 6-MWT

Project: Physical activity on prescription

Appendix 2 – Characteristics of included studies

Author, Year, Country	Study Design	Study Duration (years)	Participant characteristics	Study Groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
								HR-QoL (EQ5D-VAS)
Olsson, 2015 Sweden	RCT	2005-2007 (3 years)	Healthy but insufficiently physically active individuals with overweight and abdominal obesity.	I = PAP C = Written general information on importance of PA	101	68	43	HR-QoL (SF-36)
Sjögren, 2012 Sweden	RCT	2005-2007 (3 years)	Healthy but insufficiently physically active individuals with overweight and abdominal obesity.	I = PAP C = Written general information	73	68	40	Duration total PA (diary) Steps (pedometer)
Hendberg, 2014 Sweden	Cohort	2011-2012 (1 year)	Patients who have undergone surgery due to hip fracture	I = PAP + Rehabilitation supported by physiotherapist C = Rehabilitation with physiotherapist	34	79	47	PA (Grimby-Frändin)
Kallings, 2008 Sweden	Case series	2001-2003	Patients who have been prescribed PAP at a primary health care unit.	I = PAP	481	51	25	Adverse events

C = Control; EQ5D-VAS = EuroQoL-5 dimension visual analogue scale; HbA1c = Glycated haemoglobin; HDL = High density lipoproteins; HOMA-IR = Insulin resistance index; HR-QoL = Health-related quality of life; I = Intervention; IPAQ = International physical activity questionnaire; MVPA = Moderate-vigorous physical activity; LDL = Low density lipoproteins; PA = Physical activity; PAP = Physical activity on prescription; TIA = Transient ischemic attack; 6-MWT = Six-minute walk test; SF-36 = 36-item short form survey.

Project: Physical activity on prescription
Appendix 3: Excluded studies

Study (author, publication year	**Reason for exclusion**
Fritz, 2006	Wrong intervention
Gram, 2010	Wrong intervention
Helgadottir, 2017	Wrong intervention
Kallings, 2009	Case series with no reporting of complications
Karjalainen, 2012	Wrong intervention
Leijon, 2008	Wrong intervention, no comparison, wrong outcome
Leijon, 2009	Case series with no reporting of complications
Leijon, 2010	No comparison, wrong outcome
Leijon, 2011	No comparison, wrong outcome
Lerdal, 2013	Wrong intervention, wrong outcome
Ludvigsson, 2016a	Wrong comparison, wrong outcome
Ludvigsson, 2016b	Wrong comparison, wrong outcome
Ludvigsson, 2015	Wrong comparison, wrong outcome
Landen, Ludvigsson, 2017	No comparison, wrong outcome
Lundqvist, 2017	Case series with no reporting of complications
Sundhedsstyrelsen, 2010	HTA report with different PICO
Overmeer, Ludvigsson, 2016	Wrong comparison, wrong outcome
Pavey, 2011	HTA report with different PICO
Pedersen, 2016	Wrong intervention, no comparison
Peterson, Ludvigsson 2015	Wrong comparison, wrong outcome
Roessler, 2009	Wrong intervention, no comparison
Romé, 2009	Wrong intervention
Romé, 2010	Wrong intervention, wrong outcome
Romé, 2014	Wrong intervention
Rödjer, 2016	Case series with no reporting of complications
Saida, 2017	Wrong intervention, no comparison
Sjöling, 2011	Wrong intervention, no comparison
Sørensen, 2008	Wrong intervention, wrong comparison
Sørensen, 2011	Wrong intervention, wrong comparison
Sundquist, 2010	Wrong intervention, wrong comparison

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.1
Outcome variable: Health related Quality of Life (HRQoL)

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Morén 2016 Sweden	RCT	n=88 I=44 C=44	I=16 C=16	<u>EQ-5D VAS (0-100)</u> Baseline: 71 (16) Delta 3 months: +2 Delta 6 months: +7	<u>EQ-5D VAS (0-100)</u> Baseline: 69 (12) Delta 3 months: +3 *NS for intergroup comparison* Delta 6 months: +6 *NS for intergroup comparison*	Mixed effects modeling to estimate effect of intervention (intervention vs. control). Values are mean (sd).	+	?	?
Olsson 2015 Sweden	RCT	n=101 I=47 C=54	I=6 C=4	<u>SF-36 Health Survey</u> Baseline MCS: 84 (70-94) Delta MCS 6 months: 4.4 (-2.4-23.3) Baseline PCS: 80 (67-88) Delta PCS 6 months: 3.8 (-1.9-19.5) Proportion with baseline MCS score <88: 29 (62%). Proportion improved to MCS score ≥88 at 6 months follow-up: 18 (38%). Proportion with baseline PCS score <88: 38 (81%). Proportion improved to MCS score ≥88 at 6 months follow-up: 10 (21%).	<u>SF-36 Health Survey</u> Baseline MCS: 89 (83-94) Delta MCS 6 months: 0.0 (-4.0-4.9) *p=0.03 for intergroup comparison* Baseline PCS: 83 (73-90) Delta PCS 6 months: 0.0 (-11.3-10.6) *NS for intergroup comparison* Proportion with baseline MCS score <88: 25 (46%). Proportion improved to MCS score ≥88 at 6 months follow-up: 11 (20%). *OR=2.43 (1.00; 5.88), p<0.05 for intergroup comparison* Proportion with baseline PCS score <88: 34 (63%). Proportion improved to MCS score ≥88 at 6 months follow-up: 9 (17%). *OR=1.35 (0.50; 3.67), NS for intergroup comparison).*	MCS and PCS range 0 – 100. Values are median (inter-quartile range). Mann-Whitney U Test for between-group difference in delta. Clinically relevant improvement: a baseline score <88 and a 6 months follow-up score ≥88. Logistic regression for group difference, odds ratio (95% CI).	+	+/?	?

CI = Confidence interval; EQ-5D = EuroQoL-5 Dimension Questionnaire; MCS = Mental Component Summary; NS = Not significant; OR = Odds ratio; PCS = Physical Component Summary; SF-36 = 36-Item Short Form Health Survey.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.2
Outcome variable: Level of physical activity

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Aittasalo 2006 Finland	RCT	n=203 I=130 C=73	I=34 C=15	<u>PA sessions/week</u> Baseline: 5.9 (0.3) Delta 6 months: +1.7 <u>MVPA sessions/week</u> Baseline: 2.3 (0.2) Delta 6 months: +1.2 <u>PA duration/week (min)</u> Baseline: 344 (29) Delta 6 months: +204 <u>MVPA duration/week (min)</u> Baseline: 69 (5) Delta 6 months: +30	<u>PA sessions/week</u> Baseline: 6.3 (0.4) Delta 6 months: +0.5 *p=0.07 for intergroup comparison* <u>MVPA sessions/week</u> Baseline: 2.7 (0.2) Delta 6 months: +0.2 *p=0.023 for intergroup comparison* <u>PA duration/week (min)</u> Baseline: 430 (82) Delta 6 months: +58 *NS for intergroup comparison* <u>MVPA duration/week (min)</u> Baseline: 81 (6) Delta 6 months: +4 *NS for intergroup comparison*	Randomization of Physicians (prescribing PAP vs not prescribing PAP). Two non-PAP groups but only those receiving usual care (CON) were compared with the PAP intervention. Two follow-up measures (2 and 6 months); only 6 months follow-up is reported here. Outcome measures; PA sessions per week, PA duration per week and how many sessions and minutes were conducted with at least moderate intensity. The total number of patients included was 265, however one group (n=62) was not included in the analysis. Values are mean (sd).	+/?	?/-	+/?
Hellgren 2016 Sweden	RCT	n=96 I=66 C=30	N=27	Sedentary and low level PA decreased with 7.2%, while moderate level PA increased with 7.2 %	Sedentary and low level PA decreased with 3.8%, while moderate level PA increased with 3.8 % *NS for intergroup comparison*	Patients with impaired glucose tolerance and or impaired fasting glucose randomized to either two forms of interventions including PAP (I) compared to care as usual (C). PA level was assessed with four level scale questionnaire (sedentary, low, moderate and strenuous PA).	+	+/?	?/-

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.2
Outcome variable: Level of physical activity

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Hemmingsson 2009 Sweden	RCT	n=120 I=60 C=60	I=6 C=15	Cycling treatment success >2.0 km/d at 18 months: 38.7% Cycling treatment success >4.0 km/d at 18 months: 24.8% <u>Walking (steps/day)</u> Baseline: 8692 Delta 18 months: +1437 Walking 10 000 steps/day at 18 months: 45.7% Likely to comply with at least one treatment goal at 18 months: 60.8%	Cycling treatment success >2.0 km/d at 18 months: 8.9 % *p=0.001 for intergroup comparison* Cycling treatment success >4.0 km/d at 18 months: 4.6% *p=0.001 for intergroup comparison* <u>Walking (steps/day)</u> Baseline: 8249 Delta 18 months: +837 *NS for intergroup comparison* Walking 10 000 steps/day at 18 months: 39.3% *NS for intergroup comparison* Likely to comply with at least one treatment goal at 18 months: 41.8% *p=0.003 for intergroup comparison*	Obese middle-aged women randomized to either intervention group including groups counselling PAP, physician meeting and bicycle (I) or low-intensity support-group program and pedometers with no PAP. Follow-up at 6 and 18 months but only 18 months' follow-up is reported by the authors. Values are percent or means.	+	+/?	?

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.2
Outcome variable: Level of physical activity

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Kallings 2009 Sweden	RCT	n=101 I=47 C=54	I=6 C=4	<u>MVPA sessions/week:</u> Baseline: 2 (1-5) Delta 6 months: +3 <u>MVPA minutes/week:</u> Baseline: 120 (0-220) Delta 6 months: +159 (0-430) <u>Steps/week:</u> Baseline: 5390 (2791) Delta 6 months: +1663 <u>Increasing >3000 step/day:</u> 32%	<u>MVPA sessions/week:</u> Baseline: 2 (1-5) Delta 6 months: not presented *p<0.001 for intergroup comparison* <u>MVPA minutes/week:</u> Baseline: 130 (40-215) Delta 6 months: not presented *p<0.05 for intergroup comparison* <u>Steps/week:</u> Baseline: 4980 (2763) Delta 6 months: +871 *NS for intergroup comparison* <u>Increasing >3000 step/day:</u> 14% *p<0.05 for intergroup comparison*	Individuals with low physical activity, overweight and abdominal obesity. Randomized to either PAP or a minimal intervention. Follow-up at 6 months. Diary used to measure PA level + intensity by using Borg´s Perceived exertion scale. Pedometer to measure step/day. Values are means (sd) or medians (interquartile range).	+	+/?	?
Morén 2016 Sweden	RCT	n=88 I=44 C=44	I=16 C=16	<u>MVPA minutes/day</u> Baseline: 32 (29) Delta 3 months: +1 Delta 6 months: +3 <u>Steps/day</u> Baseline: 6191 (3541) Delta 3 months: +172	<u>MVPA minutes/day</u> Baseline: 32 (23) Delta 3 months: -2 Delta 6 months: -2 *NS both follow-ups for intergroup comparison* <u>Steps/day</u> Baseline: 7841 (8091)	Patients with transient ischemic attack (TIA) receiving care as usual + PAP (I) or care as usual only (C). Primary outcome was moderate to vigorous intensity PA measured with accelerometer. Secondary outcome steps/day. Follow-up at 3 and 6 months. The most frequent PAP activity was walking, however two patients	+	?	?

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.2
Outcome variable: Level of physical activity

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
				Delta 6 months: +529	Delta 3 months: -1615 Delta 6 months: -2027 *NS both follow-ups for intergroup comparison*	received swimming as activity. Mixed effects modeling to estimate effect of intervention (intervention vs. control). Values are mean (sd).			
Sjögren 2012 Sweden	RCT	n=73 I=30 C=43	I=17 C=11	<u>Exercise min/week</u> Baseline: 135 (40-215) Delta 6 months: +137 (0-490) <u>Steps/day</u> Baseline: 5900 (2800) Delta 6 months: +1190 (3270)	<u>Exercise min/week</u> Baseline: 120 (5-205) Delta 6 months: 0 (-105-240) *p=0.03 for intergroup comparison* <u>Steps/day</u> Baseline: 5200 (2730) Delta 6 months: +719 (2490) *NS for intergroup comparison*	Overweight and sedentary women and men. Randomization to either 6 months' lifestyle intervention with PAP or control group. PA level was assessed by pedometer and activity diary. Same population in Kallings, 2009 Values are mean (sd) or median (interquartile range).	+	+/?	?/-
Hendberg 2014 Sweden	Cohort	n=34 I=17 C=17	I=1 C=1	Patients with increased PA compared with matched control: 9/16	Increased PA level patients compared with matched control: 3/16 *p=0.039 for intergroup comparison*	Consecutive inclusion of patients with hip fracture. Matched control to each patient. Self-reported PA levels according to Grimby-Frändin was used (4 level scale). PA level calculated within the pairs, i.e. how many patients in relation to their matched control increased or decreased their PA level.	+	?/-	-

MVPA = Moderate vigorous physical activity; NS = Not significant; PA = Physical activity; PAP = physical activity on prescription.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
\- Major problems

Appendix 4.3
Outcome variable: Anthropometry

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Hellgren, 2016 Sweden	RCT	N=96 (I=66, C=30)	27	<u>Body weight (kg)</u> Baseline: not reported Delta 3 years: -0.8 (-2.1; 0.6) <u>WC (cm)</u> Baseline: 102 (10) Delta 3 years: -1.7 (-3.2; -0.3)	<u>Body weight (kg)</u> Baseline: not reported Delta 3 years: 0.1 (-2.3; 2.6) *p=0.73 for intergroup comparison* <u>WC (cm)</u> Baseline: 100 (10) Delta 3 years: -0.03 (-2.6; 2.5) *p=0.97 for intergroup comparison*	Patients 35-75 years with IGT with or without IFG. Baseline values are mean (sd). Delta values are mean (95% CI).	+	+/?	?/-
Hemmingsson, 2009 Sweden	RCT	N=99 (I=54, C=45) ITT N=120 (I=60, C=60)	25	<u>Body weight (kg)</u> Baseline: 84.6 (9.7) Delta 6 months: -0.9 (-1.9; 0.1) Delta 18 months: -0.4 (-1.6; 0.7) <u>WC (cm)</u> Baseline: 103.4 (7.3) Delta 6 months: -2.2 (-3.3; -1.1) Delta 18 months: -2.1 (-3.4; -0.8)	<u>Body weight (kg)</u> Baseline: 84.7 (9.9) Delta 6 months: -0.3 (-0.8; 0.3) Delta 18 months: -0.3 (-1.2; 0.7) <u>WC (cm)</u> Baseline: 104.2 (8.2) Delta 6 months: -1.7 (-2.7; -0.7) Delta 18 months: -2.6 (-4.0; -1.2) *NS for both variables and both follow-ups for intergroup comparison*	Women, 30-60 years, WC>=88cm Intention-to-treat Baseline values are mean (sd). Delta values are mean (95% CI).	+	+/?	?

Project: Physical activity on prescription

* + No or minor problems
? Some problems
\- Major problems

Appendix 4.3
Outcome variable: Anthropometry

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Kallings, 2009 Sweden	RCT	N=101 (I=47, C=54)	10	<u>Body weight (kg)</u> Baseline: 88.0 (14.2) Delta 6 months: -1.8 (-2.8; -0.8) <u>WC (cm)</u> Baseline: 105.2 (9.2) Delta 6 months: -2.3 (-3.5; -1.1) <u>BMI (kg·m^{-2})</u> Baseline: 29.7 (3.4) Delta 6 months: -0.6 (-0.9; -0.3) <u>Total body fat (kg)</u> Baseline: 31.5 (7.2) Delta 6 months: -1.7 (-2.5; -0.9)	<u>Body weight (kg)</u> Baseline: 88.3 (11.1) Delta 6 months: -0.5 (-1.1; 0.1) *p=0.023 for intergroup comparison* <u>WC (cm)</u> Baseline: 106.4 (7.8) Delta 6 months: -1.4 (-2.2; -0.6) *NS for intergroup comparison* <u>BMI (kg·m^{-2})</u> Baseline: 30.4 (2.9) Delta 6 months: -0.2 (-0.4; 0.0) *p=0.023 for intergroup comparison* <u>Total body fat (kg)</u> Baseline: 33.0 (7.7) Delta 6 months: -0.6 (-1.2; -0.1) *P=0.032 for intergroup comparison*	Patients, overweight BMI>=25, WC>=88 cm for women and >=102 cm for men. Body composition with bioelectrical impedance. Baseline values are mean (sd). Delta values are mean (95% CI).	+	+/?	?

BMI = Body mass index; CI = Confidence interval; IFG = Impaired fasting glucose; IGT = Impaired glucose tolerance; NS = Not significant; WC = Waist circumference.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.4
Outcome variable: Blood pressure

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Hellgren, 2016 Sweden	RCT	N=96 (I=66, C=30)	27	SBP (mmHg) Baseline: 146 (22) Delta 3 years: -15.6 (-11.0; -20.2) DBP (mmHg) Baseline: 83 (11) Delta 3 years: -5.5 (-3.1; -7.8)	SBP (mmHg) Baseline: 143 (15) Delta 3 years: -9.2 (-3.8; -14.7) *NS for intergroup comparison* DBP (mmHg) Baseline: 83 (9) Delta 3 years: -3.0 (-7.0; 0.9) *NS for intergroup comparison*	Patients 35-75 years with IGT, with or without IFG. In subgroup with IFG, significantly larger decrease of DBP in intervention group (P=0.047). Baseline values are mean (sd). Delta values are mean (95% CI).	-	+/?	?/-
Kallings, 2009 Sweden	RCT	N=91 (I=41, C=50)	10	SBP (mmHg) Baseline: 137.6 (2.2) Delta 6 months: 0.2 (-4.3; 4.7) DBP (mmHg) Baseline: 79.9 (1.5) Delta 6 months: -1.0 (-3.5; 1.6)	SBP (mmHg) Baseline: 142.3 (2.6) Delta 6 months: -4.1 (-7.5; -0.6) *NS for intergroup comparison* DBP (mmHg) Baseline: 81.6 (1.3) Delta 6 months: -1.7 (-4.4; 0.9) *NS for intergroup comparison*	Patients, overweight BMI>=25, WC>=88 cm for women and >=102 cm for men. Baseline values are mean (sd). Delta values are mean (95% CI)	-+	+/?	?

BMI = Body mass index; DBP = Diastolic blood pressure; IFG = Impaired fasting glucose; IGT = Impaired glucose tolerance; NS = Not significant; SBP = Systolic blood pressure; WC = Waist circumference.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
\- Major problems

Appendix 4.5
Outcome variable: Glucose metabolism

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Hellgren, 2016 Sweden	RCT	N=96 (I=66, C=30)	27	Developed diabetes within three years: 14% HOMA-IR Baseline: 2.9 (1.9) Delta 3 years: 0.05 (0.3; 0.4) HbA1c (mmol·mol^{-1}) Baseline: 40.2 (4.0) Delta 3 years: -2.7 (-1.7; -3.6)	Developed diabetes within three years: 19% *NS for intergroup comparison* HOMA-IR Baseline: 3.1 (2.2) Delta 3 years: 0.8 (0.3; 0.4) *p=0.066 for intergroup comparison* HbA1c (mmol·mol^{-1}) Baseline: 39.9 (2.3) Delta 3 years: -2.2 (-0.9; -3.5) *NS for intergroup comparison*	Patients 35-75 years with IGT with or without IFG. In subgroup with IGT, significantly larger decrease of HOMA-IR in intervention group compared to control group. Baseline values are mean (sd). Delta values are mean (95% CI).	+	+/?	?/-
Kallings, 2009 Sweden	RCT	N=91 (I=41, C=50)	10	Glucose (mmol·l^{-1}) Baseline: 5.5 (0.1) Delta 6 months: -0.2 (-0.3; -0.1) HbA1c (% average total Hb) Baseline: 5.0 (0.1) Delta 6 months: -0.1 (-0.2; 0.0)	Glucose (mmol·l^{-1}) Baseline: 5.4 (0.1) Delta 6 months: -0.1 (-0.2; -0.0) *NS for intergroup comparison* HbA1c (% average total Hb) Baseline: 4.8 (0.1) Delta 6 months: 0.2 (0.1; 0.3) *p=0.001 for intergroup comparison*	Patients, overweight BMI>=25, WC>=88 cm for women and >=102 cm for men. Baseline values are mean (sd). Delta values are mean (95% CI). HbA1c normal range is <5.0	+	+/?	?

BMI = Body mass index; CI = Confidence interval; Hb = Hemoglobin; HbA1c = Glycosylated haemoglobin; HOMA-IR = Homeostatic model assessment – insulin resistance; IFG = Impaired fasting glucose; IGT = Impaired glucose tolerance; NS = Not significant; WC = Waist circumference.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.6
Outcome variable: Blood lipids

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Kallings, 2009 Sweden	RCT	N=91 (I=41, C=50)	10	Cholesterol (mmol·l^{-1}) Baseline: 5.6 (0.1) Delta 6 months: -0.3 (-0.6; 0.0) Triglycerides (mmol·l^{-1}) Baseline: 1.4 (0.1) Delta 6 months: -0.2 (-0.3; -0.0) HDL (mmol·l^{-1}) Baseline: 1.7 (0.07) Delta 6 months: 0.0 (-0.1; 0.1) LDL (mmol·l^{-1}) Baseline: 3.4 (0.12) Delta 6 months: -0.1 (-0.2; 0.1)	Cholesterol (mmol·l^{-1}) Baseline: 5.5 (0.1) Delta 6 months: 0.1 (-0.1; 0.1) *p=0.042 for intergroup comparison* Triglycerides (mmol·l^{-1}) Baseline: 1.3 (0.1) Delta 6 months: -0.0 (-0.1;0.1) *NS for intergroup comparison* HDL (mmol·l^{-1}) Baseline: 1.7 (0.05) Delta 6 months: -0.0 (-0.1; 0.1) *NS for intergroup comparison* LDL (mmol·l^{-1}) Baseline: 3.2 (0.09) Delta 6 months: 0.1 (-0.1; 0.3) *NS for intergroup comparison*	Patients, overweight BMI>=25, WC>=88 cm for women and >=102 cm for men. Baseline values are mean (sd). Delta values are mean (95% CI).	+	+/?	?

BMI = Body mass index; HDL = High density lipoprotein; LDL = Low density lipoprotein; NS = Not significant; WC = Waist circumference.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

Appendix 4.7
Outcome variable: Physical function

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study ?limitations *	Precisi-on *
				Intervention	Control				
Morén 2016 Sweden	RCT	n=88 I=44 C=44	I=16 C=16	<u>6MWT (m)</u> Baseline: 430 (113) Delta 3 months: +30 Delta 6 months: +70	<u>6MWT (m)</u> Baseline: 426 (113) Delta 3 months: +20 *p=0.08 (intervention vs. control)* Delta 6 months: +31 *p=0.01 (intervention vs. control)*	Patients with transient ischemic attack (TIA) receiving care as usual + PAP (I) or care as usual only (C). Physical capacity was assessed by the 6MWT according to standard procedures. Values are mean (sd). Mixed effects modeling for effect of intervention (intervention vs. control). Increase in 6MWT walk distance of 14 – 30.5 m is a minimally clinically important difference across patient groups	?	?	?

CI = Confidence interval; PAP = Physical Activity on Prescription; 6MWT = 6-minute walk test. Directness downgraded due to selected population.

Project: Physical activity on prescription

* + No or minor problems
? Some problems
- Major problems

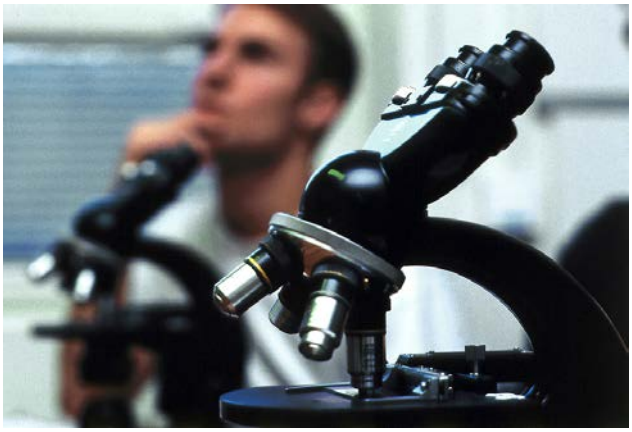
Appendix 4.8
Outcome variable: Adverse events

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention	Control				
Aittasalo 2005 Finland	RCT	n=203 I=130 C=73	2 months I=22 C=20 6 months I=34 C=15	Reported adverse effects at 2 months: 24%	Reported adverse effects at 2 months: 24% *NS for intergroup comparison*	The adverse effect mostly reported was musculoskeletal pain.	+/?	?/-	+/?
Hemmingsson 2009 Sweden	RCT	n=124 I=61 C=63	I=7 C=18	No reported adverse events at 18 months	No reported adverse events at 18 months *NS for intergroup comparison*		+	+/?	?
Morén 2016 Sweden	RCT	n=88 I=44 C=44	I=16 C=16	No reported adverse events or side effects at 6 months	No reported adverse events or side effects at 6 months *NS for intergroup comparison*		+	?	?
Sjögren 2012 Sweden	RCT	n=73 I=30 C=43	I=17 C=11	No reported adverse events or side effects at 6 months	No reported adverse events or side effects at 6 months *NS for intergroup comparison*		+	+/?	?/-
Kallings 2008a Sweden	Case series	n=481	n=183	No reported adverse events at 6 months	No control group				

NS = Not significant.

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

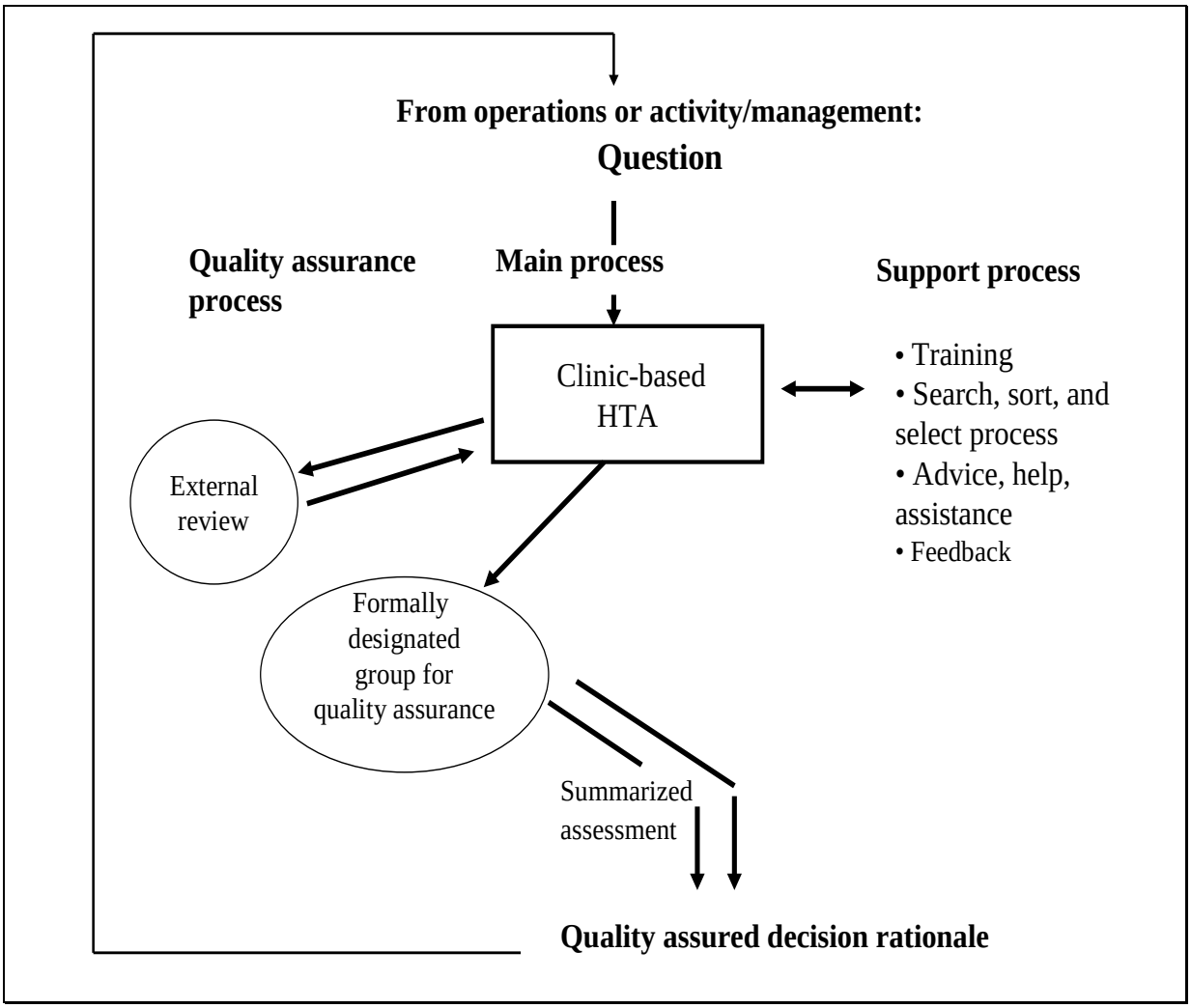
Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕O)
Low quality of evidence	= (GRADE ⊕⊕OO)
Very low quality of evidence	= (GRADE ⊕OOO)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum


From operations or activity/management:
Question
Quality assurance process
Main process
Support process
Clinic-based HTA
• Training
• Search, sort, and select process
• Advice, help, assistance
• Feedback
External review
Formally designated group for quality assurance
Summarized assessment
Quality assured decision rationale

VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Sahlgrenska Universitetssjukhuset, HTA-centrum
Röda Stråket 8, 413 45 Göteborg
www.sahlgrenska.se/hta-centrum