Effectiveness of eHealth interventions for the promotion of physical activity in older adults: A systematic review

Saskia Müllmann, Sarah Forberger, Tobias Möllers, Eileen Bröring, Hajo Zeeb, Claudia R. Pischke

DOI
10.1016/j.ypmed.2017.12.026

Published in
Preventive Medicine

Document version
Accepted manuscript

Online publication date
28 December 2017

Corresponding author
Saskia Müllmann

Citation
Müllmann S, Forberger S, Möllers T, Bröring E, Zeeb H, Pischke CR. Effectiveness of eHealth interventions for the promotion of physical activity in older adults: A systematic review. Prev Med. 2018;108:93-110.

Effectiveness of eHealth interventions for the promotion of physical activity in older adults: a systematic review

Saskia Muellmann[1], Sarah Forberger[1], Tobias Möllers[2], Eileen Bröring[1], Hajo Zeeb[1,3], Claudia R. Pischke[1]

[1]Leibniz Institute for Prevention Research and Epidemiology – BIPS, Bremen, Germany

[2]Network Aging Research, University of Heidelberg, Heidelberg, Germany

[3]Health Sciences Bremen, University of Bremen, Bremen, Germany

Corresponding author

Saskia Muellmann, M.A.

Leibniz Institute for Prevention Research and Epidemiology – BIPS

Achterstrasse 30

28359 Bremen

Germany

Phone +49 (0)421 218-56914

Fax +49 (0)421 218-56941

Email: muellmann@leibniz-bips.de

Sarah Forberger, Ph.D.: forberger@leibniz-bips.de

Tobias Möllers, M.Sc.: moellers@nar.uni-heidelberg.de

Eileen Bröring, B.A.: broering@leibniz-bips.de

Hajo Zeeb, M.D. Ph.D: zeeb@leibniz-bips.de

Claudia R. Pischke, Ph.D.: pischke@leibniz-bips.de

Word count manuscript: 4,937

Word count abstract: 246

Abstract

Regular physical activity (PA) is central to healthy ageing. However, only a minority of older adults currently meet the WHO-recommended PA levels. The aim of this systematic review is to compare the effectiveness of eHealth interventions promoting PA in older adults aged 55 years and above with either no intervention or a non-eHealth intervention (review registration: PROSPERO CRD42015023875). Eight electronic databases were searched to identify experimental and quasi-experimental studies examining the effectiveness of eHealth interventions for PA promotion in adults aged 55 years and above. Two authors independently selected and reviewed references, extracted data, and assessed study quality. In the search, 5,771 records were retrieved, 20 studies met all inclusion criteria. Studies varied greatly in intervention mode, content, duration and assessed outcomes. Study quality ranged from poor to moderate. All interventions comprised tailored PA advice and the majority of interventions included goal setting and feedback, as well as PA tracking. Participation in eHealth interventions to promote PA led to increased levels of PA in adults aged 55 years and above when compared to no intervention control groups, at least in the short term. However, the results were inconclusive regarding the question of whether eHealth interventions have a greater impact on PA behavior among older adults than non-eHealth intervention (e.g., print interventions). eHealth interventions can effectively promote PA in older adults aged 55 years and above in the short-term, while evidence regarding long-term effects and the added benefit of eHealth compared to non-eHealth interventions is still lacking.

Keywords: Systematic review, physical activity, older adults, intervention, healthy ageing, eHealth, primary prevention

Introduction

Regular physical activity (PA) is of central importance to healthy ageing because it is associated with improved physical, functional, psychological, and cognitive health [1-3]. According to the recommendations of the World Health Organization (WHO), older adults should moderately exercise 150 minutes per week to obtain health benefits. In addition, strength and flexibility training at least two times per week is recommended [4]. In the systematic review by Sun and colleagues, the percentages of older adults meeting the recommended PA levels ranged from 2% to 83%. In the majority of studies included in this systematic review, 20% to 60% of older adults met the recommendations [5]. Sun et al. explain this broad range of older adults meeting the recommendations with discrepancies and inconsistencies in the measurement of various types of PA (including instrumentation) across studies and in the guidelines or recommendations which were also not consistently applied to assess whether individuals met the guidelines or not. To promote PA in older adults, effective interventions are needed. Interventions providing information on PA in the form of printed materials or face-to-face have a long tradition and appear to be effective for PA promotion in older adults [6-8]. The increased use of the internet and mobile technologies in recent years may open new opportunities to promote PA in adult populations, including older adults [9]. In the older segments of the general population, a growing number of individuals use electronic devices, such as computers, smartphones or tablets [10]. eHealth is defined as “the use of information and communication technologies for health” [11]. Potential advantages of eHealth interventions for promoting PA are that information can be accessed easier and quicker by users, and that populations can be reached who may not otherwise get in contact with traditional person- or print-based PA interventions [12]. Results of previous systematic reviews and meta-analyses suggest that eHealth interventions are an effective intervention vehicle for the promotion of PA among adults of various ages [12-16]. However, the evidence for the effectiveness of these interventions in regard to PA promotion among older adults is mixed. Two studies [17, 18] reported increases in participants’ activity levels (aged 45-81 years) after receiving an eHealth PA intervention which was delivered by smartphone or tablet. Also, when compared to a no intervention control group, participants aged 55 years and above who received a web-based or telephone-based PA intervention showed an increase in PA-levels [19, 20]. On the other hand, Kim and Kang [21], as well as Peels and colleagues [22] could not find an added beneficial effect of eHealth PA interventions compared to non-eHealth interventions in persons aged 55 years and above (i.e., print-delivered intervention, face-to-face intervention). Müller and Khoo [23] reported that non-face-to-face PA interventions for older adults aged 50 years and above appear to positively affect uptake and maintenance of PA. However, this review did not solely compare eHealth PA interventions to non-eHealth interventions or to no intervention control groups. Hence, the current systematic review aims to compare the effectiveness of eHealth interventions promoting PA in older adults (aged 55 years and above) with either no intervention or a non-eHealth intervention.

Methods

Reporting guidelines of the "Preferred Reporting Items for Systematic Review and Meta-Analyses statement (PRISMA)" are followed for this article [24].

Study registration and protocol

This systematic review is registered at PROSPERO (registration number: CRD42015023875; http://www.crd.york.ac.uk/PROSPERO). The study protocol is published in Systematic Reviews [25].

Study inclusion and exclusion criteria

Study designs

Experimental (randomized controlled trial [RCT]) or quasi-experimental study designs that compare an eHealth PA intervention targeting older adults aged 55 and above with either a non-eHealth PA intervention or a group that is not exposed to any intervention were included in this review.

Participants

Studies examining older adults of both sexes without severe pre-existing chronic medical conditions (e.g., cancer) aged ≥55 years were included in this review. Studies that did not target the general population of older adults (e.g., patients in rehabilitation setting after stroke or heart attack, diabetic patients) were excluded. Globally, there is no consistent definition of older adulthood, definitions range somewhere between 50 and 65 years. We used a relatively low cut-off point for defining older adulthood, so that studies were eligible for inclusion if participants' mean age was at least 55 years.

Interventions

Studies on eHealth interventions promoting PA in older adults were included. eHealth interventions encompass interventions accessible via computer or other handheld devices, such as personal digital assistants (PDAs), telephones or smartphones, or tablets. Studies were included if the main intervention component was delivered via computer (i.e., website, e-mail, PDA), telephone or smartphone (i.e., telephone calls, text messaging, mobile application [app]) or tablet (i.e., app). Mass-media interventions, DVD-based interventions, and interventions delivered using gaming consoles (e.g., Nintendo Wii) were excluded.

Comparators

Comparator conditions included participation in a.) a non-eHealth intervention (e.g., paper-pencil intervention without eHealth component, face-to-face consultation, e.g., prescription of PA by a physician, or exercise in groups or with a personal trainer) or b.) no intervention. Studies that compared one or more eHealth interventions without a comparison to a non-eHealth intervention or a no intervention control group were excluded.

Outcomes

In the included studies, PA was assessed using objective (e.g., pedometer, accelerometer), subjective (e.g., PA diary, questionnaires), or a combination of objective and subjective methods. Studies that did not report data regarding intervention effectiveness for PA promotion were excluded (e.g., PA only reported as baseline variable).

Search strategy

The following databases were searched by one author (SM), including publications until the end of March 2017:

- Medline (via PubMed, 1946 to present),
- PyscINFO (via Ovid, 1806 to present),
- Web of Science including Social Sciences Citation Index and Science Citation Index Expanded (1900 to present),
- Cumulative Index to Nursing & Allied Health Literature (CINAHL) (via EBSCO Host, 1981 to present),
- Excerpta Medica database (EMBASE) (via Ovid, 1974 to present),
- Cochrane Central Register of Controlled Trials (CENTRAL) (via Cochrane Library, 1948 to present),
- Physical Education Index (PEI) (via ProQuest, 1970 to present),

- and OpenGrey (1980 to present).

The search was restricted to studies published in English or German. Keywords were related to PA, older adults, and eHealth interventions, using MeSH terms and other index terms, as well as appropriate synonyms. The keywords were combined using the Boolean operation OR and AND. Validated RCT-filters were used for the searches in Medline, PsycINFO, Web of Science, CINAHL, and EMBASE. For PEI and OpenGrey, no validated RCT-filters were available. Therefore, appropriate keywords to identify studies using an experimental or quasi-experimental study design were employed. For the search in CENTRAL, no RCT-filter was necessary because the database only includes controlled trials. The search strategy is illustrated in supplementary file 1 using the Medline search as an example and is included in the study protocol [25]. References of the included studies were checked to identify additional potentially relevant studies.

Selection of studies

First, titles and abstracts of studies identified, using the search strategy outlined above, were screened independently by two authors to select the relevant studies (SM and SF or TM). Any disagreements between the two authors regarding the selection of the articles were discussed until consensus was reached. A third author was involved in this discussion when necessary (SF or TM). In a second step, full texts of potentially relevant studies were obtained and reviewed independently by two authors (SM and SF or TM). Any disagreements between the two authors were resolved by consensus and/or discussion with a third author (SF or TM).

Quality assessment and data extraction

After selecting the relevant studies for this systematic review, quality assessment and data extraction were performed. Studies were not excluded based on the results of the quality assessment (i.e., studies with poor study quality due to a high risk of bias were still included for data extraction). Two authors independently applied the Cochrane Collaboration's tool for assessing risk of bias (SM and SF, SM and TM, SM and EB) [26]. Potential disagreements were resolved taking a similar approach as outlined above. In addition, a summary risk of bias for each study was created. For this review, the most important risk of bias domains were random sequence generation (selection bias), blinding of outcome assessment (detection bias), and incomplete outcome data (attrition bias). According to the Cochrane Collaboration's tool for assessing risk of bias, a study was classified as having a low risk of bias when it was scored low on all of the three domains, as moderate when two of the three main domains were scored as low, and as high when one or no main domain was classified as low risk of bias.

Data extraction was conducted independently by two authors (SM and SF, SM and TM, SM and EB). In case of disagreements that could not be resolved by discussion, a third author was involved (SF, TM or EB). The following information was extracted from the included studies: general information (e.g., first author, year, title, country of study), study information (e.g., aim of study, recruitment methods, inclusion/exclusion criteria randomization procedure), participant characteristics (e.g., number of participants, number of withdrawals/excluded participants), intervention information (e.g., aim of intervention, number of intervention/control groups), outcomes (e.g., primary and secondary outcomes), and results and summaries of the evidence.

Data synthesis

Quantitative data synthesis (i.e., meta-analysis) was not feasible because the included studies were too heterogeneous in regard to intervention content, PA assessment, and comparator groups. However, a narrative synthesis for summarizing the evidence with regard to intervention effects using harvest plots was performed [27]. Narrative synthesis is provided for the following subgroups: intervention mode and outcome assessment

Results

Identified studies

In the database search, 5,771 records were retrieved. Thirty-nine records were retrieved in the additional search. After screening titles and abstracts (first step) and full-texts (second step), 25 publications of 20 studies were included in this systematic review (Figure 1).

Figure 1 here

Study Quality

Overall, risk of bias of the included studies was rated as moderate [20, 28-38] to high [19, 22, 39-49]. Only one study was rated as having a low risk of bias [28]. In the majority of studies [19, 28, 30-35, 37, 38, 41-44], participants were randomly assigned to intervention and control groups (selection bias, random sequence generation; rating: low risk of bias). Concealment of the allocation to the groups was often not described in the included articles [19, 20, 22, 28, 30, 31, 36, 41, 46-49], therefore, in these cases, the risk of bias was rated as unclear (selection bias, allocation concealment). Blinding of participants and personnel was often not possible or not sufficiently well described (performance bias; rating: unclear risk of bias) [19, 20, 22, 28-30, 33, 34, 39, 40, 42-49]. Also, blinding of the outcome assessment was not possible [19, 22, 30-33, 37-44, 46-49], because subjective or a combination of subjective and objective methods was employed to measure the outcomes of interest (e.g., PA) (detection bias; rating: high risk of bias). Attrition rates per group, including reasons for attrition, were reported in most of the examined studies [20, 28-40, 49]. Also, attrition rates were relatively low (in n=13 < 20%, ranging from 0 to 41%) and similar across groups. Intention-to-treat analysis was used to analyze the data (attrition bias; rating: low risk of bias). Outcomes were described in the methods and results sections of the studies. However, it was often unclear whether all of the assessed outcomes were reported in the article or only a selection (rating: unclear risk of bias) [19, 20, 28-31, 34-38, 42-45, 49]. In addition, a published study protocol was only available for a few studies (selective reporting) [22, 32, 33, 39, 40, 46-49]. Other biases detected included small sample size [28-33, 36, 37, 39-41, 45], self-selection bias (e.g., highly educated persons and/or female are more likely to participate in PA interventions) [20, 30, 32-36, 38-40, 42-44], social desirability bias [19], baseline differences between study groups [22, 29, 39, 40, 46-49], Hawthorne effect [35] or short intervention period [31, 35, 36, 38]. A summary of the results of the risk of bias assessment of the included studies is presented in table 1.

Table 1 here

Study characteristics

Of the 20 included studies, 18 were RCTs [19, 20, 22, 28-38, 41-44, 46-49], and two studies employed a quasi-experimental design [39, 40, 45]. Eleven of the included studies were conducted in the United States of America [19, 20, 28-32, 34, 36, 41-43], three in the Netherlands [22, 35, 46-49], two in Belgium [38, 44], and one in Spain [45], Australia [39, 40], New Zealand [33], and Malaysia [37], respectively. At baseline, the 20 studies included a total sample of 6,671 participants with a range from 37 [30] to 1,971 participants [47-49]. On average, 60.9% of study participants were female across studies, proportions of females varied and ranged from 40.9% [35] to 79.6% [34]. The mean age was 65 years ranging from 56 [39, 40] to 79.8 years [34]. In 13 studies [19, 22, 30-33, 37-44, 46-49], only subjective methods were used to measure PA (i.e., questionnaires). In five studies [28, 34-36, 45], PA was measured using an objective assessment (i.e., pedometer, accelerometer). In two studies [20, 29], both subjective and objective methods were used to measure PA (i.e., questionnaire, pedometer). In the majority of the included studies, the intervention was delivered via a website (n=9) [19, 22, 28, 30, 31, 35, 38, 44, 46-49]. In seven studies, the intervention was delivered over the phone [20, 32-34, 39-43], and in four studies via text messaging [29, 36, 37, 45]. All studies that investigated the effects of eHealth interventions comprised tailored PA advice (e.g., based on age-specific PA recommendations, PA baseline lev-el, or behavioral stages of change). In the majority of studies (n=15), participants set PA goals, tracked their PA behavior (i.e., activity tracker, PA diary), and received (real-time) feedback based on the results of their self-monitoring activities. In addition, in some of the interventions, general advice on how to perform PA and information regarding local PA offers was given [22, 44, 46-49]. Intervention duration ranged from four weeks [36] to 24 months [42, 43]. Control group participants received no intervention (n=9, [19, 22, 31, 33, 35, 38, 44-49]), usual care (n=1, [42, 43]), or a non-eHealth intervention (n=10, [20, 28-30, 32, 34, 36, 37, 39-41]). Intended inter-vention dose ranged from three times per day [29] to three times in four months [22, 46-49] with the majority of studies delivering the intervention daily or weekly (n=14). 16 [19, 20, 22, 30-33, 35-44, 46-49] of the 20 interventions were theory-based (i.e., transtheoretical model [20, 22, 31-33, 41, 44, 46], social cognitive theory [22, 30-32, 39, 40, 42, 43, 46], self-determination theo-ry [22, 39, 40, 46-49], theory of planned behavior [19], ecological model [44], intervention map-ping [22, 46-49], i-change model [20, 22, 35, 46-49], health action process approach [22, 38, 46-49], precaution adoption model [22, 46], self-regulation theory [22, 38, 46-49], stages of change [35], communication theory [32], relapse prevention theory [42, 43], behavioral change tech-niques [36, 37, 49]). Study characteristics are displayed in table 2.

*** Table 2 here***

Effectiveness of interventions

A harvest plot illustrating the evidence regarding intervention effectiveness by intervention mode (i.e., website-based interventions, telephone-based interventions, text messaging-based interventions), and outcome assessment (objective or a combination of subjective and objective PA assessment, subjective PA assessment) is presented in figure 2. In the following sections, the results are described by modality and type of assessment in further detail.

Figure 2 here

Web-based interventions

Of the nine studies which delivered the intervention via website (i.e., website, PDA, virtual advi-sor), six studies compared a web-based intervention to a no intervention control group [19, 22, 31, 35, 38, 44, 46], two studies compared a web-based intervention to a non-eHealth intervention [28, 30], one study compared a web-based intervention to a no intervention control group and to a non-eHealth intervention [47-49].

In four of six studies which compared a web-based intervention to a no intervention control group, all intervention participants significantly increased their PA levels from baseline to follow-up assessment at one (for [38] total PA $p<.05$), three (for [19] $p<.001$, for [35] $p<.001$) or four months (for [31] $p=.0008$). In the study by Mouton and Cloes [44], a parallel groups design was employed involving four groups. The first intervention group received a web-based intervention only, the second intervention group a center-based (i.e., weekly group exercises at an exercise facility) intervention, the third group a combination of the web-based and center-based intervention. PA-levels of participants in all three study arms were compared with a no intervention control group at 12 months follow-up. Mouton and Cloes [44] observed a significant intervention effect only for the combined intervention (Effect size [ES]=0.20, $p=.041$), not after selective participation in the web-based (ES=0.06, $p=.247$) or center-based interventions (ES=0.14, $p=.083$). Peels and colleagues [22, 46] examined the effects of four interventions on PA behavior among participants compared to a no intervention control group: a print-based intervention vs. a web-based intervention, both of which targeted individual PA behavior, vs. a print-based intervention and a web-based intervention, both targeting PA environment. At six months follow-up, the two print-based and the web-based interventions were effective in increasing the overall number of minutes spent with PA per week (Print intervention group [IG]: ES=0.27, $p=.003$; print-environmental IG: ES=0.35, $p=.001$; web-based IG: ES=0.31, $p=.002$). At 12 months, only participation in the two print-based interventions was associated with significant changes in PA compared to the control group (Print IG: ES=0.21, $p=.017$; print-environmental IG: ES=0.32, $p=.001$) [22, 46].

In the two studies which compared a web-based intervention to a non-eHealth intervention (i.e., use of a pedometer, written health education material), the intervention was effective in increasing PA in the short-term after two months (for [28] $p=.01$, for [30] minutes/week moderate to vigorous-intensity PA $p=.048$), but this effect was not maintained at 12 months follow-up (for [28] $p=.09$).

The study which compared a web-based intervention to a no intervention control group (CG) and a non-eHealth intervention (i.e., print-based), found the following: At 12-months follow-up, participants who received the web-based intervention (i.e., an e-buddy system for promoting PA) significantly increased their PA levels compared to the no intervention CG ($\beta=62.0$, $p<.05$). Participants in this study who received the non-eHealth print-based intervention did not show any significant difference in PA increase when compared to the web-based intervention (web-based compared to print-based IG: β=48.5, p>.05) but did show an effect compared to the CG (print-based IG compared to CG: β=13.5, p>.05) [47-49].

Telephone-based interventions

Two of the seven included studies compared a telephone-based intervention to a no intervention control group [33, 41] and five studies to a non-eHealth intervention (i.e., weekly fitness program or general health education, information about available PA programs, advice by clinician, pedometer) [20, 32, 34, 39, 40, 42, 43].

In the study conducted by Jarvis and colleagues [41], no significant difference in minutes walked per week was observed between participants in the intervention and the no intervention control group at three-months follow-up (e.g., difference between IG and CG for 0 minutes/week walked at baseline: p=.019), whereas Kolt and colleagues [33] found that a telephone-based intervention was effective in increasing PA in older adults at three-months follow-up compared to a no intervention control group (e.g., walking leisure activities: p=.001). However, this effect could not be sustained until 12 months follow-up (e.g., walking leisure activities: p=.68). In the five studies [20, 32, 34, 39, 40, 42, 43] which compared effectiveness of one or more telephone-based interventions to a non-eHealth intervention, mixed evidence was reported by the authors. Three studies [20, 32, 42, 43] reported a beneficial intervention effect among persons participating in the telephone-based intervention compared to those in the non-eHealth intervention at three (for [20] p<.05), six (for [20] p<.05, for [32] p≤.05, for [42, 43] p=.003), 12 (for [32] p=≤.05, for [42, 43] p=.008), and 24-months follow-ups (for [42, 43] p=.001). On the other hand, two studies demonstrated no effects of telephone-based interventions compared to non-eHealth interventions at six (for [34] p=.21, for [39, 40] p>.05) and 18-months follow-up (for [39, 40] p>.05).

Text messaging-based interventions

Three of the four included studies compared a text messaging-based intervention to a non-eHealth control group [29, 36, 37] and one study to a no intervention control group [45].

Kim and Glanz [29] compared a text messaging-based intervention with a non-eHealth intervention and found significant differences in the number of steps per day favoring participants in the intervention group at six-week follow-up (p<.05). Martin and colleagues [36], as well as Müller and colleagues [37], compared a text messaging-based intervention to a non-eHealth intervention and reported that participants who received text messages significantly increased PA at four- (for [36] p<.001) and 12-weeks follow-ups (for [37] p=.03), but this effect was no longer observed at 24-weeks follow-up (for [37] p=.18). In the study by Muntaner-Mas and colleagues [45], effects of a training intervention, including group training sessions (warm-up, muscle-strength training, aerobic training, flexibility) twice per week, were compared to an intervention where participants performed the same exercises as the training group using videos and motivational messages made available to them via WhatsApp (to a no intervention control group). At the ten-week follow-up, both interventions were not effective in changing aerobic capacity of intervention participants compared to the control group (IG mobile vs. CG: ES=-0.73, p=.146; IG training vs. CG: ES=-0.12, p=.795). Moreover, there were no significant differences between the training and WhatsApp intervention groups (IG training vs. IG mobile: ES=0.61, p=.187) [45].

Objective or objective/subjective outcome assessment

Of the seven studies that measured PA with objective or a combination of objective and subjective methods (e.g., accelerometer and seven-day Physical Activity Recall [PAR]), two studies demonstrated no effect when comparing an eHealth intervention to a non-eHealth intervention [34] or a no intervention control group [45]. On the other hand, results of five studies suggest that participants who received an eHealth intervention significantly increased PA levels when compared to participants who received no intervention (p<.001 in [35]) or a non-eHealth intervention (for [20] p<.05, for [28] p=.01, for [29] p<.05, for [36] p<.001).

Subjective outcome assessment

Of the 13 studies assessing PA with subjective methods (e.g., International Physical Activity Questionnaire [IPAQ]), two studies reported no intervention effect when comparing an eHealth intervention to a no intervention control group [41] or a non-eHealth intervention [39, 40]. In eleven studies, a beneficial effect of the eHealth intervention compared to a no intervention control group [19, 22, 31, 33, 38, 44, 46-49] or a non-eHealth intervention [21, 30, 32, 37, 42, 43] was reported.

Delivered intervention dose and intervention engagement

12 of the 20 included studies reported information on the delivered intervention dose (n=7 web-based interventions, n=5 telephone-based interventions) [19, 20, 28, 30-33, 35, 39, 40, 42-44, 47-49]. For the web-based interventions, Bickmore and colleagues [28] reported that participants in the IG interacted with the virtual coach on average 35.8 (Standard deviation [SD] 19.7) times during the 60-day in-home intervention phase compared to an intended daily interaction.

The studies by King and colleagues [30] and Mouton and Cloes [44] reported similar engagement rates [in [30], participants completed an average of 68% of the 112 PDA entries available to them across the eight-week period, in [44], an average of 18 (SD 14) website visits for the web-based and 39 (SD 21) website visits for the mixed group in three months compared to an intended daily use]. In comparison to these studies, Irvine and colleagues [19] and King and colleagues [31] reported higher engagement rates (in [19], the mean number of website visits was 15.2 (SD 9.02) in three months compared to a intended weekly interaction; in [31], the mean number of computer interactions was 1.56 (SD = 0.65) per week compared to the recommended weekly use). For the telephone-based interventions, Freene and colleagues reported that 90% of participants received four or more of the six intended telephone calls [39, 40]. In the study by Martinson and colleagues [36], the mean number of completed course sessions was 5.12 with 39.8% of participants completing all seven intended phone sessions [42, 43]. None of the text messaging-based studies reported information regarding the delivered intervention dose (i.e., how many of the text messages sent were delivered and received and read by participants).

Discussion

Population-based strategies to promote PA are needed to improve older adults' health and quality of life, in general, and to prevent frailty and the onset or progression of chronic diseases in later stages of life. A promising approach for transporting PA interventions to wider segments of the population is the use of technology to support self-regulatory processes involved in the uptake and maintenance of PA in this population. In this systematic review, we found that eHealth interventions can effectively promote PA in older adults aged 55 years and above when compared to no intervention control groups, at least in the short term.

The majority of the included interventions were theory-based (i.e., 16 interventions); four studies did not report any use of theory leaving the question unanswered whether theory was employed for the design or the implementation of the intervention. For two of these presumably non-theory-based interventions, short-term effects on PA were observed [28, 29], for the other two, no intervention effects could be demonstrated [34, 45]. To conclude, and in line with findings by Webb and colleagues [50], our findings suggest that interventions with a theory-base were more effective in promoting PA than those that did not, regardless of intervention mode (i.e., web- vs. print-based interventions). All interventions comprised tailored PA recommendations and the great majority encouraged PA tracking either with a tracking device or an online-diary. Results of these self-monitoring activities were used to provide (real-time) feedback on individual PA-levels. This suggests that a combination of different intervention components reflecting various behavior change techniques known to support health behavior modification [51] appear to be associated with significant increases in PA in this population.

Furthermore, the number of studies employing subjective vs. objective PA assessment was not balanced. Studies employing subjective assessment still prevailed (n=13) and were not evenly distributed between web-based (n=7), telephone-based (n=5), and text messaging-based interventions (n=1). Hence, a comparison of intervention effects by different delivery modes (e.g., web-based vs. telephone-based) using objectively measure PA as the main outcome was attempted, but conclusions regarding intervention impact could not be drawn. Regarding the intervention intensity necessary for behavior change, findings by Vandelanotte and colleagues [52] indicate that greater engagement with web-based interventions is associated with larger effects on PA. In the majority of studies included in this review, intervention participants were encouraged to interact with the intervention daily or weekly (n=14), this was especially the case for web-based (n=6) and text messaging-based interventions (n=4). The results of our review suggest that participants' intervention engagement was moderate to high, but participants hardly ever reached the intended intervention dose. Subgroup analyses to further investigate the number of interactions necessary for reaching the recommended PA goals were only performed in two studies suggesting that higher levels of program interaction were significantly associated with greater changes in PA outcomes [19, 44]. In terms of the duration of follow-ups, follow-up assessments of PA in three of the four included text messaging-based interventions did not exceed three months. Web-based and telephone-based interventions were usually evaluated with longer follow-ups (web-based interventions: n=5 with follow-ups ranging from six to 12 months; telephone-based interventions: n=6 with follow-ups ranging from six to 24 months). Again, due to the heterogeneity in follow-ups, comparisons of eHealth vs. non-eHealth interventions by length of follow-up were unfortunately not possible.

Several limitations of this systematic review should be noted. While we systematically screened relevant electronic databases to identify studies, the search was restricted to studies published in English or German. Another limitation is that the technologies used for intervention delivery have changed in recent years. Most of the included studies delivered the intervention via a website or telephone, whereas only one study used apps, such as WhatsApp. In this review, no studies were included which delivered the intervention via an app developed by researchers. Moreover, we used a relatively low cut-off point for defining older adulthood which may have caused a bias because younger older adults aged 65 years or younger tend to be more experienced in using the internet or smartphones than older elderly adults aged 70 years or above. In addition, quantitative data synthesis (i.e., meta-analysis) was not feasible because the included studies were too heterogeneous in terms of intervention content and duration, outcome assessment, and comparator groups. For similar reasons, quantitative data synthesis for effects in various populations (e.g., stratified by socio-economic status) was not feasible. Using the risk of bias tool was difficult because some of its criteria could not be accurately applied to public health interventions (e. g., blinding of study personnel or participants) or information needed for determining the categories for risk of bias was not provided or unclear in the publication. Also, we decided not to exclude studies based on the risk of bias assessment (e.g., poor risk of bias).

Conclusions

To conclude, eHealth interventions can effectively promote PA in older adults aged 55 years and above in the short-term, while evidence for long-term effects is lacking. However, the findings of this systematic review have to be interpreted with caution because studies varied greatly in intervention mode, content, and duration, as well as in the outcomes assessed and the study quality ranged from poor to moderate. Further research is needed to investigate if eHealth interventions are equally, less or more beneficial in promoting PA in older adults compared to non-eHealth interventions so that future interventions will be able to provide choices based on participants' preferences. Our search yielded several study protocols describing currently ongoing studies in this research area which will have to be included in future reviews [53, 54].

Abbreviations

App: Mobile application

CENTRAL: Cochrane Central Register of Controlled Trials

CG: Control group

CINAHL: Cumulative Index to Nursing & Allied Health Literature

EMBASE: Excerpta Medica database

ES: Effect size

IG: Intervention group

IPAQ: International Physical Activity Questionnaire

PEI: Physical Education Index

PA: Physical activity

PAR: Physical Activity Recall

PDA: Personal Digital Assistant

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCT: Randomized controlled trial

SD: Standard deviation

WHO: World Health Organization

Human and animal rights: Not applicable

Competing interests: None

Funding: This systematic review was conducted as part of a dissertation. The research for the dissertation is conducted as part of the "AEQUIPA - Physical activity and health equity: primary prevention for healthy ageing" project, a regional prevention research project and network funded by the German Federal Ministry of Education and Research (grant number: 01EL1422A). The funding agency had no involvement in the execution of this systematic review and the decision to submit the article for publication.

Acknowledgements: We would like to thank our research librarian Lara Christianson (BIPS, Bremen) for providing feedback on the search strategy and the selection of the databases.

References

1. Warburton DE, Nicol CW, Bredin SS. Health benefits of physical activity: the evidence. CMAJ. 2006; 174:801-809
2. Hong SY, Hughes S, Prohaska T. Factors affecting exercise attendance and completion in sedentary older adults: a meta-analytic approach. J Phys Act Health. 2008; 5:385-397.
3. Hupin D, Roche F, Gremeaux V, Chatard JC, Oriol M, Gaspoz JM, Barthelemy JC, Edouard P. Even a low-dose of moderate-to-vigorous physical activity reduces mortality by 22% in adults aged ≥60 years: a systematic review and meta-analysis. Br J Sports Med. 2015; 49:1262-1267.
4. WHO. Global recommendations on physical activity for health. Geneva: World Health Organization; 2010.
5. Sun F, Norman IJ, While AE. Physical activity in older people: a systematic review. BMC Public Health. 2013; 13:449.
6. Noar SM, Benac CN, Harris MS. Does tailoring matter? Meta-analytic review of tailored print health behavior change interventions. Psychol Bull. 2007; 133:673-693.
7. Short CE, James EL, Plotnikoff RC, Girgis A. Efficacy of tailored-print interventions to promote physical activity: a systematic review of randomised trials. Int J Behav Nutr Phys Act. 2011; 8:113.
8. Richards J, Hillsdon M, Thorogood M, Foster C. Face-to-face interventions for promoting physical activity. Cochrane Database Syst Rev. 2013; 9:CD010392.
9. Worldbank. The little book on information and communication technology. Washington DC: World Bank; 2013.
10. Smith A. Older adults and technolgy use. 2014. http://www.pewinternet.org/2014/04/03/older-adults-and-technology-use/. Accessed 28 Sept 2015.
11. WHO. E-Health. 2015. http://www.who.int/trade/glossary/story021/en/. Accessed 28 Sept 2015.
12. Norman GJ, Zabinski MF, Adams MA, Rosenberg DE, Yaroch AL, Atienza AA. A review of eHealth interventions for physical activity and dietary behavior change. Am J Prev Med. 2007; 33:336-345.

13. Krebs P, Prochaska JO, Rossi JS. A meta-analysis of computer-tailored interventions for health behavior change. Prev Med. 2010; 51:214-221.
14. Davies CA, Spence JC, Vandelanotte C, Caperchione CM, Mummery WK. Meta-analysis of internet-delivered interventions to increase physical activity levels. Int J Behav Nutr Phys Act. 2012; 9:52.
15. Foster C, Richards J, Thorogood M, Hillsdon M. Remote and web 2.0 interventions for promoting physical activity. Cochrane Database Syst Rev. 2013; 9:CD010395.
16. Aalbers T, Baars MA, Rikkert MG. Characteristics of effective Internet-mediated interventions to change lifestyle in people aged 50 and older: a systematic review. Ageing Res Rev. 2011; 10:487-497.
17. King AC, Hekler EB, Grieco LA, Winter SJ, Sheats JL, Buman MP, Banerjee B, Robinson TN, Cirimele J. Harnessing different motivational frames via mobile phones to promote daily physical activity and reduce sedentary behavior in aging adults. PLoS One. 2013; 8:e62613.
18. Silveira P, van de Langenberg R, van Het Reve E, Daniel F, Casati F, de Bruin ED. Tablet-based strength-balance training to motivate and improve adherence to exercise in independently living older people: a phase II preclinical exploratory trial. J Med Internet Res. 2013; 15:e159.
19. Irvine AB, Gelatt VA, Seeley JR, Macfarlane P, Gau JM. Web-based intervention to promote physical activity by sedentary older adults: randomized controlled trial. J Med Internet Res. 2013; 15:e19.
20. Pinto BM, Goldstein MG, Ashba J, Sciamanna CN, Jette A. Randomized controlled trial of physical activity counseling for older primary care patients. Am J Prev Med. 2005; 29:247-255.
21. Kim CJ, Kang DH. Utility of a web-based intervention for individuals with type 2 diabetes: The impact on physical activity levels and glycemic control. CIN. 2006; 24:337-345.
22. Peels DA, Bolman C, Golsteijn RH, de Vries H, Mudde AN, van Stralen MM, Lechner L. Long-term efficacy of a printed or a Web-based tailored physical activity intervention among older adults. Int J Behav Nutr Phys Act. 2013; 10:104.
23. Müller AM, Khoo S. Non-face-to-face physical activity interventions in older adults: a systematic review. Int J Behav Nutr Phys Act. 2014; 11:35.
24. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009; 339:b2535.
25. Muellmann S, Forberger S, Mollers T, Zeeb H, Pischke CR. Effectiveness of eHealth interventions for the promotion of physical activity in older adults: a systematic review protocol. Syst Rev. 2016; 5:47.

26. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011; 343:d5928.
27. Ogilvie D, Fayter D, Petticrew M, Sowden A, Thomas S, Whitehead M, Worthy G. The harvest plot: a method for synthesising evidence about the differential effects of interventions. BMC Med Res Methodol. 2008; 8:8.
28. Bickmore TW, Silliman RA, Nelson K, Cheng DM, Winter M, Henault L, Paasche-Orlow MK. A randomized controlled trial of an automated exercise coach for older adults. J Am Geriatr Soc. 2013; 61:1676-1683.
29. Kim BH, Glanz K. Text messaging to motivate walking in older African Americans: a randomized controlled trial. Am J Prev Med. 2013; 44:71-75.
30. King AC, Ahn DK, Oliveira BM, Atienza AA, Castro CM, Gardner CD. Promoting physical activity through hand-held computer technology. Am J Prev Med. 2008; 34:138-142.
31. King AC, Bickmore TW, Campero MI, Pruitt LA, Yin JL: Employing virtual advisors in preventive care for underserved communities: results from the COMPASS study. J Health Commun. 2013; 18:1449-1464.
32. King AC, Friedman R, Marcus B, Castro C, Napolitano M, Ahn D, Baker L. Ongoing physical activity advice by humans versus computers: The Community Health Advice by Telephone (CHAT) Trial. Health Psychol. 2007; 26:718-727.
33. Kolt GS, Schofield GM, Kerse N, Garrett N, Oliver M. Effect of telephone counseling on physical activity for low-active older people in primary care: a randomized, controlled trial. J Am Geriatr Soc. 2007; 55:986-992.
34. Thompson WG, Kuhle CL, Koepp GA, McCrady-Spitzer SK, Levine JA. "Go4Life" exercise counseling, accelerometer feedback, and activity levels in older people. Arch Gerontol Geriatr. 2014; 58:314-319.
35. Wijsman CA, Westendorp RGJ, Verhagen E, Catt M, Slagboom E, de Craen AJM, Broekhuizen K, van Mechelen W, van Heemst D, van der Ouderaa F, Mooijaart SP. Effects of a Web-Based Intervention on Physical Activity and Metabolism in Older Adults: Randomized Controlled Trial. J Med Internet Res. 2013; 15:13.
36. Martin SS, Feldman DI, Blumenthal RS, Jones SR, Post WS, McKibben RA, Michos ED, Ndumele CE, Ratchford EV, Coresh J, Blaha MJ. mActive: A Randomized Clinical Trial of an Automated mHealth Intervention for Physical Activity Promotion. J Am Heart Assoc. 2015; 4.
37. Müller AM, Khoo S, Morris T. Text Messaging for Exercise Promotion in Older Adults From an Upper-Middle-Income Country: Randomized Controlled Trial. J Med Internet Res. 2016; 18:e5.

38. Van Dyck D, Plaete J, Cardon G, Crombez G, De Bourdeaudhuij I. Effectiveness of the self-regulation eHealth intervention 'MyPlan1.0.' on physical activity levels of recently retired Belgian adults: a randomized controlled trial. Health Educ Res. 2016; 31:653-664.
39. Freene N. Physiotherapist-led home-based physical activity program versus community group exercise for middle-aged adults: Quasi-experimental comparison. Open J Prev Med. 2013; 3.
40. Freene N, Waddington G, Davey R, Cochrane T. Longitudinal comparison of a physiotherapist-led, home-based and group-based program for increasing physical activity in community-dwelling middle-aged adults. Aust J Prim Health. 2015; 21:189-196.
41. Jarvis KL, Friedman RH, Heeren T, Cullinane PM. Older women and physical activity: using the telephone to walk. Womens Health Iss. 1997; 7:24-29.
42. Martinson BC, Crain AL, Sherwood NE, Hayes M, Pronk NP, O'Connor PJ. Maintaining physical activity among older adults: Six-month outcomes of the Keep Active Minnesota randomized controlled trial. Prev Med. 2008; 46:111-119.
43. Martinson BC, Sherwood NE, Crain AL, Hayes MG, King AC, Pronk NP, O'Connor PJ. Maintaining physical activity among older adults: 24-month outcomes of the Keep Active Minnesota randomized controlled trial. Prev Med. 2010; 51:37-44.
44. Mouton A, Cloes M. Efficacy of a web-based, center-based or combined physical activity intervention among older adults. Health Educ Res. 2015; 30:422-435.
45. Muntaner-Mas A, Vidal-Conti J, Borras PA, Ortega FB, Palou P. Effects of a whatsapp-delivered physical activity intervention to enhance health-related physical fitness components and cardiovascular disease risk factors in older adults. J Sports Med Phys Fitness. 2017; 57:90-102.
46. Peels DA, van Stralen MM, Bolman C, Golsteijn RHJ, de Vries H, Mudde AN, Lechner L. The differentiated effectiveness of a printed versus a Web-based tailored physical activity intervention among adults aged over 50. Health Educ Res. 2014; 29:870-882.
47. van Stralen Maartje M, de Vries H, Mudde Aart N, Bolman C, Lechner L. The working mechanisms of an environmentally tailored physical activity intervention for older adults: A randomized controlled trial. Int J Behav Nutr Phys Act. 2009; 6.
48. van Stralen MM, de Vries H, Bolman C, Mudde AN, Lechner L. Exploring the efficacy and moderators of two computer-tailored physical activity interventions for older adults: a randomized controlled trial. Ann Behav Med. 2010; 39:139-150.
49. van Stralen MM, de Vries H, Mudde AN, Bolman C, Lechner L. The long-term efficacy of two computer-tailored physical activity interventions for older adults: main effects and mediators. Health Psychol. 2011; 30:442-452.

50. Webb TL, Joseph J, Yardley L, Michie S. Using the internet to promote health behavior change: a systematic review and meta-analysis of the impact of theoretical basis, use of behavior change techniques, and mode of delivery on efficacy. J Med Internet Res. 2010; 12:e4.
51. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, Eccles MP, Cane J, Wood CE. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med. 2013; 46:81-95.
52. Vandelanotte C, Spathonis KM, Eakin EG, Owen N. Website-delivered physical activity interventions a review of the literature. Am J Prev Med. 2007; 33:54-64.
53. Muellmann S, Bragina I, Voelcker-Rehage C, Rost E, Lippke S, Meyer J, Schnauber J, Wasmann M, Toborg M, Koppelin F, et al. Development and evaluation of two web-based interventions for the promotion of physical activity in older adults: study protocol for a community-based controlled intervention trial. BMC Public Health. 2017; 17:512.
54. Peacock OJ, Western MJ, Batterham AM, Stathi A, Standage M, Tapp A, Bennett P, Thompson D. Multidimensional individualised Physical ACTivity (Mi-PACT) - a technology-enabled intervention to promote physical activity in primary care: study protocol for a randomised controlled trial. Trials. 2015; 16:381.

Table 1: Summary of risk of bias assessment of included studies.

Author, year	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Summary risk of bias
Bickmore et al. 2013 [28]	+	?	?	+	+	?	?	+
Freene et al. 2013 [39, 40]	-	-	-	-	+	+	?	-
Irvine et al. 2013 [19]	+	?	?	-	-	?	?	-
Jarvis et al. 1997 [41]	+	?	+	-	-	+	?	-
Kim & Glanz 2013 [29]	-	-	-	+	+	?	?	+/-
King et al. 2007 [32]	+	+	+	-	+	+	?	+/-
King et al. 2008 [30]	+	?	?	-	+	?	?	+/-
King et al. 2013 [31]	+	?	+	-	+	?	?	+/-
Kolt et al. 2007 [33]	+	+	?	-	+	+	?	+/-
Martin et al. 2015 [36]	?	?	+	+	+	?	?	+/-
Martinson et al. 2008 [42, 43]	+	+	?	-	?	?	?	-
Mouton & Cloes 2015 [44]	+	+	?	-	-	?	?	-
Müller et al. 2016 [37]	+	+	+	-	+	?	?	+/-
Muntaner-Mas et al. 2017 [45]	-	-	?	+	?	?	?	-
Peels et al. 2013 [22, 46]	?	?	?	-	-	+	?	-
Pinto et al. 2005 [20]	?	?	?	+	+	?	?	+/-
Thompson et al. 2014 [34]	+	+	?	+	+	?	?	+/-
Van Dyck et al. 2016 [38]	+	+	+	-	+	?	?	+/-

Van Stralen et al. 2009 [47-49]	?	?	?	-	-	+	?	-
Wijsman et al. 2013 [35]	+	+	-	+	+	?	?	+/-

+ low risk of bias +/- moderate risk of bias - high risk of bias ? unclear risk of bias

Table 2: Study characteristics of included studies.

Author, year, country	Study design, sample, age, gender	Intervention	PA outcomes	Time points measured	Results	Authors conclusions
Web-based PA interventions						
Bickmore et al. 2013 [28] USA	RCT, n=263, mean age 71.3 years, 161 females, 165 black, 75 white, 23 other, 128 >high school	Mode: ECA-computer Theory use: No information Duration: 2 months Indented intervention dose: Daily IG: Pedometer and ECA-computer, daily conversation with animated computer character (social chat, well-being check, feedback based on uploaded pedometer steps relative to goals, positive reinforcement, barriers to walking, problem-solving discussion, exercise tip of the day) CG: Pedometer	Pedometer: Average daily step-count for 30 days before the end of intervention at 2 and 12 months	Baseline, 2, 12 months	2 months IG=4,041 steps compared to CG=3,499 steps (p=.01) 12 months IG=3,861 steps compared to CG=3,383 steps (p=.09)	Intervention effective in the short-term, but not in the long-term
Irvine et al. 2013 [19] USA	RCT, n=368, mean age 60.3 years, 69.4% females, 59% Caucasian, 41% other racial/ethnic groups, 82% at least some college education	Mode: Website Theory use: Theory of Planned Behavior Duration: 3 months Indented intervention dose: Weekly IG: Active after 55 website (personal activity planning, health value of exercise, overcoming barriers, tracking progress, staying motivated, safety tips, disease-specific recommendations, library), in week 1 start-up session (personal activity program including personal goals, benefits of PA), in weeks 2-12 new exercises for personal activity program,	Self-generated Items: PA status (cardiovascular, stretching, strengthening, balance activities)	Baseline, 3, 6 months	Intervention effect at 3 months Cardiovascular activities: Eta=.067, p<.001 Stretching activities: Eta=.07, p<.001 Strengthening activities: Eta=.105, p<.001 Balance activities: Eta=.092, p<.001 Intervention effect at 6 months Cardiovascular activities: Eta=.05, p<.001	Significant increase in self-reported PA in intervention compared to CG

		personal coach presented video-based educational content CG: Waitlist, received intervention after end of study			Stretching activities: Eta=.06, p<.001 Strengthening activities: Eta=.05, p<.001 Balance activities: Eta=.081, p<.001	
King et al. 2008 [30] USA	RCT, n=37, mean age IG 60.7 years, mean age CG 59.6 years, 42.1% females IG, 44.4% females CG, 73.7% white race IG, 83.3% white race CG, mean years of education IG 16.9, mean years of education CG 16.6	Mode: PDA Theory use: Social Cognitive Theory Duration: 2 months Indented intervention dose: Daily IG: Pedometer and PDA, daily steps were recorded on PDA, education materials, goal-setting, feedback on reported PA, barriers and enablers, instruction on both routine and leisure forms of PA, personal safety and injury prevention recommendations CG: Health educational written materials related to PA in middle- and older-aged adults	CHAMPS: PA (min/week MVPA, mean caloric expenditure in kcal/kg/week in MVPA, mean caloric expenditure in kcal/week in MVPA)	Baseline, 2 months	Changes in PA over 2 months presented as baseline adjusted mean Min/week MVPA: IG=310.6 compared to CG=125.5, p=.048 Mean caloric expenditure in kcal/kg/week in MVPA: IG=19.1 compared to CG=7.8, p=.05 Mean caloric expenditure in kcal/week in MVPA: IG=1653.9 compared to CG=605.3, p=.03	Intervention effective compared to CG
King et al. 2013 [31] USA	RCT, n=40, mean age 68.3 years, 72.5% females, 37 Latino, 3 Filipino, 1 Asian, 28.2% at least some college education	Mode: Virtual advisor Theory use: Social Cognitive Theory, Transtheoretical Model Duration: 4 months Indented intervention dose: Daily (pedometer), weekly (virtual advisor) IG: Pedometer and website (virtual advisor), steps were tracked with pedometer and upload to virtual	CHAMPS: Change in walking behavior at 4 months (min/week walking)	Baseline, 2, 4 months	Mean change in walking behavior at 4 months IG=253.5 min/week compared to CG=26.8 min/week Between group-difference 226.7 min/week, p=.0008, ES=1.2	Intervention effective in increasing minutes/week walking compared to CG

		advisor, tailored feedback and advice from virtual advisor CG: Waitlist, received intervention after study completion				
Mouton & Cloes 2015 [44] Belgium	Parallel-group RCT, n=206, mean age web-based IG 61.2 years, mean age center-based IG 69.8 years, mean age mixed IG 63.2 years, mean age CG 66.1 years, 39.6% males web-based IG, 32.2% males center-based IG, 35.3% males mixed IG, 38.3% males CG, ethnicity not reported, ≥higher education level 52.9% web-based IG, 43.1% center-based IG, 45.1% mixed IG, 44% CG	Mode: Website Theory use: Transtheoretical Model, Ecological Model Duration: 3 months Indented intervention dose: Daily (website), weekly (group exercises), monthly (tailored feedback) Web-based IG: Website with benefits and recommendations of PA, success stories, tips to start being physically active, goal setting, overcome barriers, exercise examples, PA diary, tools to measure PA, local PA opportunities, online forum, news, tailored feedback based on stages of change, tips tailored to stages of change Center-based IG: Weekly group exercising including motivational and environmental PA advice Mixed IG: Both web-based and center-based intervention CG: No intervention	IPAQ short-form: PA (MET min/week)	Baseline, 3, 6, 12 months	Intervention effect compared to CG at 12 months Web-based IG=94 MET min/week compared to CG=-21 MET min/week, p=.247, ES=0.06 Center-based IG=189 MET min/week compared to CG=-21 MET min/week, p=.083, ES=0.14 Mixed IG=238 MET min/week compared to CG=-21 MET min/week, p=.041, ES=0.20	Only the mixed intervention was effective in increasing PA compared to control group, for web-based and center-based intervention no significant increases in PA observed
Peels et al. 2013 [22] Peels et al. 2014 [46]	RCT, n=1248, mean age print IG 63.2 years, mean age basic web-based IG 63.7 years, mean age print-	Mode: Website Theory use: Intervention mapping, Social Cognitive Theory, I-Change Model, Transtheoretical Model, Health Action Process Approach, Precaution Adoption Model, Self-regulation Theory, Self-	SQUASH: Min/week PA	Baseline, 3, 6, 12 months	Intervention effect compared to CG after 6 months (complete case) Print IG=231 min/week, p=.003, ES=0.27 Web-based IG=283 min/week,	6 months: Both printed interventions and the web-based intervention were effective

Netherlands	ed-environmental IG 62.6 years, mean age web-based environ-mental IG 61.6 years, mean age CG 64.1 years, 47.8% males print IG, 52.8% males web-based IG, 43.7% males printed-environmental IG, 52.8% males web-based-environmental IG, 49.0% males CG, ethnicity not reported, low education print IG 41.5%, basic web-based IG 43.5%, print-ed-environmental IG 49%, web-based envi-ronmental IG 47.4%, CG 49.5%	determination Theory Duration: 4 months Indented intervention dose: 3 times in 4 months Print IG: General information about benefits of PA, three tailored PA advices (tailored to participants personal and psychological characteristics, PA behavior, stage of change), delivered in print-version Web-based IG: see print IG, but delivered via web-site Printed-environmental IG: see print IG, additionally tailored advice on local PA possibilities Web-based-environmental IG: see printed-environmental IG, but delivered via website CG: No intervention			p=.002, ES=0.31 Printed-environmental IG=276 min/week, p=.001, ES=0.35 Web-based-environmental IG=142 min/week, p=.142, ES=0.23 CG: 49 min/week Intervention effect compared to CG after 12 months (com-plete case) Print IG=57 min/week, p=.017, ES 0.21 Web-based IG=-3 min/week, p=.581, ES 0.12 Printed-environmental IG=114 min/week, p=.001, ES 0.32 Web-based-environmental IG=-9 min/week, p=.691, ES 0.10 CG=-58 min/week	in stimulating weekly minutes of PA 12 months: The provision of the printed inter-ventions had a more sustained effect on PA behavior than the web-based condition
Van Dyck et al. 2016 [38] Belgium	RCT n=284, mean age 63.2 years, 52.8% females, ethnici-ty not reported, 53.9% college/university degree	Mode: website Theory use: Self-regulation theory, Health Action Process Approach Model Duration: 1 month Indented intervention dose: 3 times in 1 month IG: In module 1 (baseline) participants filled out online IPAQ, based on answers personal feedback and general information on PA were provided, action plan (participants were asked if they wanted to do more PA, when, where, and with whom), possibility to identify difficult situations and hin-	IPAQ: Total PA min/week, moderate PA min/week, vig-orous PA min/week	Baseline, 1 week, 1 month	Intervention effect at 1-week follow-up Total PA: IG 561.2min/week (SD 346.3), CG 623.5 min/week (SD 375.5), not significant Moderate PA: IG 476.7 min/week (SD 309.9), CG 515.0 min/week (SD 350.9), not significant Vigorous PA: IG 37.5 min/week (SD 86.7), CG 56.6 min/week (SD 115.9), not significant	Intervention effective in increasing total PA at 1-month follow-up

		dering factors for PA offered and creation of if-then plan, personal action plan was sent via email with opportunity to send it to family/friends for social support; in module 2 (activated 1 week after finishing module 1) participants received feedback about behavioral change process and goals, possibility to adopt action plan; module 3 (activated 1 month after finishing module 2) had the same content as module 2 CG: Waitlist, received intervention after end of study			Intervention effect at 1-month follow-up Total PA: IG 663.5 min/week (SD 384.2), CG 599.7 min/week (SD 356.9), p<.05 Moderate PA: IG 550.7 min/week (SD 313.7), CG 476 min/week (SD 292.3), not significant Vigorous PA: IG 66.3 min/week (SD 128.5), CG 63.6 min/week (SD 133.4), not significant	
Van Stralen et al. 2009 [47] Van Stralen et al. 2010 [48] Van Stralen et al. 2011 [49] Netherlands	Cluster RCT, n=1971, mean age 64 years, 57% females, ethnicity not reported, 48% low education	Mode: Website Theory use: Intervention mapping, I-Change Model, Health Action Process Model, Self-regulation Theory, Self-determination Theory Duration: 4 months Indented intervention dose: 3 times in 4 months Basic tailored IG: Three tailored letters with personalized PA advice (based on personal data gathered at baseline and 3 months assessment) IG plus: Same intervention as basic tailored IG, additional tailored information about local PA opportunities, access to a forum and e-buddy system on a website CG: Waitlist, after study completion participants received one tailored letter	SQUASH: Min/week PA	Baseline, 3, 6, 12 months	Intervention effect compared to CG after 12 months Basic tailored IG=7.9 min/week (β=13.5, p>.05) IG plus=73.4 min/week (β=62.0, p<.05) CG=9.6 min/week Intervention effect IG plus compared basic tailored IG β=48.5, p>.05	IG plus effective in increasing min/week PA compared to CG
Wijsman et al.	RCT,	Mode: Website	Accelerometer:	Baseline, 3	Daily PA in IG increased by	Intervention

2013 [35] Netherlands	n=235, mean age IG 64.7 years, mean age CG 64.9 years, 47 females IG, 49 females CG, ethnicity not reported, 66 high education IG, 67 high education CG	Theory use: Stages of change, I-Change Model Duration: 3 months Indented intervention dose: Daily IG: Accelerometer and website, daily activity was tracked on accelerometer and linked to personal website, e-coach provides regular updates of individual's PA status by email and gives advice to increase PAs CG: Waitlist, received intervention after study completion	Daily PA	months	46% (SE 7%, p<.001) compared to 12% (SE 3%, p<.001) in CG (p difference <.001) at 3 months	effective in increasing PA compared to CG
Telephone-based PA interventions						
Freene et al. 2013 [39] Freene et al. 2015 [40] Australia	Quasi-experimental design, n=177, mean age IG 56 years, mean age CG 59 years, 72% females, 70% born in Australia, 65% tertiary educated	Mode: Telephone Theory use: Social Cognitive Theory, Transtheoretical Model, Self-determination Theory Duration: 6 months Indented intervention dose: Monthly IG: PA advice via phone based on discussion about type, frequency, intensity, duration, benefits, barriers, goals, self-monitoring and progression of PA aiming to achieve 30 min moderate PA most days of the week, monthly telephone calls CG: Weekly community-based fitness program	Active Australia Survey: PA adherence	Baseline, 6, 18 months	Number of participants achieving sufficient PA At 6 months IG=22 vs. 45%, Z = −3.43, p=.001 CG=22 vs. 52%, Z = −4.91, p<.001 No difference between groups At 18 months IG=22 vs. 41%, $X^2(4)$ = 19.68, p=.001 CG=22 vs. 47%, $X^2(4)$ = 24.60, p<.001 No difference between groups	Both groups significantly increased PA
Jarvis et al. 1997 [41]	RCT, n=85, mean age 66.6 years,	Mode: Telephone Theory use: Transtheoretical Model	Self-generated items: Min/week	Baseline, 3 months	IG and CG increased min/week walked at 3 months compared to baseline	Both groups increased min/week

USA	52 females of whom 30% African-American, education not reported	Duration: 3 months Indented intervention dose: Weekly IG: Print material (benefits of walking, how to begin a walking program), telephone conversation using participants amount of activity and stage of change to engage participant in regular walking (benefits of walking, risks of inactivity, goal setting) CG: Print material (benefits of walking, how to begin a walking program), received intervention after end of study	walked		min/week walked, differences between IG and CG for 0 (p=.019) and 15 (p=.031) min/week walked at baseline, no difference between IG and CG for 30 (p=.062), 60 (p=.225) and 120 (p=.797) min/week walked at baseline	walked
King et al. 2007 [32] USA	RCT, n=189, mean age human advice IG 60.5 years, mean age automated advice IG 61.6 years, mean age CG 60.2 years, 70.5% females human advice IG, 69.7% females automated advice IG, 67.7% females CG, 81.87% white race human advice IG, 93.3% white race automated advice IG, 87.1% white race CG, mean years of education human advice IG 16.3, mean years of education automated advice IG 16.2, mean years of education CG	Mode: Telephone Theory use: Social Cognitive Theory, Transtheoretical Model, Communication Theory Duration: 12 months Indented intervention dose: Bi-weekly/monthly Human advice IG: Daily PA plan, bi-weekly/monthly telephone calls including individualized information, support, problem-solving, participants report on their PA, additional informational mailings, use of pedometer which provided individualized activity feedback to the participant Automated advice IG: Content similar to human advice group, but telephone contacts by automated telephone-linked computer (TLC) and not by human CG: Weekly health education classes about non-PA topics (e.g., nutrition, home safety)	7-day PAR/CHAMPS: PA (min/week MVPA)	Baseline, 6, 12 months	Mean change in min/week MVPA at 6 months Human advice IG=71 min/week MVPA (difference between IG and CG p≤.05) Automated advice IG=101.6 min/week MVPA (difference between IG and CG p≤.01) CG=8.4 min/week MVPA No differences between two IGs (p=.65) Mean change in min/week MVPA at 12 months Human advice IG=78.1 min/week MVPA (difference between IG and CG p≤.05) Automated advice IG=78.9 min/week MVPA (difference between IG and CG p>.05) CG=26.2 min/week MVPA No differences between two IGs (p=.66)	Both interventions effective compared to CG, by 12 months the effectiveness of the automated advice IG appeared to diminish relative to human advice IG

	16.1					
Kolt et al. 2007 [33] New Zealand	RCT, n=186, mean age IG 74.1 years, mean age CG 74.3 years, 58 females IG, 65 females CG, 92 New Zealand European IG, 89 New Zealand European CG, 38 university qualification/other post-high school qualification IG, 44 university qualification/other post-high school qualification CG	Mode: Telephone Theory use: Transtheoretical model Duration: 3 months Indented intervention dose: Weekly/bi-weekly IG: Eight telephone calls based on individual stage of change, strategies to increase PA were benefits of PA, risks of a sedentary lifestyle, PA opportunities, identifying motivators, problem-solving barriers, goal setting, discussion about relapse prevention, supplementary material was mailed including walking logs and pamphlets to support counseling approach CG: No intervention	AHSPAQ: Total leisure activity min/week, moderate leisure activity min/week, walking leisure activity min/week	Baseline, 3, 6, 12 months	Mean min/week at 3 months Total leisure activity: IG=184 min/week, CG=116.5 min/week, p=.02 Moderate leisure activity: IG=138.9 min/week, CG=86.7 min/week, p=.04 Walking leisure activity: IG=107.2 min/week, CG=62.4 min/week, p=.001 Mean min/week at 12 months Total leisure activity: IG=244 min/week, CG=117.3 min/week, p=.05 Moderate leisure activity: IG=197.7 min/week, CG=83.3 min/week, p=.007 Walking leisure activity: IG=91.4 min/week, CG=63.7 min/week, p=.68	3 months: IG significantly increased PA compared to CG 12 months: No significant changes for PA
Martinson et al. 2008 [42] Martinson et al. 2010 [43] USA	RCT, n=1049, mean age 57.1 years, 72.4% females, 94% white race, 66.7% 4 year degree or more	Mode: Telephone Theory use: Social cognitive theory, Relapse Prevention Theory Duration: 24 months Indented intervention dose: Bi-weekly/monthly IG: Seven telephone sessions (benefits, goal setting, action plan, types of PA, overcoming barriers, problem-solving and enhancing self-efficacy, social support, healthy eating, relapse prevention), course book, 52 week log book for monitoring	CHAMPS: Kilocalories/week total PA, kilocalories/week MVPA	Baseline, 6, 12, 24 months	Mean kilocalories/week at 6 months Total PA: IG=3848, CG=3558, p=.003 MVPA: IG=2008, CG=1764, p=.003 Mean kilocalories/week at 12 months Total PA: IG=4163, CG=3941, p=.008 MVPA: IG=2146, CG=1934, p=.004	Intervention was effective at maintaining PA in both short-term (6 months) and longer-term (12, 24 months) relative to CG

		activity and recording goals, pedometer, supplementary materials (e.g., classes in local community), after seven telephone sessions participants received monthly/bi-monthly telephone calls CG: Usual care, received information about 10,000 steps program and four newsletters on general health and wellness			Mean kilocalories/week at 24 months Total PA: IG=4309, CG=3904, p=.001 MVPA: IG=2180, CG=1903, p=.001	
Pinto et al. 2005 [20] USA	RCT, n=100, mean age 68.5 years, 60 females, 81 white race, 55 ≥college degree	Mode: Telephone Theory use: Transtheoretical Model, I-Change Model Duration: 6 months Indented intervention dose: Weekly IG: PA prescription tailored to participants' motivational readiness, three face-to-face PA counseling sessions, 12 PA counseling calls, 12 PA tip sheets CG: Advice given by clinician	7-day PAR: Kilocalories/week MVPA, PA min/week Accelerometer: weight adjusted mean counts	Baseline, 3, 6 months	Mean change in kilocalories/week MVPA At 3 months: IG=3.85, p<.05 CG=0.83 At 6 months: IG=4.19, p<.05 CG=1.11 Mean change in PA min/week At 3 months: IG=57.69, p<.05, CG=12.45 At 6 months: IG=62.84, p<.05, CG=16.6 Mean change in weight adjusted mean counts At 3 months: IG=50.79, p<.05, CG -11.11 At 6 months: IG=42.39, p<.01, CG -24.18	Intervention effective in increasing PA at 3 and 6 months compared to CG
Thompson et al. 2014 [34] USA	RCT crossover, n=49, mean age IG 79.1 years, mean age CG 79.8 years, 19 females IG, 20 females CG, ethnicity not reported, education not reported	Mode: Telephone Theory use: No information Duration: 6 months Indented intervention dose: Daily (Fitbit), weekly (telephone calls)	Accelerometer: PA units	Baseline, 6, 12 months	PA units at 6 months IG=-217.8, p=.31 CG=-583.6, p=.006 No differences between IG and CG (p=.21) PA units at 12 months Data not shown, but reported that there were no group or	Intervention not effective in increasing PA units at 6 and 12 months

		IG: Wore Fitbit accelerometer with feedback from device, exercise counseling based on Go4Life materials (education on different exercises, setting goals, exercise plan, tracking PA), telephone calls, face-to-face counseling CG: Wore Fitbit accelerometer without feedback from device, after 6 months, control group received intervention from intervention group and intervention group wore Fitbit with feedback but without counseling			between group differences from 6 to 12 months	
Text messaging-based PA interventions						
Kim & Glanz 2013 [29] USA	RCT, n=45, mean age IG 69.31 years, mean age CG 70.55 years, 21 females IG, 8 females CG, 45 African-American, education not reported	Mode: Text-messaging Theory use: No information Duration: 6 weeks Indented intervention dose: Daily (pedometer), daily 3 times a day on 3 days a week (text messages) IG: Pedometer, walking instructions manual, text messages 3 times a day, 3 days a week CG: Pedometer, walking instructions manual	LTEQ: LTEQ score in MET activity levels Pedometer: Steps/day	Baseline, 6 weeks	LTEQ score at 6 weeks IG=23.77, p=.001 CG=14.91, p=.01 Difference between IG and CG (p<.05) Steps/day at 6 weeks IG=6530.99, p=.05 CG=4780.21, p=.23 Difference between IG and CG (p<.05)	Intervention effective in increasing steps/day and LTEQ scores compared to CG
Martin et al. 2015 [36] USA	RCT, n=48, mean age 58 years, 46% females, 79% white race, education not reported	Mode: Text-messaging Theory use: Behavioral change techniques Duration: 4 weeks Indented intervention dose: Daily (Fitbug Org), 3 times a day for 2 weeks (text messages) IG text: Received unblinded Fitbug Org to track PA;	Accelerometer: Daily step-count	Baseline, weeks 2-3 (phase I), weeks 4-5 (phase II)	Mean change in daily step-count at weeks 2-3 IG text and no text: Mean change 408 steps (SD 2701) CG: Mean change -616 steps (SD 2385) Mean difference IG text and not text and CG: 1024 steps, 95% CL -580 to 2628, p=.21	Intervention effective in increasing PA with, but not without, the text-messaging component

		in week 1, assessment of baseline PA (blinded); in weeks 2-3, daily step count, (aerobic) activity time, PA history of previous day was visible on smartphone; in weeks 4-5, participants additionally received personalized texts from physician 3 times/day to encourage participants to achieve 10,000 steps/day IG no text: Received unblinded Fitbug Org to track PA; in week 1, assessment of baseline PA (blinded); in weeks 2-5, daily step count, (aerobic) activity time, PA history of previous day was visible on smartphone CG: Received blinded Fitbug Org to track PA for weeks 1-5			Mean change in daily step-count at weeks 4-5 IG text: Mean change 2334 steps (SD 1714) IG no text: Mean change -200 steps (SD 1653) CG: Mean change -1042 steps (SD 2202) Mean difference IG text and IG no text: 2534 steps, 95% CL 1318 to 3750, p<.001 Mean difference IG text and CG: 3376 steps, 95% CL 1951 to 4801, p<.001 Mean difference IG no text and CG: 842 steps, 95% CL -564 to 2248, p=.23	
Müller et al. 2016 [37] Malaysia	RCT, n=43, mean age 63.28 years, 74% females, ethnicity not reported, 68% college/university degree	Mode: Text-messaging Theory use: Behavioral change techniques Duration: 12 weeks Indented intervention dose: Daily on weekdays IG: During baseline home visit, participants received an exercise booklet (information on exercise benefits, safety instructions, description of 12 age-appropriate strengthening exercises, warm-up and cool-down section) and were introduced in a practical session to a set of exercises (arms/shoulders, trunk/neck, legs, participants were advised to exercise as often as possible), one text message with instructions on how to exercise with the exercise booklet and rewards/praise for efforts was sent to participants on weekdays	Exercise log from exercise booklet: Weekly exercise frequency	Baseline, 12, 24 weeks	Weekly exercise frequency at 12 weeks IG: Mean exercise frequency 3.74, SD 1.34 CG: Mean exercise frequency 2.52, SD 1.85 Mean difference 1.21, 95% CI 0.18 to 2.24, p=.03 Weekly exercise frequency at 24 weeks IG: Mean exercise frequency 3.07, SD 1.32 CG: Mean exercise frequency 2.33, SD 1.92 Mean difference 0.74, 95% CI -0.30 to 1.76, p=.18	Intervention effective in increasing PA at 12 weeks, but not 24 weeks, compared to CG

		CG: Received exercise booklet and set of exercises on baseline home visit				
Muntaner-Mas et al. 2017 [45] Spain	Three-group clinical trial design, n= 48, mean age 63.78 years, 75% females, ethnicity not reported, education not reported	Mode: Text-messaging Theory use: No information Duration: 10 weeks Indented intervention dose: Twice per week IG training: Twice per week group training sessions (warm-up, muscle-strength training, aerobic training, flexibility) IG mobile: Intervention content same as for IG training, but delivered via Whatsapp, all participants were added to a chat and received two videos with exercises and two messages to encourage participants to perform exercises per week CG: No intervention	Handgrip dynamometer: Muscular strength Flamingo balance test: Static balance 2-min step test: Aerobic capacity	Baseline, 10 weeks	Muscular strength at 10 weeks IG mobile vs. CG: ES=-0.04, p=.937 IG training vs. CG: ES=-0.51, p=.236 IG training vs. IG mobile: ES=-0.46, p=.337 Static balance at 10 weeks IG mobile vs. CG: ES=-1.17, p=.026 IG training vs. CG: ES=-0.07, p=.867 IG training vs. IG mobile: ES=1.11, p=.024 Aerobic capacity at 10 weeks IG mobile vs. CG: ES=-0.73, p=.146 IG training vs. CG: ES=-0.12, p=.795 IG training vs. IG mobile: ES=0.61, p=.187	Both interventions not effective in changing balance, handgrip strength, aerobic capacity

AHSPAQ: Auckland Heart Study Physical Activity Questionnaire; CG: Control group; CHAMPS: Community Healthy Activities Model Program, CL: Confidence Interval; ECA: Embodied Conversational Agent; ES: Effect size (Cohen's d); H: hours; IG: Intervention group; IPAQ: International Physical Activity Questionnaire; LTEQ: Leisure time exercise questionnaire; MET: Metabolic equivalent of task; Min: Minutes; MVPA: Moderate to vigorous-intensity physical activity, PA: Physical activity; PAR: Physical activity recall; PDA: Personal Digital Assistant; RCT: Randomized Controlled Trial; SD: Standard Deviation; SE: Standard error; SQUASH: Dutch Short Questionnaire to Assess Health Enhancing Physical Activity

Figure 1. PRISMA Flow chart.

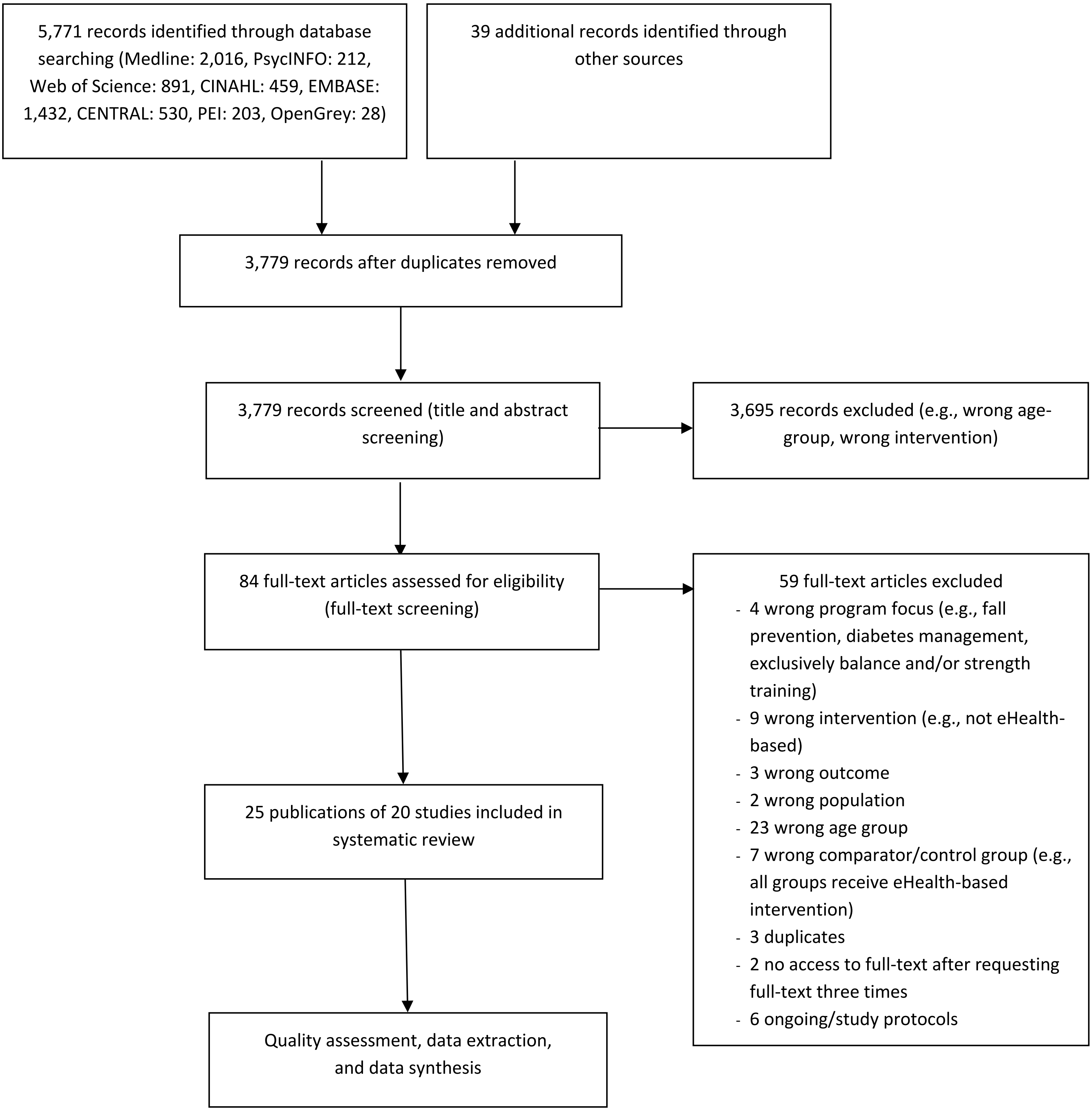
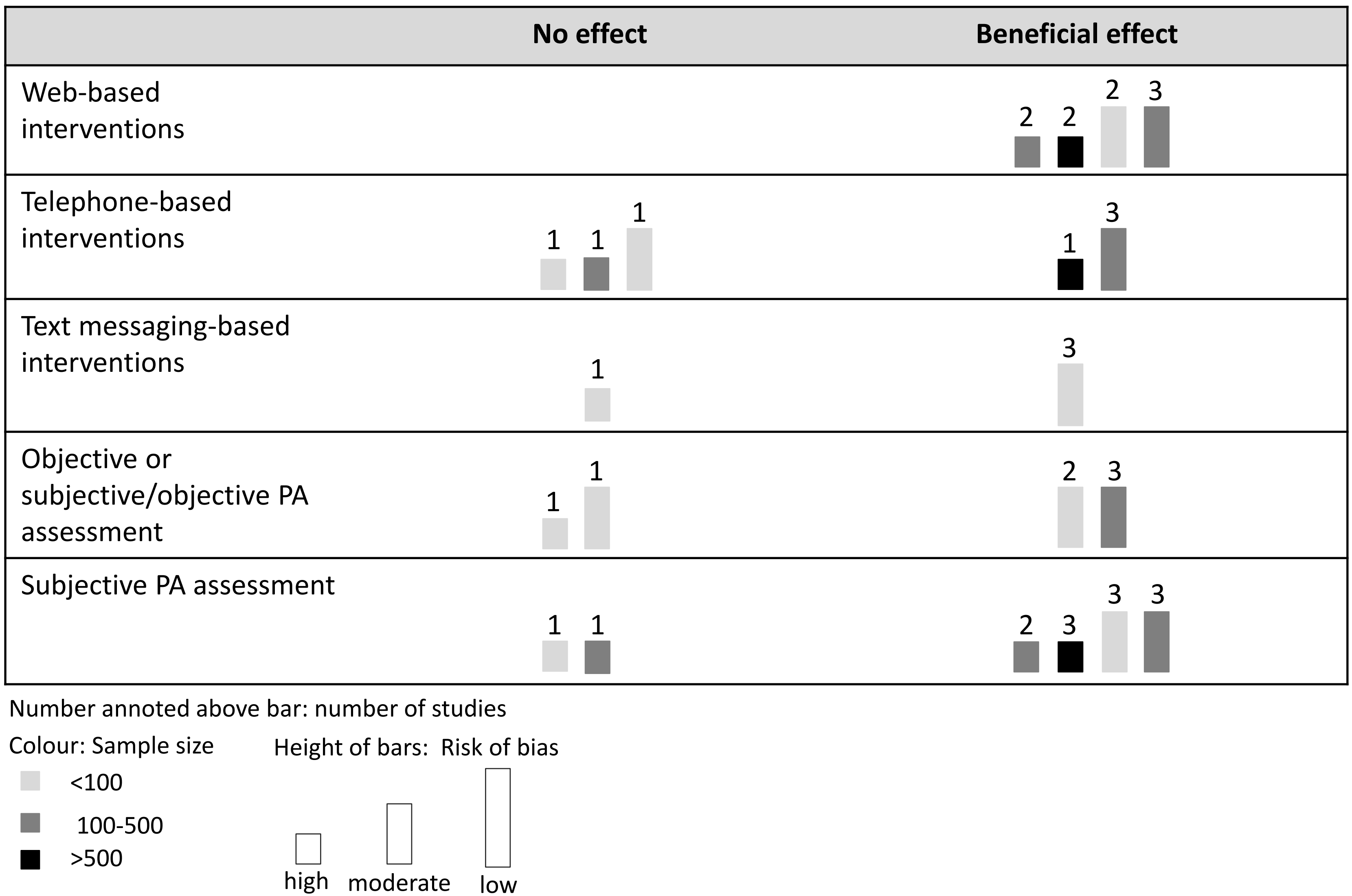


Figure 2. Harvest plot of evidence for intervention effectiveness by intervention mode and PA assessment



Additional file 1: Medline search.

Medline search (via PubMed on 30th October 2015, an update of the search was performed on 24th March 2017 and yielded 394 new hits)

Physical activity

Search name	Search query	Type of search	Results
#1	physical education and training[MeSH Terms] OR sports[MeSH Terms] OR exercise[MeSH Terms] OR physical fitness[MeSH Terms] OR exercise therapy[MeSH Terms] OR motor activity[MeSH Terms]	MeSH terms	305,405
#2	sedentary behavio*[Title/Abstract] OR physical activi*[Title/Abstract] OR physical inactivi*[Title/Abstract] OR sport*[Title/Abstract] OR exercis*[Title/Abstract] OR muscle stretching exercise*[Title/Abstract] OR resistance training[Title/Abstract] OR walk*[Title/Abstract] OR bicycle*[Title/Abstract] OR cycling[Title/Abstract] OR swim*[Title/Abstract] OR running*[Title/Abstract] OR gymnastic*[Title/Abstract] OR yoga[Title/Abstract] OR dancing[Title/Abstract] OR pilates[Title/Abstract] OR gardening[Title/Abstract]	Keyword Title/Abstract	480,553
#3	#1 OR #2		619,588

eHealth

Search name	Search query	Type of search	Results
#4	telemedicine[MeSH Terms] OR computer-assisted instruction[MeSH Terms] OR multimedia[MeSH Terms] OR computer systems[MeSH Terms] OR computers[MeSH Terms] OR cd-rom[MeSH Terms] OR electronic mail[MeSH Terms] OR cell phones[MeSH Terms] OR mobile applications[MeSH Terms] OR internet[MeSH Terms]	MeSH terms	168,712
#5	compute*[Title/Abstract] OR web*[Title/Abstract] OR online[Title/Abstract]	Keyword Title/Abstract	620,413
#6	#4 OR #5		718,731

Older adults

Search name	Search query	Type of search	Results
#7	aged[MeSH Terms]	MeSH terms	2,460,407
#8	elder*[Title/Abstract] OR older people[Title/Abstract] OR older adult*[Title/Abstract] OR old adult*[Title/Abstract] OR older person*[Title/Abstract] OR old person*[Title/Abstract] OR aging adult*[Title/Abstract] OR aging person*[Title/Abstract] OR ageing adult*[Title/Abstract] OR ageing person*[Title/Abstract] OR geriatrics[Title/Abstract] OR senior*[Title/Abstract]	Keyword Title/Abstract	295,730
#9	#7 OR #8		2,561,541

RCT-Filter: sensitivity-maximizing version (Higgins et al., 2011)

Search name	Search query	Results
#10	randomized controlled trial[Publication type]	398,286
#11	controlled clinical trial[Publication type]	89,554
#12	randomized[Title/abstract]	358,994
#13	placebo[Title/abstract]	170,382
#14	drug therapy[Subheadings]	1,790,185
#15	randomly [Title/abstract]	241,572
#16	trial[Title/abstract]	409,061
#17	groups[Title/abstract]	1,538,383
#18	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	3,679,368
#19	animals[MeSH terms] NOT humans[MeSh terms]	4,056,964
#20	#18 NOT #19	3,172,158

Summary and results

Search name	Search query	Results
#21	#3 AND #6 AND #9	4,729
#22	#3 AND #6 AND #9 AND #20	1,703
#23	#3 AND #6 AND #9 AND #20 Filters: English, German	1,622