ROLE OF PILOT TRIALS IN RCT QUALITY AND FEASIBILITY

by
Xiangji Ying

A dissertation submitted to Johns Hopkins University in conformity with the requirements for the degree of Doctor of Philosophy

Baltimore, Maryland
October 2023

Abstract

Large randomized controlled trials are crucial for assessing intervention efficacy but often fail or remain incomplete due to feasibility issues. Pilot trials may increase full-scale trial success but come with methodological challenges, including the debate over estimating efficacy. Design modifications post-pilot are common but their impact on feasibility is not fully understood. Furthermore, the association between pilot trials and the quality of full-scale trials is underexplored.

This meta-epidemiological study tackles these challenges by assembling two datasets. We searched PubMed for pilot trials published between 2005 and 2018 and their subsequent full-scale trials. The meta-analysis of the full-scale trials was then used to identify other full-scale trials on the same research topic but without a pilot trial.

In Paper 1, we analyzed 248 pairs of pilot and full-scale trials. Full-scale trials with a significant pilot trial were 2.72 times more likely to find a significant result for the primary efficacy outcome than those with a non-significant pilot trial. In 73% of the pairs, the pilot trial yielded a larger point estimate than the full-scale trial, yet in 87% of cases, the pilot's 95% confidence interval encompassed the full-scale point estimate. Paper 2 analyzed 249 pilot and full-scale trial pairs. Using feasibility progression criteria in pilot trials and maintaining the same masking status as the full-scale trial may improve the chances of successful screening, whereas adding extra content to the intervention, changing to active or more frequent control, and altering follow-up lengths and visits may decrease the chances of retaining participants in full-scale trials. In Paper 3, 58 full-scale trials with a pilot trial and 151 full-scale trials without were identified from 47 meta-analyses. A pilot trial's presence was associated with lower risk of bias in full-scale trial random sequence generation, allocation concealment, and participants/researchers masking, but not outcome assessment masking, incomplete outcome data, and selective reporting.

Pilot trials can offer early signals on intervention efficacy. Researchers and funders should weigh both the data from pilot trials and proposed design modifications when evaluating full-scale trials. Pilot trials may improve the quality of ensuing full-scale trials and warrant more frequent consideration.

Primary Dissertation Readers

Stephan Ehrhardt, MD, MPH; Adviser

Elizabeth Colantuoni, PhD

Janet Holbrook, PhD

Karen A. Robinson, PhD

Alternate Dissertation Readers

Pablo Martinez Amezcua, PhD

Jamie Perin, PhD

Leiyu Shi, DrPH

Acknowledgments

Completing this dissertation was made possible by the collective support of numerous individuals whom I am fortunate to know. I am immensely grateful to my adviser, Dr. Stephan Ehrhardt, for his consistent guidance and for setting a standard that challenged me to grow as an independent researcher. I would also like to thank him for providing me with exciting research opportunities in both preliminary and large-scale trials.

My sincere appreciation goes to Drs. Karen A. Robinson and Bryan Lau, whose incisive advice significantly refined my research ideas. My heartfelt thanks extend to all members and alternate members of my departmental, school-wide, and final oral examination committees (Drs. Stephan Ehrhardt, Sheriza Baksh, Ian J. Saldanha, Joanne Katz, Jennifer Deal, Xiangrong Kong, John McGready, Karen A. Robinson, Elizabeth Colantuoni, Janet Holbrook, Ann-Margret Ervin, Pablo Martinez Amezcua, Jamie Perin, and Leiyu Shi). Your questions and suggestions were incredibly thought-provoking and useful.

I also want to acknowledge the faculty and staff of my track, department, and school, as well as my peers, for their unending support. My former mentor and colleagues in China have been a continuous source of inspiration and encouragement, for which I am thankful. This journey would not have been possible without the financial support from the Department of Epidemiology and the Mary B. Meyer Memorial Fund Scholarship.

My deep gratitude goes to the peer reviewers and journal editors of my dissertation-related papers, whose constructive critiques and suggestions greatly enriched this work and motivated me to strive for research excellence.

Finally, I dedicate this dissertation to my family and friends, without whom I would not be where I am today. Thank you for your steadfast support while I pursue my dream.

Table of Contents

List of Tables

List of Figures

Chapter 1 Introduction

1. Impact of Unsuccessful RCTs

Randomized controlled trials (RCTs) are crucial for assessing the effectiveness or efficacy of interventions. However, conducting large-scale trials, such as pivotal drug development trials, demands significant time and resources. The entire process, encompassing planning, conducting, analyzing, and reporting of clinical trials, often spans years. A study of 138 pivotal trials for 59 FDA-approved drugs revealed a median cost of $19 million per trial and roughly $40,000 per patient in 2015. This cost can fluctuate dramatically, with estimates varying up to 100-fold [1–3].

Despite the high investment, approximately 45% of trials with results posted on ClinicalTrials.gov from 2000 to 2019 were not completed [4]. The feasibility of a trial heavily relies on a viable protocol, characterized by successful recruitment, participant adherence, and retention. Yet, approximately 45% of trials fail to meet the planned enrollment target, a figure that has remained fairly constant over time [5]. Noncompliance with prescribed medication is alarmingly high in real-world practice, with rates estimated at around 50%, leading to roughly 89,000 premature deaths and annual costs exceeding $100 billion [6]. Trial drop-outs are common, occurring in 81-95% of trials [7], and in certain fields like obesity interventions, the attrition rate can surge to 80% [8]. Even among trials that reach completion, a significant portion does not demonstrate efficacy. For instance, literature suggests that success rates for oncology drug trials hover between 3.4% and 6.7% [9,10].

Unsuccessful trials contribute to research inefficiencies by delaying results, inflating costs, and potentially biasing findings. The implications of a failed definitive trial extend beyond the direct trial costs and also encompass opportunity costs and expenses associated with previous

research efforts. After factoring in the probability of failure and opportunity costs, the research and development costs for drugs are estimated to lie between $200 million and $2.9 billion [11].

2. Utilizing Pilot Trials to Boost RCT Success Rates

A pilot or feasibility study is “a small-scale investigation designed either to test the feasibility of methods and procedures for later use on a large scale, or to search for possible effects and associations that may be worth following up in a subsequent larger study [12].” In particular, external randomized pilot studies or pilot trials are stand-alone pilot studies that incorporate a randomization procedure [13]. Although a pilot or feasibility study does not ensure success in the subsequent main study, it is generally perceived to enhance the likelihood of success, efficiency, and validity [14].

Over the past two decades, pilot and feasibility studies have gained increased attention [15,16]. In 2015, a new journal titled 'Pilot and Feasibility Studies' was launched, dedicated solely to these types of studies [17]. Additionally, two reporting guidelines for randomized and nonrandomized pilot and feasibility studies have been recently made available [18,19].

There has been a noticeable surge in the publication of pilot and feasibility studies. Data from PubMed shows an increase in articles containing the MeSH terms "pilot project" or "feasibility study", from 3,430 in 2000 to 12,563 in 2021. The ratio of pilot-to-main trials has also risen significantly from 1.4/100 in 2000 to 15.7/100 in 2022. Notably, approximately 33% to 42% of these published studies on an annual basis were pilot trials.

3. The Central Debate: Efficacy Estimation in Pilot Trials

Historically, the primary emphasis of pilot trials was on efficacy estimation. Hypothesis testing was conducted in 81% of pilot randomized controlled trials published in seven high-impact medical journals during 2007 and 2008 [20]. In a similar vein, 69 out of 93 (67.7%) pilot studies

published in Indian journals in 2013 employed at least one statistical test to discern any significant intergroup differences [21].

However, these practices have raised methodological concerns due to the potential for underpowered hypothesis testing, leading to a general discouragement of efficacy estimation in pilot trials [18]. Current consensus leans more towards the view that pilot studies or trials are typically not designed to gauge intervention efficacy, but rather to inform study processes and feasibility measures which will impact the design and execution of a larger, subsequent study [22,23].

Yet, a need often arises for preliminary efficacy evidence before committing significant investments in definitive trials. This begs the question: given the limited sample size of pilot trials, how informative can they be regarding efficacy estimation for a larger trial?

4. The Unsettled Question: How Valuable are Pilot Trials for Assessing Feasibility after Design Modifications?

The primary purpose of conducting a pilot trial, as advocated by many, has become feasibility estimation. This process inherently assumes that the feasibility parameters derived from the pilot trial are reliable indicators of the feasibility of the forthcoming trial. Yet, even if the only difference between the pilot and the full trial is the scale of the study, it might be overly optimistic to anticipate the larger-scale trial to reproduce the results of the smaller-scale pilot trial [24]. Furthermore, if alterations are made to the study design (for example, eligibility criteria), the pilot trial's feasibility outcomes may not necessarily extend to the main trial [25].

Cooper et al. identified a systematic bias and substantial variations between the feasibility parameters (namely, randomization and attrition proportions) predicted in the pilot trials and those observed in the definitive trials [26]. These differences could be due to modifications in the trial design following the pilot trial. However, the study was based on a relatively small sample of

16 pairs of pilot and corresponding full-scale trials, which restricts further investigations into how trial modifications influence feasibility.

It is quite common for researchers to alter trial design after the pilot trial. In fact, such modifications are often necessary to enhance the feasibility of the trial or the efficacy of the intervention. Beets et al found that 75% of full trials were different from the pilot trial in at least one domain, including intervention intensity and implementation support [27]. Regrettably, these alterations are often implemented without a clear understanding of their potential impact on trial feasibility, considering that it would be impractical to rerun the pilot trial for another round of feasibility estimation. Consequently, there is an urgent requirement for evidence regarding the influence and extent to which trial modifications might impact trial feasibility. This would optimize the utilization of pilot trials in guiding the feasibility of full-scale trials.

5. The Gap in Evidence: Do Pilot Trials Enhance the Quality of Full-scale Trials?

Trial quality, defined as the "absence of errors that matter to decision-making" [28] , is vital not only for achieving scientific objectives but also for safeguarding the rights and well-being of participants. Since errors can be categorized into random errors and systematic errors or bias, the absence of bias is considered a cornerstone of trial quality. Unfortunately, a significant number of randomized controlled trials to date have suffered from poor methodological quality or a high risk of bias. A study that analyzed over 170,000 RCTs published between 1966 and 2018 revealed a positive trend in trial quality over time [29]. However, there remains an urgent need for enhancement, given the persistently high probabilities of bias in treatment allocation, randomization, and masking processes. A similar conclusion was drawn in an earlier 2015 study, which found that 43% of trials had a high risk of bias in at least one domain of the Cochrane Risk of Bias (RoB) Assessment tool [30]. Simulations conducted in the study showed

that 50% of these biases and the associated wastage of resources could have been circumvented.

In the last decade, the focus on trial quality has shifted from being a secondary, retrospective aspect of trial science to becoming a central part of trial design [31]. The idea is that reliance on retrospective quality audits should be reduced, with the trial protocol acting as the blueprint for quality [32]. Since information from pilot trials is incorporated into the design of the main trial, it is reasonable to anticipate that conducting a pilot trial would enhance the main trial's quality. However, the role of pilot trials in improving the quality of the subsequent main trial has been sparingly discussed. Such evidence could carry significant implications for researchers and funders when distributing resources, as well as for reviewers and journal editors during the peer-review process of papers.

6. Objectives of the Study

AIM 1. To evaluate the role of pilot trials in informing full-scale trials' efficacy estimation. Specifically, we examine (1) the agreement in efficacy estimates between pilot and full-scale trials, (2) the impact on the full-scale trials' power when parameters estimated from pilot trials are used for sample size calculation, and (3) the association between the statistical significance and other characteristics of pilot trials with the efficacy results of full-scale trials.

Hypothesis: (1) Pilot trials tend to overestimate the effect size; (2) Using the effect size or standard deviation derived from pilot trials directly for sample size calculation can result in underpowered full-scale trials; (3) Achieving statistical significance in a pilot trial is independently associated with a "positive" outcome in the main trial.

AIM 2. To contrast feasibility estimates between pilot and full-scale trials and to investigate whether characteristics of pilot trials and subsequent modifications are associated with equivalent or improved feasibility in full-scale trials.

AIM 3. To examine the association between the presence of a pilot trial and the methodological quality of the main trial as assessed by the Cochrane Risk of Bias Assessment tool.

Hypothesis: The conduct of a pilot trial is associated with an enhanced quality of the main trial.

Chapter 2 Paper 1

Re-evaluating the role of pilot trials in informing effect and sample size estimates for full-scale trials: a meta-epidemiological study

Xiangji Ying ,[1] Karen A Robinson,[1,2,3] Stephan Ehrhardt[1]

[1] Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

[2] Department of Medicine, School of Medicine, Johns Hopkins University, Baltimore, Maryland, USA

[3] Section Evidence-Based Practice, Western Norway University of Applied Sciences, Bergen, Norway

This paper has been published with *BMJ Evidence-Based Medicine.* doi:10.1136/bmjebm-2023-112358.

Abstract

Background Some have argued that pilot trials have little value for informing the expected effect size of a subsequent large trial. This study aims to empirically evaluate the roles of pilot trials in informing the effect and sample size estimates of a full-scale trial.

Methods We conducted a search in PubMed on 19 February 2022, for all pilot trials published between 2005 and 2018 and their subsequent full-scale trials. We analyzed the agreement in results by comparing the direction and magnitude of the effect size in the pilot trial and full-scale

trial. Logistic regression was used to explore whether a significant pilot trial and other characteristics were associated with a significant full-scale trial.

Results A total of 248 pairs of pilot and full-scale trials were analyzed. Full-scale trials with a significant pilot trial were 2.72 times more likely to find a significant result for the primary efficacy outcome than those with a non-significant pilot trial (95%CI 1.52 to 4.86, p=0.001). The association remained significant irrespective of changes made to the trial design. In 73% of the pairs, the pilot trial produced a larger point estimate than the subsequent full-scale trial, but 87% of pairs had a 95%CI estimated by the pilot trial that covered the full-scale trial point estimate. Full-scale trials with a sample size estimated using the SD from the pilot trial were less likely to yield a significant result (OR=0.26, 95%CI 0.10 to 0.65, p=0.004).

Conclusion Pilot trials can provide strong signals on intervention efficacy. When determining the sample size for full-scale trials, using the CI bounds from the pilot trials instead of the point estimate may improve power estimation.

Introduction

Large randomized controlled trials are time consuming and resource consuming. Careful planning is needed before substantial investment in a well-powered trial. This is critical not only for scientific reasons but also to protect the rights and well-being of participants. A major consideration is whether the intervention is efficacious enough so that it is worthwhile to perform a full-scale trial. Such information may be provided by preliminary studies [1 2]. In a typical drug development process, phase II trials provide preliminary evidence on efficacy, which is subsequently used to justify larger definitive phase III trials. For non-pharmaceutical interventions, trialists often perform a pilot trial to test the potential effects of the intervention. A pilot trial is a type of pilot study that uses a randomized controlled design [3].

However, many have questioned the usefulness of pilot trials in informing a subsequent large trial about the magnitude of the effect of an intervention. It has also been argued that the effect size or SD estimated from the pilot data should not be used for full-scale trial sample size calculation [4]. Because pilot trials are usually small in size, the efficacy signals can be missed or exaggerated, leading to false conclusions. For instance, in one study using statistical simulations, even when the true effect size was moderate or large and the sample size was determined using the effect size from the pilot trial, the full-scale trial was found to be underpowered 32% and 23% of the time, respectively [5]. Furthermore, trialists might modify trial design after the pilot trial to improve key aspects, but very few have investigated how those modifications influenced the subsequent efficacy estimates [6,7].

The aim of this meta-epidemiological study is to evaluate the role of pilot trials in informing full-scale trials' efficacy estimation. Specifically, we examine (1) the agreement in efficacy estimates between pilot and full-scale trials, (2) the impact on the power of full-scale trials when parameters estimated from pilot trials are used for sample size calculation and (3) the association between the statistical significance and other characteristics of pilot trials with the efficacy results of full-scale trials. We follow guidelines for reporting meta-epidemiological methodology research [8].

Methods

Literature search

PubMed was searched on 19 February 2022 to identify pilot trials. The search strategy included three concepts: pilot or feasibility study, randomized controlled trial and feasibility parameters. All concepts were searched as MeSH terms and keywords (eTable 1 in Appendix A). A date restriction of 2005–2018 was imposed. This was because few pilot trials were published before 2005 and this ensured that a time window was left after the pilot trial for the full-scale trials to be

conducted and published. The search was restricted to the English language. To maximize the number of pilot full-scale trial pairs, we did not limit the search to a specific research area or disease type.

Study selection

Any pilot trials using a randomized controlled design were eligible for inclusion, except for internal pilot trials in which the data were pooled with the full-scale trial data in the final analysis. We then identified the subsequent full-scale trial by screening similar articles noted by PubMed and papers citing the pilot trial. A study was considered as the full-scale trial of the pilot if the study's result paper acknowledged the pilot trial as a foundation or basis for its design or execution. It was also required that the full-scale trial be conducted by the same research team and have at least one arm that was the same or similar to the pilot trial. Moreover, there had to be an overlap in population characteristics between the pilot and full-scale trials. In cases where the full-scale trial paper did not directly cite the pilot trial, but referenced a study protocol (published or provided as an appendix), we reviewed the protocol to determine if it was based on the pilot trial. We conducted iterative screenings of citations until we located the full-scale trial or determined its non-existence. We excluded full-scale trials that were informed by multiple pilot trials simultaneously to avoid ambiguity in isolating one specific pilot full-scale pair. However, if pilot trials were conducted sequentially and the full-scale trial was primarily informed by the final pilot trial, we included the pair consisting of the final pilot trial and the full-scale trial. We also included pairs where the full-scale trial was informed by one pilot trial alongside other preliminary work. The initial identification of pilot trials and their subsequent full-scale trials was carried out by one investigator (XY) following a predetermined plan. The selection of the final sample was subsequently discussed and agreed on by two investigators (XY and SE).

Data collection and preparation

One investigator (XY) performed data extraction in Covidence[9] using a pilot-tested form. For each identified pair of pilot and full-scale trials, trial characteristics and results (eg, effect size, p value and CI) were extracted from trial result papers, protocols, statistical analysis plans and trial registries. In the few cases where information was contradictory across different sources, priority was given to protocols and published trial result papers.

Trial characteristics of the full-scale trials were compared with their pilot trials to determine if any modifications had been made to the participant eligibility, intervention, control or outcome. Specifically, we examined whether the intervention and control groups in both trials had the same content, duration and frequency. An intervention or control was classified as the same across both studies if all three aspects were unchanged. We regarded the intervention or control as modified if the intervention or control of the full-scale trial contained more or less content, was longer or shorter in duration or was more or less frequent than it was in the pilot trial. If the changes extended beyond simple additions or reductions in content, the intervention or control was categorized as having other differences. Appendix A eTable 2 provides further definitions and examples of what was considered a modification.

Effect sizes (eg, mean difference, Cohen's d, OR, etc) were extracted from each pilot trial and full-scale trial only if they referred to the same efficacy endpoint, measured using the same methodology and taken at the same or nearest time points. If effect sizes were not directly reported, we extracted the necessary information for their calculation. For continuous outcomes, we calculated Cohen's d based on the appropriate SD for the given design [10,11]. For binary or time-to-event data, relative measures of association were calculated. When feasible, we employed the same analytic approach for both pilot and full-scale trials to ensure comparability of the estimates. The effect size was considered medium to large in magnitude if Cohen's d >0.5 or ratio >2.74 for a positive association and if Cohen's d <-0.5 or ratio <0.36 for a negative association [12].

A full-scale trial was deemed ‘positive’ if the stated primary hypothesis of the trial was met. A pilot trial was considered statistically significant if the p value was less than 0.05 for the between-group comparison on the efficacy endpoint that was subsequently used as the primary endpoint in the full-scale trial. We performed appropriate statistical tests on efficacy if the pilot trial did not test for differences between groups.

Statistical analysis

We compared the direction and magnitude of the point estimate of the effect in the full-scale trial to that of the pilot trial. We assessed whether the 95% CI of the effect estimated in the pilot trial included the point estimate of the effect in the full-scale trial. For point estimates sharing the same direction, we calculated the absolute difference by deducting the value of the full-scale trial from that of the pilot trial (ie, pilot − full-scale). Subsequently, we determined the relative difference by dividing this absolute difference by the effect size of the full-scale trial. This relative difference measure facilitated a comparison of the magnitude of the discrepancy relative to the actual value under examination. In cases where both associations were negative, we used the absolute value of Cohen’s d or the inverse of the ratio in our calculations. This ensured that a positive difference would always be indicative of a larger magnitude of association in the pilot trial than in the full-scale trial, regardless of the direction of the association.

Since each pair of pilot and subsequent full-scale trial is clustered by the research team and topic, but the study sample in the pilot and full-scale trials are independent from one another, the statistical significance and other characteristics of pilot trial results were analyzed using logistic regression analyses with robust variance estimates to estimate whether one or more factors were predictive of positive full-scale trials [13]. Both univariable and multivariable analyses were conducted for the primary exposure of interest (ie, statistical significance of the full-scale trial’s primary endpoint in the pilot trial), with the multivariable analysis model being adjusted for the characteristics of the pilot trial that were associated with the significance of the full-scale

trial. For the remaining trial design and modification characteristics, we reported the estimates while adjusting for intervention type. Additionally, we conducted subgroup analyses based on trial design modification status and other characteristics to explore their impact on the association between pilot trial significance and full-scale trial significance.

All analyses were performed using Stata (V.16; StataCorp, TX, USA) and RStudio (V.2022.12.0+353).

Patient and public involvement

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

Results

Trial characteristics

The initial search yielded 8739 unique citations of potential pilot trials, with the detailed numbers and reasons for exclusion depicted in figure 1. We identified 249 pairs of pilot and full-scale trials (full list available in eTable 3 in Appendix A). One full-scale trial published baseline characteristics, but the primary endpoint was not yet reached. This pair was excluded from the sample, resulting in 248 pairs in the analysis. Two hundred pilot trials assessed and reported efficacy outcomes, and 46% of those trials found a statistically significant between-group difference. One hundred and twenty nine (52%) full-scale trials were positive.

The pilot trial characteristics and modifications are summarized in table 1 and table 2. Most pilot trials (69%) investigated behavioral interventions. The mean number of participants enrolled in pilot trials was 121 (range=7–3318), and the mean pilot-to-full-scale sample size ratio was 24% (IQR=12%–32%). On average, the full-scale trials were published 5 years (IQR=3–7 years) after

the publication of the pilot trial. Sixty-nine per cent, 40% and 15% of trials were modified after the pilot trial on participant eligibility, intervention and control, respectively.

Agreement with full-scale trial effect size

Among the 125 pairs of pilot and full-scale trials that had effect size estimates available for agreement analysis, 26 pairs (21%) had point estimates of effect in the opposite direction. Among the remaining 99 pairs with point estimates in the same direction, 72 (73%) of the pilot trials yielded a larger point estimate than their subsequent full-scale trials (average absolute difference: 0.37, 95%CI −0.96 to 1.70; figure 2A). Approximately half of the pilot trials had a point estimate 53% larger than the full-scale trial (median relative difference: 53%, IQR=−2% to 187%; figure 2B). The magnitude and variation of the relative differences appeared to decrease when both pilot and full-scale trials had larger sample sizes (figure 2B). Approximately 87% (109 out of 125) of the point estimates from the full-scale trial fell within the 95%CI estimated by the pilot trial.

Association with full-scale trial significance

Pilot trial characteristics and modifications

Tables 3 and 4 show the associations of pilot trial characteristics and subsequent modifications with the full-scale trial significance. Pharmaceutical interventions were less likely to have a positive full-scale trial than behavioral interventions (unadjusted OR=0.27, 95%CI 0.13 to 0.58, p=0.001). When the sample size per arm of the pilot trial was more than 15% of the sample size per arm of the full-scale trial, the odds of a significant outcome for the full-scale trial was higher (adjusted OR=1.86, 95%CI 1.09 to 3.18, p=0.023). Using the pilot trial's SD for the full-scale trial sample size calculation was associated with reduced odds of the full-scale trial being positive (adjusted OR=0.26, 95%CI 0.10 to 0.65, p=0.004). If the full-scale trial increased the length of

the intervention relative to the pilot trial, we observed an increased odds of a positive trial result (adjusted OR=2.11, 95%CI 1.22 to 3.66, p=0.008).

Pilot trial statistical significance

Positive pilot trials were more likely to lead to positive full-scale trials (68% vs 44%, unadjusted OR=2.72, 95%CI 1.52 to 4.86, p=0.001). The OR was 2.41 (95% CI 1.32 to 4.42, p=0.004) after adjusting for pilot trial characteristics significantly linked to the likelihood of a positive full-scale trial, including intervention type, cluster randomized design, participant masking status and ratio of sample size per arm.

We investigated the effect of post-pilot trial modification on the association between pilot trial significance and full-scale trial significance by stratifying the pairs into two subgroups: with modifications and without modifications. Our findings revealed a significant strong association in the no modification subgroup (unadjusted OR=4.78, 95% CI 1.10 to 20.72, p=0.036; adjusted OR=6.87, 95% CI 1.07 to 44.12, p=0.042). We also observed a significant association in the modification subgroup (unadjusted OR=2.33, 95% CI 1.23 to 4.43, p=0.010; adjusted OR=1.99, 95% CI 1.02 to 3.88, p=0.044). The results of subgroup analyses based on other trial design characteristics can be found in figure 3. It is worth noting that the association between pilot trial significance and full-scale trial significance was no longer statistically significant when the analyses were limited to subgroups where the effect size or SD estimated from the pilot trial was used for the calculation of the full-scale trial's sample size (both p>0.05).

Discussion

Our analysis revealed that pilot trials, while not designed for definitive evidence, can still provide strong signals of efficacy. A moderate to strong association was found between pilot and full-scale trial statistical significance, and in most cases, the pilot trial's 95% CI covered the point estimate of the full-scale trial.

Concerns about the usefulness of pilot trials in determining intervention efficacy include modifications made to the trial design and unreliable estimates due to small sample sizes. However, our analysis found that even for pairs with modifications, there was a significant association between pilot and full-scale trial significance, with increased intervention length being the only significant modification. These results suggest that pilot trials remain informative regardless of modifications made to the trial design. While pilot trials tended to produce a larger point estimate than the full-scale trial, most pairs had a 95% CI that covered the full-scale trial point estimate, suggesting that using the CI bound for sample size calculation may be more reasonable than the point estimate of effect size or SD. Statistical methods have been developed to adjust sample size based on pilot estimates, with some advocating for the use of the CI bound [14–16].

The required sample size for pilot trials has been discussed in the literature. Rules of thumb include 12 participants per arm,[17] 30[14] and 70 overall,[18] and calculation methods for different study objectives are available [19–21]. Our results suggest that the pilot-to-full-scale sample size ratio rather than the pilot trial sample size itself predicted whether the full-scale trial showed a positive result. Moreover, full-scale trials appeared to be less likely to be significant when the pilot trial had a larger sample size (70+ vs < 30). This was because a higher proportion of non-significant full-scale trials had pilot trials that were cluster randomized trials with typically larger sample sizes than individual randomized controlled trials. Nonetheless, when pilot trial results are used to inform the full-scale trial, the relative size of pilot trials to full-scale trials may be a more relevant metric. Larger pilot trials can yield more precise estimates, leading to a smaller sample size needed for the full-scale trial [22 23]. Therefore, an optimal sample size for pilot trials (or the pilot-to-full-scale trial sample size ratio) might exist, which minimizes the total sample size of pilot and full-scale trials combined. Other authors also proposed that the pilot trial's

sample size should be chosen based on the full-scale trial's possible sample size, and the recommended percentage is at least 9% [19].

It is worth noting that most trials included in our analysis investigated behavioral interventions. An earlier study reported that a positive phase II trial was predictive of success in a phase III trial for pharmaceutical cancer therapies [24]. Our study relies on published literature, which raises concerns about potential selection bias due to publication bias. However, we believe that this might bias our results toward the null. This is because pairs of negative pilot and negative full-scale trials are the least likely to be published among the four combinations of pilot and full-scale trial publication status. Consequently, these pairs are undersampled (ie, cell d in the two-by-two table) in our study, which may lead to an underestimation of the OR. The current study was not preregistered but had a prespecified protocol.

Conclusion

While pilot trials do not typically provide definitive evidence on intervention efficacy, they can offer important preliminary evidence and strong signals regarding efficacy. When calculating the full-scale trial sample size, it may be more reasonable to use the CI bound than the point estimate of effect size or SD.

(Paper 1) Table 1 Characteristics of pilot trials (N=248)

Variables	N (%)
Publication year	
2004-2009	74 (30%)
2010-2014	103 (42%)
2015-2019	71 (29%)
Disease	
Addiction	24 (10%)
Mental health	34 (14%)
Obesity & physical activity	26 (10%)
Oncology	21 (8%)
Other [1]	143 (58%)
Intervention	
Behavioral	171 (69%)
Pharmaceutical	41 (17%)
Other [2]	36 (15%)
Funding source	
Non-industry	219 (88%)
Industry	6 (2%)
None or not reported	23 (9%)
Cluster randomization	
No	232 (94%)
Yes	16 (6%)
Non-inferiority hypothesis	
No	246 (99%)
Yes	2 (1%)
Participants masked	
No	208 (84%)
Yes	40 (16%)
Caregiver/investigator masked	
No	215 (87%)
Yes	33 (13%)
Evaluator masked	
No	173 (70%)
Yes	75 (30%)
Analyst masked	
No	236 (95%)
Yes	12 (5%)
Number of parties masked	
0	138 (56%)
1	74 (30%)
2	23 (9%)

3	12 (5%)
4	1 (0%)
Pilot sample size, mean±SD	121±300
Pilot sample size, median (IQR)	53 (31, 100)
Pilot sample size per arm, mean±SD	56±147
Pilot sample size per arm, median (IQR)	25 (15, 46)
Sample size ratio (pilot/full-scale), %, mean±SD	24±17
Sample size ratio (pilot/full-scale), %, median (IQR)	20 (12, 32)
Sample size per arm ratio (pilot/full-scale), %, mean±SD	24±17
Sample size per arm ratio (pilot/full-scale), %, median (IQR)	20 (13, 31)
Effect size used for sample size calculation	
No	183 (74%)
Yes	47 (19%)
Yes, but adapted	18 (7%)
Standard deviation used for sample size calculation	
No	219 (88%)
Yes	25 (10%)
Yes, but adapted	4 (2%)
Pilot purpose: assess efficacy	
No	47 (19%)
Yes	153 (81%)
Pilot purpose: assess trial feasibility	
No	155 (77%)
Yes	45 (23%)
Pilot purpose: assess intervention feasibility	
No	96 (48%)
Yes	104 (52%)

SD: standard deviation; IQR: interquartile range

[1] Other include HIV (n=11), pain (n=9), stroke (n=7), diabetes (n=7), heart disease (n=7), and so on.

[2] Other includes interventions related to devices (n=19), complementary therapies (n=11), occupational therapies (n=4), surgical treatments (n=3), and psychotherapies (n=2).

(Paper 1) Table 2 Characteristics of trial modifications (N=248)

Variables	N (%)
Publication gap year, median (IQR)	5 (3, 7)
Eligibility criteria modification	
Same	76 (31%)
Modified	172 (69%)
Disease criteria	
Same	169 (68%)
Less severe	30 (12%)
More severe	49 (20%)
Other criteria (e.g., age)	
Same	171 (69%)
Less stringent	59 (24%)
More stringent	18 (7%)
Intervention modification	
Same	137 (55%)
Modified	99 (40%)
Other difference	12 (5%)
Intervention content	
Same	176 (71%)
Added content	52 (21%)
Reduced content	8 (3%)
Missing	12 (5%)
Intervention duration	
Same	181 (73%)
Longer duration	48 (19%)
Shorter duration	7 (3%)
Missing	12 (5%)
Intervention frequency	
Same	227 (92%)
More frequent	6 (2%)
Less frequent	3 (1%)
Missing	12 (5%)
Control modification	
Same	165 (67%)
Modified	36 (15%)
Active in main, placebo in pilot	20 (8%)
Placebo in main, active in pilot	10 (4%)
Other difference	17 (7%)
Control content	
Same	178 (72%)
Added content	16 (6%)

Reduced content	7 (3%)
Missing	47 (19%)
Control duration	
Same	189 (76%)
Longer duration	7 (3%)
Shorter duration	5 (2%)
Missing	47 (19%)
Control frequency	
Same	196 (79%)
More frequent	2 (1%)
Less frequent	3 (1%)
Missing	47 (19%)
Length of follow-up	
Same	73 (29%)
Longer	134 (54%)
Shorter	26 (10%)
Missing	15 (6%)

IQR: interquartile range

(Paper 1) Table 3 Associations of pilot trial characteristics with full-scale trial efficacy outcome by logistic regressions with robust variance estimate

	OR	95%CI	P value
General characteristics			
Publication year			
2004-2009	Ref		
2010-2014	1.4	0.76 - 2.55	0.278
2015-2019	0.82	0.43 - 1.58	0.553
Disease			
Addiction	Ref		
Mental health	1.62	0.56 - 4.66	0.375
Obesity & physical activity	1.00	0.33 - 3.04	1
Oncology	1.33	0.41 - 4.34	0.633
Other[1]	0.99	0.41 - 2.35	0.975
Intervention			
Behavioral	Ref		
Pharmaceutical	0.27	0.13 - 0.58	0.001
Other[2]	0.93	0.45 - 1.92	0.847
Funding source			
Non-industry	Ref		
Industry	0.18	0.02 - 1.58	0.122
None or not reported	1.18	0.49 - 2.80	0.715
Design characteristics[3]			
Cluster randomization			
No	Ref		
Yes	0.22	0.07 - 0.72	0.012
Participants masked			
No	Ref		
Yes	0.68	0.30 - 1.50	0.338
Caregiver/investigator masked			
No	Ref		
Yes	0.78	0.33 - 1.84	0.57
Evaluator masked			
No	Ref		
Yes	0.96	0.55 - 1.68	0.889
Analyst masked			
No	Ref		
Yes	0.39	0.11 - 1.34	0.135
Number of parties masked			
0	Ref		

1	0.58	0.33 - 1.03	0.063
2	1	0.36 - 2.74	0.996
>2	0.65	0.17 - 2.50	0.529
Effect size used for sample size calculation			
No	Ref		
Yes	1.52	0.78 - 2.93	0.217
Yes, but adapted	0.56	0.20 - 1.62	0.287
Standard deviation used for sample size calculation			
No	Ref		
Yes	0.26	0.10 - 0.65	0.004
Yes, but adapted	0.64	0.09 - 4.65	0.662
Pilot sample size			
≤30	Ref		
30-70	0.92	0.47 - 1.79	0.799
>70	0.55	0.28 - 1.09	0.086
Sample size ratio (pilot/full-scale)[4]			
<15%	Ref		
>15%	1.58	0.93 - 2.67	0.089
Pilot sample size per arm			
≤15	Ref		
15-30	0.86	0.44 - 1.69	0.665
>30	0.59	0.31 - 1.13	0.11
Sample size per arm ratio (pilot/full-scale) [4]			
<15%	Ref		
>15%	1.86	1.09 - 3.18	0.023
Pilot purpose: assess efficacy			
No	Ref		
Yes	1.76	0.98 - 3.19	0.061
Pilot purpose: assess trial feasibility			
No	Ref		
Yes	0.58	0.32 - 1.04	0.069
Pilot purpose: assess intervention feasibility			
No	Ref		
Yes	0.63	0.37 - 1.08	0.091

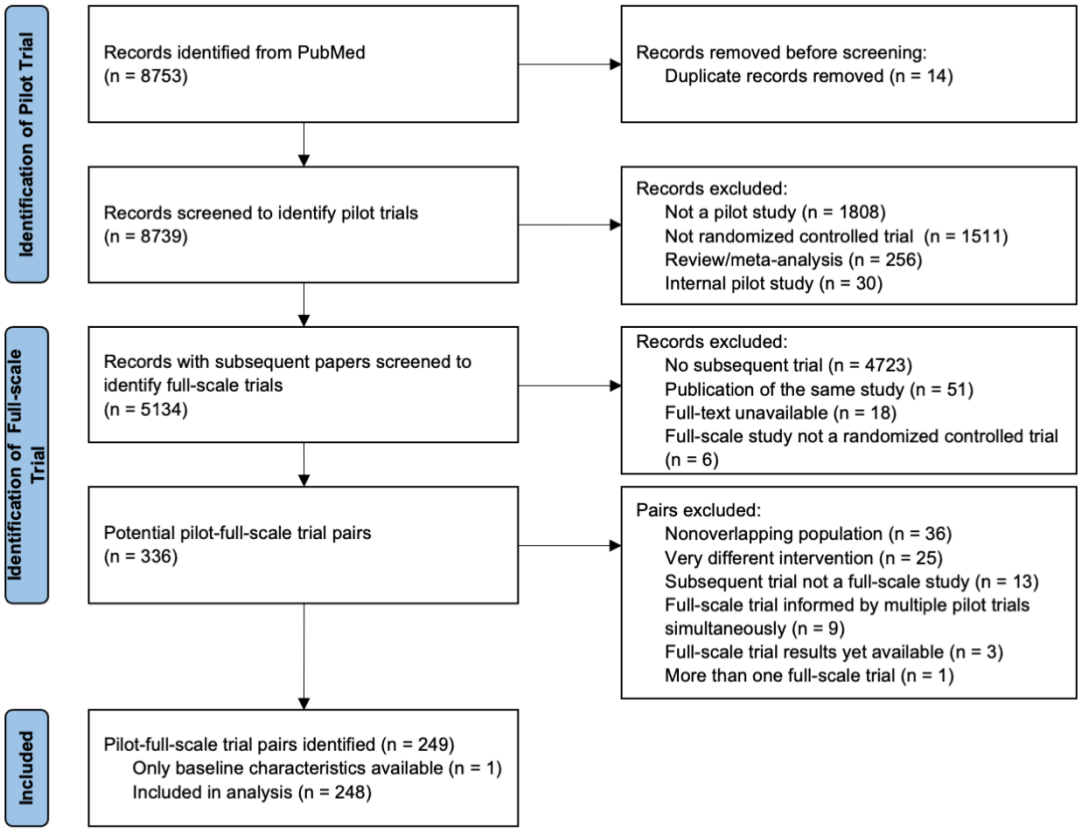
[1] Other include HIV (n=11), pain (n=9), stroke (n=7), diabetes (n=7), heart disease (n=7), and so on.
[2] Other includes interventions related to devices (n=19), complementary therapies (n=11), occupational therapies (n=4), surgical treatments (n=3), and psychotherapies (n=2).
[3] Estimates are adjusted for intervention type.
[4] The 15% cutoff is the optimal value that maximizes the product of sensitivity and specificity when using the sample size ratio to predict the statistical significance of the full-scale trial.

(Paper 1) Table 4 Associations of trial modification characteristics with full-scale trial efficacy outcome by logistic regressions with robust variance estimate and adjusted for intervention type

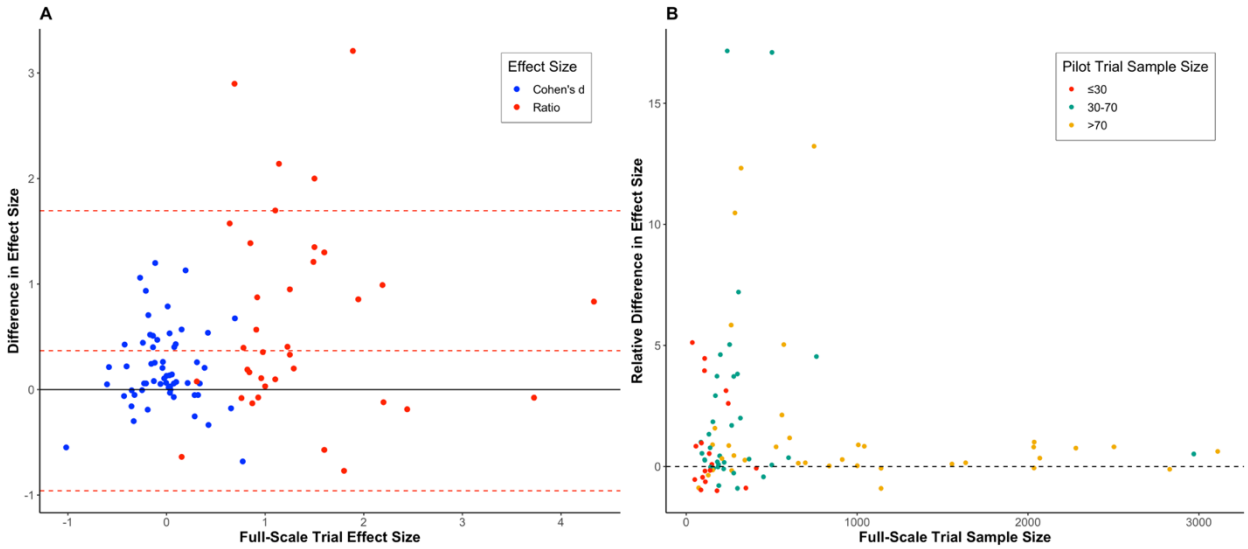
	OR	95%CI	P value
Publication gap year	0.98	0.89 - 1.08	0.656
Eligibility criteria modification			
Same	Ref		
Modified	1.18	0.67 - 2.05	0.569
Disease criteria			
Same	Ref		
Less severe	0.59	0.25 - 1.39	0.229
More severe	1.31	0.69 - 2.49	0.418
Other criteria (e.g., age)			
Same	Ref		
Less stringent	1.59	0.85 - 2.98	0.146
More stringent	0.86	0.31 - 2.38	0.771
Intervention modification			
Same	Ref		
Modified	2.11	1.22 - 3.66	0.008
Other difference	2.15	0.61 - 7.64	0.236
Intervention content			
Same	Ref		
Added content	1.23	0.64 - 2.36	0.531
Reduced content	1.37	0.31 - 6.00	0.674
Intervention duration			
Same	Ref		
Longer duration	3.34	1.60 - 6.97	0.001
Shorter duration	1.96	0.35 - 10.88	0.443
Intervention frequency			
Same	Ref		
More frequent	0.75	0.15 - 3.85	0.729
Less frequent	0.38	0.03 - 4.27	0.433
Control modification			
Same	Ref		
Modified	1.90	0.91 - 3.96	0.086
Active in main, placebo in pilot	1.50	0.56 - 4.05	0.422
Placebo in main, active in pilot	1.50	0.35 - 6.38	0.582
Other difference	1.38	0.46 - 4.10	0.568
Control content			
Same	Ref		
Added content	1.18	0.44 - 3.17	0.739

Reduced content	-	-	-
Control duration			
Same	Ref		
Longer duration	1.16	0.28 - 4.76	0.84
Shorter duration	5.32	0.76 - 37.30	0.093
Control frequency			
Same	Ref		
More frequent	-	-	-
Less frequent	-	-	-
Length of follow-up			
Same	Ref		
Longer	0.98	0.54 - 1.77	0.947
Shorter	0.52	0.20 - 1.36	0.184

(Paper 1) Figure 1 Flowchart

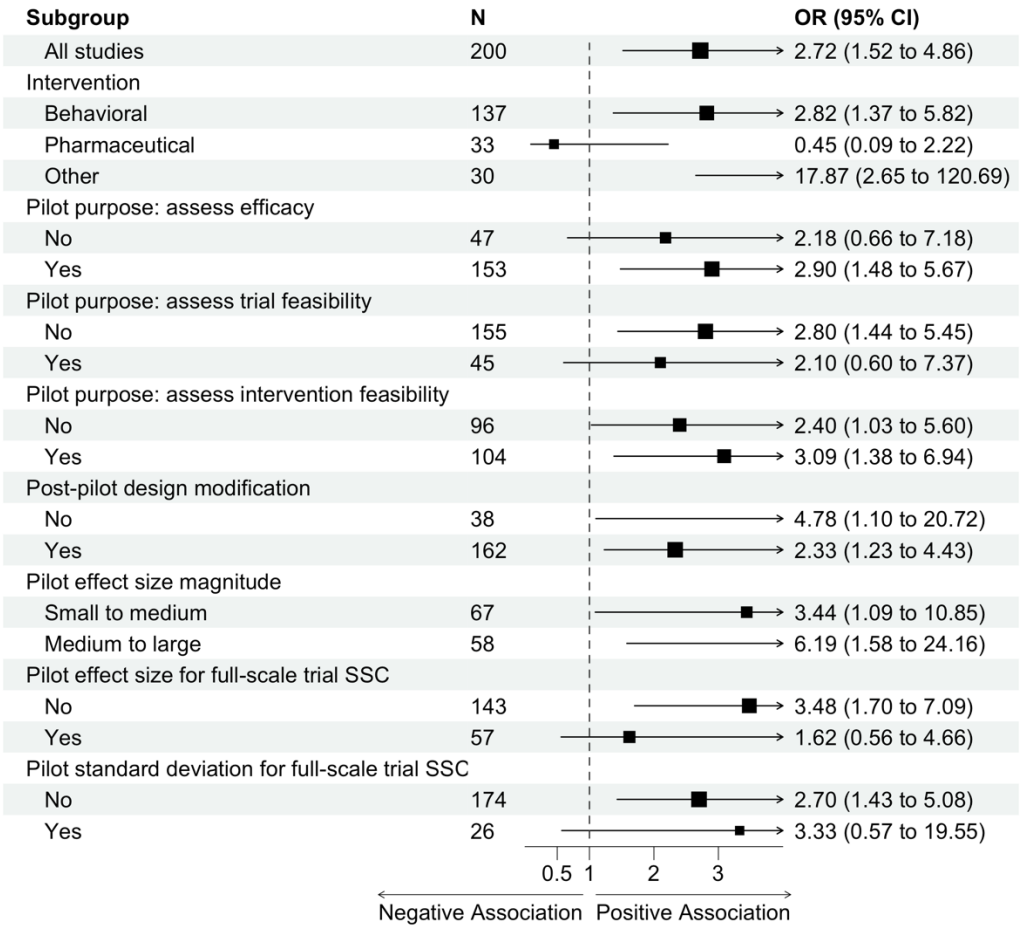


(Paper 1) Figure 2 Bland-Altman plot (A) and scatterplot (B) of differences in effect size estimates between pilot and full-scale trials



(A) The y-axis represents the absolute difference in effect size between the pilot and full-scale trials, obtained by subtracting the value of the full-scale trial from the pilot trial (ie, pilot − full-scale). The three red dashed lines, presented from top to bottom, indicate the upper bound of the 95% CI of the average absolute difference (1.70), the average absolute difference (0.37) and the lower bound of the 95% confidence interval of the average absolute difference (−0.96). To enhance clarity and focus on the main distribution of data points, three outlier pairs were excluded from the graph. These outliers consisted of 2 pairs where the pilot trial estimated an odds ratio larger than 20 and 1 pair where the full-scale trial estimated a Cohen's d larger than 3. (B) The y-axis represents the relative difference in effect size between the pilot and full-scale trials, obtained by dividing the absolute difference by the value of the full-scale trial (ie, (pilot − full-scale)/full-scale). To enhance clarity and focus on the main distribution of data points, eight outlier pairs were excluded from the graph. These outliers consisted of 2 pairs where the relative difference is larger than 20 and 6 pairs where the full-scale trial sample size is larger than 5000.

(Paper 1) Figure 3 Analyses of the association between the significance of a pilot trial and that of a full-scale trial by subgroups of pilot trial characteristics



SSC, sample size calculation. *Other intervention includes interventions related to devices (n=19), complementary therapies (n=11), occupational therapies (n=4), surgical treatments (n=3) and psychotherapies (n=2).

References

1 Moore CG, Carter RE, Nietert PJ, et al. Recommendations for planning pilot studies in clinical and translational research. Clin Transl Sci 2011;4:332–7.

2 Beets MW, von Klinggraeff L, Weaver RG, et al. Small studies, big decisions: the role of pilot/feasibility studies in incremental science and premature scale-up of behavioral interventions. Pilot Feasibility Stud 2021;7:173.

3 Arain M, Campbell MJ, Cooper CL, et al. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Med Res Methodol 2010;10:67.

4 Sim J. Should treatment effects be estimated in pilot and feasibility studies? Pilot Feasibility Stud 2019;5:107.

5 Westlund E, Stuart EA. The Nonuse, misuse, and proper use of pilot studies in experimental evaluation research. Am J Eval 2017;38:246–61.

6 Beets MW, von Klinggraeff L, Burkart S, et al. Impact of risk of generalizability biases in adult obesity interventions: a meta-epidemiological review and meta-analysis. Obes Rev 2022;23:e13369.

7 Beets MW, Weaver RG, Ioannidis JPA, et al. Identification and evaluation of risk of Generalizability biases in pilot versus efficacy/effectiveness trials: a systematic review and meta-analysis. Int J Behav Nutr Phys Act 2020;17:19.

8 Murad MH, Wang Z. Guidelines for reporting meta-epidemiological methodology research. Evid Based Med 2017;22:139–42.

9 Veritas Health Innovation. Covidence systematic review software. Melbourne, Australia. Available: www.covidence.org

10 Lipsey MW, Wilson DB. Practical meta-analysis. Thousand Oaks, Calif: Sage Publications, 2001.

11 Morris SB. Estimating effect sizes from pretest-posttest-control group designs. Organ Res Methods 2008;11:364–86.

12 Chen H, Cohen P, Chen S. How big is a big odds ratio? Interpreting the magnitudes of odds ratios in epidemiological studies. Commun Stat - Simul Comput 2010;39:860–4.

13 Desai M, Bryson SW, Robinson T. On the use of robust Estimators for standard errors in the presence of clustering when clustering membership is misspecified. Contemp Clin Trials 2013;34:248–56.

14 Browne RH. On the use of a pilot sample for sample size determination. Stat Med 1995;14:1933–40.

15 Julious SA, Owen RJ. Sample size calculations for clinical studies allowing for uncertainty about the variance. Pharm Stat 2006;5:29–37.

16 Wang S-J, Hung HMJ, O'Neill RT. Adapting the sample size planning of a phase III trial based on phase II data. Pharmaceut Statist 2006;5:85–97.

17 Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharm Stat 2005;4:287–91.

18 Teare MD, Dimairo M, Shephard N, et al. Sample size requirements to estimate key design parameters from external pilot randomized controlled trials: a simulation study. Trials 2014;15:264.

19 Cocks K, Torgerson DJ. Sample size calculations for pilot randomized trials: a confidence interval approach. J Clin Epidemiol 2013;66:197–201.

20 Viechtbauer W, Smits L, Kotz D, et al. A simple formula for the calculation of sample size in pilot studies. J Clin Epidemiol 2015;68:1375–9.

21 Hertzog MA. Considerations in determining sample size for pilot studies. Res Nurs Health 2008;31:180–91.

22 Whitehead AL, Julious SA, Cooper CL, et al. Estimating the sample size for a pilot randomized trial to minimize the overall trial sample size for the external pilot and main trial for a continuous outcome variable. Stat Methods Med Res 2016;25:1057–73.

23 Kieser M, Wassmer G. On the use of the upper confidence limit for the variance from a pilot sample for sample size determination. Biom J 1996;38:941–9.

24 Chan JK, Ueda SM, Sugiyama VE, et al. Analysis of phase II studies on targeted agents and subsequent phase III trials: what are the predictors for success. J Clin Oncol 2008;26:1511–8.

Chapter 3 Paper 2

Pilot trial characteristics, postpilot design modifications, and feasibility of full-scale trials

Xiangji Ying ,[1] Stephan Ehrhardt[1]

[1] Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

This paper has been published with *JAMA Network Open*.

doi:10.1001/jamanetworkopen.2023.33642

Abstract

Importance Pilot trials often lead to study design changes in subsequent full-scale trials. Yet, it remains unclear whether these modifications improve the feasibility of the larger trial.

Objective To compare feasibility estimates between pilot and full-scale trials and identify pilot trial characteristics and modifications associated with equivalent or improved feasibility in the full-scale trial.

Design Cohort study

Setting PubMed searched on February 19th, 2022.

Participants Pilot trials published between 2005 and 2018 and their corresponding full-scale trials.

Exposures Pilot trial characteristics and post-pilot trial design modifications.

Main outcomes and measures The outcome of interest was difference in three feasibility parameters: successful screening probability, enrollment rate, and retention probability. We defined these metrics as equivalent or improved if the full-scale trial's estimate was within or exceeding 10% of the pilot trial's estimate.

Results Two hundred forty-nine pairs of trials were analyzed, with 43%, 77%, and 82% of full-scale trials having equivalent or improved successful screening probabilities, enrollment rates, and retention probabilities, respectively. When pilot trials employed feasibility progression criteria (RR=1.94, 95% CI: 1.02-5.97) and maintained masking for participants (RR=1.82, 95% CI: 1.04-4.33) or healthcare practitioners (RR=1.81, 95% CI: 1.03-3.97) consistent with the full-scale trial, the likelihood of achieving equivalent or improved screening success in full-scale trials increased. Increasing study sites post-pilot was associated with higher likelihood of equivalent or improved enrollment rates (RR=1.03, 95% CI: 1.01-1.08). Adding extra content to the intervention (RR=0.82, 95% CI: 0.66-0.98), changing to active control (RR=0.74, 95% CI: 0.48-0.99), administrating the control treatment more frequently (RR=0.60, 95% CI: 0.29-0.93), different follow-up lengths (RR=0.85, 95% CI: 0.73-0.97), and more follow-up visits (RR=0.86, 95% CI: 0.75-0.98) were associated with lower likelihood of equivalent or improved retention probability in the full-scale trial.

Conclusions and relevance In this cohort study of pilot and full-scale trial pairs, pilot trial characteristics and post-pilot modifications had varying association with full-scale trial’s feasibility. If full-scale trials planned for masking, it was desirable to use it in the pilot. Modifications increasing participant burden might decrease full-scale trial feasibility. Trialists and funders should consider both pilot trial data and proposed design changes when assessing full-scale trials.

Introduction

In the past two decades, there has been growing attention on pilot studies. A basic PubMed search using the term "pilot study" yielded 668 articles in 2000 and 5484 articles in 2020. Traditionally, pilot studies served the purpose of evaluating feasibility and providing preliminary evidence on efficacy [1]. However, the appropriateness of pilot studies in evaluating efficacy has been questioned due to their small sample sizes [2-6]. It has been recommended that pilot studies should focus primarily on feasibility estimation, such as calculating probabilities of recruitment, randomization, intervention adherence, and attrition [7].

Pilot trials are a specific type of pilot study that utilizes a randomized controlled design [8,9]. Although the emphasis is on using pilot studies or pilot trials for feasibility, few studies have examined the accuracy of their estimates in predicting parameters for full-scale trials. A recent empirical analysis of 16 pairs found that, on average, pilot trials provided variable but unbiased estimates for randomization and attrition probabilities [10]. The authors speculated that the differences could be due to remedial action taken in the full trial to address issues identified in the pilot [10].

It is not uncommon for trials to modify their designs after the pilot trial, as identifying areas requiring modification is one of the key objectives of conducting a pilot trial. A recent analysis found that 75% of full-scale intervention trials on obesity differed from the pilot trial in at least one domain, such as intervention intensity and implementation support [11]. However, it is often unclear how those modifications will impact the feasibility of conducting the full-scale trial, especially when multiple aspects of the trial are being modified, which adds an extra layer of complexity. Ideally, a new pilot trial incorporating those changes would provide the most current feasibility data, but this comes with additional resource demands and potential delays in

generating definitive evidence [12]. Moreover, repeating this approach may not be practical should further modifications be required after the new pilot.

This study therefore aims to compare feasibility estimates between pilot and full-scale trials and explore whether certain pilot trial characteristics and modifications are associated with equivalent or improved feasibility in full-scale trials.

Methods

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies [13]. Since the analysis was conducted at the study level without involving human participants, it did not require ethics approval or informed consent.

Literature search and study selection

A systematic search in PubMed was conducted on February 19th, 2022, to identify pilot trials published between January 2005 and December 2018. The search was restricted to English and included three concepts: pilot or feasibility study, randomized controlled trial, and feasibility parameters (eTable 1 in Appendix B). A pilot study was defined as a small-scale investigation aimed at testing feasibility of methodologies for large-scale application, or exploring potential effects and associations to be examined in a future larger study [1]. Stand-alone pilot studies that utilized a randomized controlled design were considered for inclusion. We employed these inclusive early definitions to cover the timeline and to account for the varied use of the term "pilot trial" in literature.

To identify the subsequent full-scale trial that was conducted by the same research team and had an overlap in population characteristics with the pilot, we screened articles that cited the pilot trial. A full-scale trial was included if it had at least one arm that was the same or similar to the pilot. We excluded the full-scale trial if it was informed by multiple pilot trials simultaneously.

Data extraction

We gathered information on trial characteristics, feasibility and efficacy estimates for each pilot and full-scale trial pair in Covidence [14] using a form that had been pilot-tested. Our selection of these characteristics was guided by research on factors influencing trial generalizability [15-17] or participant recruitment and retention [18-24]. To ensure data accuracy and minimize missingness, we extracted and cross-checked information from trial reports, protocols, and registries, prioritizing trial reports in case of discrepancies. Protocols were crucial for supplementary details when the trial report did not adequately describe elements such as intervention procedures and outcome measurements. We compared the trial characteristics of the full-scale trials with their pilot trials to identify any modifications made to trial design, participant eligibility, intervention, control, and outcome measurement.

Feasibility parameters

The study examined three feasibility parameters: probability of successful screening, enrollment rate, and retention probability.

Successful screening means that a study participant is both eligible and willing to be randomized. We calculated the probability of successful screening by dividing the number of randomized participants by the total number of participants screened.

The enrollment rate was calculated by dividing the number of participants randomized by the duration of recruitment in weeks. A site-average rate was also computed by dividing this overall rate by the number of sites. Unless specifically mentioned otherwise, any reference to 'enrollment rate' in this paper pertains to the overall, not per-site, estimate.

For the probability of retention, we divided the number of participants who completed the study by the number of participants who were initially randomized. Noncompletion can be caused by competing events, withdrawal, loss to follow-up, and protocol deviations. To maintain

consistency, we used the same definition of dropout within each pair of pilot and full-scale trials, as different studies had varying definitions. Whenever possible, we calculated the retention probabilities at the same timepoint in both the pilot and full-scale trials.

Statistical analysis

We described the feasibility estimates from pilot and full-scale trials using either the mean and standard deviation (SD) or median and interquartile range (IQR) if the estimate was heavily skewed. To evaluate the agreement between the pilot and full-scale trials, we calculated the percentage difference by dividing the difference between the two studies (i.e., pilot - full-scale) by their mean [25].

All pilot trials in our sample progressed to full-scale trials, indicating that the trialists deemed the full-scale trial feasible, either initially or after making protocol modifications. We considered the full-scale trial's feasibility estimate to be equivalent if it fell within 10% of the pilot trial's estimate, in either direction, or improved if it was more than 10% greater than the pilot trial estimate. We chose the 10% threshold because it accounted for possible random fluctuations and was commonly used in sample size calculations to adjust for dropouts. We used logistic regression to identify characteristics and modifications of pilot trials associated with equivalent or improved feasibility in the full-scale trial. The resulting odd ratios were converted to relative risk (RRs), and corresponding percentile-based confidence intervals (CIs) were calculated using 10000 bootstrap replications [26].

All analyses were performed using Stata (Version 16; StataCorp, TX) and RStudio (Version 2022.12.0+353). A two-sided P value smaller than .05 was considered statistically significant.

Results

Study characteristics

A total of 249 pairs of pilot and subsequent full-scale trials were identified (eFigure 1 in Appendix B). These pairs investigated a range of diseases (eTable 2 in Appendix B), with the majority (69%) focusing on behavioral interventions (Table 1). Most pilot trials (75%) were conducted in a single center, while more than half (54%) of full-scale trials were multicenter. The proportion of trials with two arms was the same for both pilot and full-scale trials (84%). On average, 121 individuals (SD: 300, median: 53) were randomized in pilot trials, while full-scale trials randomized an average of 1164 individuals (SD: 4111, median: 264). The average and median follow-up duration in full-scale trials were approximately twice as long as in pilot trials (321 vs. 166 days for average and 182 vs. 91 days for median).

Data on successful screening probability, enrollment rate, and retention probability were available in 183, 177, and 238 pairs of pilot and full-scale trials, respectively. Comparisons of characteristics between pairs with and without missing data for these parameters are provided in Supplemental text, eTable 3, and eTable 4 in Appendix B.

Successful screening

On average, the successful screening proportion (n=183) was 47% (SD: 27%) for pilot trials and 41% (SD: 27%) for full-scale trials. The mean percentage difference between pilot and full-scale trials was 15% (SD: 60%; median: 14%; IQR: -21% – 47%). As shown in Figure 1, the percentage differences are symmetrically distributed around the mean, with a tendency for both the magnitude and variability to decrease as the sample size of the pilot trial increases.

The full-scale trial showed equivalent (n=35) or improved (n=54) successful screening in 89 of the 183 pairs (43%). The likelihood of achieving equivalent or improved successful screening in the full-scale trials were higher when the pilot trial utilized masking/blinding (RR=1.41, 95% CI: 1.05 – 1.93) and feasibility progression criteria (RR=1.94, 95% CI: 1.02 – 5.97) (Table 2). When the pilot trial was single-center, the full-scale trial had higher likelihood of achieving an

equivalent or improved successful screening if it was also conducted at a single center (RR=1.50, 95% CI: 1.04 – 2.31) (Table 3). When participants or healthcare practitioners were masked in the full-scale trials, the likelihood of observing an equivalent or improved successful screening probability were higher if the pilot trial also masked the participants or healthcare practitioners compared to situations where they were unmasked (RR=1.82, 95% CI: 1.04 – 4.33; RR=1.81, 95% CI: 1.03 – 3.97, respectively) (Table 3).

Enrollment rate

The median overall enrollment rate (n=177) was 1.7 participants per week (IQR: 0.6 – 5.4) for pilot trials and 2.9 participants per week (IQR: 1.3 – 8.5) for full-scale trials. The mean percentage difference between the two was -52% (SD: 85%, median: -59%, IQR: -121% – 4%). For the site-average enrollment rate, pilot trials had a median rate of 1.2 participants per week per site (IQR: 0.5 – 3.3), while full-scale trials had a median rate of 1.0 participants per week per site (IQR: 0.4 – 3.3). The mean percentage difference was 7% (SD: 92%, median: 7%, IQR: -56% – 83%).

Out of 177 pairs, 136 (77%) had equivalent (n=9) or improved (n=127) overall enrollment rates in the full-scale trial compared to the pilot trial. Having one more study site in the full-scale trial was associated with 1.03 times higher likelihood of equivalent or improved enrollment rates (95% CI: 1.01 – 1.08) (Table 3). When healthcare practitioners were unmasked in the pilot trial, the full-scale trial had higher likelihood of achieving an equivalent or improved enrollment rate if trialists did not change this design feature (RR=1.51, 95% CI: 1.02 – 2.83) (Table 3). However, modifying the intervention was associated with lower likelihood of equivalent or improved enrollment rates (RR=0.84, 95% CI: 0.70 – 0.99), as was extending the length of follow-up in the full-scale trial (RR=0.81, 95% CI: 0.68 – 0.96) (Table 4).

Retention probability

The retention probability (n=238) was found to be similar for both pilot and full-scale trials, with an average of 83.5% (SD: 15%) and 84.2% (SD: 13%), respectively (mean percentage difference: -1%, SD: 19%, median: 0%, IQR: -9% – 6%) (eFigure 2 in Appendix B).

Approximately 82% (194/238) of full-scale trials achieved an equivalent (n=138) or improved (n=56) retention probability. If the pilot trial had a sample size between 30 and 50, the retention probability had higher likelihood of being equivalent or improved compared to pilot trials with a sample size below 30 (RR=1.21, 95% CI: 1.03 – 1.44) (Table 2). The likelihood of having an equivalent or improved retention probability were lower if the full-scale trial added extra content to the intervention (RR=0.82, 95% CI: 0.66 – 0.98), changed the comparison group from placebo or no treatment to active control as opposed to simple modification (RR=0.74, 95% CI: 0.48 – 0.99), administrated the control intervention more frequently (RR=0.60, 95% CI: 0.29 – 0.93), had a different length of follow-up (RR=0.85, 95% CI: 0.73 – 0.97), or conducted more follow-up visits (RR=0.86, 95% CI: 0.75 – 0.98) (Table 4).

Discussion

This study first compared feasibility estimates between pilot and full-scale trials. On average, screening success was slightly lower (7%) in full-scale trials, with only 43% of trials showing improved screening. However, 77% of full-scale trials had better enrollment rates (average increase of 52%). Estimated retention probability had good agreement between pilot and full-scale trials, with a 1% difference and over half of the values within the 10% equivalence margin. This aligns with a previous study comparing 16 pairs of pilot and full-scale trials [10].

The observed decrease in screening proportion and increase in enrollment rates in full-scale trials could be attributed to the greater number of study sites compared to pilot trials. While multi-site trials can expedite enrollment through simultaneous recruitment at different sites, they also face a more diverse participant pool. This diversity may lower the screening proportion as

not all seemingly eligible participants ultimately qualify. Our associational analysis indeed showed that trials with more sites than their pilot often achieved higher enrollment, but multi-center full-scale trials following single-center pilots had lower likelihood of similar or improved screening success. Therefore, researchers conducting full-scale trials at multiple sites may anticipate faster recruitment but should also prepare for a larger screening pool to reach the target sample size.

Masking has been widely recognized as a factor that can hinder study recruitment [18,27-29]. We found that masking was one of the few design features in pilot trials that was associated with an equivalent or improved probability of successful screening. Our results also suggest that if masking is envisioned in the full-scale trial, it is desirable to use it in the pilot trial. We recommend that the pilot and full-scale trials be consistent in terms of masking to maximize recruitment feasibility.

Our analyses also found that protocol modifications may decrease the feasibility of full-scale trials if they impose a greater burden on participants. Such modifications include additional intervention content, changing the comparator from placebo or no treatment to active treatment, administrating the control treatment more frequently, prolonged follow-up periods, and increasing the number of follow-up visits. Previous qualitative and quantitative evidence has suggested that potential trial participants may perceive high time commitments and demanding follow-up schedules as too burdensome [30-33], leading to increased screen failure and dropouts [34]. Quantifying participant burden and incorporating it into study protocol to evaluate feasibility has been suggested [35-37].

It has been recommended that pilot trials incorporate prespecified progression criteria to aid in the decision-making process for proceeding with a full-scale trial [7]. Typically, these criteria set a threshold above which the full-scale trial is deemed feasible. The decision to proceed can be made in a binary fashion by comparing the feasibility parameter's point estimate to the threshold

or by testing if the CI around the estimate includes the threshold. While progression criteria have been used in research practice [38], few studies have investigated whether their use improves the performance of pilot trials in informing the feasibility of full-scale trials. Our analysis suggests that using feasibility progression criteria in the pilot trial may result in an equivalent or improved probability of successful screening in the full-scale trial. However, we did not observe a similar association for recruitment rate or retention probability. Further examination of the data revealed that this difference may be attributed to subsequent modifications made to the trial design. These modifications were associated with worse retention probability and recruitment rate, while maintaining or enhancing screening probability. Our findings imply that the utility of progression criteria might be undermined by modifications made after the pilot phase.

In the current study, we adopted a broad definition of pilot trials, not excluding studies solely due to the implementation of effect size estimation or hypothesis testing, despite concerns have been raised about these practices [2-6]. This approach is partially based on the understanding that treatment efficacy could affect trial retention and participant recruitment. We also presumed that studies, even if not explicitly assessing feasibility, inherently do so during execution. Nonetheless, pilot trials primarily focusing on efficacy estimation were excluded at the analysis stage if they did not report the three feasibility parameters of interest.

This study has certain limitations. First, we did not differentiate between “true” pilot trials and those potentially mislabeled. However, we posit that post-hoc mislabeling of studies as pilot trials to excuse small sample sizes, low methodological quality, or incomplete studies is less likely in our dataset, considering all studies informed a full-scale trial. Second, by excluding pilot trials not followed by full-scale trials, we may have observed an attenuated association. The absence of a full-scale trial may indicate its infeasibility even with significant modifications. The association between trial modifications and feasibility would be stronger in such cases because

the modifications altered the full-scale trial from being infeasible to feasible. Thirdly, we employed a complete case analysis, excluding pairs with missing feasibility estimates. This non-reporting indicates a lack of adherence to the Consolidated Standards of Reporting Trials (CONSORT) guidelines [39] and possibly inferior methodological quality, as reporting quality often proxies for methodological quality [40]. Forth, there are other important factors that can influence trial recruitment and retention, such as the use of incentives and the follow-up format [18,19], which we were not able to examine in our study. Fifth, multiple trial aspects may be modified simultaneously, and these modifications may influence the feasibility of the full-scale trial in different ways and magnitudes. Lastly, the current study examined various characteristics. However, per nature of its design, the width of the confidence intervals was not adjusted for multiple comparisons, and the results should be viewed as exploratory.

Using pilot trial estimates to inform the full-scale trial's feasibility can be challenging due to biases introduced by modifications and random errors magnified by the small sample size. While the agreement between pilot and full trials may improve with larger sample sizes, systematic errors may still persist. Trialists and funders should consider potential impacts of protocol modifications on feasibility when planning or assessing a full-scale trial. On average, full-scale trials had slightly lower screening success, better enrollment rates, and comparable retention probabilities than the pilot trial. Consistency in masking is desirable, and the pilot trial's use of feasibility progression criteria might improve full-scale trial feasibility. Modifications that increase participant burden may make full-scale trials less feasible.

(Paper 2) Table 1 Key characteristics shared by pilot trials and subsequent full-scale trials

	No. (%)	
	Pilot trial (n=249)	Full-scale trial (n=249)
Disease [a]		
Addiction	24 (10)	
Mental health	34 (14)	
Obesity & physical activity	27 (11)	
Oncology	21 (8)	
Other	143 (57)	
Intervention		
Behavioral	172 (69)	
Pharmaceutical & other	77 (31)	
Publication year		
2004-2009	74 (30)	6 (2)
2010-2014	103 (41)	51 (20)
2015-2019	72 (29)	123 (49)
2020-2022	0 (0)	69 (28)
Funding source		
Non-industry	220 (88)	230 (92)
Industry	6 (2)	12 (5)
None or not reported	23 (9)	7 (3)
Cluster randomization		
No	233 (94)	211 (85)
Yes	16 (6)	38 (15)
No. of sites		
Single center	186 (75)	115 (46)
Multicenter	63 (25)	134 (54)
No. of arms		
2	210 (84)	210 (84)
>2	39 (16)	39 (16)
Sample size		
Mean (SD)	121 (300)	1164 (4111)
Median (IQR)	53 (31, 100)	264 (143, 600)
Masking used		
No	139 (56)	90 (36)
Yes	110 (44)	159 (64)
Primary length of follow-up (days)		
Mean (SD)	166 (237)	321 (428)
Median (IQR)	91 (42, 182)	182 (91, 365)
Intervention efficacy		
Not statistically significant	109 (44)	119 (48)
Statistically significant	92 (37)	129 (52)
Not evaluated	48 (19)	1 (0)

Abbreviations: SD, standard deviation; IQR, interquartile range.

[a] The diseases listed represent the top four most frequently occurring within the dataset. All other disease types are grouped under the category labeled as "other." A complete list of diseases is available in eTable 2 in Appendix B.

(Paper 2) Table 2 Association of pilot trial characteristics with concordance in feasibility estimates

	Successful screening probability (n=183)	Enrollment rate per week (n=177)	Retention probability (n=238)
	Relative risk (95%CI)	Relative risk (95%CI)	Relative risk (95%CI)
General characteristics			
Disease [b]			
Addiction	1 [Reference]	1 [Reference]	1 [Reference]
Mental health	1.46 (0.75 - 3.75)	1.21 (0.85 - 1.85)	1.07 (0.86 - 1.38)
Obesity & physical activity	1.29 (0.59 - 3.36)	0.84 (0.41 - 1.43)	0.92 (0.67 - 1.24)
Oncology	1.58 (0.70 - 4.16)	0.92 (0.54 - 1.52)	1.08 (0.84 - 1.38)
Other	1.32 (0.78 - 3.27)	1.20 (0.91 - 1.82)	0.96 (0.81 - 1.24)
Intervention			
Behavioral	1 [Reference]	1 [Reference]	1 [Reference]
Pharmaceutical & others	1.18 (0.85 - 1.93)	1.03 (0.91 - 1.46)	1.30 (1.02 - 2.41) [a]
Publication year			
2004-2009	1 [Reference]	1 [Reference]	1 [Reference]
2010-2014	1.22 (0.81 - 1.97)	1.07 (0.88 - 1.33)	1.09 (0.94 - 1.28)
2015-2019	1.64 (1.11 - 2.62) [a]	0.95 (0.76 - 1.21)	1.07 (0.91 - 1.28)
Funding source			
Non-industry	1 [Reference]	1 [Reference]	1 [Reference]
Industry	1.03 (0.39 - 1.74)	NA	NA
None or not reported	1.03 (0.53 - 1.60)	0.90 (0.54 - 1.20)	0.93 (0.69 – 1.15)
Cluster randomization			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	0.93 (0.32 - 1.61)	1.11 (0.78 - 1.29)	0.89 (0.59 - 1.14)
Recruitment number			
No. of sites			
Single center	1 [Reference]	1 [Reference]	1 [Reference]
Multicenter	0.93 (0.73 - 1.37)	1.02 (0.90 - 1.46)	1.14 (0.97 - 1.89)
No. of arms			
2	1 [Reference]	1 [Reference]	1 [Reference]
>2	1.14 (0.85 - 2.30)	1.07 (0.94 - 3.64)	0.97 (0.95 - 1.47)
Sample size			
≤30	1 [Reference]	1 [Reference]	1 [Reference]
30-50	0.93 (0.53 - 1.62)	0.98 (0.74 - 1.29)	1.21 (1.03 - 1.44) [a]
50-100	1.38 (0.94 - 2.23)	1.07 (0.86 - 1.36)	1.10 (0.92 - 1.33)

>100	1.04 (0.63 - 1.76)	1.00 (0.79 - 1.28)	1.05 (0.86 - 1.30)
Sample size per arm			
≤15	1 [Reference]	1 [Reference]	1 [Reference]
15-45	1.12 (0.78 - 1.72)	0.99 (0.81 - 1.24)	1.12 (0.97 - 1.31)
>45	1.03 (0.64 - 1.65)	1.04 (0.84 - 1.31)	1.05 (0.87 - 1.26)
Masking usage			
Masking used			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.41 (1.05 - 1.93) [a]	1.03 (0.87 - 1.21)	1.04 (0.92 - 1.17)
Participants masked			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.64 (1.20 - 2.19) [a]	0.96 (0.75 - 1.17)	1.05 (0.88 - 1.20)
Healthcare practitioner masked			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.04 (0.39 - 1.76)	NA	0.87 (0.40 - 1.10)
Assessor masked			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.10 (0.79 - 1.48)	1.10 (0.94 - 1.30)	1.00 (0.87 - 1.13)
Analyst masked			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.91 (1.24 - 2.24) [a]	0.75 (0.35 - 1.11)	1.00 (0.67 - 1.16)
Outcome and aims			
Primary length of follow-up (months)	1.01 (0.97 - 1.03)	1.01 (1.00 - 1.04)	1.00 (0.99 - 1.01)
Intervention efficacy			
Not statistically significant	1 [Reference]	1 [Reference]	1 [Reference]
Statistically significant	1.16 (0.83 - 1.61)	1.12 (0.94 - 1.35)	1.00 (0.88 - 1.14)
Not evaluated	1.02 (0.59 - 1.56)	1.01 (0.78 - 1.27)	0.90 (0.73 - 1.08)
Pilot aim: efficacy			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	0.96 (0.70 - 1.37)	0.91 (0.77 - 1.08)	1.07 (0.93 - 1.26)
Pilot aim: safety			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.17 (0.84 - 1.75)	1.05 (0.88 - 1.27)	0.95 (0.85 - 1.08)
Pilot aim: feasibility			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.03 (0.51 - 1.61)	1.03 (0.76 - 1.26)	1.07 (0.87 - 1.22)

Feasibility progression criteria used			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.94 (1.02 - 5.97) [a]	0.96 (0.85 - 1.61)	0.94 (0.87 - 1.26)

Abbreviations: NA, not available.

[a] P<.05.

[b] The diseases listed represent the top four most frequently occurring within the dataset. All other disease types are grouped under the category labeled as "other." A complete list of diseases is available in eTable 2 in Appendix B..

(Paper 2) Table 3 Association of modifications on recruitment number and masking usage with concordance in feasibility estimates

Modifications compared to pilot	Successful screening probability (N=183)	Enrollment rate per week (N=177)	Retention probability (N=238)
	Relative risk (95%CI)	Relative risk (95%CI)	Relative risk (95%CI)
Recruitment number			
Ratio of sample size per arm (pilot/full-scale)			
<50%	1 [Reference]	1 [Reference]	1 [Reference]
>50%	1.36 (0.78 - 1.95)	0.70 (0.31 - 1.08)	1.10 (0.87 - 1.22)
Effect size used for sample size calculation			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.28 (0.93 - 1.72)	1.02 (0.83 - 1.21)	1.04 (0.91 - 1.18)
Standard deviation used for sample size calculation			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	0.81 (0.61 - 1.30)	1.02 (0.88 - 1.72)	1.00 (0.90 - 1.61)
Difference in no. of sites	1.00 (0.98 - 1.00)	1.03 (1.01 - 1.08) [a]	1.00 (1.00 - 1.02)
No. of sites			
Pilot single-center, full-scale multi-center	1 [Reference]	1 [Reference]	1 [Reference]
Both single-center	1.50 (1.04 - 2.31) [a]	0.90 (0.74 - 1.10)	0.95 (0.82 - 1.11)
Both multi-center	1.20 (0.74 - 1.94)	0.97 (0.79 - 1.18)	1.06 (0.91 - 1.23)
No. of countries			
Same	1 [Reference]	1 [Reference]	1 [Reference]
More	1.66 (0.75 - 5.94)	1.17 (0.88 - 2.15)	NA
Masking usage			
Number of parties masked			
Same	1 [Reference]	1 [Reference]	1 [Reference]
More	0.97 (0.68 - 1.35)	1.00 (0.85 - 1.19)	1.05 (0.92 - 1.19)
Fewer	1.56 (0.997 - 2.19)	0.86 (0.52 - 1.18)	0.95 (0.69 - 1.18)
Participant masking status			
Pilot unmasked, full-scale masked	1 [Reference]	1 [Reference]	1 [Reference]
Both unmasked	1.15 (0.69 - 2.82)	1.36 (0.96 - 2.38)	0.90 (0.79 - 1.07)
Both masked	1.82 (1.04 - 4.33) [a]	1.39 (0.93 - 2.46)	0.94 (0.77 - 1.16)
Pilot masked, full-scale unmasked	2.06 (0.80 - 4.50)	0.85 (0.28 - 1.80)	0.98 (0.60 - 1.15)
Healthcare practitioner masking status			

Pilot unmasked, full-scale masked	1 [Reference]	1 [Reference]	1 [Reference]
Both unmasked	0.99 (0.60 - 2.20)	1.51 (1.02 - 2.83) [a]	0.95 (0.82 - 1.17)
Both masked	1.81 (1.03 - 3.97) [a]	1.55 (0.89 - 2.90)	1.08 (0.80 - 1.30)
Pilot masked, full-scale unmasked	NA	NA	NA
Assessor masking status			
Pilot unmasked, full-scale masked	1 [Reference]	1 [Reference]	1 [Reference]
Both unmasked	0.91 (0.62 - 1.35)	1.01 (0.82 - 1.27)	0.92 (0.80 - 1.06)
Both masked	0.98 (0.64 - 1.49)	1.07 (0.85 - 1.35)	1.00 (0.86 - 1.16)
Pilot masked, full-scale unmasked	1.23 (0.63 - 1.99)	NA	0.75 (0.46 - 1.03)
Analyst masking status			
Pilot unmasked, full-scale masked	1 [Reference]	1 [Reference]	1 [Reference]
Both unmasked	0.75 (0.52 - 1.24)	0.85 (0.75 - 1.06)	1.10 (0.89 - 1.47)
Both masked	1.11 (0.42 - 1.78)	0.74 (0.28 - 1.05)	0.80 (0.29 - 1.26)
Pilot masked, full-scale unmasked	NA	0.56 (0.19 - 0.96) [a]	NA

Abbreviations: NA, not available.

[a] P<.05.

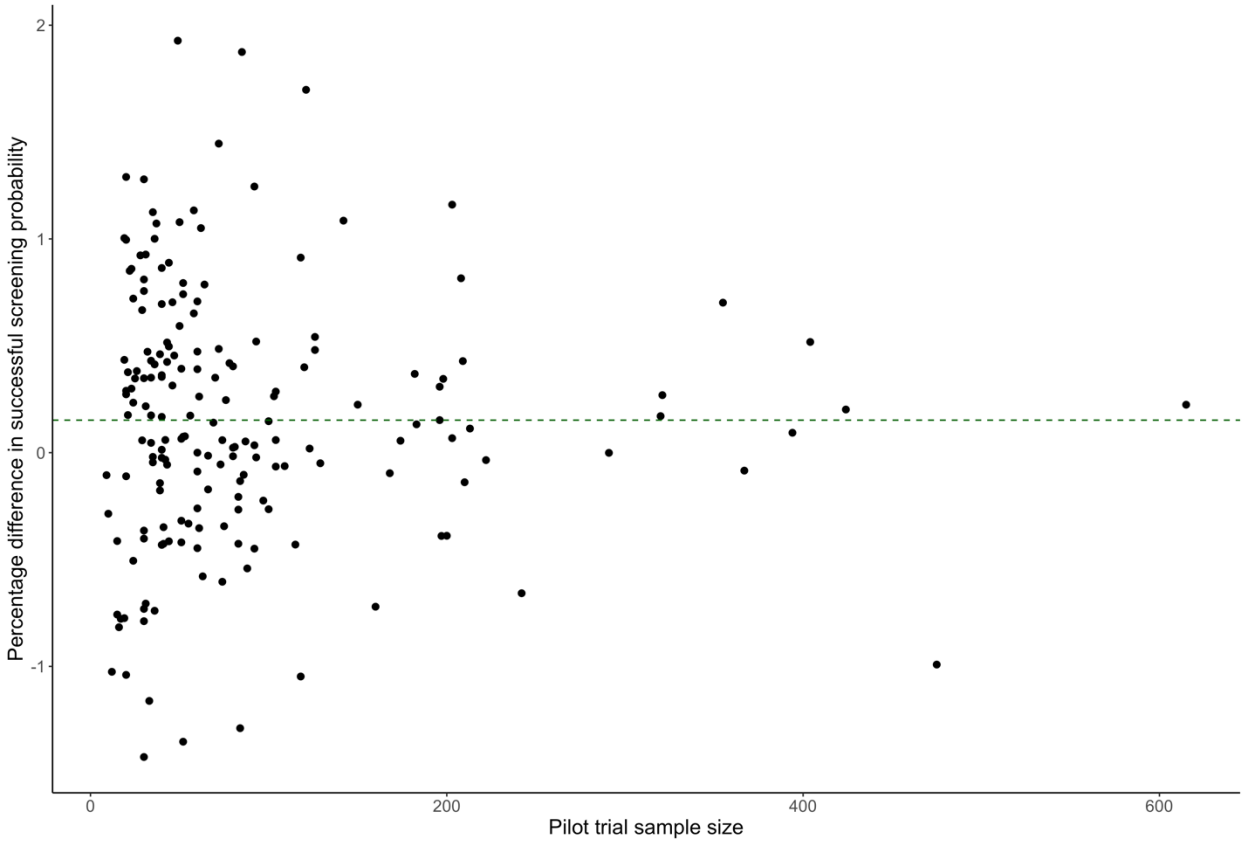
(Paper 2) Table 4 Association of modifications on PICO components with concordance in feasibility estimates

Modifications compared to pilot	Successful screening probability (N=183)	Enrollment rate per week (N=177)	Retention probability (N=238)
	Relative risk (95%CI)	Relative risk (95%CI)	Relative risk (95%CI)
Population (P)			
Eligibility modified			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	0.83 (0.61 - 1.13)	0.98 (0.83 - 1.17)	0.99 (0.88 - 1.14)
Eligibility modification type			
Broader	1 [Reference]	1 [Reference]	1 [Reference]
Narrower	0.89 (0.51 - 1.39)	0.91 (0.70 - 1.14)	1.04 (0.88 - 1.23)
Same	0.96 (0.68 - 1.39)	0.92 (0.77 - 1.10)	1.00 (0.87 - 1.17)
Intervention (I)			
No. of arms			
Same	1 [Reference]	1 [Reference]	1 [Reference]
More	0.78 (0.33 - 1.33)	1.08 (0.79 - 1.29)	1.00 (0.78 - 1.18)
Fewer	1.01 (0.57 - 1.49)	0.96 (0.63 - 1.23)	0.98 (0.76 - 1.17)
Intervention modification type			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Modified	0.93 (0.67 - 1.26)	0.84 (0.70 – 0.99) [a]	0.97 (0.84 - 1.09)
Other difference	0.43 (0.16 - 1.07)	0.85 (0.46 - 1.12)	0.99 (0.65 - 1.16)
Intervention modified			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	0.88 (0.63 - 1.18)	0.84 (0.70 - 0.99) [a]	0.97 (0.85 - 1.09)
Intervention content			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Added content	0.74 (0.45 - 1.07)	1.00 (0.81 - 1.20)	0.82 (0.66 - 0.98) [a]
Reduced content	0.37 (0.21 - 1.22)	0.51 (0.19 - 1.01)	1.03 (0.64 - 1.12)
Intervention duration			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Longer duration	1.12 (0.75 - 1.54)	0.85 (0.63 - 1.08)	1.00 (0.84 – 1.15)
Shorter duration	1.24 (0.44 - 1.86)	0.94 (0.40 - 1.11)	NA
Intervention frequency			
Same	1 [Reference]	1 [Reference]	1 [Reference]
More frequent	0.80 (0.29 - 1.60)	0.64 (0.30 - 1.00)	1.02 (0.51 – 1.13)
Less frequent	0.99 (0.46 - 1.57)	0.64 (0.30 - 1.00)	NA

Comparison (C)			
Control modified			
No	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.15 (0.83 - 1.56)	1.01 (0.84 - 1.19)	0.99 (0.86 - 1.12)
Control modification type			
Modified	1 [Reference]	1 [Reference]	1 [Reference]
Same	0.89 (0.60 - 1.50)	0.97 (0.80 - 1.23)	0.93 (0.82 - 1.09)
Active in main, placebo in pilot	0.96 (0.44 - 1.83)	1.03 (0.66 - 1.35)	0.74 (0.48 – 0.99) [a]
Placebo in main, active in pilot	1.28 (0.50 - 2.25)	0.63 (0.23 - 1.08)	0.71 (0.29 - 1.03)
Other difference	1.04 (0.46 - 1.98)	0.97 (0.63 - 1.33)	1.07 (0.86 - 1.22)
Control content			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Added content	1.33 (0.69 - 1.99)	1.11 (0.79 - 1.29)	1.06 (0.82 - 1.20)
Reduced content	0.72 (0.36 - 1.68)	1.05 (0.44 - 1.20)	1.01 (0.49 - 1.11)
Control duration			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Longer duration	0.85 (0.32 - 1.70)	0.64 (0.22 - 1.08)	NA
Shorter duration	1.41 (0.51 - 1.88)	NA	NA
Control frequency			
Same	1 [Reference]	1 [Reference]	1 [Reference]
More frequent	NA	0.65 (0.31 - 1.01)	0.60 (0.29 - 0.93) [a]
Less frequent	NA	NA	NA
Outcome (O)			
Length of follow-up (longest)			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Longer	0.95 (0.68 - 1.38)	0.81 (0.68 - 0.96) [a]	0.93 (0.81 - 1.06)
Shorter	0.78 (0.33 - 1.38)	0.94 (0.71 - 1.14)	0.99 (0.78 - 1.16)
Length of follow-up (primary)			
Same	1 [Reference]	1 [Reference]	1 [Reference]
Different	1.32 (0.98 - 1.78)	0.84 (0.69 - 0.99) [a]	0.85 (0.73 - 0.97) [a]
No. of follow-up visits			
Same	1 [Reference]	1 [Reference]	1 [Reference]
More	0.93 (0.66 - 1.27)	1.01 (0.84 - 1.22)	0.86 (0.75 - 0.98) [a]
Fewer	0.87 (0.40 - 1.43)	1.20 (0.94 - 1.41)	0.94 (0.74 - 1.10)

Abbreviations: PICO, patient/population/problem, intervention, comparison, outcome; NA, not available.
[a] P<.05.

(Paper 2) Figure 1 Scatterplot of percentage difference in successful screening probability vs pilot trial sample size



Dots represent the percentage difference, calculated by dividing the difference between the two studies (i.e., pilot - full-scale) by their mean value. The dashed line represents the average percentage difference.

References

1. Everitt BS. Medical Statistics from A to Z: A Guide for Clinicians and Medical Students. 2nd ed. Cambridge University Press; 2006. doi:10.1017/CBO9780511544453

2. Kraemer HC, Mintz J, Noda A, Tinklenberg J, Yesavage JA. Caution Regarding the Use of Pilot Studies to Guide Power Calculations for Study Proposals. Arch Gen Psychiatry. 2006;63(5):484-489. doi:10.1001/archpsyc.63.5.484

3. Arain M, Campbell MJ, Cooper CL, Lancaster GA. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Med Res Methodol. 2010;10:67. doi:10.1186/1471-2288-10-67

4. Kistin C, Silverstein M. Pilot Studies: A Critical but Potentially Misused Component of Interventional Research. JAMA. 2015;314(15):1561-1562. doi:10.1001/jama.2015.10962

5. Leon AC, Davis LL, Kraemer HC. The Role and Interpretation of Pilot Studies in Clinical Research. J Psychiatr Res. 2011;45(5):626-629. doi:10.1016/j.jpsychires.2010.10.008

6. Sim J. Should treatment effects be estimated in pilot and feasibility studies? Pilot Feasibility Stud. 2019;5(1):107. doi:10.1186/s40814-019-0493-7

7. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355:i5239. doi:10.1136/bmj.i5239

8. Arnold DM, Burns KEA, Adhikari NKJ, et al. The design and interpretation of pilot trials in clinical research in critical care. Crit Care Med. 2009;37(1 Suppl):S69-74. doi:10.1097/CCM.0b013e3181920e33

9. Whitehead AL, Sully BGO, Campbell MJ. Pilot and feasibility studies: is there a difference from each other and from a randomised controlled trial? Contemp Clin Trials. 2014;38(1):130-133. doi:10.1016/j.cct.2014.04.001

10. Cooper CL, Whitehead A, Pottrill E, Julious SA, Walters SJ. Are pilot trials useful for predicting randomisation and attrition rates in definitive studies: A review of publicly funded trials. Clin Trials. 2018;15(2):189-196. doi:10.1177/1740774517752113

11. Beets MW, von Klinggraeff L, Burkart S, et al. Impact of risk of generalizability biases in adult obesity interventions: A meta-epidemiological review and meta-analysis. Obes Rev. 2022;23(2):e13369. doi:10.1111/obr.13369

12. Morgan B, Hejdenberg J, Hinrichs-Krapels S, Armstrong D. Do feasibility studies contribute to, or avoid, waste in research? PLOS ONE. 2018;13(4):e0195951. doi:10.1371/journal.pone.0195951

13. Vandenbroucke JP, Elm E von, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and Elaboration. PLOS Med. 2007;4(10):e297. doi:10.1371/journal.pmed.0040297

14. Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. www.covidence.org

15. Rothwell PM. External validity of randomised controlled trials: “to whom do the results of this trial apply?” Lancet Lond Engl. 2005;365(9453):82-93. doi:10.1016/S0140-6736(04)17670-8

16. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. BMJ. 2015;350:h2147. doi:10.1136/bmj.h2147

17. Beets MW, Weaver RG, Ioannidis JPA, et al. Identification and evaluation of risk of generalizability biases in pilot versus efficacy/effectiveness trials: a systematic review and meta-analysis. Int J Behav Nutr Phys Act. 2020;17(1):19. doi:10.1186/s12966-020-0918-y

18. Treweek S, Pitkethly M, Cook J, et al. Strategies to improve recruitment to randomised trials. Cochrane Database Syst Rev. 2018;2(2):MR000013. doi:10.1002/14651858.MR000013.pub6

19. Gillies K, Kearney A, Keenan C, et al. Strategies to improve retention in randomised trials. Cochrane Database Syst Rev. 2021;(3). doi:10.1002/14651858.MR000032.pub3

20. Koog YH, Gil M, We SR, Wi H, Min BI. Barriers to participant retention in knee osteoarthritis clinical trials: a systematic review. Semin Arthritis Rheum. 2013;42(4):346-354. doi:10.1016/j.semarthrit.2012.07.006

21. Cui Z, Seburg EM, Sherwood NE, Faith MS, Ward DS. Recruitment and retention in obesity prevention and treatment trials targeting minority or low-income children: a review of the clinical trials registration database. Trials. 2015;16:564. doi:10.1186/s13063-015-1089-z

22. Davis LL, Broome ME, Cox RP. Maximizing Retention in Community-based Clinical Trials. J Nurs Scholarsh. 2002;34(1):47-53. doi:10.1111/j.1547-5069.2002.00047.x

23. Dias L, Schoenfeld E, Thomas J, et al. Reasons for high retention in pediatric clinical trials: comparison of participant and staff responses in the Correction of Myopia Evaluation Trial. Clin Trials Lond Engl. 2005;2(5):443-452. doi:10.1191/1740774505cn113oa

24. Bricca A, Swithenbank Z, Scott N, et al. Predictors of recruitment and retention in randomized controlled trials of behavioural smoking cessation interventions: a systematic review and meta-regression analysis. Addict Abingdon Engl. 2022;117(2):299-311. doi:10.1111/add.15614

25. Cole TJ, Altman DG. Statistics Notes: What is a percentage difference? BMJ. Published online August 16, 2017:j3663. doi:10.1136/bmj.j3663

26. Localio AR, Margolis DJ, Berlin JA. Relative risks and confidence intervals were easily computed indirectly from multivariable logistic regression. J Clin Epidemiol. 2007;60(9):874-882. doi:10.1016/j.jclinepi.2006.12.001

27. Avenell A, Grant AM, McGee M, et al. The effects of an open design on trial participant recruitment, compliance and retention--a randomized controlled trial comparison with a blinded, placebo-controlled design. Clin Trials Lond Engl. 2004;1(6):490-498. doi:10.1191/1740774504cn053oa

28. Hemminki E, Hovi SL, Veerus P, et al. Blinding decreased recruitment in a prevention trial of postmenopausal hormone therapy. J Clin Epidemiol. 2004;57(12):1237-1243. doi:10.1016/j.jclinepi.2004.04.009

29. Ravikoff JE, Cole EB, Korzenik JR. Barriers to enrollment in inflammatory bowel disease randomized controlled trials: an investigation of patient perspectives. Inflamm Bowel Dis. 2012;18(11):2092-2098. doi:10.1002/ibd.22872

30. Houghton C, Dowling M, Meskell P, et al. Factors that impact on recruitment to randomised trials in health care: a qualitative evidence synthesis. Cochrane Database Syst Rev. 2020;10(10):MR000045. doi:10.1002/14651858.MR000045.pub2

31. Naidoo N, Nguyen VT, Ravaud P, et al. The research burden of randomized controlled trial participation: a systematic thematic synthesis of qualitative evidence. BMC Med. 2020;18(1):6. doi:10.1186/s12916-019-1476-5

32. Getz K, Sethuraman V, Rine J, Peña Y, Ramanathan S, Stergiopoulos S. Assessing Patient Participation Burden Based on Protocol Design Characteristics. Ther Innov Regul Sci. Published online August 19, 2019:2168479019867284. doi:10.1177/2168479019867284

33. Bodart S, Byrom B, Crescioni M, Eremenco S, Flood E. Perceived Burden of Completion of Patient-Reported Outcome Measures in Clinical Trials:: Results of a Preliminary Study. Ther Innov Regul Sci. 2019;53(3):318-323. doi:10.1177/2168479018788053

34. Ulrich CM, Ratcliffe SJ, Zhou Q, et al. Association of Perceived Benefit or Burden of Research Participation With Participants' Withdrawal From Cancer Clinical Trials. JAMA Netw Open. 2022;5(11):e2244412. doi:10.1001/jamanetworkopen.2022.44412

35. Cameron D, Willoughby C, Messer D, Lux M, Aitken M, Getz K. Assessing Participation Burden in Clinical Trials: Introducing the Patient Friction Coefficient. Clin Ther. 2020;42(8):e150-e159. doi:10.1016/j.clinthera.2020.06.015

36. Gabel M, Bollinger RM, Knox M, et al. Perceptions of Research Burden and Retention Among Participants in ADRC Cohorts. Alzheimer Dis Assoc Disord. 2022;36(4):281-287. doi:10.1097/WAD.0000000000000514

37. Smith Z, Wilkinson M, Carney C, Grove N, Qutab B, Getz K. Enhancing the Measure of Participation Burden in Protocol Design to Incorporate Logistics, Lifestyle, and Demographic Characteristics. Ther Innov Regul Sci. 2021;55(6):1239-1249. doi:10.1007/s43441-021-00336-2

38. Mellor K, Eddy S, Peckham N, et al. Progression from external pilot to definitive randomised controlled trial: a methodological review of progression criteria reporting. BMJ Open. 2021;11(6):e048178. doi:10.1136/bmjopen-2020-048178

39. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c869. doi:10.1136/bmj.c869

40. Huwiler-Müntener K, Jüni P, Junker C, Egger M. Quality of reporting of randomized trials as a measure of methodologic quality. JAMA. 2002;287(21):2801-2804. doi:10.1001/jama.287.21.2801

Chapter 4 Paper 3

Pilot trials may improve the quality of full-scale trials: a meta-research study

Xiangji Ying ,[1] Stephan Ehrhardt[1]

[1] Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA

This paper has been published with *J Clin Epidemiol*. doi: 10.1016/j.jclinepi.2023.06.017.

Abstract

Objectives

Evidence on the value of pilot trials for subsequent trial's quality is scarce. This study aims to determine if a pilot trial improves the quality of the full-scale trial.

Study Design and Setting

We searched PubMed for pilot trials and their subsequent full-scale trials. The meta-analysis of the full-scale trials was used to identify other full-scale trials on the same research topic but without a pilot trial. Markers of trial quality included publication outcomes and Cochrane Risk of Bias (RoB) assessment.

Results

Fifty-eight full-scale trials with a pilot trial and 151 full-scale trials without were identified from 47 meta-analyses. Trials with a pilot trial were published 0.9 years sooner (mean ± standard deviation: 1.7 ± 1.0 vs. 2.6 ± 2.0, P = 0.005) and in peer-reviewed journals with higher impact

factors (60.9 ± 75.0 vs. 24.8 ± 50.3, P < 0.001). A pilot trial's presence was associated with lower risk of bias in full-scale trial random sequence generation (OR [95% CI]: 4.05 [1.27–12.91]), allocation concealment (2.89 [1.07–7.83]), and participants/researchers masking (4.31 [1.37–13.50]), but not outcome assessment masking (1.03 [0.49–2.18]), incomplete outcome data (1.27 [0.47–3.42]), and selective reporting (1.23 [0.44–3.46]).

Conclusion

Conducting a pilot trial may enhance the quality of the subsequent full-scale trial.

Introduction

Trial quality is a concept that is often discussed but hard to define. It is multidimensional and relates to the design, conduct, and analysis of a trial [1]. The Clinical Trials Transformation Initiative defines that quality is the “absence of errors that matter to decision-making” [2]. Hence, lack of bias is one mainstay of trial quality. However, until now, a considerable number of randomized controlled trials (RCTs) have suffered from poor methodological quality, including a high risk of bias. One study analyzed over 170,000 RCTs published between 1966 and 2018 [3]. A positive time trend in trial quality was found, but there existed an urgent need for improvement, as relatively high probabilities of bias remained in the processes of treatment allocation, randomization, and masking. Similar results were found in an earlier paper published in 2015, where colleagues found that 43% of trials had a high risk of bias in at least one domain of the Cochrane Risk of Bias (RoB) assessment tool [4]. Pilot and feasibility studies are designed to generate sufficient evidence that researchers and funding agencies may use to assess whether it is worthwhile or feasible to carry out a larger trial [5].

This study aims to assess whether conducting a pilot trial is associated with improved quality of full-scale trials. As randomization is a critical aspect of conducting RCTs, we will limit our focus

to external pilot trials that utilize a randomized controlled design. These pilot studies serve as stand-alone studies that precede the full-scale trial [6].

Materials and methods

Literature search and study selection

We searched PubMed on February 19, 2022, for pilot trials published between 2005 and 2018. The search strategy and study selection criteria are detailed in Appendix C, and the study selection process is illustrated in Figure 1. We identified stand-alone pilot trials that utilized a randomized controlled design and searched for subsequent full-scale trials conducted by the same research team by reviewing papers that cited the pilot trial. We then looked for meta-analyses on the primary endpoint of the full-scale trial by reviewing papers that cited the trial. When multiple meta-analyses were available, the most relevant or recently published one was chosen, with a preference for Cochrane meta-analyses.

Using the meta-analysis, we identified other full-scale trials on the same research topic but without a pilot trial. Systematic reviews alone were not used as a source to identify other trials, because the inability to perform a meta-analysis often indicates substantial heterogeneity. To ensure the comparability of trials, we manually reviewed the patient, population or problem, intervention, comparison, and outcome (PICO) components of each trial in the meta-analyses. Only trials that were most similar to our trial with a preceding pilot were included for comparison. In most cases, we relied on the subgroup that had already been defined by the meta-analysis author. The full-text of the similar trials was reviewed to determine if they were full-scale trials and if they were informed by a pilot trial or any other forms of preliminary work. Trials were excluded if they were informed by any preliminary work or if the information available was insufficient to determine even after consulting trial protocol and registration information. A full-scale trial was considered to have a preceding pilot trial if explicitly stated in the paper,

regardless of whether the pilot trial was published or not. Any trial newly found to be informed by a pilot trial was moved to the group of prepiloted full-scale trials. We included both individual and cluster randomized trials. The initial study selection was carried out independently of the outcome status and according to a predetermined plan by one investigator (XY). A second investigator (SE) reviewed the selected studies. Both investigators agreed on the final sample.

Data collection

Two-level data were collected by one investigator (XY) from the meta-analysis, original trial paper, and other sources, such as trial registry. Meta-analysis level characteristics included publication information, study field, intervention format, and PICO components. Individual trial level variables included trial design features, research team experience, publication outcomes, intervention efficacy results, trial feasibility measures, and Cochrane RoB assessment results. To maintain the independence of outcome adjudication, we mainly relied on the RoB assessment made by the meta-analysis authors. We cross-checked the meta-analysts' judgment on the incomplete outcome data domain with the dropout rate extracted from the original trial. Five meta-analyses did not rate all domains. We made these assessments without knowledge of pilot trial status and checked for consistency between our assessment and that of other meta-analyses, if available.

Measurement of trial quality

Both publication outcomes and RoB results were proxies of trial quality. We calculated the time lag between study completion and print publication date. We obtained publishing journal impact factors (IF) from Clarivate's Web of Science Journal Citation Reports for the year in which the trial was published, as well as for the most recent year of available data as of our search date (2021). Additionally, we recorded the corresponding author's H-index as of January 2023 from the Web of Science [7]. The original version of the Cochrane RoB assessment tool was used to

measure the methodologic quality of the trials. Although a revised version of this tool was proposed recently [8], the original version is still by far the most commonly used. Results across these two versions are largely consistent [9].

Statistical analysis

We recalculated the I-squared statistic for each set of similar trials as a simple check of between-trial heterogeneity. We examined the crude associations between the presence of pilot trials and the statistical significance of intervention efficacy, feasibility outcomes, funding status, and publication outcomes of the full-scale trial.

The original Cochrane RoB assessment tool included seven domains, namely, random sequence generation (selection bias), allocation concealment (selection bias), masking of participants and personnel/researchers (information bias), masking of outcome assessment (information bias), incomplete outcome data (selection bias), selective reporting (reporting bias), and other bias [10]. Each domain was analyzed separately. The last domain of other bias was not assessed in most meta-analyses and therefore was not included in our analyses. Domains were rated as having a low, high, or unclear risk of bias.

We compared the dichotomized risk of biases (low vs. high or unclear) from full-scale trials with and without a pilot trial using random-effects logit models with a clustered sandwich estimator of variances, considering that the trials are clustered within the meta-analysis. Default adaptive quadrature was used in the analysis with a quadrature check conducted after each random-effects model. If needed, the number of quadrature points was increased to ensure reliable model fit [11]. We also performed logistic regressions with robust variance estimators (RVE), treating trials within each meta-analysis independently as a comparison to the random-effects model results.

Adjusted and unadjusted analyses were conducted, with adjustment variables selected based on prior knowledge, statistical significance, and magnitude of associations in univariable analyses. All adjusted models included study region, number of authors, presence or absence of group author, corresponding author's H-index 1 year before the (pilot) trial, study field, and year of study initiation (before or after 2005). Number of authors and corresponding author's H-index were continuous variables and quadratic terms were added to the model to account for nonlinear associations if needed. Additionally, the analysis of the domain “masking of participants and personnel” accounted for sample size and intervention format, while “masking of outcome assessment” was analyzed by adjusting for sample size. Finally, the length of follow-up was included in the model for “incomplete outcome data” and “selective reporting”.

All statistical analyses were performed using Stata (Version 16; StataCorp, TX) with a two-sided P value <0.05 considered statistically significant.

Results

Study characteristics

A total of 47 meta-analyses were retrieved (Table 1). Half of them were published in 2020 and onward (range: 2013–2022). Approximately one-third of them were Cochrane reviews and meta-analyses. The most frequently examined intervention type was behavioral intervention (31.9%), followed by psychological intervention (29.8%) and pharmacological intervention (17.0%).

From those meta-analyses, 58 full-scale trials had a preceding pilot trial, and 151 full-scale trials did not (Table 2). Participant average age and gender distribution were similar between trials with and without a pilot. The median sample size was significantly larger in trials with a pilot than in those without (341.0 vs. 229.0, P = 0.018). Full-scale trials with a pilot trial were more recently conducted, more recently published, had more authors, and were more likely to have group authorship (all P < 0.05). Regardless of the presence or absence of a pilot trial, researchers

were at approximately the same stage of their career before the pilot or full-scale trial started (median H-index of corresponding author: 8.0 vs. 8.0, P = 0.910).

Efficacy, feasibility, funding status, and publication outcomes

Among full-scale trials with and without a pilot trial, 31.0% and 39.7%, respectively, found a statistically significant difference in the primary efficacy endpoint (Table 3). Two trials with a pilot trial stopped early for futility, and three trials without a pilot trial were terminated early for reasons of futility (n = 1), efficacy (n = 1), and failure to enroll (n = 1). Regardless of the presence or absence of a pilot trial, full-scale trials spent similar time on recruitment (mean: 2.1 vs. 2.2 years) and had comparable recruitment rates (median: 18.8 vs. 16.0 participants per month) and dropout percentages (mean: 12.6% vs. 13.5%). There was a higher proportion of full-scale trials with a pilot trial receiving government funding (82.8% vs. 56.3%, P < 0.001) and multiple sources of funding (24.1% vs. 17.9%, P = 0.041) compared to those without a pilot trial. Trials with a pilot trial were on average published 0.9 years sooner after trial completion (1.7 ± 1.0 vs. 2.6 ± 2.0 years, P = 0.005) and were published in peer-reviewed journals that had a higher IF (60.9 ± 75.0 vs. 24.8 ± 50.3 as of 2021, P < 0.001) than trials without a pilot trial.

Risk of bias

Most full-scale trials fell under the low risk of bias category (Table 4). The exception was that for the domain of masking of participants and researchers, only 31 (20.5%) full-scale trials without a pilot trial and 20 (34.5%) full-scale trials with a pilot trial were rated as having a low risk of bias. Across all domains, the proportion of being categorized as “low risk of bias” appeared to be higher among trials with a pilot trial than trials without a pilot.

Table 5 shows the results of the unadjusted and adjusted regression analyses for the associations of pilot trials with the risk of bias in the subsequent full-scale trial. Logistic regression with RVE indicated that the presence of a pilot trial was significantly associated with

a higher probability of achieving a low risk of bias in the random sequence generation of the full-scale trial (OR = 3.2, 95% CI: 1.18–8.64; adjusted OR = 4.05, 95% CI: 1.27–12.91), but this association was not observed in the random-effects model. The presence of a pilot trial was also associated with a low risk of bias in the full-scale trial's allocation concealment (OR = 4.95, 95% CI: 1.94–12.68; adjusted OR = 2.89, 95% CI: 1.07–7.83) and masking of participants and researchers (OR = 4.2, 95% CI: 1.80–9.79; adjusted OR = 4.31, 95% CI: 1.37–13.50) both before and after adjustment. No significant association was found in either model for masking of outcome data or incomplete outcome data. An unadjusted analysis indicated a positive association between pilot trials and selective reporting in the full-scale trial (OR = 2.78, 95% CI: 1.04–7.45), but this association became null after the adjustment (OR = 1.23, 95% CI: 0.44–3.46).

Discussion

Pilot studies are designed to answer the question “Can we do this?” by testing the performance characteristics of study designs, outcome measures, procedures, recruitment criteria, and operational strategies [12,13]. Our analyses found that RCTs with pilot trials were published sooner and in higher-impact peer-reviewed journals. We also saw strong positive associations between the pilot trial and a lower risk of bias in the full-scale trial's allocation concealment and masking. This may be attributed to the fact that allocation concealment and masking procedures have been tested during the pilot, and can therefore be more smoothly implemented during the full-scale trial.

The logistic regression with RVE found statistically significant associations between conducting a pilot trial and the domain of random sequence generation in both unadjusted and adjusted analyses. However, the random-effects logit models did not show statistically significant associations. It is worth noting that in these models, the point estimate for the association

(unadjusted OR = 3.37, adjusted OR = 4.93) was large enough to be considered substantively important. Nevertheless, due to the wide confidence interval (CI) that included the null value, the evidence supporting the association was not sufficiently strong.

The smallest point estimate was found for masking of outcome assessment across all domains. This is likely due to the fact that the ability to mask outcome assessment is largely determined by the nature of the outcome. In our sample, both RCTs with and without a preceding pilot trial shared the same outcome. If the outcome assessment cannot be masked by nature (e.g., patient-reported outcomes where patients cannot be masked), conducting a pilot trial may not make a significant difference.

In our unadjusted analyses, we observed a lower risk of bias in selective reporting among full-scale trials that conducted pilot trials. It is possible that researchers used the pilot trials to test various outcomes of interest and selected the most reliable and valid ones for use in full-scale trials, thereby reducing the likelihood of selective reporting. However, this significant association was no longer present after adjusting for whether the study was initiated before or after 2005, the year when journals began mandating trial protocol registration. This finding suggests that pilot trials may not have as significant an impact on selective reporting, or at least not as significant as the trial registration requirement.

Theoretically, the presence of a pilot trial may improve the feasibility of a full-scale trial, resulting in fewer incomplete outcome data. However, the point estimate (OR = 1.27) for the incomplete outcome data domain may be too small to be of importance, although the confidence interval extends to values (3.42) that could be significant. These findings align with the null associations of pilot trials with the recruitment rate and attrition proportion of full-scale trials in our study, which are two other crucial feasibility parameters.

It is possible that the point estimate for domain incomplete outcome data is confounded by indication, as the presence of a pilot trial may indicate feasibility concerns. Without a pilot trial, the full-scale trial may have faced more feasibility issues. To eliminate “confounding by indication,” we restricted comparisons to full-scale trials on the same/similar research question and adjusted for factors such as trial size, context, research team experience, and design features like length of follow-up in the analysis. However, residual confounding may still exist. Additionally, our analyses were based solely on published papers, which could be another source of bias, as studies that failed to complete due to feasibility issues may be less likely to be published in peer-reviewed journals. Therefore, our study may have observed an underestimated association between pilot trials and full-scale trial feasibility by undersampling full-scale trials that did not have a pilot trial and failed to complete and publish due to feasibility issues.

Furthermore, the generalizability of pilot trial feasibility results to a full-scale trial may be limited by modifications made to the trial design after the pilot phase [14]. An analysis of 16 pairs of pilot and full-scale trials found that pilot trials underestimated attrition and overestimated enrollment capacity as compared to their full-scale trials [15]. Another recent analysis revealed that 75% of full-scale trials differed from the pilot trial in at least one domain, such as intervention intensity and implementation support [16]. There is a need for methods that can better predict the feasibility of a full-scale trial based on pilot data. In particular, trialists need to understand how modifications based on pilot-trial data change key trial performance metrics of full-scale trials.

There are several limitations inherent in the current study. Firstly, approximately one-third of the trials investigated nondrug interventions, which may impact the generalizability of our findings to pharmaceutical interventions, particularly in masking-related domains. Secondly, some of the included studies were cluster randomized trials, which require specific risk of bias considerations in addition to those for individual randomized trials. Thirdly, an overall risk of bias

score was not computed or compared as this is discouraged when using the original RoB assessment tool [17]. Finally, while our study had a prespecified protocol, it was not preregistered.

Conclusion

The study sheds light on the association between pilot trials and the quality of subsequent full-scale trials. Full-scale trials with a pilot trial were published sooner and in journals with higher impact factors. A published pilot trial was associated with a higher likelihood of a low risk of bias particularly in allocation concealment and masking. These findings have important implications for researchers and funders when allocating resources, as well as for reviewers and journal editors during the paper peer-review process.

(Paper 3) Table 1 Characteristics of the 47 meta-analyses that contributed 58 full-scale trials with a pilot trial and 151 full-scale trials without a pilot trial

	N (%)
Publication year, median (range)	2020 (2018, 2021)
Journal impact factor, median (range)	10.3 (4.6, 12.0)
Cochrane review	
No	32 (68.1%)
Yes	15 (31.9%)
Research field	
Clinical medicine	23 (48.9%)
Epidemiology and health behavior	16 (34.0%)
Healthcare services	8 (17.0%)
Patient, population or problem	
Cancer	6 (12.8%)
Cardiovascular conditions	3 (6.4%)
Endocrinal, nutritional and metabolic disorders	4 (8.5%)
Healthcare delivery	7 (14.9%)
Infections	3 (6.4%)
Lifestyle and wellbeing	7 (14.9%)
Mental health and behavioral conditions	9 (19.1%)
Musculoskeletal conditions	6 (12.8%)
Other	2 (4.3%)
Intervention format	
Medical procedure or device	3 (6.4%)
Medicine	9 (19.1%)
Program	35 (74.5%)
Intervention content	
Behavioral therapies	15 (31.9%)
Complementary and alternative therapies	3 (6.4%)
Healthcare delivery interventions	6 (12.8%)
Medical devices	1 (2.1%)
Pharmacological interventions	8 (17.0%)
Psychological therapies	14 (29.8%)
Outcome	
Compliance with treatment	3 (6.4%)
Function	2 (4.3%)
Infection	2 (4.3%)
Mental health	8 (17.0%)
Mortality	4 (8.5%)
Other	10 (21.3%)
Pain	7 (14.9%)
Resource use	3 (6.4%)

Smoking cessation	2 (4.3%)
Weight/physical activity	6 (12.8%)
I-squared	
>50	17 (39.5%)
≤50	26 (60.5%)

SD: standard deviation

(Paper 3) Table 2 Characteristics of 209 full-scale trials by the presence or absence of a pilot trial

	With pilot (N=58)	Without pilot (N=151)	P-value*
Age of study participants (average ± SD)	41.8±22.2	42.8±24.4	0.79
Percent women (average ± SD)	60.7±25.4	57.8±25.1	0.46
Study region			0.13
Africa	0 (0.0%)	5 (3.3%)	
America	20 (34.5%)	48 (31.8%)	
Asia	3 (5.2%)	21 (13.9%)	
Australia	7 (12.1%)	11 (7.3%)	
Europe	21 (36.2%)	58 (38.4%)	
International	7 (12.1%)	8 (5.3%)	
Cluster randomized controlled trial			0.50
No	46 (79.3%)	113 (74.8%)	
Yes	12 (20.7%)	38 (25.2%)	
Number of participants randomized			
Average ± SD	878.0±1291.3	934.2±2310.6	0.86
Median (range)	341.0 (205.0, 755.0)	229.0 (100.0, 702.0)	0.018
Time from baseline to last follow-up, months			
Average ± SD	7.6±6.1	10.5±11.5	0.071
Median (range)	6.0 (3.0, 12.0)	7.0 (3.0, 12.0)	0.17
Study start year			
1989-2005	3 (5.3%)	55 (40.4%)	<0.001
2006-2018	54 (94.7%)	81 (59.6%)	
Publication year			<0.001
1990-2010	6 (10.3%)	52 (34.4%)	
2011-2021	52 (89.7%)	99 (65.6%)	
Number of authors			
Average ± SD	11.3±7.0	7.4±4.2	<0.001
Median (range)	9.0 (7.0, 13.0)	6.0 (4.0, 9.0)	<0.001
Group author			0.007
No	45 (77.6%)	138 (91.4%)	
Yes	13 (22.4%)	13 (8.6%)	
H-index of corresponding author			
Average ± SD	12.3±13.6	14.8±18.5	0.34
Median (range)	8.0 (3.0, 18.0)	8.0 (1.0, 23.0)	0.91

SD: standard deviation

* P values are derived from Student's t tests for means, Wilcoxon rank-sum tests for medians, Pearson's Chi-squared tests for frequencies if all cell counts exceed 5 or Fisher's Exact tests if at least one cell count is less than or equal to 5.

(Paper 3) Table 3 Intervention efficacy, feasibility, funding status, and publication outcomes of full-scale trials by the presence or absence of a pilot trial

	With pilot (N=58)	Without pilot (N=151)	P-value*
Efficacy significant			0.24
No	40 (79.0%)	91 (60.3%)	
Yes	85 (31.0%)	60 (39.7%)	
Trial early stop			0.62
No	56 (96.6%)	148 (98.0%)	
Yes	2 (3.4%)	3 (2.0%)	
Recruitment length, years			
Average ± SD	2.1±1.4	2.2±1.7	0.81
Median (range)	1.9 (1.2, 2.7)	1.6 (1.0, 2.9)	0.84
Recruitment rate, per month			
Average ± SD	95.6±274.5	217.9±1049.2	0.49
Median (range)	18.8 (7.4, 45.5)	16.0 (4.4, 46.4)	0.50
Dropout, %			
Average ± SD	12.6±12.4	13.5±12.0	0.62
Median (range)	10.5 (2.5, 19.6)	11.0 (4.4, 22.0)	0.57
Industry funding			0.16
No	56 (96.6%)	136 (90.1%)	
Yes	2 (3.4%)	15 (9.9%)	
Government funding			<0.001
No	10 (17.2%)	66 (43.7%)	
Yes	48 (82.8%)	85 (56.3%)	
Organization funding			0.66
No	38 (65.5%)	94 (62.3%)	
Yes	20 (34.5%)	57 (37.7%)	
Number of funding sources			0.041
None/not reported	2 (3.4%)	23 (15.2%)	
1	42 (72.4%)	101 (66.9%)	
2 or more	14 (24.1%)	27 (17.9%)	
Journal impact factor (publication year)			
Average ± SD	19.1±20.7	7.9±12.7	<0.001
Median (range)	8.1 (4.5, 21.7)	3.9 (2.5, 5.6)	<0.001
Time from study completion to publication, years			
Average ± SD	1.7±1.0	2.6±2.0	0.005
Median (range)	1.6 (1.0, 2.1)	2.3 (1.4, 3.2)	0.003
Journal impact factor (2021)			
Average ± SD	60.9±75.0	24.8±50.3	<0.001
Median (range)	17.5 (6.5, 96.2)	5.6 (3.8, 10.7)	<0.001
H-index of corresponding author (2023)			

Average ± SD	36.3±25.0	32.4±27.6	0.34
Median (range)	29.5 (20.0, 44.0)	25.0 (11.0, 45.0)	0.090

SD: standard deviation

*P values are derived from Student's t tests for means, Wilcoxon rank-sum tests for medians, Pearson's Chi-squared tests for frequencies if all cell counts exceed 5 or Fisher's Exact tests if at least one cell count is less than or equal to 5.

(Paper 3) Table 4 Assessment of risk of bias of the full-scale trials by the presence or absence of a pilot trial

	With pilot (N=58)	Without pilot (N=151)	P-value*
Random sequence generation (selection bias)			0.043
Low risk of bias	53 (91.4%)	116 (76.8%)	
High risk of bias	0 (0.0%)	6 (4.0%)	
Unknown risk of bias	5 (8.6%)	29 (19.2%)	
Allocation concealment (selection bias)			<0.001
Low risk of bias	49 (84.5%)	81 (53.6%)	
High risk of bias	0 (0.0%)	22 (14.6%)	
Unknown risk of bias	9 (15.5%)	48 (31.8%)	
Masking of participants and researchers (information bias)			0.013
Low risk of bias	20 (34.5%)	31 (20.5%)	
High risk of bias	31 (53.4%)	75 (49.7%)	
Unknown risk of bias	7 (12.1%)	45 (29.8%)	
Masking of outcome assessment (information bias)			0.51
Low risk of bias	38 (65.5%)	88 (58.3%)	
High risk of bias	9 (15.5%)	23 (15.2%)	
Unknown risk of bias	11 (19.0%)	40 (26.5%)	
Incomplete outcome data (selection bias)			0.32
Low risk of bias	44 (75.9%)	102 (67.5%)	
High risk of bias	9 (15.5%)	24 (15.9%)	
Unknown risk of bias	5 (8.6%)	25 (16.6%)	
Selective reporting (reporting bias)			0.014
Low risk of bias	46 (79.3%)	87 (57.6%)	
High risk of bias	3 (5.2%)	15 (9.9%)	
Unknown risk of bias	9 (15.5%)	49 (32.5%)	

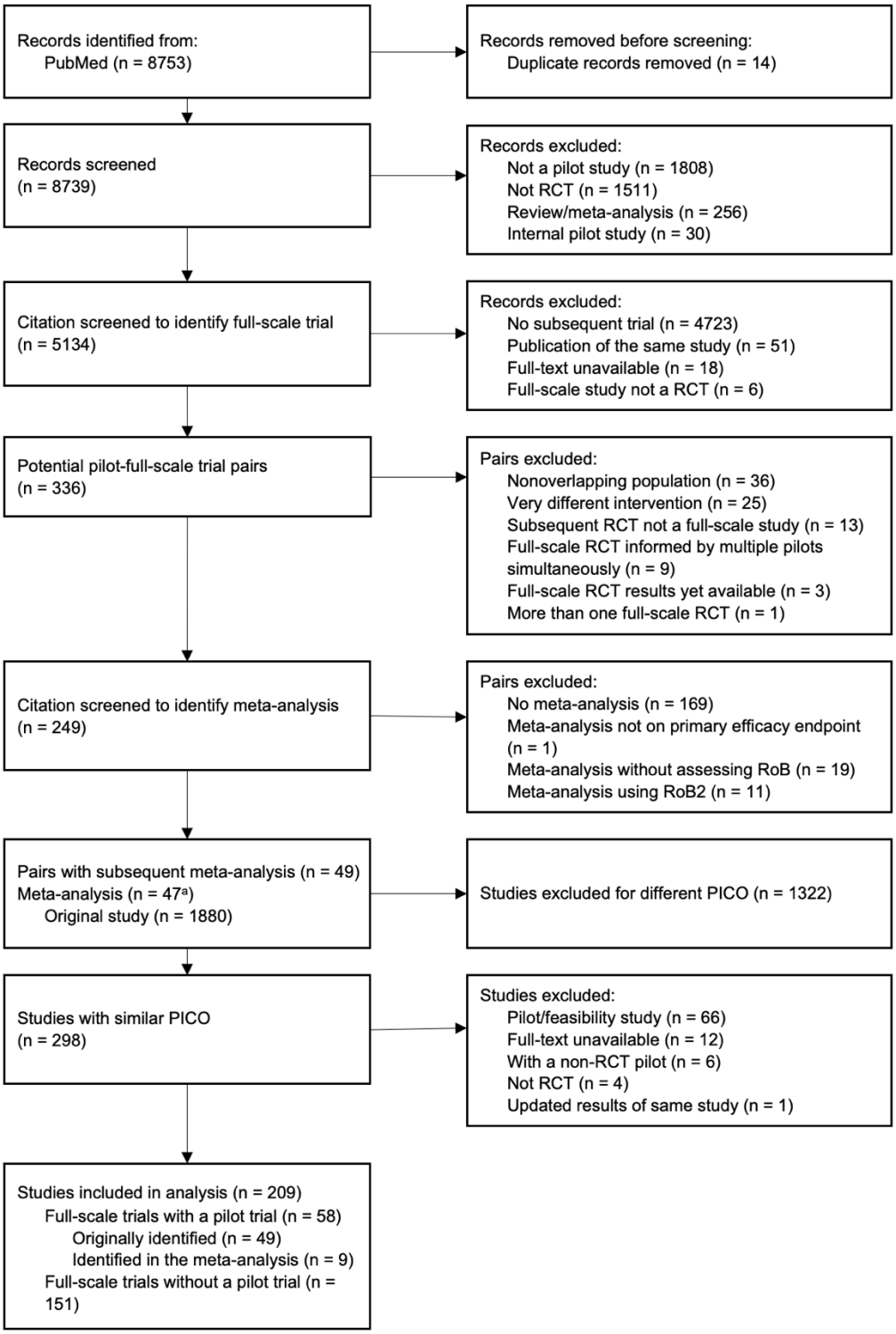
*P-values are calculated for the 3-level risk of bias assessment results by Pearson's Chi-squared tests if none of the cell count <5 or Fisher's Exact tests if at least one cell count ≤5

(Paper 3) Table 5 Association of pilot trials with risk of bias in the full-scale trials

	Unadjusted analyses		Adjusted analyses	
	Random-effects logit model	Logistic regression with RVE	Random-effects logit model	Logistic regression with RVE
Random sequence generation (selection bias)				
High risk of bias	Reference	Reference	Reference	Reference
Low risk of bias	3.37 (0.87 - 13.07)	3.2 (1.18 - 8.64)	4.93 (0.92 – 26.36)	4.05 (1.27 - 12.91)
Allocation concealment (selection bias)				
High risk of bias	Reference	Reference	Reference	Reference
Low risk of bias	4.95 (1.94 - 12.68)	4.71 (2.15 - 10.28)	2.89 (1.07 – 7.83)	3.09 (1.09 – 8.77)
Blinding of participants and researchers (information bias)				
High risk of bias	Reference	Reference	Reference	Reference
Low risk of bias	4.2 (1.80 - 9.79)	2.04 (1.04 - 3.99)	4.31 (1.37 - 13.50)	2.74 (1.001 – 7.48)
Blinding of outcome assessment (information bias)				
High risk of bias	Reference	Reference	Reference	Reference
Low risk of bias	1.59 (0.80 - 3.12)	1.36 (0.72 - 2.56)	1.03 (0.49 - 2.18)	1.09 (0.52 - 2.29)
Incomplete outcome data (selection bias)				
High risk of bias	Reference	Reference	Reference	Reference
Low risk of bias	1.45 (0.66 - 3.16)	1.51 (0.76 - 3.02)	1.27 (0.47 - 3.42)	1.23 (0.54 – 2.84)
Selective reporting (reporting bias)				
High risk of bias	Reference	Reference	Reference	Reference
Low risk of bias	2.78 (1.04 - 7.45)	2.82 (1.38 - 5.76)	1.23 (0.44 – 3.46)	1.77 (0.70 – 4.49)

RVE: robust variance estimate

(Paper 3) Figure 1 Process of identifying full-scale trials with or without a pilot trial



Abbreviations: RCT, randomized controlled trial; RoB, risk of bias; PICO, patient, population or problem, intervention, comparison, and outcome. [a]Four pairs shared the same two meta-analyses.

References

1 Juni P, Altman DG, Egger M. Assessing the quality of controlled clinical trials. BMJ 2001;323:42e6.

2 Bhatt A. Quality of clinical trials: a moving target. Perspect Clin Res 2011;2:124e8.

3 Vinkers CH, Lamberink HJ, Tijdink JK, Heus P, Bouter L, Glasziou P, et al. The methodological quality of 176,620 randomized controlled trials published between 1966 and 2018 reveals a positive trend but also an urgent need for improvement. PLoS Biol 2021;19:e3001162.

4 Yordanov Y, Dechartres A, Porcher R, Boutron I, Altman DG, Ravaud P. Avoidable waste of research related to inadequate methods in clinical trials. BMJ 2015;350:h809.

5 Beets MW, von Klinggraeff L, Weaver RG, Armstrong B, Burkart S. Small studies, big decisions: the role of pilot/feasibility studies in incremental science and premature scale-up of behavioral interventions. Pilot Feasibility Stud 2021;7:173.

6 Arain M, Campbell MJ, Cooper CL, Lancaster GA. What is a pilot or feasibility study? A review of current practice and editorial policy. BMC Med Res Methodol 2010;10:67.

7 Memisevic H, Taljic I, Hadziomerovic AM. Making use of H-index: the shape of science at the University of Sarajevo. Acta Inform Med 2017;25:187e90.

8 Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.

9 Richter B, Hemmingsen B. Comparison of the Cochrane risk of bias tool 1 (RoB 1) with the updated Cochrane risk of bias tool 2 (RoB 2). London, UK: Cochrane. 2021. Available at https://community. cochrane.org/sites/default/files/uploads/inline-files/RoB1_2_project_ 220529_BR%20KK%20formatted.pdf. Accessed January 23, 2023.

10 Higgins JPT, Altman DG, Gøtzsche PC, J€uni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.

11 Hayes RJ, Moulton LH. Cluster randomised trials Boca Raton, FL: :Chapman and Hall/CRC; 2017.

12 Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. J Eval Clin Pract 2004; 10:307e12.

13 Moore CG, Carter RE, Nietert PJ, Stewart PW. Recommendations for planning pilot studies in clinical and translational research. Clin Transl Sci 2011;4:332e7.

14 Beets MW, Weaver RG, Ioannidis JPA, Geraci M, Brazendale K, Decker L, et al. Identification and evaluation of risk of generalizability biases in pilot versus efficacy/effectiveness trials: a systematic review and meta-analysis. Int J Behav Nutr Phys Act 2020;17:19.

15 Cooper CL, Whitehead A, Pottrill E, Julious SA, Walters SJ. Are pilot trials useful for predicting randomisation and attrition rates in definitive studies: a review of publicly funded trials. Clin Trials 2018;15:189e96.

16 Beets MW, von Klinggraeff L, Burkart S, Jones A, Ioannidis JPA, Weaver RG, et al. Impact of risk of generalizability biases in adult obesity interventions: a meta-epidemiological review and meta-analysis. Obes Rev 2022;23:e13369.

17 Higgins JPT, Green S. In: Cochrane Handbook for Systematic Reviews of Interventions. London, UK: Cochrane; 2011.

Chapter 5 Conclusion

1. Summary of Findings and Implications

In our first paper, we found that pilot trials tend to overestimate the point estimate of the effect size on average. Yet, most 95% confidence interval surrounding this estimate did incorporate the point estimate from the full-scale trial. Moreover, having a significant pilot trial appeared to be a moderate to strong indicator for the full-scale trial's significance. It is important to clarify that this discovery does not endorse the pursuit of statistical significance in pilot trials. Instead, we aim to prompt the scientific community to reconsider the relevance of statistical testing within these trials.

From our findings, we propose several recommendations. Significance testing regarding efficacy can be performed in pilot trials, though its results should not be perceived as definitive proof of efficacy. Provided that the evidence is deemed preliminary, a significant difference in efficacy between the intervention and control groups typically signifies a large effect size within the pilot trial. As a result, there is a high likelihood that a full-scale trial will yield significant findings, indicating that further testing of the intervention is warranted.

If the pilot trial does not produce a significant p-value, we suggest researchers examine the confidence interval around the point estimate to determine if it includes values of potential clinical relevance. This objective analysis should be supplemented with a subjective understanding of the intervention's potential effect. By combining these evaluations, researchers may be better equipped to make informed decisions about the necessity of a definitive trial to further assess the intervention's efficacy.

Paper 2 concluded that the characteristics of pilot trials and subsequent modifications might influence the feasibility of full-scale trials to varying degrees. Implementing feasibility

progression criteria in pilot stages and retaining the same masking status as in the full-scale trial can enhance the likelihood of successful screening. While adding more sites after the pilot phase correlated with quicker recruitment, it might diminish the probability of successful screening. Changes that increase the burden on participants may undermine the feasibility of a full-scale trial. For example, expanding intervention content, shifting to an active or more frequently administrated control, and increasing the frequency of follow-ups can lead to decreased participant retention in full-scale trials.

While our findings echo established evidence from non-pilot contexts about factors influencing participant recruitment and retention in RCTs [33,34], to our understanding, this was the first exploration of such evidence within the context of pilot RCTs. The distinctive nature of pilot trials, which offers a unique setting for testing trial procedures, could have shifted the impact of these factors. Our data underscore the importance for both trialists and funders to review pilot trial results and post-pilot design alterations when gauging the feasibility of full-scale trials. Additionally, as researchers make changes to trial designs, they can draw upon the detailed evidence from this study to make well-informed decisions on feasibility. This may hold true even when various elements of the trial are being modified, as understanding the specific impacts of different changes can guide an overarching assessment. As a result, a new pilot trial with updated design features might not always be essential to reassess feasibility, sparing both time and the resources a new trial demands.

Paper 3 reported that conducting a pilot trial could decrease bias in a subsequent full-scale trial, particularly in the generation of random sequences, allocation concealment, and participant masking. This finding aligns with the purpose of pilot trials, which serve as preparatory studies designed to evaluate study procedures and operational strategies for later, typically larger, investigations [35,36].

Many research grant applications necessitate information regarding any preliminary work done before the current proposal. Our study provides empirical support for this prerequisite by demonstrating pilot trials may enhance the quality of full-scale trials. The results suggest that pilot trials might warrant more frequent consideration by researchers and funding bodies. This is particularly relevant for early-career researchers who might lack the experience of seasoned researchers in executing a randomized controlled trial, or in instances where the trial is expected to face practical challenges during the study implementation.

2. Future Directions

This dissertation offers several potential avenues for further research.

Our current investigation focused on pilot trials implementing a randomization process, but other pilot study forms such as one-arm or non-randomized pilot studies could be explored. Given that randomization frequently presents practical challenges, an examination of this process in pilot trials is needed, particularly when the goal is to enhance feasibility or improve quality. Yet, informing intervention efficacy might not necessitate the use of randomization. With recent advances in Bayesian statistics and the strategy of borrowing information from external controls [37], it is plausible that pilot studies could effectively inform efficacy without an accompanying concurrent randomized control group. Therefore, it could be informative to assess whether randomization is required during the pilot phase when the intention is to inform intervention efficacy.

We analyzed pilot trials across a broad range of fields in this work. Future research might narrow its scope to specific subgroups. For instance, as clustered randomized trials are often more susceptible to bias than individual randomized trials [38,39], a deeper look into whether pilot trials are especially beneficial for the methodological quality of clustered randomized trials could

be enlightening. It could also be valuable to determine if a pilot trial needs to adopt a clustered randomized design if the subsequent full-scale trial is planned in this format.

Our current findings associate pilot trials with improved quality in the ensuing trial. Future studies might explore whether a pilot trial must maintain a high quality to optimally inform the quality of a full-scale trial. Given the widespread belief that the term 'pilot' is often misused to justify poor study quality, it might also be insightful to investigate whether empirical evidence indeed suggests that pilot trials are of lower quality than definitive trials.

Finally, while our research centered on methodological quality, future studies could consider the reporting quality by assessing adherence of both pilot and full-scale trials to the relevant CONSORT guidelines, as well as how adherence in each may be correlated.

In summary, this dissertation contributes to our understanding of the role of pilot trials in informing efficacy, feasibility, and quality for subsequent full-scale trials. Pilot trials can offer early signals on intervention efficacy. Researchers and funders should weigh both the data from pilot trials and proposed design modifications when evaluating full-scale trials. Pilot trials may improve the quality of ensuing full-scale trials and warrant more frequent consideration. Future research is needed to explore other types of pilot studies and evaluate their impact on full-scale trials.

Appendices

Appendix A: Supplementary Materials for Paper 1

eTable 1. Search strategy

#1	"Pilot Projects"[Mesh] OR "Feasibility Studies"[Mesh]
#2	(Feasib*[Title/Abstract] OR pilot[Title/Abstract]) AND (study[Title/Abstract] OR trial[Title/Abstract])
#3	#1 OR #2
#4	retention[Title/Abstract] OR attrition[Title/Abstract] OR recruitment[Title/Abstract] OR randomization[Title/Abstract] OR participation[Title/Abstract] OR adherence[Title/Abstract] OR compliance[Title/Abstract] OR acceptability[Title/Abstract] OR completion[Title/Abstract] OR attendance[Title/Abstract]
#5	randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] NOT (animals [mh] NOT humans [mh])
#6	random*[Title/Abstract]
#7	#5 AND #6
#8	#3 AND # 4 AND #7

eTable 2. Illustration of modifications on the content, duration, and frequency of the intervention and comparator

	Pilot trial	Full-scale trial	Example
Content: intervention component (duration and frequency can vary)			
Same	A	A	Pair #2: Pilot: simvastatin 20 mg plus ezetimibe 10 mg daily Full: simvastatin 20 mg plus ezetimibe 10 mg daily
Added content	A	A+B	Pair #25: Pilot: 0.6% vaginal and neonate wipe performed every 4 hours (up to 3 times maximum) until delivery Full: 0.6% vaginal and neonate wipe performed every 4 hours (up to 3 times maximum) until delivery+minimum of one wash at least an hour before delivery
Reduced content	A+B	A	Pair #46: Pilot: 10-week Viewing IDVD at home+peer support group teleconferences (PSGTs)+Usual WIC care Full: 16-week Viewing IDVD at home+peer support group teleconferences (PSGTs)
Other difference	A+B	A+C	Pair #235: Pilot: 12 week wechat articles three to five times a week+12 SMS text message greetings and reminders Full: 12 week wechat articles three to five times a week+physical activity promotion program+ most read articles as booster
	A delivered by P	A delivered by Q	Pair #13: Pilot: clinic-based cognitive-behavioral therapy partially delivered by internet Full: internet-based cognitive-behavioral therapy
	A	Revised A	Pair #95: Pilot: DECISION+ program (3 three-hour on-site interactive workshops, reminders and feedback over a four- to six-month period) Full: revised DECISION+ program (a 2-hour web-based tutorial followed by a 2-hour on-site interactive workshop followed by reminders)
Duration: intervention length, in hours/days/weeks/months (content can vary)			
Same	X	X	Pair #5: Pilot: definitive radiotherapy (70 Gy in 7 weeks) + cisplatin (75 mg/m2) plus

			tirapazamine (290 mg/m2/d) on day 2 of weeks 1, 4, and7, and tirapazamine alone (160 mg/m2/d) on days 1, 3, and 5 of weeks 2 and 3 Full: definitive radiotherapy (70 Gy in 7 weeks) + cisplatin (75 mg/m2) plus tirapazamine (290 mg/m2/d) on day 1 of weeks 1, 4, and 7, and tirapazamine alone (160 mg/m2/d) on days 1, 3, and 5 of weeks 2 and 3
Longer duration	X	>X	Pair #46: Pilot: 10-week Viewing IDVD at home+peer support group teleconferences (PSGTs)+Usual WIC care Full: 16-week Viewing IDVD at home+peer support group teleconferences (PSGTs)
Shorter duration	X	<X	Pair #71: Pilot: injectable hydromorphone over 12 months Full: injectable hydromorphone over 6 months
Frequency: number of sessions (content can vary)			
Same	Y	Y	Pair #5: Pilot: definitive radiotherapy (70 Gy in 7 weeks) + cisplatin (75 mg/m2) plus tirapazamine (290 mg/m2/d) on day 2 of weeks 1, 4, and7, and tirapazamine alone (160 mg/m2/d) on days 1, 3, and 5 of weeks 2 and 3 Full: definitive radiotherapy (70 Gy in 7 weeks) + cisplatin (75 mg/m2) plus tirapazamine (290 mg/m2/d) on day 1 of weeks 1, 4, and 7, and tirapazamine alone (160 mg/m2/d) on days 1, 3, and 5 of weeks 2 and 3
More frequent	Y	>Y	Pair #67: Pilot:16 weeks weekly 90-minute yoga classes + newsletters on back care Full: 24 weeks twice weekly 90-minute yoga classes
Less frequent	Y	<Y	Pair #11: Pilot: 90-minute after-school Physical Activity Club offered five days a week Full: 90-minute after-school physical activity club offered 3 days/week

eTable 3. List of 248 pilot-full-scale trial pairs

Pair #	Pilot trial	Full-scale trial
1	Ames, S. C.; Patten, C. A.; Offord, K. P.; Pennebaker, J. W.; Croghan, I. T.; Tri, D. M.; Stevens, S. R.; Hurt, R. D. Expressive writing intervention for young adult cigarette smokers. J Clin Psychol. 2005;61(12):1555-70. doi:10.1002/jclp.20208	Ames, Steven C.; Patten, Christi A.; Werch, Chudley E.; Schroeder, Darrell R.; Stevens, Susanna R.; Fredrickson, Paul A.; Echols, J. Dan; Pennebaker, James W.; Hurt, Richard D. Expressive writing as a smoking cessation treatment adjunct for young adult smokers. Nicotine Tob Res. 2007;9(2):185-194. doi:10.1080/14622200601078525
2	Landray, Martin; Baigent, Colin; Leaper, Craig; Adu, Dwomoa; Altmann, Paul; Armitage, Jane; Ball, Simon; Baxter, Alex; Blackwell, Lisa; Cairns, Hugh S.; Carr, Sue; Collins, Rory; Kourellias, Karen; Rogerson, Mary; Scoble, John E.; Tomson, Charles R. V.; Warwick, Graham; Wheeler, David C. The second United Kingdom Heart and Renal Protection (UK-HARP-II) Study: a randomized controlled study of the biochemical safety and efficacy of adding ezetimibe to simvastatin as initial therapy among patients with CKD. Am J Kidney Dis. 2006;47(3):385-395. doi:10.1053/j.ajkd.2005.11.018	Baigent, Colin; Landray, Martin J.; Reith, Christina; Emberson, Jonathan; Wheeler, David C.; Tomson, Charles; Wanner, Christoph; Krane, Vera; Cass, Alan; Craig, Jonathan; Neal, Bruce; Jiang, Lixin; Hooi, Lai Seong; Levin, Adeera; Agodoa, Lawrence; Gaziano, Mike; Kasiske, Bertram; Walker, Robert; Massy, Ziad A.; Feldt-Rasmussen, Bo; Krairittichai, Udom; Ophascharoensuk, Vuddidhej; Fellström, Bengt; Holdaas, Hallvard; Tesar, Vladimir; Wiecek, Andrzej; Grobbee, Diederick; de Zeeuw, Dick; Grönhagen-Riska, Carola; Dasgupta, Tanaji; Lewis, David; Herrington, William; Mafham, Marion; Majoni, William; Wallendszus, Karl; Grimm, Richard; Pedersen, Terje; Tobert, Jonathan; Armitage, Jane; Baxter, Alex; Bray, Christopher; Chen, Yiping; Chen, Zhengming; Hill, Michael; Knott, Carol; Parish, Sarah; Simpson, David; Sleight, Peter; Young, Alan; Collins, Rory; SHARP Investigators The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. 2011;377(9784):2181-2192. doi:10.1016/S0140-6736(11)60739-3
3	Gohagan, J. K.; Marcus, P. M.; Fagerstrom, R. M.; Pinsky, P. F.; Kramer, B. S.; Prorok, P. C.; Ascher, S.; Bailey, W.; Brewer, B.; Church, T.; Engelhard, D.; Ford, M.; Fouad, M.; Freedman, M.; Gelmann, E.; Gierada, D.; Hocking, W.; Inampudi, S.; Irons, B.; Johnson, C. C.; Jones, A.; Kucera, G.; Kvale, P.; Lappe, K.; Manor, W.; Moore, A.; Nath, H.; Neff, S.; Oken, M.; Plunkett, M.; Price, H.; Reding, D.; Riley, T.; Schwartz, M.; Spizarny, D.; Yoffie, R.; Zylak, C. Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest X-ray screening for lung cancer. Lung Cancer. 2005;47(1):45184. doi:10.1016/j.lungcan.2004.06.007	National Lung Screening Trial Research Team; Church, Timothy R.; Black, William C.; Aberle, Denise R.; Berg, Christine D.; Clingan, Kathy L.; Duan, Fenghai; Fagerstrom, Richard M.; Gareen, Ilana F.; Gierada, David S.; Jones, Gordon C.; Mahon, Irene; Marcus, Pamela M.; Sicks, JoRean D.; Jain, Amanda; Baum, Sarah Results of initial low-dose computed tomographic screening for lung cancer. N Engl J Med. 2013;368(21):1980-1991. doi:10.1056/NEJMoa1209120

4	LIFE Study Investigators; Pahor, Marco; Blair, Steven N.; Espeland, Mark; Fielding, Roger; Gill, Thomas M.; Guralnik, Jack M.; Hadley, Evan C.; King, Abby C.; Kritchevsky, Stephen B.; Maraldi, Cinzia; Miller, Michael E.; Newman, Anne B.; Rejeski, Walter J.; Romashkan, Sergei; Studenski, Stephanie Effects of a physical activity intervention on measures of physical performance: Results of the lifestyle interventions and independence for Elders Pilot (LIFE-P) study. J Gerontol A Biol Sci Med Sci. 2006;61(11):1157-1165. doi:10.1093/gerona/61.11.1157	Pahor, Marco; Guralnik, Jack M.; Ambrosius, Walter T.; Blair, Steven; Bonds, Denise E.; Church, Timothy S.; Espeland, Mark A.; Fielding, Roger A.; Gill, Thomas M.; Groessl, Erik J.; King, Abby C.; Kritchevsky, Stephen B.; Manini, Todd M.; McDermott, Mary M.; Miller, Michael E.; Newman, Anne B.; Rejeski, W. Jack; Sink, Kaycee M.; Williamson, Jeff D.; LIFE study investigators Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA. 2014;311(23):2387-2396. doi:10.1001/jama.2014.5616
5	Rischin, D.; Peters, L.; Fisher, R.; Macann, A.; Denham, J.; Poulsen, M.; Jackson, M.; Kenny, L.; Penniment, M.; Corry, J.; Lamb, D.; McClure, B. Tirapazamine, Cisplatin, and Radiation versus Fluorouracil, Cisplatin, and Radiation in patients with locally advanced head and neck cancer: a randomized phase II trial of the Trans-Tasman Radiation Oncology Group (TROG 98.02). J Clin Oncol. 2005;23(1):79-87. doi:10.1200/jco.2005.01.072	Rischin, Danny; Peters, Lester J.; O'Sullivan, Brian; Giralt, Jordi; Fisher, Richard; Yuen, Kally; Trotti, Andy; Bernier, Jacques; Bourhis, Jean; Ringash, Jolie; Henke, Michael; Kenny, Lizbeth Tirapazamine, cisplatin, and radiation versus cisplatin and radiation for advanced squamous cell carcinoma of the head and neck (TROG 02.02, HeadSTART): a phase III trial of the Trans-Tasman Radiation Oncology Group. J Clin Oncol. 2010;28(18):2989-2995. doi:10.1200/JCO.2009.27.4449
6	Safren, S. A.; Otto, M. W.; Sprich, S.; Winett, C. L.; Wilens, T. E.; Biederman, J. Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. Behav Res Ther. 2005;43(7):831-42. doi:10.1016/j.brat.2004.07.001	Safren, Steven A.; Sprich, Susan; Mimiaga, Matthew J.; Surman, Craig; Knouse, Laura; Groves, Meghan; Otto, Michael W. Cognitive behavioral therapy vs relaxation with educational support for medication-treated adults with ADHD and persistent symptoms: a randomized controlled trial. JAMA. 2010;304(8):875-880. doi:10.1001/jama.2010.1192
7	Sirey, J. A.; Bruce, M. L.; Alexopoulos, G. S. The Treatment Initiation Program: an intervention to improve depression outcomes in older adults. Am J Psychiatry. 2005;162(1):184-6. doi:10.1176/appi.ajp.162.1.184	Sirey, Jo Anne; Banerjee, Samprit; Marino, Patricia; Bruce, Martha L.; Halkett, Ashley; Turnwald, Molly; Chiang, Claire; Liles, Brian; Artis, Amanda; Blow, Fred; Kales, Helen C. Adherence to Depression Treatment in Primary Care: A Randomized Clinical Trial. JAMA Psychiatry. 2017;74(11):1129-1135. doi:10.1001/jamapsychiatry.2017.3047
8	Amaro, S.; Viggiano, A.; Di Costanzo, A.; Madeo, I.; Viggiano, A.; Baccari, M. E.; Marchitelli, E.; Raia, M.; Viggiano, E.; Deepak, S.; Monda, M.; De Luca, B. Kalèdo, a new educational board-game, gives nutritional rudiments and encourages healthy eating in children: a pilot cluster randomized trial. Eur J Pediatr. 2006;165(9):630-5. doi:10.1007/s00431-006-0153-9	Viggiano, Alessandro; Viggiano, Emanuela; Di Costanzo, Anna; Viggiano, Andrea; Andreozzi, Eleonora; Romano, Vincenzo; Rianna, Ines; Vicidomini, Claudia; Gargano, Giuliana; Incarnato, Lucia; Fevola, Celeste; Volta, Pietro; Tolomeo, Caterina; Scianni, Giuseppina; Santangelo, Caterina; Battista, Roberta; Monda, Marcellino; Viggiano, Adela; De Luca, Bruno; Amaro, Salvatore Kaledo, a board game for nutrition education of children and adolescents at school: cluster randomized controlled trial of healthy lifestyle promotion. Eur J Pediatr. 2015;174(2):217-228. doi:10.1007/s00431-014-2381-8

9	Mackintosh, J.; White, M.; Howel, D.; Chadwick, T.; Moffatt, S.; Deverill, M.; Sandell, A. Randomised controlled trial of welfare rights advice accessed via primary health care: pilot study [ISRCTN61522618]. BMC Public Health. 2006;6():162. doi:10.1186/1471-2458-6-162	Howel, Denise; Moffatt, Suzanne; Haighton, Catherine; Bryant, Andrew; Becker, Frauke; Steer, Melanie; Lawson, Sarah; Aspray, Terry; Milne, Eugene M. G.; Vale, Luke; McColl, Elaine; White, Martin Does domiciliary welfare rights advice improve health-related quality of life in independent-living, socio-economically disadvantaged people aged ≥60 years? Randomised controlled trial, economic and process evaluations in the North East of England. PLoS One. 2019;14(1):e0209560. doi:10.1371/journal.pone.0209560
10	Moody, K.; Finlay, J.; Mancuso, C.; Charlson, M. Feasibility and safety of a pilot randomized trial of infection rate: neutropenic diet versus standard food safety guidelines. J Pediatr Hematol Oncol. 2006;28(3):126-33. doi:10.1097/01.mph.0000210412.33630.fb	Moody, Karen M.; Baker, Rebecca A.; Santizo, Ruth O.; Olmez, Inan; Spies, Jeanie M.; Buthmann, Amanda; Granowetter, Linda; Dulman, Robin Y.; Ayyanar, Kanyalakshmi; Gill, Jonathan B.; Carroll, Aaron E. A randomized trial of the effectiveness of the neutropenic diet versus food safety guidelines on infection rate in pediatric oncology patients. Pediatr Blood Cancer. 2018;65(1):. doi:10.1002/pbc.26711
11	Robbins, L. B.; Gretebeck, K. A.; Kazanis, A. S.; Pender, N. J. Girls on the move program to increase physical activity participation. Nurs Res. 2006;55(3):206-16. doi:10.1097/00006199-200605000-00007	Robbins, Lorraine B.; Ling, Jiying; Sharma, Dhruv B.; Dalimonte-Merckling, Danielle M.; Voskuil, Vicki R.; Resnicow, Kenneth; Kaciroti, Niko; Pfeiffer, Karin A. Intervention Effects of "Girls on the Move" on Increasing Physical Activity: A Group Randomized Trial. Ann Behav Med. 2019;53(5):493-500. doi:10.1093/abm/kay054
12	Sackley, C.; Wade, D. T.; Mant, D.; Atkinson, J. C.; Yudkin, P.; Cardoso, K.; Levin, S.; Lee, V. B.; Reel, K. Cluster randomized pilot controlled trial of an occupational therapy intervention for residents with stroke in UK care homes. Stroke. 2006;37(9):2336-41. doi:10.1161/01.Str.0000237124.20596.92	Sackley, Catherine M.; Walker, Marion F.; Burton, Christopher R.; Watkins, Caroline L.; Mant, Jonathan; Roalfe, Andrea K.; Wheatley, Keith; Sheehan, Bart; Sharp, Leslie; Stant, Katie E.; Fletcher-Smith, Joanna; Steel, Kerry; Wilde, Kate; Irvine, Lisa; Peryer, Guy; OTCH trial investigators An occupational therapy intervention for residents with stroke related disabilities in UK care homes (OTCH): cluster randomised controlled trial. BMJ. 2015;350():h468. doi:10.1136/bmj.h468
13	Spence, S. H.; Holmes, J. M.; March, S.; Lipp, O. V. The feasibility and outcome of clinic plus internet delivery of cognitive-behavior therapy for childhood anxiety. J Consult Clin Psychol. 2006;74(3):614-21. doi:10.1037/0022-006x.74.3.614	March, Sonja; Spence, Susan H.; Donovan, Caroline L. The efficacy of an internet-based cognitive-behavioral therapy intervention for child anxiety disorders. J Pediatr Psychol. 2009;34(5):474-487. doi:10.1093/jpepsy/jsn099
14	Stremler, R.; Hodnett, E.; Lee, K.; MacMillan, S.; Mill, C.; Ongcangco, L.; Willan, A. A behavioral-educational intervention to promote maternal and infant sleep: a pilot randomized, controlled trial. Sleep. 2006;29(12):1609-15. doi:10.1093/sleep/29.12.1609	Stremler, Robyn; Hodnett, Ellen; Kenton, Laura; Lee, Kathryn; Weiss, Shelly; Weston, Julie; Willan, Andrew Effect of behavioural-educational intervention on sleep for primiparous women and their infants in early postpartum: multisite randomised controlled trial. BMJ. 2013;346():f1164. doi:10.1136/bmj.f1164
15	Tan, E. J.; Xue, Q. L.; Li, T.; Carlson, M. C.; Fried, L. P. Volunteering: a physical activity intervention for older adults--The Experience	Gruenewald, Tara L.; Tanner, Elizabeth K.; Fried, Linda P.; Carlson, Michelle C.; Xue, Qian-Li; Parisi, Jeanine M.; Rebok, George W.;

	Corps program in Baltimore. J Urban Health. 2006;83(5):954-69. doi:10.1007/s11524-006-9060-7	Yarnell, Lisa M.; Seeman, Teresa E. The Baltimore Experience Corps Trial: Enhancing Generativity via Intergenerational Activity Engagement in Later Life. J Gerontol B Psychol Sci Soc Sci. 2016;71(4):661-670. doi:10.1093/geronb/gbv005
16	Crew, K. D.; Capodice, J. L.; Greenlee, H.; Apollo, A.; Jacobson, J. S.; Raptis, G.; Blozie, K.; Sierra, A.; Hershman, D. L. Pilot study of acupuncture for the treatment of joint symptoms related to adjuvant aromatase inhibitor therapy in postmenopausal breast cancer patients. J Cancer Surviv. 2007;1(4):283-91. doi:10.1007/s11764-007-0034-x	Crew, Katherine D.; Capodice, Jillian L.; Greenlee, Heather; Brafman, Lois; Fuentes, Deborah; Awad, Danielle; Yann Tsai, Wei; Hershman, Dawn L. Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated joint symptoms in women with early-stage breast cancer. J Clin Oncol. 2010;28(7):1154-1160. doi:10.1200/JCO.2009.23.4708
17	Elder, C.; Ritenbaugh, C.; Mist, S.; Aickin, M.; Schneider, J.; Zwickey, H.; Elmer, P. Randomized trial of two mind-body interventions for weight-loss maintenance. J Altern Complement Med. 2007;13(1):67-78. doi:10.1089/acm.2006.6237	Elder, Charles R.; Gullion, Christina M.; Debar, Lynn L.; Funk, Kristine L.; Lindberg, Nangel M.; Ritenbaugh, Cheryl; Meltesen, Gayle; Gallison, Cherri; Stevens, Victor J. Randomized trial of Tapas Acupressure Technique for weight loss maintenance. BMC Complement Altern Med. 2012;12():19. doi:10.1186/1472-6882-12-19
18	Greenfield, S. F.; Trucco, E. M.; McHugh, R. K.; Lincoln, M.; Gallop, R. J. The Women's Recovery Group Study: a Stage I trial of women-focused group therapy for substance use disorders versus mixed-gender group drug counseling. Drug Alcohol Depend. 2007;90(1):39-47. doi:10.1016/j.drugalcdep.2007.02.009	Greenfield, Shelly F.; Sugarman, Dawn E.; Freid, Cathryn M.; Bailey, Genie L.; Crisafulli, Michele A.; Kaufman, Julia S.; Wigderson, Sara; Connery, Hilary S.; Rodolico, John; Morgan-Lopez, Antonio A.; Fitzmaurice, Garrett M. Group therapy for women with substance use disorders: results from the Women's Recovery Group Study. Drug Alcohol Depend. 2014;142():245-253. doi:10.1016/j.drugalcdep.2014.06.035
19	Haerens, L.; Deforche, B.; Vandelanotte, C.; Maes, L.; De Bourdeaudhuij, I. Acceptability, feasibility and effectiveness of a computer-tailored physical activity intervention in adolescents. Patient Educ Couns. 2007;66(3):303-10. doi:10.1016/j.pec.2007.01.003	Haerens, Leen; Maes, Lea; Vereecken, Carine; De Henauw, Stefaan; Moreno, Luis; De Bourdeaudhuij, Ilse Effectiveness of a computer tailored physical activity intervention in adolescents compared to a generic advice. Patient Educ Couns. 2009;77(1):38-41. doi:10.1016/j.pec.2009.03.020
20	Kampman, K. M.; Pettinati, H. M.; Lynch, K. G.; Whittingham, T.; Macfadden, W.; Dackis, C.; Tirado, C.; Oslin, D. W.; Sparkman, T.; O'Brien, C. P. A double-blind, placebo-controlled pilot trial of quetiapine for the treatment of Type A and Type B alcoholism. J Clin Psychopharmacol. 2007;27(4):344-51. doi:10.1097/JCP.0b013e3180ca86e5	Litten, Raye Z.; Fertig, Joanne B.; Falk, Daniel E.; Ryan, Megan L.; Mattson, Margaret E.; Collins, Joseph F.; Murtaugh, Cristin; Ciraulo, Domenic; Green, Alan I.; Johnson, Bankole; Pettinati, Helen; Swift, Robert; Afshar, Maryam; Brunette, Mary F.; Tiouririne, Nassima A.-D.; Kampman, Kyle; Stout, Robert; NCIG 001 Study Group A double-blind, placebo-controlled trial to assess the efficacy of quetiapine fumarate XR in very heavy-drinking alcohol-dependent patients. Alcohol Clin Exp Res. 2012;36(3):406-416. doi:10.1111/j.1530-0277.2011.01649.x
21	Ludman, E. J.; Simon, G. E.; Grothaus, L. C.; Luce, C.; Markley, D. K.; Schaefer, J. A pilot study of telephone care management and structured disease self-management groups for chronic depression. Psychiatr	Ludman, Evette J.; Simon, Gregory E.; Grothaus, Louis C.; Richards, Julie Elissa; Whiteside, Ursula; Stewart, Christine Organized Self-Management Support Services for Chronic Depressive Symptoms: A Randomized

	Serv. 2007;58(8):1065-72. doi:10.1176/ps.2007.58.8.1065	Controlled Trial. Psychiatr Serv. 2016;67(1):29-36. doi:10.1176/appi.ps.201400295
22	Magee, L. A.; von Dadelszen, P.; Chan, S.; Gafni, A.; Gruslin, A.; Helewa, M.; Hewson, S.; Kavuma, E.; Lee, S. K.; Logan, A. G.; McKay, D.; Moutquin, J. M.; Ohlsson, A.; Rey, E.; Ross, S.; Singer, J.; Willan, A. R.; Hannah, M. E. The Control of Hypertension In Pregnancy Study pilot trial. Bjog. 2007;114(6):770, e13-20. doi:10.1111/j.1471-0528.2007.01315.x	Magee, Laura A.; von Dadelszen, Peter; Rey, Evelyne; Ross, Susan; Asztalos, Elizabeth; Murphy, Kellie E.; Menzies, Jennifer; Sanchez, Johanna; Singer, Joel; Gafni, Amiram; Gruslin, Andrée; Helewa, Michael; Hutton, Eileen; Lee, Shoo K.; Lee, Terry; Logan, Alexander G.; Ganzevoort, Wessel; Welch, Ross; Thornton, Jim G.; Moutquin, Jean-Marie Less-tight versus tight control of hypertension in pregnancy. N Engl J Med. 2015;372(5):407-417. doi:10.1056/NEJMoa1404595
23	Nikander, R.; Sievänen, H.; Ojala, K.; Oivanen, T.; Kellokumpu-Lehtinen, P. L.; Saarto, T. Effect of a vigorous aerobic regimen on physical performance in breast cancer patients - a randomized controlled pilot trial. Acta Oncol. 2007;46(2):181-6. doi:10.1080/02841860600833145	Saarto, T.; Sievänen, H.; Kellokumpu-Lehtinen, P.; Nikander, R.; Vehmanen, L.; Huovinen, R.; Kautiainen, H.; Järvenpää, S.; Penttinen, H. M.; Utriainen, M.; Jääskeläinen, A. S.; Elme, A.; Ruohola, J.; Palva, T.; Vertio, H.; Rautalahti, M.; Fogelholm, M.; Luoto, R.; Blomqvist, C. Effect of supervised and home exercise training on bone mineral density among breast cancer patients. A 12-month randomised controlled trial. Osteoporos Int. 2012;23(5):1601-1612. doi:10.1007/s00198-011-1761-4
24	Pears, K. C.; Fisher, P. A.; Bronz, K. D. An Intervention to Promote Social Emotional School Readiness in Foster Children: Preliminary Outcomes From a Pilot Study. School Psych Rev. 2007;36(4):665-673. doi:	Pears, Katherine C.; Fisher, Philip A.; Kim, Hyoun K.; Bruce, Jacqueline; Healey, Cynthia V.; Yoerger, Karen Immediate Effects of a School Readiness Intervention for Children in Foster Care. Early Educ Dev. 2013;24(6):771-791. doi:10.1080/10409289.2013.736037
25	Saleem, S.; Reza, T.; McClure, E. M.; Pasha, O.; Moss, N.; Rouse, D. J.; Bartz, J.; Goldenberg, R. L. Chlorhexidine vaginal and neonatal wipes in home births in Pakistan: a randomized controlled trial. Obstet Gynecol. 2007;110(5):977-85. doi:10.1097/01.Aog.0000285653.17869.26	Saleem, Sarah; Rouse, Dwight J.; McClure, Elizabeth M.; Zaidi, Anita; Reza, Tahira; Yahya, Y.; Memon, I. A.; Khan, N. H.; Memon, G.; Soomro, N.; Pasha, Omrana; Wright, Linda L.; Moore, Janet; Goldenberg, Robert L. Chlorhexidine vaginal and infant wipes to reduce perinatal mortality and morbidity: a randomized controlled trial. Obstet Gynecol. 2010;115(6):1225-1232. doi:10.1097/AOG.0b013e3181e00ff0
26	Vernacchio, L.; Vezina, R. M.; Mitchell, A. A. Tolerability of oral xylitol solution in young children: implications for otitis media prophylaxis. Int J Pediatr Otorhinolaryngol. 2007;71(1):89-94. doi:10.1016/j.ijporl.2006.09.008	Vernacchio, Louis; Corwin, Michael J.; Vezina, Richard M.; Pelton, Steven I.; Feldman, Henry A.; Coyne-Beasley, Tamera; Mitchell, Allen A. Xylitol syrup for the prevention of acute otitis media. Pediatrics. 2014;133(2):289-295. doi:10.1542/peds.2013-2373
27	Ananworanich, J.; Kosalaraksa, P.; Siangphoe, U.; Engchanil, C.; Pancharoen, C.; Lumbiganon, P.; Intasan, J.; Apateerapong, W.; Chuenyam, T.; Ubolyam, S.; Bunupuradah, T.; Lange, J.; Cooper, D. A.; Phanuphak, P. A feasibility study of immediate versus deferred antiretroviral therapy in children with HIV infection. AIDS Res Ther. 2008;5():24. doi:10.1186/1742-6405-5-24	Puthanakit, Thanyawee; Saphonn, Vonthanak; Ananworanich, Jintanat; Kosalaraksa, Pope; Hansudewechakul, Rawiwan; Vibol, Ung; Kerr, Stephen J.; Kanjanavanit, Suparat; Ngampiyaskul, Chaiwat; Wongsawat, Jurai; Luesomboon, Wicharn; Ngo-Giang-Huong, Nicole; Chettra, Kea; Cheunyam, Theshinee; Suwarnlerk, Tulathip; Ubolyam, Sasiwimol; Shearer, William T.; Paul, Robert; Mofenson, Lynne M.; Fox, Lawrence; Law, Matthew G.;

		Cooper, David A.; Phanuphak, Praphan; Vun, Mean Chhi; Ruxrungtham, Kiat; PREDICT Study Group Early versus deferred antiretroviral therapy for children older than 1 year infected with HIV (PREDICT): a multicentre, randomised, open-label trial. Lancet Infect Dis. 2012;12(12):933-941. doi:10.1016/S1473-3099(12)70242-6
28	Cohen, B. E.; Chang, A. A.; Grady, D.; Kanaya, A. M. Restorative yoga in adults with metabolic syndrome: a randomized, controlled pilot trial. Metab Syndr Relat Disord. 2008;6(3):223-9. doi:10.1089/met.2008.0016	Kanaya, Alka M.; Araneta, Maria Rosario G.; Pawlowsky, Sarah B.; Barrett-Connor, Elizabeth; Grady, Deborah; Vittinghoff, Eric; Schembri, Michael; Chang, Ann; Carrion-Petersen, Mary Lou; Coggins, Traci; Tanori, Daniah; Armas, Jean M.; Cole, Roger J. Restorative yoga and metabolic risk factors: the Practicing Restorative Yoga vs. Stretching for the Metabolic Syndrome (PRYSMS) randomized trial. J Diabetes Complications. 2014;28(3):406-412. doi:10.1016/j.jdiacomp.2013.12.001
29	Cowling, B. J.; Fung, R. O.; Cheng, C. K.; Fang, V. J.; Chan, K. H.; Seto, W. H.; Yung, R.; Chiu, B.; Lee, P.; Uyeki, T. M.; Houck, P. M.; Peiris, J. S.; Leung, G. M. Preliminary findings of a randomized trial of non-pharmaceutical interventions to prevent influenza transmission in households. PLoS One. 2008;3(5):e2101. doi:10.1371/journal.pone.0002101	Cowling, Benjamin J.; Chan, Kwok-Hung; Fang, Vicky J.; Cheng, Calvin K. Y.; Fung, Rita O. P.; Wai, Winnie; Sin, Joey; Seto, Wing Hong; Yung, Raymond; Chu, Daniel W. S.; Chiu, Billy C. F.; Lee, Paco W. Y.; Chiu, Ming Chi; Lee, Hoi Che; Uyeki, Timothy M.; Houck, Peter M.; Peiris, J. S. Malik; Leung, Gabriel M. Facemasks and hand hygiene to prevent influenza transmission in households: a cluster randomized trial. Ann Intern Med. 2009;151(7):437-446. doi:10.7326/0003-4819-151-7-200910060-00142
30	Drexel, H.; Saely, C. H.; Langer, P.; Loruenser, G.; Marte, T.; Risch, L.; Hoefle, G.; Aczel, S. Metabolic and anti-inflammatory benefits of eccentric endurance exercise - a pilot study. Eur J Clin Invest. 2008;38(4):218-26. doi:10.1111/j.1365-2362.2008.01937.x	Drexel, Heinz; Mader, Arthur; Saely, Christoph H.; Tautermann, Gerda; Dopheide, Jörn F.; Vonbank, Alexander Downhill hiking improves low-grade inflammation, triglycerides, body weight and glucose tolerance. Sci Rep. 2021;11(1):14503. doi:10.1038/s41598-021-93879-1
31	Frech, S. A.; Dupont, H. L.; Bourgeois, A. L.; McKenzie, R.; Belkind-Gerson, J.; Figueroa, J. F.; Okhuysen, P. C.; Guerrero, N. H.; Martinez-Sandoval, F. G.; Meléndez-Romero, J. H.; Jiang, Z. D.; Asturias, E. J.; Halpern, J.; Torres, O. R.; Hoffman, A. S.; Villar, C. P.; Kassem, R. N.; Flyer, D. C.; Andersen, B. H.; Kazempour, K.; Breisch, S. A.; Glenn, G. M. Use of a patch containing heat-labile toxin from Escherichia coli against travellers' diarrhoea: a phase II, randomised, double-blind, placebo-controlled field trial. Lancet. 2008;371(9629):2019-25. doi:10.1016/s0140-6736(08)60839-9	Behrens, Ronald H.; Cramer, Jakob P.; Jelinek, Tomas; Shaw, Hilary; von Sonnenburg, Frank; Wilbraham, Darren; Weinke, Thomas; Bell, David J.; Asturias, Edwin; Pauwells, Hermann L. Enkerlin; Maxwell, Roberto; Paredes-Paredes, Mercedes; Glenn, Gregory M.; Dewasthaly, Shailesh; Stablein, Donald M.; Jiang, Zhi-Dong; DuPont, Herbert L. Efficacy and safety of a patch vaccine containing heat-labile toxin from Escherichia coli against travellers' diarrhoea: a phase 3, randomised, double-blind, placebo-controlled field trial in travellers from Europe to Mexico and Guatemala. Lancet Infect Dis. 2014;14(3):197-204. doi:10.1016/S1473-3099(13)70297-4
32	Janicke, David M.; Sallinen, Bethany J.; Perri, Michael G.; Lutes, Lesley D.; Huerta, Milagros; Silverstein, Janet H.; Brumback, Babette Comparison of parent-only vs	Janicke, David M.; Lim, Crystal S.; Perri, Michael G.; Mathews, Anne E.; Bobroff, Linda B.; Gurka, Matthew J.; Parish, Alice; Brumback, Babette A.; Dumont-Driscoll, Marilyn; Silverstein, Janet H.

	family-based interventions for overweight children in underserved rural settings: outcomes from project STORY. Arch Pediatr Adolesc Med. 2008;162(12):1119-1125. doi:10.1001/archpedi.162.12.1119	Featured Article: Behavior Interventions Addressing Obesity in Rural Settings: The E-FLIP for Kids Trial. J Pediatr Psychol. 2019;44(8):889-901. doi:10.1093/jpepsy/jsz029
33	Kennard, B. D.; Emslie, G. J.; Mayes, T. L.; Nightingale-Teresi, J.; Nakonezny, P. A.; Hughes, J. L.; Jones, J. M.; Tao, R.; Stewart, S. M.; Jarrett, R. B. Cognitive-behavioral therapy to prevent relapse in pediatric responders to pharmacotherapy for major depressive disorder. J Am Acad Child Adolesc Psychiatry. 2008;47(12):1395-404. doi:10.1097/CHI.0b013e31818914a1	Kennard, Betsy D.; Emslie, Graham J.; Mayes, Taryn L.; Nakonezny, Paul A.; Jones, Jessica M.; Foxwell, Aleksandra A.; King, Jessica Sequential treatment with fluoxetine and relapse--prevention CBT to improve outcomes in pediatric depression. Am J Psychiatry. 2014;171(10):1083-1090. doi:10.1176/appi.ajp.2014.13111460
34	Lancastle, D.; Boivin, J. A feasibility study of a brief coping intervention (PRCI) for the waiting period before a pregnancy test during fertility treatment. Hum Reprod. 2008;23(10):2299-307. doi:10.1093/humrep/den257	Ockhuijsen, Henrietta; van den Hoogen, Agnes; Eijkemans, Marinus; Macklon, Nick; Boivin, Jacky The impact of a self-administered coping intervention on emotional well-being in women awaiting the outcome of IVF treatment: a randomized controlled trial. Hum Reprod. 2014;29(7):1459-1470. doi:10.1093/humrep/deu093
35	Meeks, S.; Looney, S. W.; Van Haitsma, K.; Teri, L. BE-ACTIV: a staff-assisted behavioral intervention for depression in nursing homes. Gerontologist. 2008;48(1):105-14. doi:10.1093/geront/48.1.105	Meeks, Suzanne; Van Haitsma, Kimberly; Schoenbachler, Ben; Looney, Stephen W. BE-ACTIV for depression in nursing homes: primary outcomes of a randomized clinical trial. J Gerontol B Psychol Sci Soc Sci. 2015;70(1):13-23. doi:10.1093/geronb/gbu026
36	Morone, Natalia E.; Rollman, Bruce L.; Moore, Charity G.; Li, Qin; Weiner, Debra K. A mind-body program for older adults with chronic low back pain: results of a pilot study. Pain Med. 2009;10(8):1395-1407. doi:10.1111/j.1526-4637.2009.00746.x	Morone, Natalia E.; Greco, Carol M.; Moore, Charity G.; Rollman, Bruce L.; Lane, Bridget; Morrow, Lisa A.; Glynn, Nancy W.; Weiner, Debra K. A Mind-Body Program for Older Adults With Chronic Low Back Pain: A Randomized Clinical Trial. JAMA Intern Med. 2016;176(3):329-337. doi:10.1001/jamainternmed.2015.8033
37	Nelson, M. R.; Reid, C. M.; Ames, D. A.; Beilin, L. J.; Donnan, G. A.; Gibbs, P.; Johnston, C. I.; Krum, H.; Storey, E.; Tonkin, A.; Wolfe, R.; Woods, R.; McNeil, J. J. Feasibility of conducting a primary prevention trial of low-dose aspirin for major adverse cardiovascular events in older people in Australia: results from the ASPirin in Reducing Events in the Elderly (ASPREE) pilot study. Med J Aust. 2008;189(2):105-9. doi:10.5694/j.1326-5377.2008.tb01932.x	McNeil, John J.; Woods, Robyn L.; Nelson, Mark R.; Reid, Christopher M.; Kirpach, Brenda; Wolfe, Rory; Storey, Elsdon; Shah, Raj C.; Lockery, Jessica E.; Tonkin, Andrew M.; Newman, Anne B.; Williamson, Jeff D.; Margolis, Karen L.; Ernst, Michael E.; Abhayaratna, Walter P.; Stocks, Nigel; Fitzgerald, Sharyn M.; Orchard, Suzanne G.; Trevaks, Ruth E.; Beilin, Lawrence J.; Donnan, Geoffrey A.; Gibbs, Peter; Johnston, Colin I.; Ryan, Joanne; Radziszewska, Barbara; Grimm, Richard; Murray, Anne M.; ASPREE Investigator Group Effect of Aspirin on Disability-free Survival in the Healthy Elderly. N Engl J Med. 2018;379(16):1499-1508. doi:10.1056/NEJMoa1800722
38	Oh, B.; Butow, P.; Mullan, B.; Clarke, S. Medical Qigong for cancer patients: pilot study of impact on quality of life, side effects of treatment and inflammation. Am J Chin	Oh, B.; Butow, P.; Mullan, B.; Clarke, S.; Beale, P.; Pavlakis, N.; Kothe, E.; Lam, L.; Rosenthal, D. Impact of medical Qigong on quality of life, fatigue, mood and inflammation in cancer patients: a randomized controlled trial. Ann

	Med. 2008;36(3):459-72. doi:10.1142/s0192415x08005904	Oncol. 2010;21(3):608-614. doi:10.1093/annonc/mdp479
39	Park, P.; Simmons, R. K.; Prevost, A. T.; Griffin, S. J. Screening for type 2 diabetes is feasible, acceptable, but associated with increased short-term anxiety: a randomised controlled trial in British general practice. BMC Public Health. 2008;8():350. doi:10.1186/1471-2458-8-350	Simmons, Rebecca K.; Echouffo-Tcheugui, Justin B.; Sharp, Stephen J.; Sargeant, Lincoln A.; Williams, Kate M.; Prevost, A. Toby; Kinmonth, Ann Louise; Wareham, Nicholas J.; Griffin, Simon J. Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): a cluster-randomised controlled trial. Lancet. 2012;380(9855):1741-1748. doi:10.1016/S0140-6736(12)61422-6
40	Ritenbaugh, C.; Hammerschlag, R.; Calabrese, C.; Mist, S.; Aickin, M.; Sutherland, E.; Leben, J.; Debar, L.; Elder, C.; Dworkin, S. F. A pilot whole systems clinical trial of traditional Chinese medicine and naturopathic medicine for the treatment of temporomandibular disorders. J Altern Complement Med. 2008;14(5):475-87. doi:10.1089/acm.2007.0738	Ritenbaugh, Cheryl; Hammerschlag, Richard; Dworkin, Samuel F.; Aickin, Mikel G.; Mist, Scott D.; Elder, Charles R.; Harris, Richard E. Comparative effectiveness of traditional Chinese medicine and psychosocial care in the treatment of temporomandibular disorders-associated chronic facial pain. J Pain. 2012;13(11):1075-1089. doi:10.1016/j.jpain.2012.08.002
41	Sprigg, N.; Gray, L. J.; England, T.; Willmot, M. R.; Zhao, L.; Sare, G. M.; Bath, P. M. A randomised controlled trial of triple antiplatelet therapy (aspirin, clopidogrel and dipyridamole) in the secondary prevention of stroke: safety, tolerability and feasibility. PLoS One. 2008;3(8):e2852. doi:10.1371/journal.pone.0002852	Bath, Philip M.; Woodhouse, Lisa J.; Appleton, Jason P.; Beridze, Maia; Christensen, Hanne; Dineen, Robert A.; Duley, Lelia; England, Timothy J.; Flaherty, Katie; Havard, Diane; Heptinstall, Stan; James, Marilyn; Krishnan, Kailash; Markus, Hugh S.; Montgomery, Alan A.; Pocock, Stuart J.; Randall, Marc; Ranta, Annemarei; Robinson, Thompson G.; Scutt, Polly; Venables, Graham S.; Sprigg, Nikola; TARDIS Investigators Antiplatelet therapy with aspirin, clopidogrel, and dipyridamole versus clopidogrel alone or aspirin and dipyridamole in patients with acute cerebral ischaemia (TARDIS): a randomised, open-label, phase 3 superiority trial. Lancet. 2018;391(10123):850-859. doi:10.1016/S0140-6736(17)32849-0
42	Talmor, D.; Sarge, T.; Malhotra, A.; O'Donnell, C. R.; Ritz, R.; Lisbon, A.; Novack, V.; Loring, S. H. Mechanical ventilation guided by esophageal pressure in acute lung injury. N Engl J Med. 2008;359(20):2095-104. doi:10.1056/NEJMoa0708638	Beitler, Jeremy R.; Sarge, Todd; Banner-Goodspeed, Valerie M.; Gong, Michelle N.; Cook, Deborah; Novack, Victor; Loring, Stephen H.; Talmor, Daniel; EPVent-2 Study Group Effect of Titrating Positive End-Expiratory Pressure (PEEP) With an Esophageal Pressure-Guided Strategy vs an Empirical High PEEP-Fio2 Strategy on Death and Days Free From Mechanical Ventilation Among Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA. 2019;321(9):846-857. doi:10.1001/jama.2019.0555
43	Bakas, Tamilyn; Farran, Carol J.; Austin, Joan K.; Given, Barbara A.; Johnson, Elizabeth A.; Williams, Linda S. Stroke caregiver outcomes from the Telephone Assessment and Skill-Building Kit (TASK). Top Stroke Rehabil. 2009;16(2):105-121. doi:10.1310/tsr1602-105	Bakas, Tamilyn; Austin, Joan K.; Habermann, Barbara; Jessup, Nenette M.; McLennon, Susan M.; Mitchell, Pamela H.; Morrison, Gwendolyn; Yang, Ziyi; Stump, Timothy E.; Weaver, Michael T. Telephone Assessment and Skill-Building Kit for Stroke Caregivers: A Randomized Controlled

		Clinical Trial. Stroke. 2015;46(12):3478-3487. doi:10.1161/STROKEAHA.115.011099
44	Bowen, S.; Chawla, N.; Collins, S. E.; Witkiewitz, K.; Hsu, S.; Grow, J.; Clifasefi, S.; Garner, M.; Douglass, A.; Larimer, M. E.; Marlatt, A. Mindfulness-based relapse prevention for substance use disorders: a pilot efficacy trial. Subst Abus. 2009;30(4):295-305. doi:10.1080/08897070903250084	Bowen, Sarah; Witkiewitz, Katie; Clifasefi, Seema L.; Grow, Joel; Chawla, Neharika; Hsu, Sharon H.; Carroll, Haley A.; Harrop, Erin; Collins, Susan E.; Lustyk, M. Kathleen; Larimer, Mary E. Relative efficacy of mindfulness-based relapse prevention, standard relapse prevention, and treatment as usual for substance use disorders: a randomized clinical trial. JAMA Psychiatry. 2014;71(5):547-556. doi:10.1001/jamapsychiatry.2013.4546
45	Burns, D. S.; Robb, S. L.; Haase, J. E. Exploring the feasibility of a therapeutic music video intervention in adolescents and young adults during stem-cell transplantation. Cancer Nurs. 2009;32(5):E8-e16. doi:10.1097/NCC.0b013e3181a4802c	Robb, Sheri L.; Burns, Debra S.; Stegenga, Kristin A.; Haut, Paul R.; Monahan, Patrick O.; Meza, Jane; Stump, Timothy E.; Cherven, Brooke O.; Docherty, Sharron L.; Hendricks-Ferguson, Verna L.; Kintner, Eileen K.; Haight, Ann E.; Wall, Donna A.; Haase, Joan E. Randomized clinical trial of therapeutic music video intervention for resilience outcomes in adolescents/young adults undergoing hematopoietic stem cell transplant: a report from the Children's Oncology Group. Cancer. 2014;120(6):909-917. doi:10.1002/cncr.28355
46	Chang, Mei-Wei; Nitzke, Susan; Brown, Roger Design and outcomes of a Mothers In Motion behavioral intervention pilot study. J Nutr Educ Behav. 2010;42(3 Suppl):S11-21. doi:10.1016/j.jneb.2010.01.010	Chang, Mei-Wei; Brown, Roger; Nitzke, Susan Results and lessons learned from a prevention of weight gain program for low-income overweight and obese young mothers: Mothers In Motion. BMC Public Health. 2017;17(1):182. doi:10.1186/s12889-017-4109-y
47	Clarke, C. E.; Furmston, A.; Morgan, E.; Patel, S.; Sackley, C.; Walker, M.; Bryan, S.; Wheatley, K. Pilot randomised controlled trial of occupational therapy to optimise independence in Parkinson's disease: the PD OT trial. J Neurol Neurosurg Psychiatry. 2009;80(9):976-8. doi:10.1136/jnnp.2007.138586	Clarke, Carl E.; Patel, Smitaa; Ives, Natalie; Rick, Caroline E.; Dowling, Francis; Woolley, Rebecca; Wheatley, Keith; Walker, Marion F.; Sackley, Catherine M.; PD REHAB Collaborative Group Physiotherapy and Occupational Therapy vs No Therapy in Mild to Moderate Parkinson Disease: A Randomized Clinical Trial. JAMA Neurol. 2016;73(3):291-299. doi:10.1001/jamaneurol.2015.4452
48	Conrozier, T.; Jerosch, J.; Beks, P.; Kemper, F.; Euller-Ziegler, L.; Bailleul, F.; Chevalier, X. Prospective, multi-centre, randomised evaluation of the safety and efficacy of five dosing regimens of viscosupplementation with hylan G-F 20 in patients with symptomatic tibio-femoral osteoarthritis: a pilot study. Arch Orthop Trauma Surg. 2009;129(3):417-23. doi:10.1007/s00402-008-0601-2	Chevalier, X.; Jerosch, J.; Goupille, P.; van Dijk, N.; Luyten, F. P.; Scott, D. L.; Bailleul, F.; Pavelka, K. Single, intra-articular treatment with 6 ml hylan G-F 20 in patients with symptomatic primary osteoarthritis of the knee: a randomised, multicentre, double-blind, placebo controlled trial. Ann Rheum Dis. 2010;69(1):113-119. doi:10.1136/ard.2008.094623
49	DeVito Dabbs, A.; Dew, M. A.; Myers, B.; Begey, A.; Hawkins, R.; Ren, D.; Dunbar-Jacob, J.; Oconnell, E.; McCurry, K. R. Evaluation of a hand-held, computer-based intervention to promote early self-care behaviors after lung transplant. Clin	DeVito Dabbs, A.; Song, M. K.; Myers, B. A.; Li, R.; Hawkins, R. P.; Pilewski, J. M.; Bermudez, C. A.; Aubrecht, J.; Begey, A.; Connolly, M.; Alrawashdeh, M.; Dew, M. A. A Randomized Controlled Trial of a Mobile Health Intervention to Promote Self-Management After Lung

	Transplant. 2009;23(4):537-45. doi:10.1111/j.1399-0012.2009.00992.x	Transplantation. Am J Transplant. 2016;16(7):2172-2180. doi:10.1111/ajt.13701
50	Donaldson, C.; Tallis, R.; Miller, S.; Sunderland, A.; Lemon, R.; Pomeroy, V. Effects of conventional physical therapy and functional strength training on upper limb motor recovery after stroke: a randomized phase II study. Neurorehabil Neural Repair. 2009;23(4):389-97. doi:10.1177/1545968308326635	Hunter, Susan M.; Johansen-Berg, Heidi; Ward, Nick; Kennedy, Niamh C.; Chandler, Elizabeth; Weir, Christopher John; Rothwell, John; Wing, Alan M.; Grey, Michael J.; Barton, Garry; Leavey, Nick Malachy; Havis, Claire; Lemon, Roger N.; Burridge, Jane; Dymond, Amy; Pomeroy, Valerie M. Functional Strength Training and Movement Performance Therapy for Upper Limb Recovery Early Poststroke-Efficacy, Neural Correlates, Predictive Markers, and Cost-Effectiveness: FAST-INdiCATE Trial. Front Neurol. 2017;8():733. doi:10.3389/fneur.2017.00733
51	Free, C.; Whittaker, R.; Knight, R.; Abramsky, T.; Rodgers, A.; Roberts, I. G. Txt2stop: a pilot randomised controlled trial of mobile phone-based smoking cessation support. Tob Control. 2009;18(2):88-91. doi:10.1136/tc.2008.026146	Free, Caroline; Knight, Rosemary; Robertson, Steven; Whittaker, Robyn; Edwards, Phil; Zhou, Weiwei; Rodgers, Anthony; Cairns, John; Kenward, Michael G.; Roberts, Ian Smoking cessation support delivered via mobile phone text messaging (txt2stop): a single-blind, randomised trial. Lancet. 2011;378(9785):49-55. doi:10.1016/S0140-6736(11)60701-0
52	Chappell, Lucy C.; Gurung, Vinita; Seed, Paul T.; Chambers, Jenny; Williamson, Catherine; Thornton, James G.; PITCH Study Consortium Ursodeoxycholic acid versus placebo, and early term delivery versus expectant management, in women with intrahepatic cholestasis of pregnancy: semifactorial randomised clinical trial. BMJ. 2012;344():e3799. doi:10.1136/bmj.e3799	Chappell, Lucy C.; Bell, Jennifer L.; Smith, Anne; Linsell, Louise; Juszczak, Edmund; Dixon, Peter H.; Chambers, Jenny; Hunter, Rachael; Dorling, Jon; Williamson, Catherine; Thornton, Jim G.; PITCHES study group Ursodeoxycholic acid versus placebo in women with intrahepatic cholestasis of pregnancy (PITCHES): a randomised controlled trial. Lancet. 2019;394(10201):849-860. doi:10.1016/S0140-6736(19)31270-X
53	Haug, Severin; Meyer, Christian; Schorr, Gudrun; Bauer, Stephanie; John, Ulrich Continuous individual support of smoking cessation using text messaging: a pilot experimental study. Nicotine Tob Res. 2009;11(8):915-923. doi:10.1093/ntr/ntp084	Haug, Severin; Schaub, Michael P.; Venzin, Vigeli; Meyer, Christian; John, Ulrich Efficacy of a text message-based smoking cessation intervention for young people: a cluster randomized controlled trial. J Med Internet Res. 2013;15(8):e171. doi:10.2196/jmir.2636
54	Lyon, M. E.; Garvie, P. A.; Briggs, L.; He, J.; McCarter, R.; D'Angelo, L. J. Development, feasibility, and acceptability of the Family/Adolescent-Centered (FACE) Advance Care Planning intervention for adolescents with HIV. J Palliat Med. 2009;12(4):363-72. doi:10.1089/jpm.2008.0261	Dallas, Ronald H.; Kimmel, Allison; Wilkins, Megan L.; Rana, Sohail; Garcia, Ana; Cheng, Yao I.; Wang, Jichuan; Lyon, Maureen E.; Adolescent Palliative Care Consortium. Acceptability of Family-Centered Advanced Care Planning for Adolescents With HIV. Pediatrics. 2016;138(6):e20161854. doi:10.1542/peds.2016-1854
55	Murphy, D. J.; MacGregor, H.; Munishankar, B.; McLeod, G. A randomised controlled trial of oxytocin 5IU and placebo infusion versus oxytocin 5IU and 30IU infusion for the control of blood loss at elective caesarean section--pilot study. ISRCTN 40302163. Eur J Obstet Gynecol Reprod Biol. 2009;142(1):30-3. doi:10.1016/j.ejogrb.2008.09.004	Sheehan, Sharon R.; Montgomery, Alan A.; Carey, Michael; McAuliffe, Fionnuala M.; Eogan, Maeve; Gleeson, Ronan; Geary, Michael; Murphy, Deirdre J.; ECSSIT Study Group Oxytocin bolus versus oxytocin bolus and infusion for control of blood loss at elective caesarean section: double blind, placebo controlled, randomised trial. BMJ. 2011;343():d4661. doi:10.1136/bmj.d4661

56	Naar-King, Sylvie; Wright, Kathryn; Parsons, Jeffrey T.; Frey, Maureen; Templin, Thomas; Lam, Phebe; Murphy, Debra Healthy choices: motivational enhancement therapy for health risk behaviors in HIV-positive youth. AIDS Educ Prev. 2006;18(1):44937. doi:10.1521/aeap.2006.18.1.1	Naar-King, Sylvie; Parsons, Jeffrey T.; Murphy, Debra A.; Chen, Xinguang; Harris, D. Robert; Belzer, Marvin E. Improving health outcomes for youth living with the human immunodeficiency virus: a multisite randomized trial of a motivational intervention targeting multiple risk behaviors. Arch Pediatr Adolesc Med. 2009;163(12):1092-1098. doi:10.1001/archpediatrics.2009.212
57	Ni Mhurchu, C.; Roberts, V.; Maddison, R.; Dorey, E.; Jiang, Y.; Jull, A.; Tin Tin, S. Effect of electronic time monitors on children's television watching: pilot trial of a home-based intervention. Prev Med. 2009;49(5):413-7. doi:10.1016/j.ypmed.2009.09.003	Maddison, Ralph; Marsh, Samantha; Foley, Louise; Epstein, Leonard H.; Olds, Timothy; Dewes, Ofa; Heke, Ihirangi; Carter, Karen; Jiang, Yannan; Mhurchu, Cliona Ni Screen-Time Weight-loss Intervention Targeting Children at Home (SWITCH): a randomized controlled trial. Int J Behav Nutr Phys Act. 2014;11():111. doi:10.1186/s12966-014-0111-2
58	Pekmezi, D. W.; Neighbors, C. J.; Lee, C. S.; Gans, K. M.; Bock, B. C.; Morrow, K. M.; Marquez, B.; Dunsiger, S.; Marcus, B. H. A culturally adapted physical activity intervention for Latinas: a randomized controlled trial. Am J Prev Med. 2009;37(6):495-500. doi:10.1016/j.amepre.2009.08.023	Marcus, Bess H.; Dunsiger, Shira I.; Pekmezi, Dorothy W.; Larsen, Britta A.; Bock, Beth C.; Gans, Kim M.; Marquez, Becky; Morrow, Kathleen M.; Tilkemeier, Peter The Seamos Saludables study: A randomized controlled physical activity trial of Latinas. Am J Prev Med. 2013;45(5):598-605. doi:10.1016/j.amepre.2013.07.006
59	Quagliarello, V.; Juthani-Mehta, M.; Ginter, S.; Towle, V.; Allore, H.; Tinetti, M. Pilot testing of intervention protocols to prevent pneumonia in nursing home residents. J Am Geriatr Soc. 2009;57(7):1226-31. doi:10.1111/j.1532-5415.2009.02311.x	Juthani-Mehta, Manisha; Van Ness, Peter H.; McGloin, Joanne; Argraves, Stephanie; Chen, Shu; Charpentier, Peter; Miller, Laura; Williams, Kathleen; Wall, Diane; Baker, Dorothy; Tinetti, Mary; Peduzzi, Peter; Quagliarello, Vincent J. A cluster-randomized controlled trial of a multicomponent intervention protocol for pneumonia prevention among nursing home elders. Clin Infect Dis. 2015;60(6):849-857. doi:10.1093/cid/ciu935
60	Rogers, L. Q.; Hopkins-Price, P.; Vicari, S.; Pamenter, R.; Courneya, K. S.; Markwell, S.; Verhulst, S.; Hoelzer, K.; Naritoku, C.; Jones, L.; Dunnington, G.; Lanzotti, V.; Wynstra, J.; Shah, L.; Edson, B.; Graff, A.; Lowy, M. A randomized trial to increase physical activity in breast cancer survivors. Med Sci Sports Exerc. 2009;41(4):935-46. doi:10.1249/MSS.0b013e31818e0e1b	Rogers, Laura Q.; Courneya, Kerry S.; Anton, Philip M.; Hopkins-Price, Patricia; Verhulst, Steven; Vicari, Sandra K.; Robbs, Randall S.; Mocharnuk, Robert; McAuley, Edward Effects of the BEAT Cancer physical activity behavior change intervention on physical activity, aerobic fitness, and quality of life in breast cancer survivors: a multicenter randomized controlled trial. Breast Cancer Res Treat. 2015;149(1):109-119. doi:10.1007/s10549-014-3216-z
61	Ruokonen, E.; Parviainen, I.; Jakob, S. M.; Nunes, S.; Kaukonen, M.; Shepherd, S. T.; Sarapohja, T.; Bratty, J. R.; Takala, J. Dexmedetomidine versus propofol/midazolam for long-term sedation during mechanical ventilation. Intensive Care Med. 2009;35(2):282-90. doi:10.1007/s00134-008-1296-0	Jakob, Stephan M.; Ruokonen, Esko; Grounds, R. Michael; Sarapohja, Toni; Garratt, Chris; Pocock, Stuart J.; Bratty, J. Raymond; Takala, Jukka; Dexmedetomidine for Long-Term Sedation Investigators Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA. 2012;307(11):1151-1160. doi:10.1001/jama.2012.304

62	Saper, R. B.; Sherman, K. J.; Cullum-Dugan, D.; Davis, R. B.; Phillips, R. S.; Culpepper, L. Yoga for chronic low back pain in a predominantly minority population: a pilot randomized controlled trial. Altern Ther Health Med. 2009;15(6):18-27. doi:	Saper, Robert B.; Lemaster, Chelsey; Delitto, Anthony; Sherman, Karen J.; Herman, Patricia M.; Sadikova, Ekaterina; Stevans, Joel; Keosaian, Julia E.; Cerrada, Christian J.; Femia, Alexandra L.; Roseen, Eric J.; Gardiner, Paula; Gergen Barnett, Katherine; Faulkner, Carol; Weinberg, Janice Yoga, Physical Therapy, or Education for Chronic Low Back Pain: A Randomized Noninferiority Trial. Ann Intern Med. 2017;167(2):85-94. doi:10.7326/M16-2579
63	Schroer, S.; Macpherson, H. Acupuncture, or non-directive counselling versus usual care for the treatment of depression: a pilot study. Trials. 2009;10():3. doi:10.1186/1745-6215-10-3	MacPherson, Hugh; Richmond, Stewart; Bland, Martin; Brealey, Stephen; Gabe, Rhian; Hopton, Ann; Keding, Ada; Lansdown, Harriet; Perren, Sara; Sculpher, Mark; Spackman, Eldon; Torgerson, David; Watt, Ian Acupuncture and counselling for depression in primary care: a randomised controlled trial. PLoS Med. 2013;10(9):e1001518. doi:10.1371/journal.pmed.1001518
64	Schuppert, H. M.; Giesen-Bloo, J.; van Gemert, T. G.; Wiersema, H. M.; Minderaa, R. B.; Emmelkamp, P. M.; Nauta, M. H. Effectiveness of an emotion regulation group training for adolescents--a randomized controlled pilot study. Clin Psychol Psychother. 2009;16(6):467-78. doi:10.1002/cpp.637	Schuppert, H. Marieke; Timmerman, Marieke E.; Bloo, Josephine; van Gemert, Tonny G.; Wiersema, Herman M.; Minderaa, Ruud B.; Emmelkamp, Paul M. G.; Nauta, Maaike H. Emotion regulation training for adolescents with borderline personality disorder traits: a randomized controlled trial. J Am Acad Child Adolesc Psychiatry. 2012;51(12):1314-1323.e2. doi:10.1016/j.jaac.2012.09.002
65	Song, M. K.; Ward, S. E.; Happ, M. B.; Piraino, B.; Donovan, H. S.; Shields, A. M.; Connolly, M. C. Randomized controlled trial of SPIRIT: an effective approach to preparing African-American dialysis patients and families for end of life. Res Nurs Health. 2009;32(3):260-73. doi:10.1002/nur.20320	Song, Mi-Kyung; Ward, Sandra E.; Fine, Jason P.; Hanson, Laura C.; Lin, Feng-Chang; Hladik, Gerald A.; Hamilton, Jill B.; Bridgman, Jessica C. Advance care planning and end-of-life decision making in dialysis: a randomized controlled trial targeting patients and their surrogates. Am J Kidney Dis. 2015;66(5):813-822. doi:10.1053/j.ajkd.2015.05.018
66	Weigensberg, M. J.; Lane, C. J.; Winners, O.; Wright, T.; Nguyen-Rodriguez, S.; Goran, M. I.; Spruijt-Metz, D. Acute effects of stress-reduction Interactive Guided Imagery(SM) on salivary cortisol in overweight Latino adolescents. J Altern Complement Med. 2009;15(3):297-303. doi:10.1089/acm.2008.0156	Weigensberg, Marc J.; Àvila, Quintila; Spruijt-Metz, Donna; Davis, Jaimie N.; Wen, Cheng K. F.; Goodman, Kim; Perdomo, Marisa; Wadé, Niquelle Brown; Ding, Li; Lane, Christianne J. Imagine HEALTH: Randomized Controlled Trial of a Guided Imagery Lifestyle Intervention to Improve Obesity-Related Lifestyle Behaviors in Predominantly Latinx Adolescents. J Altern Complement Med. 2021;27(9):738-749. doi:10.1089/acm.2020.0515
67	Williams, Kimberly; Abildso, Christiaan; Steinberg, Lois; Doyle, Edward; Epstein, Beverly; Smith, David; Hobbs, Gerry; Gross, Richard; Kelley, George; Cooper, Linda Evaluation of the effectiveness and efficacy of Iyengar yoga therapy on chronic low back pain. Spine (Phila Pa 1976). 2009;34(19):2066-2076. doi:10.1097/BRS.0b013e3181b315cc	Williams, Kimberly; Abildso, Christiaan; Steinberg, Lois; Doyle, Edward; Epstein, Beverly; Smith, David; Hobbs, Gerry; Gross, Richard; Kelley, George; Cooper, Linda Evaluation of the effectiveness and efficacy of Iyengar yoga therapy on chronic low back pain. Spine (Phila Pa 1976). 2009;34(19):2066-2076. doi:10.1097/BRS.0b013e3181b315cc

68	Harrison, James D.; Young, Jane M.; Solomon, Michael J.; Butow, Phyllis N.; Secomb, Robyn; Masya, Lindy Randomized pilot evaluation of the supportive care intervention "CONNECT" for people following surgery for colorectal cancer. Dis Colon Rectum. 2011;54(5):622-631. doi:10.1007/DCR.0b013e31820bc152	Young, Jane M.; Butow, Phyllis N.; Walsh, Jennifer; Durcinoska, Ivana; Dobbins, Timothy A.; Rodwell, Laura; Harrison, James D.; White, Kate; Gilmore, Andrew; Hodge, Bruce; Hicks, Henry; Smith, Stephen; O'Connor, Geoff; Byrne, Christopher M.; Meagher, Alan P.; Jancewicz, Stephen; Sutherland, Andrew; Ctercteko, Grahame; Pathma-Nathan, Nimalan; Curtin, Austin; Townend, David; Abraham, Ned S.; Longfield, Greg; Rangiah, David; Young, Christopher J.; Eyers, Anthony; Lee, Peter; Fisher, Dean; Solomon, Michael J. Multicenter randomized trial of centralized nurse-led telephone-based care coordination to improve outcomes after surgical resection for colorectal cancer: the CONNECT intervention. J Clin Oncol. 2013;31(28):3585-3591. doi:10.1200/JCO.2012.48.1036
69	Sur, Ranjan; Donde, Bernard; Falkson, Conrad; Ahmed, Sheikh Nisar; Levin, Victor; Nag, Subir; Wong, Raimond; Jones, Glenn Randomized prospective study comparing high-dose-rate intraluminal brachytherapy (HDRILBT) alone with HDRILBT and external beam radiotherapy in the palliation of advanced esophageal cancer. Brachytherapy. 2004;3(4):191-195. doi:10.1016/j.brachy.2004.09.004	Rosenblatt, Eduardo; Jones, Glenn; Sur, Ranjan K.; Donde, Bernard; Salvajoli, Joao V.; Ghosh-Laskar, Sarbani; Frobe, Ana; Suleiman, Ahmed; Xiao, Zefen; Nag, Subir Adding external beam to intra-luminal brachytherapy improves palliation in obstructive squamous cell oesophageal cancer: a prospective multi-centre randomized trial of the International Atomic Energy Agency. Radiother Oncol. 2010;97(3):488-494. doi:10.1016/j.radonc.2010.09.001
70	Hess, Erik P.; Knoedler, Meghan A.; Shah, Nilay D.; Kline, Jeffrey A.; Breslin, Maggie; Branda, Megan E.; Pencille, Laurie J.; Asplin, Brent R.; Nestler, David M.; Sadosty, Annie T.; Stiell, Ian G.; Ting, Henry H.; Montori, Victor M. The chest pain choice decision aid: a randomized trial. Circ Cardiovasc Qual Outcomes. 2012;5(3):251-259. doi:10.1161/CIRCOUTCOMES.111.964791	Hess, Erik P.; Hollander, Judd E.; Schaffer, Jason T.; Kline, Jeffrey A.; Torres, Carlos A.; Diercks, Deborah B.; Jones, Russell; Owen, Kelly P.; Meisel, Zachary F.; Demers, Michel; Leblanc, Annie; Shah, Nilay D.; Inselman, Jonathan; Herrin, Jeph; Castaneda-Guarderas, Ana; Montori, Victor M. Shared decision making in patients with low risk chest pain: prospective randomized pragmatic trial. BMJ. 2016;355():i6165. doi:10.1136/bmj.i6165
71	Oviedo-Joekes, E.; Guh, D.; Brissette, S.; Marsh, D. C.; Nosyk, B.; Krausz, M.; Anis, A.; Schechter, M. T. Double-blind injectable hydromorphone versus diacetylmorphine for the treatment of opioid dependence: a pilot study. J Subst Abuse Treat. 2010;38(4):408-11. doi:10.1016/j.jsat.2010.03.003	Oviedo-Joekes, Eugenia; Guh, Daphne; Brissette, Suzanne; Marchand, Kirsten; MacDonald, Scott; Lock, Kurt; Harrison, Scott; Janmohamed, Amin; Anis, Aslam H.; Krausz, Michael; Marsh, David C.; Schechter, Martin T. Hydromorphone Compared With Diacetylmorphine for Long-term Opioid Dependence: A Randomized Clinical Trial. JAMA Psychiatry. 2016;73(5):447-455. doi:10.1001/jamapsychiatry.2016.0109
72	Moore, Simon C.; Murphy, Simon; Moore, Susan N.; Brennan, Iain; Byrne, Ellie; Shepherd, Jonathan; Moore, Laurence An exploratory randomised controlled trial of a premises-level intervention to reduce alcohol-related harm including violence in the United Kingdom. BMC Public Health.	Moore, Simon C.; Alam, M. Fasihul; Heikkinen, Marjukka; Hood, Kerenza; Huang, Chao; Moore, Laurence; Murphy, Simon; Playle, Rebecca; Shepherd, Jonathan; Shovelton, Claire; Sivarajasingam, Vaseekaran; Williams, Anne The effectiveness of an intervention to reduce alcohol-related violence in premises licensed for the sale and on-site consumption of alcohol: a

	2012;12():412. doi:10.1186/1471-2458-12-412	randomized controlled trial. Addiction. 2017;112(11):1898-1906. doi:10.1111/add.13878
73	Malekzadeh, F.; Marshall, T.; Pourshams, A.; Gharravi, M.; Aslani, A.; Nateghi, A.; Rastegarpanah, M.; Khoshnia, M.; Semnani, S.; Salahi, R.; Thomas, G. N.; Larijani, B.; Cheng, K. K.; Malekzadeh, R. A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy ('polypill') on cardiovascular risk factors. Int J Clin Pract. 2010;64(9):1220-7. doi:10.1111/j.1742-1241.2010.02412.x	Roshandel, Gholamreza; Khoshnia, Masoud; Poustchi, Hossein; Hemming, Karla; Kamangar, Farin; Gharavi, Abdolsamad; Ostovaneh, Mohammad Reza; Nateghi, Alireza; Majed, Masoud; Navabakhsh, Behrooz; Merat, Shahin; Pourshams, Akram; Nalini, Mahdi; Malekzadeh, Fatemeh; Sadeghi, Masoumeh; Mohammadifard, Noushin; Sarrafzadegan, Nizal; Naemi-Tabiei, Mohammad; Fazel, Abdolreza; Brennan, Paul; Etemadi, Arash; Boffetta, Paolo; Thomas, Neil; Marshall, Tom; Cheng, Kar Keung; Malekzadeh, Reza Effectiveness of polypill for primary and secondary prevention of cardiovascular diseases (PolyIran): a pragmatic, cluster-randomised trial. Lancet. 2019;394(10199):672-683. doi:10.1016/S0140-6736(19)31791-X
74	Reynolds, Julie A.; Bland, J. Martin; MacPherson, Hugh Acupuncture for irritable bowel syndrome an exploratory randomised controlled trial. Acupunct Med. 2008;26(1):45154. doi:10.1136/aim.26.1.8	MacPherson, Hugh; Tilbrook, Helen; Bland, J. Martin; Bloor, Karen; Brabyn, Sally; Cox, Helen; Kang'ombe, Arthur Ricky; Man, Mei-See; Stuardi, Tracy; Torgerson, David; Watt, Ian; Whorwell, Peter Acupuncture for irritable bowel syndrome: primary care based pragmatic randomised controlled trial. BMC Gastroenterol. 2012;12():150. doi:10.1186/1471-230X-12-150
75	Gokee LaRose, J.; Tate, D. F.; Gorin, A. A.; Wing, R. R. Preventing weight gain in young adults: a randomized controlled pilot study. Am J Prev Med. 2010;39(1):63-8. doi:10.1016/j.amepre.2010.03.011	Wing, Rena R.; Tate, Deborah F.; Espeland, Mark A.; Lewis, Cora E.; LaRose, Jessica Gokee; Gorin, Amy A.; Bahnson, Judy; Perdue, Letitia H.; Hatley, Karen E.; Ferguson, Erica; Garcia, Katelyn R.; Lang, Wei; Study of Novel Approaches to Weight Gain Prevention (SNAP) Research Group Innovative Self-Regulation Strategies to Reduce Weight Gain in Young Adults: The Study of Novel Approaches to Weight Gain Prevention (SNAP) Randomized Clinical Trial. JAMA Intern Med. 2016;176(6):755-762. doi:10.1001/jamainternmed.2016.1236
76	Fulkerson, J. A.; Rydell, S.; Kubik, M. Y.; Lytle, L.; Boutelle, K.; Story, M.; Neumark-Sztainer, D.; Dudovitz, B.; Garwick, A. Healthy Home Offerings via the Mealtime Environment (HOME): feasibility, acceptability, and outcomes of a pilot study. Obesity (Silver Spring). 2010;18 Suppl 1(Suppl 1):S69-74. doi:10.1038/oby.2009.434	Fulkerson, Jayne A.; Friend, Sarah; Horning, Melissa; Flattum, Colleen; Draxten, Michelle; Neumark-Sztainer, Dianne; Gurvich, Olga; Garwick, Ann; Story, Mary; Kubik, Martha Y. Family Home Food Environment and Nutrition-Related Parent and Child Personal and Behavioral Outcomes of the Healthy Home Offerings via the Mealtime Environment (HOME) Plus Program: A Randomized Controlled Trial. J Acad Nutr Diet. 2018;118(2):240-251. doi:10.1016/j.jand.2017.04.006
77	Fjeldsoe, B. S.; Miller, Y. D.; Marshall, A. L. MobileMums: a randomized controlled trial of an SMS-based physical activity intervention. Ann Behav Med. 2010;39(2):101-11. doi:10.1007/s12160-010-9170-z	Fjeldsoe, Brianna S.; Miller, Yvette D.; Graves, Nicholas; Barnett, Adrian G.; Marshall, Alison L. Randomized Controlled Trial of an Improved Version of MobileMums, an Intervention for Increasing Physical Activity in Women with Young Children. Ann Behav Med.

		2015;49(4):487-499. doi:10.1007/s12160-014-9675-y
78	Da, Dudley; Ad, Okely; P, Pearson; J, Peat Engaging adolescent girls from linguistically diverse and low income backgrounds in school sport: a pilot randomised controlled trial. . 2010;13(2):. doi:10.1016/j.jsams.2009.04.008	Dudley, Dean A.; Okely, Anthony D.; Pearson, Philip; Peat, Jennifer Engaging adolescent girls from linguistically diverse and low income backgrounds in school sport: a pilot randomised controlled trial. J Sci Med Sport. 2010;13(2):217-224. doi:10.1016/j.jsams.2009.04.008
79	Druss, B. G.; Zhao, L.; von Esenwein, S. A.; Bona, J. R.; Fricks, L.; Jenkins-Tucker, S.; Sterling, E.; Diclemente, R.; Lorig, K. The Health and Recovery Peer (HARP) Program: a peer-led intervention to improve medical self-management for persons with serious mental illness. Schizophr Res. 2010;118(44929):264-70. doi:10.1016/j.schres.2010.01.026	Druss, Benjamin G.; Singh, Manasvini; von Esenwein, Silke A.; Glick, Gretl E.; Tapscott, Stephanie; Tucker, Sherry Jenkins; Lally, Cathy A.; Sterling, Evelina W. Peer-Led Self-Management of General Medical Conditions for Patients With Serious Mental Illnesses: A Randomized Trial. Psychiatr Serv. 2018;69(5):529-535. doi:10.1176/appi.ps.201700352
80	Cook, P. F.; Bremer, R. W.; Ayala, A. J.; Kahook, M. Y. Feasibility of motivational interviewing delivered by a glaucoma educator to improve medication adherence. Clin Ophthalmol. 2010;4():1091-101. doi:10.2147/opth.S12765	Cook, Paul F.; Schmiege, Sarah J.; Mansberger, Steven L.; Sheppler, Christina; Kammer, Jeffrey; Fitzgerald, Timothy; Kahook, Malik Y. Motivational interviewing or reminders for glaucoma medication adherence: Results of a multi-site randomised controlled trial. Psychol Health. 2017;32(2):145-165. doi:10.1080/08870446.2016.1244537
81	Clemson, L.; Singh, M. F.; Bundy, A.; Cumming, R. G.; Weissel, E.; Munro, J.; Manollaras, K.; Black, D. LiFE Pilot Study: A randomised trial of balance and strength training embedded in daily life activity to reduce falls in older adults. Aust Occup Ther J. 2010;57(1):42-50. doi:10.1111/j.1440-1630.2009.00848.x	Clemson, Lindy; Fiatarone Singh, Maria A.; Bundy, Anita; Cumming, Robert G.; Manollaras, Kate; O'Loughlin, Patricia; Black, Deborah Integration of balance and strength training into daily life activity to reduce rate of falls in older people (the LiFE study): randomised parallel trial. BMJ. 2012;345():e4547. doi:10.1136/bmj.e4547
82	Breitbart, W.; Rosenfeld, B.; Gibson, C.; Pessin, H.; Poppito, S.; Nelson, C.; Tomarken, A.; Timm, A. K.; Berg, A.; Jacobson, C.; Sorger, B.; Abbey, J.; Olden, M. Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. Psychooncology. 2010;19(1):21-8. doi:10.1002/pon.1556	Breitbart, William; Rosenfeld, Barry; Pessin, Hayley; Applebaum, Allison; Kulikowski, Julia; Lichtenthal, Wendy G. Meaning-centered group psychotherapy: an effective intervention for improving psychological well-being in patients with advanced cancer. J Clin Oncol. 2015;33(7):749-754. doi:10.1200/JCO.2014.57.2198
83	Bogner, H. R.; de Vries, H. F. Integrating type 2 diabetes mellitus and depression treatment among African Americans: a randomized controlled pilot trial. Diabetes Educ. 2010;36(2):284-92. doi:10.1177/0145721709356115	Bogner, Hillary R.; Morales, Knashawn H.; de Vries, Heather F.; Cappola, Anne R. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. Ann Fam Med. 2012;10(1):15-22. doi:10.1370/afm.1344
84	Bleidorn, Jutta; Gágyor, Ildikó; Kochen, Michael M.; Wegscheider, Karl; Hummers-Pradier, Eva Symptomatic treatment (ibuprofen) or antibiotics (ciprofloxacin) for uncomplicated urinary tract infection?--results of a randomized controlled pilot trial.	Gágyor, Ildikó; Bleidorn, Jutta; Kochen, Michael M.; Schmiemann, Guido; Wegscheider, Karl; Hummers-Pradier, Eva Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial. BMJ. 2015;351():h6544. doi:10.1136/bmj.h6544

	BMC Med. 2010;8():30. doi:10.1186/1741-7015-8-30	
85	Barton, R.; English, A.; Nabb, S.; Rigby, A. S.; Johnson, M. J. A randomised trial of high vs low intensity training in breathing techniques for breathless patients with malignant lung disease: a feasibility study. Lung Cancer. 2010;70(3):313-9. doi:10.1016/j.lungcan.2010.03.007	Johnson, Miriam J.; Kanaan, Mona; Richardson, Gerry; Nabb, Samantha; Torgerson, David; English, Anne; Barton, Rachael; Booth, Sara A randomised controlled trial of three or one breathing technique training sessions for breathlessness in people with malignant lung disease. BMC Med. 2015;13():213. doi:10.1186/s12916-015-0453-x
86	Ackermann, R. T.; Finch, E. A.; Caffrey, H. M.; Lipscomb, E. R.; Hays, L. M.; Saha, C. Long-term effects of a community-based lifestyle intervention to prevent type 2 diabetes: the DEPLOY extension pilot study. Chronic Illn. 2011;7(4):279-90. doi:10.1177/1742395311407532	Ackermann, Ronald T.; Liss, David T.; Finch, Emily A.; Schmidt, Karen K.; Hays, Laura M.; Marrero, David G.; Saha, Chandan A Randomized Comparative Effectiveness Trial for Preventing Type 2 Diabetes. Am J Public Health. 2015;105(11):2328-2334. doi:10.2105/AJPH.2015.302641
87	Chang, J. Y.; Talley, N. J.; Locke, G. R., 3rd; Katzka, D. A.; Schleck, C. D.; Zinsmeister, A. R.; Dunagan, K. T.; Wu, T. T.; Wang, K. K.; Prasad, G. A. Population screening for barrett esophagus: a prospective randomized pilot study. Mayo Clin Proc. 2011;86(12):1174-80. doi:10.4065/mcp.2011.0396	Sami, Sarmed S.; Dunagan, Kelly T.; Johnson, Michele L.; Schleck, Cathy D.; Shah, Nilay D.; Zinsmeister, Alan R.; Wongkeesong, Louis-Michel; Wang, Kenneth K.; Katzka, David A.; Ragunath, Krish; Iyer, Prasad G. A randomized comparative effectiveness trial of novel endoscopic techniques and approaches for Barrett's esophagus screening in the community. Am J Gastroenterol. 2015;110(1):148-158. doi:10.1038/ajg.2014.362
88	Cho, H.; Hallfors, D. D.; Mbai, II; Itindi, J.; Milimo, B. W.; Halpern, C. T.; Iritani, B. J. Keeping adolescent orphans in school to prevent human immunodeficiency virus infection: evidence from a randomized controlled trial in Kenya. J Adolesc Health. 2011;48(5):523-6. doi:10.1016/j.jadohealth.2010.08.007	Cho, Hyunsan; Mbai, Isabella; Luseno, Winnie Kavulani; Hobbs, Marcia; Halpern, Carolyn; Hallfors, Denise Dion School Support as Structural HIV Prevention for Adolescent Orphans in Western Kenya. J Adolesc Health. 2018;62(1):44-51. doi:10.1016/j.jadohealth.2017.07.015
89	Davis, A. M.; James, R. L.; Boles, R. E.; Goetz, J. R.; Belmont, J.; Malone, B. The use of TeleMedicine in the treatment of paediatric obesity: feasibility and acceptability. Matern Child Nutr. 2011;7(1):71-9. doi:10.1111/j.1740-8709.2010.00248.x	Davis, Ann McGrath; Sampilo, Marilyn; Gallagher, Katherine Steiger; Landrum, Yasuko; Malone, Brett Treating rural pediatric obesity through telemedicine: outcomes from a small randomized controlled trial. J Pediatr Psychol. 2013;38(9):932-943. doi:10.1093/jpepsy/jst005
90	Duncan, S.; McPhee, J. C.; Schluter, P. J.; Zinn, C.; Smith, R.; Schofield, G. Efficacy of a compulsory homework programme for increasing physical activity and healthy eating in children: the healthy homework pilot study. Int J Behav Nutr Phys Act. 2011;8():127. doi:10.1186/1479-5868-8-127	Duncan, Scott; Stewart, Tom; McPhee, Julia; Borotkanics, Robert; Prendergast, Kate; Zinn, Caryn; Meredith-Jones, Kim; Taylor, Rachael; McLachlan, Claire; Schofield, Grant Efficacy of a compulsory homework programme for increasing physical activity and improving nutrition in children: a cluster randomised controlled trial. Int J Behav Nutr Phys Act. 2019;16(1):80. doi:10.1186/s12966-019-0840-3
91	Ferrara, A.; Hedderson, M. M.; Albright, C. L.; Ehrlich, S. F.; Quesenberry, C. P., Jr.; Peng, T.; Feng, J.; Ching, J.; Crites, Y. A pregnancy and postpartum lifestyle	Ferrara, Assiamira; Hedderson, Monique M.; Brown, Susan D.; Albright, Cheryl L.; Ehrlich, Samantha F.; Tsai, Ai-Lin; Caan, Bette J.; Sternfeld, Barbara; Gordon, Nancy P.;

	intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial. Diabetes Care. 2011;34(7):1519-25. doi:10.2337/dc10-2221	Schmittdiel, Julie A.; Gunderson, Erica P.; Mevi, Ashley A.; Herman, William H.; Ching, Jenny; Crites, Yvonne; Quesenberry, Charles P. The Comparative Effectiveness of Diabetes Prevention Strategies to Reduce Postpartum Weight Retention in Women With Gestational Diabetes Mellitus: The Gestational Diabetes' Effects on Moms (GEM) Cluster Randomized Controlled Trial. Diabetes Care. 2016;39(1):65-74. doi:10.2337/dc15-1254
92	Hamann, J.; Mendel, R.; Meier, A.; Asani, F.; Pausch, E.; Leucht, S.; Kissling, W. "How to speak to your psychiatrist": shared decision-making training for inpatients with schizophrenia. Psychiatr Serv. 2011;62(10):1218-21. doi:10.1176/ps.62.10.pss6210_1218	Hamann, Johannes; Parchmann, Anna; Sassenberg, Nina; Bronner, Katharina; Albus, Margot; Richter, Alwin; Hoppstock, Sandra; Kissling, Werner Training patients with schizophrenia to share decisions with their psychiatrists: a randomized-controlled trial. Soc Psychiatry Psychiatr Epidemiol. 2017;52(2):175-182. doi:10.1007/s00127-016-1327-z
93	Akerblom, H. K.; Virtanen, S. M.; Ilonen, J.; Savilahti, E.; Vaarala, O.; Reunanen, A.; Teramo, K.; Hämäläinen, A.-M.; Paronen, J.; Riikjärv, M.-A.; Ormisson, A.; Ludvigsson, J.; Dosch, H.-M.; Hakulinen, T.; Knip, M.; National TRIGR Study Groups Dietary manipulation of beta cell autoimmunity in infants at increased risk of type 1 diabetes: a pilot study. Diabetologia. 2005;48(5):829-837. doi:10.1007/s00125-005-1733-3	Knip, Mikael; Åkerblom, Hans K.; Becker, Dorothy; Dosch, Hans-Michael; Dupre, John; Fraser, William; Howard, Neville; Ilonen, Jorma; Krischer, Jeffrey P.; Kordonouri, Olga; Lawson, Margaret L.; Palmer, Jerry P.; Savilahti, Erkki; Vaarala, Outi; Virtanen, Suvi M.; TRIGR Study Group Hydrolyzed infant formula and early β-cell autoimmunity: a randomized clinical trial. JAMA. 2014;311(22):2279-2287. doi:10.1001/jama.2014.5610
94	Kramer, U.; Berger, T.; Kolly, S.; Marquet, P.; Preisig, M.; de Roten, Y.; Despland, J. N.; Caspar, F. Effects of motive-oriented therapeutic relationship in early-phase treatment of borderline personality disorder: a pilot study of a randomized trial. J Nerv Ment Dis. 2011;199(4):244-50. doi:10.1097/NMD.0b013e3182125d19	Kramer, Ueli; Kolly, Stéphane; Berthoud, Laurent; Keller, Sabine; Preisig, Martin; Caspar, Franz; Berger, Thomas; de Roten, Yves; Marquet, Pierre; Despland, Jean-Nicolas Effects of motive-oriented therapeutic relationship in a ten-session general psychiatric treatment of borderline personality disorder: a randomized controlled trial. Psychother Psychosom. 2014;83(3):176-186. doi:10.1159/000358528
95	Légaré, F.; Labrecque, M.; LeBlanc, A.; Njoya, M.; Laurier, C.; Côté, L.; Godin, G.; Thivierge, R. L.; O'Connor, A.; St-Jacques, S. Training family physicians in shared decision making for the use of antibiotics for acute respiratory infections: a pilot clustered randomized controlled trial. Health Expect. 2011;14 Suppl 1(Suppl 1):96-110. doi:10.1111/j.1369-7625.2010.00616.x	Légaré, France; Labrecque, Michel; Cauchon, Michel; Castel, Josette; Turcotte, Stéphane; Grimshaw, Jeremy Training family physicians in shared decision-making to reduce the overuse of antibiotics in acute respiratory infections: a cluster randomized trial. CMAJ. 2012;184(13):E726-734. doi:10.1503/cmaj.120568
96	Miller, E.; Decker, M. R.; McCauley, H. L.; Tancredi, D. J.; Levenson, R. R.; Waldman, J.; Schoenwald, P.; Silverman, J. G. A family planning clinic partner violence intervention to reduce risk associated with reproductive coercion. Contraception. 2011;83(3):274-80. doi:10.1016/j.contraception.2010.07.013	Miller, Elizabeth; Tancredi, Daniel J.; Decker, Michele R.; McCauley, Heather L.; Jones, Kelley A.; Anderson, Heather; James, Lisa; Silverman, Jay G. A family planning clinic-based intervention to address reproductive coercion: a cluster randomized controlled trial. Contraception. 2016;94(1):58-67. doi:10.1016/j.contraception.2016.02.009
97	Murphy, Susan L.; Lyden, Angela K.; Smith, Dylan M.; Dong, Qian; Koliba, Jessica F.	Murphy, Susan L.; Kratz, Anna L.; Kidwell, Kelley; Lyden, Angela K.; Geisser, Michael E.;

	Effects of a tailored activity pacing intervention on pain and fatigue for adults with osteoarthritis. Am J Occup Ther. 2010;64(6):869-876. doi:10.5014/ajot.2010.09198	Williams, David A. Brief time-based activity pacing instruction as a singular behavioral intervention was not effective in participants with symptomatic osteoarthritis. Pain. 2016;157(7):1563-1573. doi:10.1097/j.pain.0000000000000549
98	Cotter, Gad; Dittrich, Howard C.; Weatherley, Beth Davison; Bloomfield, Daniel M.; O'Connor, Christopher M.; Metra, Marco; Massie, Barry M.; Protect Steering Committee, Investigators, and Coordinators The PROTECT pilot study: a randomized, placebo-controlled, dose-finding study of the adenosine A1 receptor antagonist rolofylline in patients with acute heart failure and renal impairment. J Card Fail. 2008;14(8):631-640. doi:10.1016/j.cardfail.2008.08.010	Massie, Barry M.; O'Connor, Christopher M.; Metra, Marco; Ponikowski, Piotr; Teerlink, John R.; Cotter, Gad; Weatherley, Beth Davison; Cleland, John G. F.; Givertz, Michael M.; Voors, Adriaan; DeLucca, Paul; Mansoor, George A.; Salerno, Christina M.; Bloomfield, Daniel M.; Dittrich, Howard C.; PROTECT Investigators and Committees Rolofylline, an adenosine A1-receptor antagonist, in acute heart failure. N Engl J Med. 2010;363(15):1419-1428. doi:10.1056/NEJMoa0912613
99	Russell, C.; Conn, V.; Ashbaugh, C.; Madsen, R.; Wakefield, M.; Webb, A.; Coffey, D.; Peace, L. Taking immunosuppressive medications effectively (TIMELink): a pilot randomized controlled trial in adult kidney transplant recipients. Clin Transplant. 2011;25(6):864-70. doi:10.1111/j.1399-0012.2010.01358.x	Russell, Cynthia L.; Hathaway, Donna; Remy, Laura M.; Aholt, Dana; Clark, Debra; Miller, Courtney; Ashbaugh, Catherine; Wakefield, Mark; Ye, Sangbeak; Staggs, Vincent S.; Ellis, Rebecca J.; Goggin, Kathy Improving medication adherence and outcomes in adult kidney transplant patients using a personal systems approach: SystemCHANGE™ results of the MAGIC randomized clinical trial. Am J Transplant. 2020;20(1):125-136. doi:10.1111/ajt.15528
100	Szanton, S. L.; Thorpe, R. J.; Boyd, C.; Tanner, E. K.; Leff, B.; Agree, E.; Xue, Q. L.; Allen, J. K.; Seplaki, C. L.; Weiss, C. O.; Guralnik, J. M.; Gitlin, L. N. Community aging in place, advancing better living for elders: a bio-behavioral-environmental intervention to improve function and health-related quality of life in disabled older adults. J Am Geriatr Soc. 2011;59(12):2314-20. doi:10.1111/j.1532-5415.2011.03698.x	Szanton, Sarah L.; Xue, Qian-Li; Leff, Bruce; Guralnik, Jack; Wolff, Jennifer L.; Tanner, Elizabeth K.; Boyd, Cynthia; Thorpe, Roland J.; Bishai, David; Gitlin, Laura N. Effect of a Biobehavioral Environmental Approach on Disability Among Low-Income Older Adults: A Randomized Clinical Trial. JAMA Intern Med. 2019;179(2):204-211. doi:10.1001/jamainternmed.2018.6026
101	Ter Heide, F. J.; Mooren, T. M.; Kleijn, W.; de Jongh, A.; Kleber, R. J. EMDR versus stabilisation in traumatised asylum seekers and refugees: results of a pilot study. Eur J Psychotraumatol. 2011;2():. doi:10.3402/ejpt.v2i0.5881	Ter Heide, F. Jackie June; Mooren, Trudy M.; van de Schoot, Rens; de Jongh, Ad; Kleber, Rolf J. Eye movement desensitisation and reprocessing therapy v. stabilisation as usual for refugees: randomised controlled trial. Br J Psychiatry. 2016;209(4):311-318. doi:10.1192/bjp.bp.115.167775
102	Thorn, B. E.; Day, M. A.; Burns, J.; Kuhajda, M. C.; Gaskins, S. W.; Sweeney, K.; McConley, R.; Ward, C. L.; Cabbil, C. Randomized trial of group cognitive behavioral therapy compared with a pain education control for low-literacy rural people with chronic pain. Pain. 2011;152(12):2710-2720. doi:10.1016/j.pain.2011.07.007	Thorn, Beverly E.; Eyer, Joshua C.; Van Dyke, Benjamin P.; Torres, Calia A.; Burns, John W.; Kim, Minjung; Newman, Andrea K.; Campbell, Lisa C.; Anderson, Brian; Block, Phoebe R.; Bobrow, Bentley J.; Brooks, Regina; Burton, Toya T.; Cheavens, Jennifer S.; DeMonte, Colette M.; DeMonte, William D.; Edwards, Crystal S.; Jeong, Minjeong; Mulla, Mazheruddin M.; Penn, Terence; Smith, Laura J.; Tucker, Deborah H. Literacy-Adapted Cognitive Behavioral Therapy Versus Education for

		Chronic Pain at Low-Income Clinics: A Randomized Controlled Trial. Ann Intern Med. 2018;168(7):471-480. doi:10.7326/M17-0972
103	Seivewright, Helen; Green, John; Salkovskis, Paul; Barrett, Barbara; Nur, Ula; Tyrer, Peter Cognitive-behavioural therapy for health anxiety in a genitourinary medicine clinic: randomised controlled trial. Br J Psychiatry. 2008;193(4):332-337. doi:10.1192/bjp.bp.108.052936	Tyrer, Peter; Salkovskis, Paul; Tyrer, Helen; Wang, Duolao; Crawford, Michael J.; Dupont, Simon; Cooper, Sylvia; Green, John; Murphy, David; Smith, Georgina; Bhogal, Sharandeep; Nourmand, Shaeda; Lazarevic, Valentina; Loebenberg, Gemma; Evered, Rachel; Kings, Stephanie; McNulty, Antoinette; Lisseman-Stones, Yvonne; McAllister, Sharon; Kramo, Kofi; Nagar, Jessica; Reid, Steven; Sanatinia, Rahil; Whittamore, Katherine; Walker, Gemma; Philip, Aaron; Warwick, Hilary; Byford, Sarah; Barrett, Barbara Cognitive-behaviour therapy for health anxiety in medical patients (CHAMP): a randomised controlled trial with outcomes to 5 years. Health Technol Assess. 2017;21(50):21186. doi:10.3310/hta21500
104	Vera, M.; Reyes-Rabanillo, M. L.; Juarbe, D.; Pérez-Pedrogo, C.; Olmo, A.; Kichic, R.; Chaplin, W. F. Prolonged exposure for the treatment of Spanish-speaking Puerto Ricans with posttraumatic stress disorder: a feasibility study. BMC Res Notes. 2011;4():415. doi:10.1186/1756-0500-4-415	Vera, Mildred; Obén, Adriana; Juarbe, Deborah; Hernández, Norberto; Kichic, Rafael; Hembree, Elizabeth A. A randomized clinical trial of prolonged exposure and applied relaxation for the treatment of Latinos with posttraumatic stress disorder. J Trauma Stress. 2022;35(2):593-604. doi:10.1002/jts.22773
105	Anderson, Craig S.; Huang, Yining; Wang, Ji Guang; Arima, Hisatomi; Neal, Bruce; Peng, Bin; Heeley, Emma; Skulina, Christian; Parsons, Mark W.; Kim, Jong Sung; Tao, Qing Ling; Li, Yue Chun; Jiang, Jian Dong; Tai, Li Wen; Zhang, Jin Li; Xu, En; Cheng, Yan; Heritier, Stephane; Morgenstern, Lewis B.; Chalmers, John; INTERACT Investigators Intensive blood pressure reduction in acute cerebral haemorrhage trial (INTERACT): a randomised pilot trial. Lancet Neurol. 2008;7(5):391-399. doi:10.1016/S1474-4422(08)70069-3	Anderson, Craig S.; Heeley, Emma; Huang, Yining; Wang, Jiguang; Stapf, Christian; Delcourt, Candice; Lindley, Richard; Robinson, Thompson; Lavados, Pablo; Neal, Bruce; Hata, Jun; Arima, Hisatomi; Parsons, Mark; Li, Yuechun; Wang, Jinchao; Heritier, Stephane; Li, Qiang; Woodward, Mark; Simes, R. John; Davis, Stephen M.; Chalmers, John; INTERACT2 Investigators Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med. 2013;368(25):2355-2365. doi:10.1056/NEJMoa1214609
106	Burrow-Sanchez, J. J.; Wrona, M. Comparing culturally accommodated versus standard group CBT for Latino adolescents with substance use disorders: a pilot study. Cultur Divers Ethnic Minor Psychol. 2012;18(4):373-383. doi:10.1037/a0029439	Burrow-Sánchez, Jason J.; Minami, Takuya; Hops, Hyman Cultural accommodation of group substance abuse treatment for Latino adolescents: Results of an RCT. Cultur Divers Ethnic Minor Psychol. 2015;21(4):571-583. doi:10.1037/cdp0000023
107	Citro, A.; Cantarelli, E.; Maffi, P.; Nano, R.; Melzi, R.; Mercalli, A.; Dugnani, E.; Sordi, V.; Magistretti, P.; Daffonchio, L.; Ruffini, P. A.; Allegretti, M.; Secchi, A.; Bonifacio, E.; Piemonti, L. CXCR1/2 inhibition enhances pancreatic islet survival after transplantation. J Clin Invest. 2012;122(10):3647-51. doi:10.1172/jci63089	Maffi, Paola; Lundgren, Torbjörn; Tufveson, Gunnar; Rafael, Ehab; Shaw, James A. M.; Liew, Aaron; Saudek, Frantisek; Witkowski, Piotr; Golab, Karolina; Bertuzzi, Federico; Gustafsson, Bengt; Daffonchio, Luisa; Ruffini, Pier Adelchi; Piemonti, Lorenzo; REP0211 Study Group Targeting CXCR1/2 Does Not Improve Insulin Secretion After Pancreatic Islet Transplantation: A Phase 3, Double-Blind, Randomized, Placebo-Controlled Trial in Type 1 Diabetes. Diabetes

		Care. 2020;43(4):710-718. doi:10.2337/dc19-1480
108	Diacon, A. H.; Donald, P. R.; Pym, A.; Grobusch, M.; Patientia, R. F.; Mahanyele, R.; Bantubani, N.; Narasimooloo, R.; De Marez, T.; van Heeswijk, R.; Lounis, N.; Meyvisch, P.; Andries, K.; McNeeley, D. F. Randomized pilot trial of eight weeks of bedaquiline (TMC207) treatment for multidrug-resistant tuberculosis: long-term outcome, tolerability, and effect on emergence of drug resistance. Antimicrob Agents Chemother. 2012;56(6):3271-6. doi:10.1128/aac.06126-11	Diacon, Andreas H.; Pym, Alexander; Grobusch, Martin P.; de los Rios, Jorge M.; Gotuzzo, Eduardo; Vasilyeva, Irina; Leimane, Vaira; Andries, Koen; Bakare, Nyasha; De Marez, Tine; Haxaire-Theeuwes, Myriam; Lounis, Nacer; Meyvisch, Paul; De Paepe, Els; van Heeswijk, Rolf P. G.; Dannemann, Brian; TMC207-C208 Study Group Multidrug-resistant tuberculosis and culture conversion with bedaquiline. N Engl J Med. 2014;371(8):723-732. doi:10.1056/NEJMoa1313865
109	Greer, Joseph A.; Traeger, Lara; Bemis, Heather; Solis, Jessica; Hendriksen, Ellen S.; Park, Elyse R.; Pirl, William F.; Temel, Jennifer S.; Prigerson, Holly G.; Safren, Steven A. A pilot randomized controlled trial of brief cognitive-behavioral therapy for anxiety in patients with terminal cancer. Oncologist. 2012;17(10):1337-1345. doi:10.1634/theoncologist.2012-0041	Greer, Joseph A.; Jacobs, Jamie; Pensak, Nicole; MacDonald, James J.; Fuh, Charn-Xin; Perez, Giselle K.; Ward, Alina; Tallen, Colleen; Muzikansky, Alona; Traeger, Lara; Penedo, Frank J.; El-Jawahri, Areej; Safren, Steven A.; Pirl, William F.; Temel, Jennifer S. Randomized Trial of a Tailored Cognitive-Behavioral Therapy Mobile Application for Anxiety in Patients with Incurable Cancer. Oncologist. 2019;24(8):1111-1120. doi:10.1634/theoncologist.2018-0536
110	Grossmann, R. E.; Zughaier, S. M.; Kumari, M.; Seydafkan, S.; Lyles, R. H.; Liu, S.; Sueblinvong, V.; Schechter, M. S.; Stecenko, A. A.; Ziegler, T. R.; Tangpricha, V. Pilot study of vitamin D supplementation in adults with cystic fibrosis pulmonary exacerbation: A randomized, controlled trial. Dermatoendocrinol. 2012;4(2):191-7. doi:10.4161/derm.20332	Tangpricha, Vin; Lukemire, Joshua; Chen, Yuqing; Binongo, José Nilo G.; Judd, Suzanne E.; Michalski, Ellen S.; Lee, Moon J.; Walker, Seth; Ziegler, Thomas R.; Tirouvanziam, Rabin; Zughaier, Susu M.; Chesdachai, Supavit; Hermes, Wendy A.; Chmiel, James F.; Grossmann, Ruth E.; Gaggar, Amit; Joseph, Patricia M.; Alvarez, Jessica A. Vitamin D for the Immune System in Cystic Fibrosis (DISC): a double-blind, multicenter, randomized, placebo-controlled clinical trial. Am J Clin Nutr. 2019;109(3):544-553. doi:10.1093/ajcn/nqy291
111	Jago, R.; Sebire, S. J.; Cooper, A. R.; Haase, A. M.; Powell, J.; Davis, L.; McNeill, J.; Montgomery, A. A. Bristol girls dance project feasibility trial: outcome and process evaluation results. Int J Behav Nutr Phys Act. 2012;9():83. doi:10.1186/1479-5868-9-83	Jago, Russell; Edwards, Mark J.; Sebire, Simon J.; Tomkinson, Keeley; Bird, Emma L.; Banfield, Kathryn; May, Thomas; Kesten, Joanna M.; Cooper, Ashley R.; Powell, Jane E.; Blair, Peter S. Effect and cost of an after-school dance programme on the physical activity of 11-12 year old girls: The Bristol Girls Dance Project, a school-based cluster randomised controlled trial. Int J Behav Nutr Phys Act. 2015;12():128. doi:10.1186/s12966-015-0289-y
112	Jerosch-Herold, C.; Shepstone, L.; Miller, L. Sensory relearning after surgical treatment for carpal tunnel syndrome: a pilot clinical trial. Muscle Nerve. 2012;46(6):885-90. doi:10.1002/mus.23421	Jerosch-Herold, C.; Houghton, J.; Miller, L.; Shepstone, L. Does sensory relearning improve tactile function after carpal tunnel decompression? A pragmatic, assessor-blinded, randomized clinical trial. J Hand Surg Eur Vol. 2016;41(9):948-956. doi:10.1177/1753193416657760
113	Kolko, D. J.; Campo, J. V.; Kilbourne, A. M.; Kelleher, K. Doctor-office collaborative care for pediatric behavioral problems: a	Kolko, David J.; Campo, John; Kilbourne, Amy M.; Hart, Jonathan; Sakolsky, Dara; Wisniewski, Stephen Collaborative care outcomes for

	preliminary clinical trial. Arch Pediatr Adolesc Med. 2012;166(3):224-31. doi:10.1001/archpediatrics.2011.201	pediatric behavioral health problems: a cluster randomized trial. Pediatrics. 2014;133(4):e981-992. doi:10.1542/peds.2013-2516
114	Kwekkeboom, Kristine L.; Abbott-Anderson, Kristen; Cherwin, Catherine; Roiland, Rachel; Serlin, Ronald C.; Ward, Sandra E. Pilot randomized controlled trial of a patient-controlled cognitive-behavioral intervention for the pain, fatigue, and sleep disturbance symptom cluster in cancer. J Pain Symptom Manage. 2012;44(6):810-822. doi:10.1016/j.jpainsymman.2011.12.281	Kwekkeboom, Kristine; Zhang, Yingzi; Campbell, Toby; Coe, Christopher L.; Costanzo, Erin; Serlin, Ronald C.; Ward, Sandra Randomized controlled trial of a brief cognitive-behavioral strategies intervention for the pain, fatigue, and sleep disturbance symptom cluster in advanced cancer. Psychooncology. 2018;27(12):2761-2769. doi:10.1002/pon.4883
115	Lauche, R.; Wübbeling, K.; Lüdtke, R.; Cramer, H.; Choi, K. E.; Rampp, T.; Michalsen, A.; Langhorst, J.; Dobos, G. J. Randomized controlled pilot study: pain intensity and pressure pain thresholds in patients with neck and low back pain before and after traditional East Asian "gua sha" therapy. Am J Chin Med. 2012;40(5):905-17. doi:10.1142/s0192415x1250067x	Saha, Felix J.; Brummer, Gianna; Lauche, Romy; Ostermann, Thomas; Choi, Kyung-Eun; Rampp, Thomas; Dobos, Gustav; Cramer, Holger Gua Sha therapy for chronic low back pain: A randomized controlled trial. Complement Ther Clin Pract. 2019;34():64-69. doi:10.1016/j.ctcp.2018.11.002
116	O'Neil, S.; Coulton, S.; Deluca, P.; Deverill, M.; Drummond, C.; Gilvarry, E.; Graybill, E.; Harle, C.; Howel, D.; Kaner, E.; McArdle, P.; McColl, E.; McGovern, R.; Speed, C.; Stamp, E.; Tate, L.; Newbury-Birch, D. Brief intervention to prevent hazardous drinking in young people aged 14-15 in a high school setting (SIPS JR-HIGH): study protocol for a randomized controlled trial. Trials. 2012;13():166. doi:10.1186/1745-6215-13-166	Giles, Emma L.; McGeechan, Grant J.; Coulton, Simon; Deluca, Paolo; Drummond, Colin; Howel, Denise; Kaner, Eileen; McColl, Elaine; McGovern, Ruth; Scott, Stephanie; Stamp, Elaine; Sumnall, Harry; Todd, Liz; Vale, Luke; Albani, Viviana; Boniface, Sadie; Ferguson, Jennifer; Gilvarry, Eilish; Hendrie, Nadine; Howe, Nicola; Mossop, Helen; Ramsay, Amy; Stanley, Grant; Newbury-Birch, Dorothy Brief alcohol intervention for risky drinking in young people aged 14–15 years in secondary schools: the SIPS JR-HIGH RCT. . 2019;():. doi:
117	Price, Cynthia J.; Wells, Elizabeth A.; Donovan, Dennis M.; Rue, Tessa Mindful awareness in body-oriented therapy as an adjunct to women's substance use disorder treatment: a pilot feasibility study. J Subst Abuse Treat. 2012;43(1):94-107. doi:10.1016/j.jsat.2011.09.016	Price, Cynthia J.; Thompson, Elaine A.; Crowell, Sheila E.; Pike, Kenneth; Cheng, Sunny C.; Parent, Sara; Hooven, Carole Immediate effects of interoceptive awareness training through Mindful Awareness in Body-oriented Therapy (MABT) for women in substance use disorder treatment. Subst Abus. 2019;40(1):102-115. doi:10.1080/08897077.2018.1488335
118	Sheeber, L. B.; Seeley, J. R.; Feil, E. G.; Davis, B.; Sorensen, E.; Kosty, D. B.; Lewinsohn, P. M. Development and pilot evaluation of an Internet-facilitated cognitive-behavioral intervention for maternal depression. J Consult Clin Psychol. 2012;80(5):739-749. doi:10.1037/a0028820	Sheeber, Lisa B.; Feil, Edward G.; Seeley, John R.; Leve, Craig; Gau, Jeff M.; Davis, Betsy; Sorensen, Erik; Allan, Steve Mom-net: Evaluation of an internet-facilitated cognitive behavioral intervention for low-income depressed mothers. J Consult Clin Psychol. 2017;85(4):355-366. doi:10.1037/ccp0000175
119	Tegeler, C. H.; Kumar, S. R.; Conklin, D.; Lee, S. W.; Gerdes, L.; Turner, D. P.; Tegeler, C. L.; B, C. Fidali; Houle, T. T. Open label, randomized, crossover pilot trial of high-resolution, relational, resonance-based, electroencephalic mirroring to relieve insomnia. Brain Behav. 2012;2(6):814-24. doi:10.1002/brb3.101	Tegeler, Catherine L.; Shaltout, Hossam A.; Lee, Sung W.; Simpson, Sean L.; Gerdes, Lee; Tegeler, Charles H. High-resolution, relational, resonance-based, electroencephalic mirroring (HIRREM) improves symptoms and autonomic function for insomnia: A randomized, placebo-controlled clinical trial. Brain Behav. 2020;10(11):e01826. doi:10.1002/brb3.1826

120	Shah, Sarwat; Ainsworth, Hannah; Fairhurst, Caroline; Tilbrook, Helen; Sheikh, Aziz; Amos, Amanda; Parrott, Steve; Torgerson, David; Thompson, Heather; King, Rebecca; Mir, Ghazala; Siddiqi, Kamran Muslim communities learning about second-hand smoke: a pilot cluster randomised controlled trial and cost-effectiveness analysis. NPJ Prim Care Respir Med. 2015;25():15052. doi:10.1038/npjpcrm.2015.52	Mdege, Noreen Dadirai; Fairhurst, Caroline; Wang, Han-I.; Ferdous, Tarana; Marshall, Anna-Marie; Hewitt, Catherine; Huque, Rumana; Jackson, Cath; Kellar, Ian; Parrott, Steve; Semple, Sean; Sheikh, Aziz; Wu, Qi; Azdi, Zunayed Al; Siddiqi, Kamran; MCLASS II trial team Efficacy and cost-effectiveness of a community-based smoke-free-home intervention with or without indoor-air-quality feedback in Bangladesh (MCLASS II): a three-arm, cluster-randomised, controlled trial. Lancet Glob Health. 2021;9(5):e639-e650. doi:10.1016/S2214-109X(21)00040-1
121	Ankolekar, S.; Fuller, M.; Cross, I.; Renton, C.; Cox, P.; Sprigg, N.; Siriwardena, A. N.; Bath, P. M. Feasibility of an ambulance-based stroke trial, and safety of glyceryl trinitrate in ultra-acute stroke: the rapid intervention with glyceryl trinitrate in Hypertensive Stroke Trial (RIGHT, ISRCTN66434824). Stroke. 2013;44(11):3120-8. doi:10.1161/strokeaha.113.001301	RIGHT-2 Investigators Prehospital transdermal glyceryl trinitrate in patients with ultra-acute presumed stroke (RIGHT-2): an ambulance-based, randomised, sham-controlled, blinded, phase 3 trial. Lancet. 2019;393(10175):1009-1020. doi:10.1016/S0140-6736(19)30194-1
122	Apter, A. J.; Wan, F.; Reisine, S.; Bogen, D. K.; Rand, C.; Bender, B.; Bennett, I. M.; Gonzalez, R.; Priolo, C.; Sonnad, S. S.; Bryant-Stephens, T.; Ferguson, M.; Boyd, R. C.; Ten Have, T.; Roy, J. Feasibility, acceptability and preliminary effectiveness of patient advocates for improving asthma outcomes in adults. J Asthma. 2013;50(8):850-60. doi:10.3109/02770903.2013.812655	Apter, Andrea J.; Perez, Luzmercy; Han, Xiaoyan; Ndicu, Grace; Localio, Anna; Park, Hami; Mullen, Alyssa N.; Klusaritz, Heather; Rogers, Marisa; Cidav, Zuleyha; Bryant-Stephens, Tyra; Bender, Bruce G.; Reisine, Susan T.; Morales, Knashawn H. Patient Advocates for Low-Income Adults with Moderate to Severe Asthma: A Randomized Clinical Trial. J Allergy Clin Immunol Pract. 2020;8(10):3466-3473.e11. doi:10.1016/j.jaip.2020.06.058
123	Barnett, A. G.; Lucas, M.; Platts, D.; Whiting, E.; Fraser, J. F. The benefits of thermal clothing during winter in patients with heart failure: a pilot randomised controlled trial. BMJ Open. 2013;3(4):. doi:10.1136/bmjopen-2013-002799	Barnett, Adrian Gerard; Stewart, Ian; Beevers, Andrea; Fraser, John F.; Platts, David Thermal clothing to reduce heart failure morbidity during winter: a randomised controlled trial. BMJ Open. 2017;7(10):e017592. doi:10.1136/bmjopen-2017-017592
124	Bricker, J.; Wyszynski, C.; Comstock, B.; Heffner, J. L. Pilot randomized controlled trial of web-based acceptance and commitment therapy for smoking cessation. Nicotine Tob Res. 2013;15(10):1756-64. doi:10.1093/ntr/ntt056	Bricker, Jonathan B.; Mull, Kristin E.; McClure, Jennifer B.; Watson, Noreen L.; Heffner, Jaimee L. Improving quit rates of web-delivered interventions for smoking cessation: full-scale randomized trial of WebQuit.org versus Smokefree.gov. Addiction. 2018;113(5):914-923. doi:10.1111/add.14127
125	Carter, A. M.; Daley, A. J.; Kesterton, S. W.; Woodroofe, N. M.; Saxton, J. M.; Sharrack, B. Pragmatic exercise intervention in people with mild to moderate multiple sclerosis: a randomised controlled feasibility study. Contemp Clin Trials. 2013;35(2):40-7. doi:10.1016/j.cct.2013.04.003	Carter, A.; Daley, A.; Humphreys, L.; Snowdon, N.; Woodroofe, N.; Petty, J.; Roalfe, A.; Tosh, J.; Sharrack, B.; Saxton, J. M. Pragmatic intervention for increasing self-directed exercise behaviour and improving important health outcomes in people with multiple sclerosis: a randomised controlled trial. Mult Scler. 2014;20(8):1112-1122. doi:10.1177/1352458513519354

126	Cavanagh, K.; Strauss, C.; Cicconi, F.; Griffiths, N.; Wyper, A.; Jones, F. A randomised controlled trial of a brief online mindfulness-based intervention. Behav Res Ther. 2013;51(9):573-8. doi:10.1016/j.brat.2013.06.003	Cavanagh, Kate; Churchard, Alasdair; O'Hanlon, Puffin; Mundy, Thomas; Votolato, Phoebe; Jones, Fergal; Gu, Jenny; Strauss, Clara A Randomised Controlled Trial of a Brief Online Mindfulness-Based Intervention in a Non-clinical Population: Replication and Extension. Mindfulness (N Y). 2018;9(4):1191-1205. doi:10.1007/s12671-017-0856-1
127	Cormie, P.; Newton, R. U.; Spry, N.; Joseph, D.; Taaffe, D. R.; Galvão, D. A. Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. Prostate Cancer Prostatic Dis. 2013;16(4):328-35. doi:10.1038/pcan.2013.22	Galvão, Daniel A.; Taaffe, Dennis R.; Spry, Nigel; Cormie, Prue; Joseph, David; Chambers, Suzanne K.; Chee, Raphael; Peddle-McIntyre, Carolyn J.; Hart, Nicolas H.; Baumann, Freerk T.; Denham, James; Baker, Michael; Newton, Robert U. Exercise Preserves Physical Function in Prostate Cancer Patients with Bone Metastases. Med Sci Sports Exerc. 2018;50(3):393-399. doi:10.1249/MSS.0000000000001454
128	Crawley, E.; Mills, N.; Beasant, L.; Johnson, D.; Collin, S. M.; Deans, Z.; White, K.; Montgomery, A. The feasibility and acceptability of conducting a trial of specialist medical care and the Lightning Process in children with chronic fatigue syndrome: feasibility randomized controlled trial (SMILE study). Trials. 2013;14():415. doi:10.1186/1745-6215-14-415	Crawley, Esther M.; Gaunt, Daisy M.; Garfield, Kirsty; Hollingworth, William; Sterne, Jonathan A. C.; Beasant, Lucy; Collin, Simon M.; Mills, Nicola; Montgomery, Alan A. Clinical and cost-effectiveness of the Lightning Process in addition to specialist medical care for paediatric chronic fatigue syndrome: randomised controlled trial. Arch Dis Child. 2018;103(2):155-164. doi:10.1136/archdischild-2017-313375
129	de Bruin, E. D.; van Het Reve, E.; Murer, K. A randomized controlled pilot study assessing the feasibility of combined motor-cognitive training and its effect on gait characteristics in the elderly. Clin Rehabil. 2013;27(3):215-25. doi:10.1177/0269215512453352	van het Reve, Eva; de Bruin, Eling D. Strength-balance supplemented with computerized cognitive training to improve dual task gait and divided attention in older adults: a multicenter randomized-controlled trial. BMC Geriatr. 2014;14():134. doi:10.1186/1471-2318-14-134
130	Van Voorhees, Benjamin W.; Vanderplough-Booth, Karen; Fogel, Joshua; Gladstone, Tracy; Bell, Carl; Stuart, Scott; Gollan, Jackie; Bradford, Nathan; Domanico, Rocco; Fagan, Blake; Ross, Ruth; Larson, Jon; Watson, Natalie; Paunesku, Dave; Melkonian, Stephanie; Kuwabara, Sachiko; Holper, Tim; Shank, Nicholas; Saner, Donald; Butler, Amy; Chandler, Amy; Louie, Tina; Weinstein, Cynthia; Collins, Shannon; Baldwin, Melinda; Wassel, Abigail; Reinecke, Mark A. Integrative internet-based depression prevention for adolescents: a randomized clinical trial in primary care for vulnerability and protective factors. J Can Acad Child Adolesc Psychiatry. 2008;17(4):184-196. doi:	Van Voorhees, Benjamin; Gladstone, Tracy R. G.; Sobowale, Kunmi; Brown, C. Hendricks; Aaby, David A.; Terrizzi, Daniela A.; Canel, Jason; Ching, Eumene; Berry, Anita D.; Cantorna, James; Eder, Milton; Beardslee, William; Fitzgibbon, Marian; Marko-Holguin, Monika; Schiffer, Linda; Lee, Miae; de Forest, Sarah A.; Sykes, Emily E.; Suor, Jennifer H.; Crawford, Theodore J.; Burkhouse, Katie L.; Goodwin, Brady C.; Bell, Carl 24-Month Outcomes of Primary Care Web-Based Depression Prevention Intervention in Adolescents: Randomized Clinical Trial. J Med Internet Res. 2020;22(10):e16802. doi:10.2196/16802
131	Fabrizio, C. S.; Lam, T. H.; Hirschmann, M. R.; Stewart, S. M. A Brief Parenting Intervention to Enhance the Parent-Child Relationship in Hong Kong: Harmony@Home. J Child Fam Stud.	Fabrizio, Cecilia S.; Stewart, Sunita M.; Ip, Alison K. Y.; Lam, Tai Hing Enhancing the parent-child relationship: a Hong Kong community-based randomized controlled trial. J Fam Psychol. 2014;28(1):42-53. doi:10.1037/a0035275

	2013;22(5):603-613. doi:10.1007/s10826-012-9614-0	
132	Gray, C. M.; Hunt, K.; Mutrie, N.; Anderson, A. S.; Treweek, S.; Wyke, S. Weight management for overweight and obese men delivered through professional football clubs: a pilot randomized trial. Int J Behav Nutr Phys Act. 2013;10():121. doi:10.1186/1479-5868-10-121	Hunt, Kate; Wyke, Sally; Gray, Cindy M.; Anderson, Annie S.; Brady, Adrian; Bunn, Christopher; Donnan, Peter T.; Fenwick, Elisabeth; Grieve, Eleanor; Leishman, Jim; Miller, Euan; Mutrie, Nanette; Rauchhaus, Petra; White, Alan; Treweek, Shaun A gender-sensitised weight loss and healthy living programme for overweight and obese men delivered by Scottish Premier League football clubs (FFIT): a pragmatic randomised controlled trial. Lancet. 2014;383(9924):1211-1221. doi:10.1016/S0140-6736(13)62420-4
133	Lasser, Karen E.; Kenst, Karey S.; Quintiliani, Lisa M.; Wiener, Renda Soylemez; Murillo, Jennifer; Pbert, Lori; Xuan, Ziming; Bowen, Deborah J. Patient navigation to promote smoking cessation among low-income primary care patients: a pilot randomized controlled trial. J Ethn Subst Abuse. 2013;12(4):374-390. doi:10.1080/15332640.2013.819311	Lasser, Karen E.; Quintiliani, Lisa M.; Truong, Ve; Xuan, Ziming; Murillo, Jennifer; Jean, Cheryl; Pbert, Lori Effect of Patient Navigation and Financial Incentives on Smoking Cessation Among Primary Care Patients at an Urban Safety-Net Hospital: A Randomized Clinical Trial. JAMA Intern Med. 2017;177(12):1798-1807. doi:10.1001/jamainternmed.2017.4372
134	Leahey TM, Wing RR. A randomized controlled pilot study testing three types of health coaches for obesity treatment: Professional, peer, and mentor. Obesity (Silver Spring). 2013;21(5):928-934. doi:10.1002/oby.20271	Leahey, Tricia M.; Huedo-Medina, Tania B.; Grenga, Andrea; Gay, Linda; Fernandes, Denise; Denmat, Zeely; Doyle, Caroline; Areny-Joval, Remei; Wing, Rena R. Patient-provided e-support in reduced intensity obesity treatment: The INSPIRE randomized controlled trial. Health Psychol. 2020;39(12):1037-1047. doi:10.1037/hea0000996
135	Lee, T. S.; Goh, S. J.; Quek, S. Y.; Phillips, R.; Guan, C.; Cheung, Y. B.; Feng, L.; Teng, S. S.; Wang, C. C.; Chin, Z. Y.; Zhang, H.; Ng, T. P.; Lee, J.; Keefe, R.; Krishnan, K. R. A brain-computer interface based cognitive training system for healthy elderly: a randomized control pilot study for usability and preliminary efficacy. PLoS One. 2013;8(11):e79419. doi:10.1371/journal.pone.0079419	Yeo, Si Ning; Lee, Tih Shih; Sng, Wei Theng; Heo, Min Quan; Bautista, Dianne; Cheung, Yin Bun; Zhang, Hai Hong; Wang, Chuanchu; Chin, Zheng Yang; Feng, Lei; Zhou, Juan; Chong, Mei Sian; Ng, Tze Pin; Krishnan, K. Ranga; Guan, Cuntai Effectiveness of a Personalized Brain-Computer Interface System for Cognitive Training in Healthy Elderly: A Randomized Controlled Trial. J Alzheimers Dis. 2018;66(1):127-138. doi:10.3233/JAD-180450
136	Lin, P. R.; Zhao, Z. W.; Cheng, K. K.; Lam, T. H. The effect of physician's 30 s smoking cessation intervention for male medical outpatients: a pilot randomized controlled trial. J Public Health (Oxf). 2013;35(3):375-83. doi:10.1093/pubmed/fdt018	Cheung, Yee Tak Derek; Jiang, Nan; Jiang, Chao Qiang; Zhuang, Run Sen; Gao, Wen Hui; Zhou, Jian; Lu, Jin Hong; Li, Hui; Wang, Jun Feng; Lai, Yi Sheng; Sun, Jun Sheng; Wu, Jiu Chang; Ye, Chiang; Li, Na; Zhou, Gang; Chen, Jing Ying; Ou, Xiu Yan; Liu, Liu Qing; Huang, Zhuang Hong; Ho, Sai Yin; Li, Ho Cheung William; Su, Sheng Hua; Yang, Yan; Jiang, Yuan; Zhu, Wei Hua; Yang, Lie; Lin, Peiru; He, Yao; Cheng, Kar Keung; Lam, Tai Hing Physicians' very brief (30-sec) intervention for smoking cessation on 13 671 smokers in China: a pragmatic randomized controlled trial. Addiction. 2021;116(5):1172-1185. doi:10.1111/add.15262

137	Lurie, J. D.; Zagaria, A. B.; Pidgeon, D. M.; Forman, J. L.; Spratt, K. F. Pilot comparative effectiveness study of surface perturbation treadmill training to prevent falls in older adults. BMC Geriatr. 2013;13():49. doi:10.1186/1471-2318-13-49	Lurie, Jon D.; Zagaria, Alexandra B.; Ellis, Lisa; Pidgeon, Dawna; Gill-Body, Kathleen M.; Burke, Christina; Armbrust, Kurt; Cass, Sharil; Spratt, Kevin F.; McDonough, Christine M. Surface Perturbation Training to Prevent Falls in Older Adults: A Highly Pragmatic, Randomized Controlled Trial. Phys Ther. 2020;100(7):1153-1162. doi:10.1093/ptj/pzaa023
138	Lyon, M. E.; Jacobs, S.; Briggs, L.; Cheng, Y. I.; Wang, J. Family-centered advance care planning for teens with cancer. JAMA Pediatr. 2013;167(5):460-7. doi:10.1001/jamapediatrics.2013.943	Needle, Jennifer Susan; Friebert, Sarah; Thompkins, Jessica D.; Grossoehme, Daniel H.; Baker, Justin N.; Jiang, JiJi; Wang, Jichuan; Lyon, Maureen E. Effect of the Family-Centered Advance Care Planning for Teens with Cancer Intervention on Sustainability of Congruence About End-of-Life Treatment Preferences: A Randomized Clinical Trial. JAMA Netw Open. 2022;5(7):e2220696. doi:10.1001/jamanetworkopen.2022.20696
139	MacPhail, C.; Adato, M.; Kahn, K.; Selin, A.; Twine, R.; Khoza, S.; Rosenberg, M.; Nguyen, N.; Becker, E.; Pettifor, A. Acceptability and feasibility of cash transfers for HIV prevention among adolescent South African women. AIDS Behav. 2013;17(7):2301-12. doi:10.1007/s10461-013-0433-0	Pettifor, Audrey; MacPhail, Catherine; Hughes, James P.; Selin, Amanda; Wang, Jing; Gómez-Olivé, F. Xavier; Eshleman, Susan H.; Wagner, Ryan G.; Mabuza, Wonderful; Khoza, Nomhle; Suchindran, Chirayath; Mokoena, Immitrude; Twine, Rhian; Andrew, Philip; Townley, Ellen; Laeyendecker, Oliver; Agyei, Yaw; Tollman, Stephen; Kahn, Kathleen The effect of a conditional cash transfer on HIV incidence in young women in rural South Africa (HPTN 068): a phase 3, randomised controlled trial. Lancet Glob Health. 2016;4(12):e978-e988. doi:10.1016/S2214-109X(16)30253-4
140	Mogollon, J. A.; Bujold, E.; Lemieux, S.; Bourdages, M.; Blanchet, C.; Bazinet, L.; Couillard, C.; Noël, M.; Dodin, S. Blood pressure and endothelial function in healthy, pregnant women after acute and daily consumption of flavanol-rich chocolate: a pilot, randomized controlled trial. Nutr J. 2013;12():41. doi:10.1186/1475-2891-12-41	Babar, Asma; Bujold, Emmanuel; Leblanc, Vicky; Lavoie-Lebel, Élise; Paquette, Joalee; Bazinet, Laurent; Lemieux, Simone; Marc, Isabelle; Abdous, Belkacem; Dodin, Sylvie Changes in endothelial function, arterial stiffness and blood pressure in pregnant women after consumption of high-flavanol and high-theobromine chocolate: a double blind randomized clinical trial. Hypertens Pregnancy. 2018;37(2):68-80. doi:10.1080/10641955.2018.1446977
141	Moore, B. A.; Fazzino, T.; Barry, D. T.; Fiellin, D. A.; Cutter, C. J.; Schottenfeld, R. S.; Ball, S. A. The Recovery Line: A pilot trial of automated, telephone-based treatment for continued drug use in methadone maintenance. J Subst Abuse Treat. 2013;45(1):63-9. doi:10.1016/j.jsat.2012.12.011	Moore, Brent A.; Buono, Frank D.; Lloyd, Daniel P.; Printz, Destiny M. B.; Fiellin, David A.; Barry, Declan T. A randomized clinical trial of the Recovery Line among methadone treatment patients with ongoing illicit drug use. J Subst Abuse Treat. 2019;97():68-74. doi:10.1016/j.jsat.2018.11.011
142	Moyle, W.; Cooke, M.; Beattie, E.; Jones, C.; Klein, B.; Cook, G.; Gray, C. Exploring the effect of companion robots on emotional expression in older adults with dementia: a pilot randomized controlled trial. J Gerontol Nurs. 2013;39(5):46-53. doi:10.3928/00989134-20130313-03	Moyle, Wendy; Jones, Cindy J.; Murfield, Jenny E.; Thalib, Lukman; Beattie, Elizabeth R. A.; Shum, David K. H.; O'Dwyer, Siobhan T.; Mervin, M. Cindy; Draper, Brian M. Use of a Robotic Seal as a Therapeutic Tool to Improve Dementia Symptoms: A Cluster-Randomized Controlled Trial. J Am Med Dir Assoc.

		2017;18(9):766-773. doi:10.1016/j.jamda.2017.03.018
143	Nyamathi, A.; Sinha, S.; Ganguly, K. K.; Ramakrishna, P.; Suresh, P.; Carpenter, C. L. Impact of protein supplementation and care and support on body composition and CD4 count among HIV-infected women living in rural India: results from a randomized pilot clinical trial. AIDS Behav. 2013;17(6):2011-21. doi:10.1007/s10461-013-0420-5	Carpenter, Catherine L.; Kapur, Kavita; Ramakrishna, Padma; Pamujula, Suresh; Yadav, Kartik; Giovanni, Jennifer E.; Julian, Olivia; Ekstrand, Maria L.; Sinha, Sanjeev; Nyamathi, Adeline M. Lean Mass Improvement from Nutrition Education and Protein Supplementation among Rural Indian Women Living with HIV/AIDS: Results from Cluster Randomized Factorial Trial at 18-Month Follow-Up. Nutrients. 2021;14(1):179. doi:10.3390/nu14010179
144	Palmer, Rebecca; Enderby, Pam; Cooper, Cindy; Latimer, Nick; Julious, Steven; Paterson, Gail; Dimairo, Munyaradzi; Dixon, Simon; Mortley, Jane; Hilton, Rose; Delaney, Audrey; Hughes, Helen Computer therapy compared with usual care for people with long-standing aphasia poststroke: a pilot randomized controlled trial. Stroke. 2012;43(7):1904-1911. doi:10.1161/STROKEAHA.112.650671	Palmer, Rebecca; Dimairo, Munyaradzi; Cooper, Cindy; Enderby, Pam; Brady, Marian; Bowen, Audrey; Latimer, Nicholas; Julious, Steven; Cross, Elizabeth; Alshreef, Abualbishr; Harrison, Madeleine; Bradley, Ellen; Witts, Helen; Chater, Tim Self-managed, computerised speech and language therapy for patients with chronic aphasia post-stroke compared with usual care or attention control (Big CACTUS): a multicentre, single-blinded, randomised controlled trial. Lancet Neurol. 2019;18(9):821-833. doi:10.1016/S1474-4422(19)30192-9
145	Peris, T. S.; Piacentini, J. Optimizing treatment for complex cases of childhood obsessive compulsive disorder: a preliminary trial. J Clin Child Adolesc Psychol. 2013;42(1):44934. doi:10.1080/15374416.2012.673162	Peris, Tara S.; Rozenman, Michelle S.; Sugar, Catherine A.; McCracken, James T.; Piacentini, John Targeted Family Intervention for Complex Cases of Pediatric Obsessive-Compulsive Disorder: A Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2017;56(12):1034-1042.e1. doi:10.1016/j.jaac.2017.10.008
146	Poston, L.; Briley, A. L.; Barr, S.; Bell, R.; Croker, H.; Coxon, K.; Essex, H. N.; Hunt, C.; Hayes, L.; Howard, L. M.; Khazaezadeh, N.; Kinnunen, T.; Nelson, S. M.; Oteng-Ntim, E.; Robson, S. C.; Sattar, N.; Seed, P. T.; Wardle, J.; Sanders, T. A.; Sandall, J. Developing a complex intervention for diet and activity behaviour change in obese pregnant women (the UPBEAT trial); assessment of behavioural change and process evaluation in a pilot randomised controlled trial. BMC Pregnancy Childbirth. 2013;13():148. doi:10.1186/1471-2393-13-148	Poston, Lucilla; Bell, Ruth; Croker, Helen; Flynn, Angela C.; Godfrey, Keith M.; Goff, Louise; Hayes, Louise; Khazaezadeh, Nina; Nelson, Scott M.; Oteng-Ntim, Eugene; Pasupathy, Dharmintra; Patel, Nashita; Robson, Stephen C.; Sandall, Jane; Sanders, Thomas A. B.; Sattar, Naveed; Seed, Paul T.; Wardle, Jane; Whitworth, Melissa K.; Briley, Annette L.; UPBEAT Trial Consortium Effect of a behavioural intervention in obese pregnant women (the UPBEAT study): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2015;3(10):767-777. doi:10.1016/S2213-8587(15)00227-2
147	Samaan, Z.; Schulze, K. M.; Middleton, C.; Irvine, J.; Joseph, P.; Mente, A.; Shah, B. R.; Pare, G.; Desai, D.; Anand, S. S. South Asian Heart Risk Assessment (SAHARA): Randomized Controlled Trial Design and Pilot Study. JMIR Res Protoc. 2013;2(2):e33. doi:10.2196/resprot.2621	Anand, Sonia S.; Samaan, Zainab; Middleton, Catherine; Irvine, Jane; Desai, Dipika; Schulze, Karleen M.; Sothiratnam, Stena; Hussain, Fathima; Shah, Baiju R.; Pare, Guillaume; Beyene, Joseph; Lear, Scott A.; South Asian Heart Risk Assessment Investigators A Digital Health Intervention to Lower Cardiovascular Risk: A Randomized Clinical Trial. JAMA Cardiol. 2016;1(5):601-606. doi:10.1001/jamacardio.2016.1035

148	Sturkenboom, I. H.; Graff, M. J.; Borm, G. F.; Veenhuizen, Y.; Bloem, B. R.; Munneke, M.; Nijhuis-van der Sanden, M. W. The impact of occupational therapy in Parkinson's disease: a randomized controlled feasibility study. Clin Rehabil. 2013;27(2):99-112. doi:10.1177/0269215512448382	Sturkenboom, Ingrid H. W. M.; Graff, Maud J. L.; Hendriks, Jan C. M.; Veenhuizen, Yvonne; Munneke, Marten; Bloem, Bastiaan R.; Nijhuis-van der Sanden, Maria W.; OTiP study group Efficacy of occupational therapy for patients with Parkinson's disease: a randomised controlled trial. Lancet Neurol. 2014;13(6):557-566. doi:10.1016/S1474-4422(14)70055-9
149	Hip Fracture Accelerated Surgical Treatment and Care Track (HIP ATTACK) Investigators Accelerated care versus standard care among patients with hip fracture: the HIP ATTACK pilot trial. CMAJ. 2014;186(1):E52-60. doi:10.1503/cmaj.130901	HIP ATTACK Investigators Accelerated surgery versus standard care in hip fracture (HIP ATTACK): an international, randomised, controlled trial. Lancet. 2020;395(10225):698-708. doi:10.1016/S0140-6736(20)30058-1
150	Anderson, A. S.; Macleod, M.; Mutrie, N.; Sugden, J.; Dobson, H.; Treweek, S.; O'Carroll, R. E.; Thompson, A.; Kirk, A.; Brennan, G.; Wyke, S. Breast cancer risk reduction--is it feasible to initiate a randomised controlled trial of a lifestyle intervention programme (ActWell) within a national breast screening programme?. Int J Behav Nutr Phys Act. 2014;11():156. doi:10.1186/s12966-014-0156-2	Anderson, Annie S.; Chong, Huey Yi; Craigie, Angela M.; Donnan, Peter T.; Gallant, Stephanie; Hickman, Amy; McAdam, Chloe; McKell, Jennifer; McNamee, Paul; Macaskill, E. Jane; Mutrie, Nanette; O'Carroll, Ronan E.; Rauchhaus, Petra; Sattar, Naveed; Stead, Martine; Treweek, Shaun A novel approach to increasing community capacity for weight management a volunteer-delivered programme (ActWELL) initiated within breast screening clinics: a randomised controlled trial. Int J Behav Nutr Phys Act. 2021;18(1):34. doi:10.1186/s12966-021-01099-7
151	Bricker, J. B.; Mull, K. E.; Kientz, J. A.; Vilardaga, R.; Mercer, L. D.; Akioka, K. J.; Heffner, J. L. Randomized, controlled pilot trial of a smartphone app for smoking cessation using acceptance and commitment therapy. Drug Alcohol Depend. 2014;143():87-94. doi:10.1016/j.drugalcdep.2014.07.006	Bricker, Jonathan B.; Watson, Noreen L.; Mull, Kristin E.; Sullivan, Brianna M.; Heffner, Jaimee L. Efficacy of Smartphone Applications for Smoking Cessation: A Randomized Clinical Trial. JAMA Intern Med. 2020;180(11):1472-1480. doi:10.1001/jamainternmed.2020.4055
152	Busse, J. W.; Bhandari, M.; Einhorn, T. A.; Heckman, J. D.; Leung, K. S.; Schemitsch, E.; Tornetta, P., 3rd; Walter, S. D.; Guyatt, G. H. Trial to re-evaluate ultrasound in the treatment of tibial fractures (TRUST): a multicenter randomized pilot study. Trials. 2014;15():206. doi:10.1186/1745-6215-15-206	TRUST Investigators writing group; Busse, Jason W.; Bhandari, Mohit; Einhorn, Thomas A.; Schemitsch, Emil; Heckman, James D.; Tornetta, Paul; Leung, Kwok-Sui; Heels-Ansdell, Diane; Makosso-Kallyth, Sun; Della Rocca, Gregory J.; Jones, Clifford B.; Guyatt, Gordon H. Re-evaluation of low intensity pulsed ultrasound in treatment of tibial fractures (TRUST): randomized clinical trial. BMJ. 2016;355():i5351. doi:10.1136/bmj.i5351
153	Capa-Grasa, A.; Rojo-Manaute, J. M.; Rodríguez, F. C.; Martín, J. V. Ultra minimally invasive sonographically guided carpal tunnel release: an external pilot study. Orthop Traumatol Surg Res. 2014;100(3):287-92. doi:10.1016/j.otsr.2013.11.015	Rojo-Manaute, Jose Manuel; Capa-Grasa, Alberto; Chana-Rodríguez, Francisco; Perez-Mañanes, Ruben; Rodriguez-Maruri, Guillermo; Sanz-Ruiz, Pablo; Muñoz-Ledesma, Jorge; Aburto-Bernardo, Mikel; Esparragoza-Cabrera, Luis; Cerro-Gutiérrez, Miguel Del; Vaquero-Martín, Javier Ultra-Minimally Invasive Ultrasound-Guided Carpal Tunnel Release: A Randomized Clinical Trial. J Ultrasound Med. 2016;35(6):1149-1157. doi:10.7863/ultra.15.07001

154	Cederbom, S.; Rydwik, E.; Söderlund, A.; Denison, E.; Frändin, K.; von Heideken Wågert, P. A behavioral medicine intervention for older women living alone with chronic pain - a feasibility study. Clin Interv Aging. 2014;9():1383-97. doi:10.2147/cia.S66943	Cederbom, Sara; Leveille, Suzanne G.; Bergland, Astrid Effects of a behavioral medicine intervention on pain, health, and behavior among community-dwelling older adults: a randomized controlled trial. Clin Interv Aging. 2019;14():1207-1220. doi:10.2147/CIA.S208102
155	Dowling, G. A.; Merrilees, J.; Mastick, J.; Chang, V. Y.; Hubbard, E.; Moskowitz, J. T. Life enhancing activities for family caregivers of people with frontotemporal dementia. Alzheimer Dis Assoc Disord. 2014;28(2):175-81. doi:10.1097/WAD.0b013e3182a6b905	Moskowitz, Judith T.; Cheung, Elaine O.; Snowberg, Karin E.; Verstaen, Alice; Merrilees, Jennifer; Salsman, John M.; Dowling, Glenna A. Randomized controlled trial of a facilitated online positive emotion regulation intervention for dementia caregivers. Health Psychol. 2019;38(5):391-402. doi:10.1037/hea0000680
156	Eleftheriadou, V.; Thomas, K.; Ravenscroft, J.; Whitton, M.; Batchelor, J.; Williams, H. Feasibility, double-blind, randomised, placebo-controlled, multi-centre trial of hand-held NB-UVB phototherapy for the treatment of vitiligo at home (HI-Light trial: Home Intervention of Light therapy). Trials. 2014;15():51. doi:10.1186/1745-6215-15-51	Batchelor, Jonathan M.; Thomas, Kim S.; Akram, Perways; Azad, Jaskiran; Bewley, Anthony; Chalmers, Joanne R.; Cheung, Seau Tak; Duley, Lelia; Eleftheriadou, Viktoria; Ellis, Robert; Ferguson, Adam; Goulding, Jonathan Mr; Haines, Rachel H.; Hamad, Hamdi; Ingram, John R.; Laguda, Bisola; Leighton, Paul; Levell, Nick; Makrygeorgou, Areti; Meakin, Garry D.; Millington, Adam; Ogboli, Malobi; Rajasekaran, Amirtha; Ravenscroft, Jane C.; Rogers, Andrew; Sach, Tracey H.; Santer, Miriam; Stainforth, Julia; Tan, Wei; Wahie, Shyamal; White, Jennifer; Whitton, Maxine E.; Williams, Hywel C.; Wright, Andrew; Montgomery, Alan A. Home-based narrowband UVB, topical corticosteroid or combination for children and adults with vitiligo: HI-Light Vitiligo three-arm RCT. Health Technol Assess. 2020;24(64):1-128. doi:10.3310/hta24640
157	Franchi, C.; Mari, D.; Tettamanti, M.; Pasina, L.; Djade, C. D.; Mannucci, P. M.; Onder, G.; Bernabei, R.; Gussoni, G.; Bonassi, S.; Nobili, A. E-learning to improve the drug prescribing in the hospitalized elderly patients: the ELICADHE feasibility pilot study. Aging Clin Exp Res. 2014;26(4):435-43. doi:10.1007/s40520-013-0187-6	Franchi, Carlotta; Tettamanti, Mauro; Djade, Codjo Dgnefa; Pasina, Luca; Mannucci, Pier Mannuccio; Onder, Graziano; Gussoni, Gualberto; Manfellotto, Dario; Bonassi, Stefano; Salerno, Francesco; Nobili, Alessandro; ELICADHE Investigators E-learning in order to improve drug prescription for hospitalized older patients: a cluster-randomized controlled study. Br J Clin Pharmacol. 2016;82(1):53-63. doi:10.1111/bcp.12922
158	Gaffney, H.; Mansell, W.; Edwards, R.; Wright, J. Manage Your Life Online (MYLO): a pilot trial of a conversational computer-based intervention for problem solving in a student sample. Behav Cogn Psychother. 2014;42(6):731-46. doi:10.1017/s135246581300060x	Bird, Timothy; Mansell, Warren; Wright, Jason; Gaffney, Hannah; Tai, Sara Manage Your Life Online: A Web-Based Randomized Controlled Trial Evaluating the Effectiveness of a Problem-Solving Intervention in a Student Sample. Behav Cogn Psychother. 2018;46(5):570-582. doi:10.1017/S1352465817000820
159	Green, C. A.; Janoff, S. L.; Yarborough, B. J.; Yarborough, M. T. A 12-week weight reduction intervention for overweight individuals taking antipsychotic medications. Community Ment Health J. 2014;50(8):974-80. doi:10.1007/s10597-014-9716-9	Green, Carla A.; Yarborough, Bobbi Jo H.; Leo, Michael C.; Yarborough, Micah T.; Stumbo, Scott P.; Janoff, Shannon L.; Perrin, Nancy A.; Nichols, Greg A.; Stevens, Victor J. The STRIDE weight loss and lifestyle intervention for individuals taking antipsychotic medications: a

		randomized trial. Am J Psychiatry. 2015;172(1):71-81. doi:10.1176/appi.ajp.2014.14020173
160	Jaser, S. S.; Patel, N.; Rothman, R. L.; Choi, L.; Whittemore, R. Check it! A randomized pilot of a positive psychology intervention to improve adherence in adolescents with type 1 diabetes. Diabetes Educ. 2014;40(5):659-67. doi:10.1177/0145721714535990	Jaser, Sarah S.; Whittemore, Robin; Choi, Leena; Nwosu, Samuel; Russell, William E. Randomized Trial of a Positive Psychology Intervention for Adolescents With Type 1 Diabetes. J Pediatr Psychol. 2019;44(5):620-629. doi:10.1093/jpepsy/jsz006
161	Littlewood, C.; Malliaras, P.; Mawson, S.; May, S.; Walters, S. J. Self-managed loaded exercise versus usual physiotherapy treatment for rotator cuff tendinopathy: a pilot randomised controlled trial. Physiotherapy. 2014;100(1):54-60. doi:10.1016/j.physio.2013.06.001	Littlewood, Chris; Bateman, Marcus; Brown, Kim; Bury, Julie; Mawson, Sue; May, Stephen; Walters, Stephen J. A self-managed single exercise programme versus usual physiotherapy treatment for rotator cuff tendinopathy: a randomised controlled trial (the SELF study). Clin Rehabil. 2016;30(7):686-696. doi:10.1177/0269215515593784
162	Nakimuli-Mpungu, Etheldreda; Wamala, Kizito; Okello, James; Alderman, Stephen; Odokonyero, Raymond; Mojtabai, Ramin; Mills, Edward J.; Kanters, Steve; Nachega, Jean B.; Musisi, Seggane Group support psychotherapy for depression treatment in people with HIV/AIDS in northern Uganda: a single-centre randomised controlled trial. Lancet HIV. 2015;2(5):e190-199. doi:10.1016/S2352-3018(15)00041-7	Nakimuli-Mpungu, Etheldreda; Musisi, Seggane; Wamala, Kizito; Okello, James; Ndyanabangi, Sheila; Birungi, Josephine; Nanfuka, Mastula; Etukoit, Micheal; Mayora, Chrispus; Ssengooba, Freddie; Mojtabai, Ramin; Nachega, Jean B.; Harari, Ofir; Mills, Edward J. Effectiveness and cost-effectiveness of group support psychotherapy delivered by trained lay health workers for depression treatment among people with HIV in Uganda: a cluster-randomised trial. Lancet Glob Health. 2020;8(3):e387-e398. doi:10.1016/S2214-109X(19)30548-0
163	Ribeiro, D. C.; Sole, G.; Abbott, J. H.; Milosavljevic, S. The effectiveness of a lumbopelvic monitor and feedback device to change postural behavior: a feasibility randomized controlled trial. J Orthop Sports Phys Ther. 2014;44(9):702-11. doi:10.2519/jospt.2014.5009	Ribeiro, Daniel Cury; Milosavljevic, Stephan; Terry, Jane; Abbott, J. H. Effectiveness of a lumbopelvic monitor and feedback device to change postural behaviour: the ELF cluster randomised controlled trial. Occup Environ Med. 2020;77(7):462-469. doi:10.1136/oemed-2019-106293
164	Roffe, C.; Nevatte, T.; Crome, P.; Gray, R.; Sim, J.; Pountain, S.; Handy, L.; Handy, P. The Stroke Oxygen Study (SO2S) - a multi-center, study to assess whether routine oxygen treatment in the first 72 hours after a stroke improves long-term outcome: study protocol for a randomized controlled trial. Trials. 2014;15():99. doi:10.1186/1745-6215-15-99	Roffe, Christine; Nevatte, Tracy; Sim, Julius; Bishop, Jon; Ives, Natalie; Ferdinand, Phillip; Gray, Richard; Stroke Oxygen Study Investigators and the Stroke OxygenStudy Collaborative Group Effect of Routine Low-Dose Oxygen Supplementation on Death and Disability in Adults With Acute Stroke: The Stroke Oxygen Study Randomized Clinical Trial. JAMA. 2017;318(12):1125-1135. doi:10.1001/jama.2017.11463
165	Stacey, D.; Hawker, G.; Dervin, G.; Tugwell, P.; Boland, L.; Pomey, M. P.; O'Connor, A. M.; Taljaard, M. Decision aid for patients considering total knee arthroplasty with preference report for surgeons: a pilot randomized controlled trial. BMC Musculoskelet Disord. 2014;15():54. doi:10.1186/1471-2474-15-54	Stacey, D.; Taljaard, M.; Dervin, G.; Tugwell, P.; O'Connor, A. M.; Pomey, M. P.; Boland, L.; Beach, S.; Meltzer, D.; Hawker, G. Impact of patient decision aids on appropriate and timely access to hip or knee arthroplasty for osteoarthritis: a randomized controlled trial. Osteoarthritis Cartilage. 2016;24(1):99-107. doi:10.1016/j.joca.2015.07.024

166	Straudi, S.; Martinuzzi, C.; Pavarelli, C.; Sabbagh Charabati, A.; Benedetti, M. G.; Foti, C.; Bonato, M.; Zancato, E.; Basaglia, N. A task-oriented circuit training in multiple sclerosis: a feasibility study. BMC Neurol. 2014;14():124. doi:10.1186/1471-2377-14-124	Straudi, Sofia; De Marco, Gianluca; Martinuzzi, Carlotta; Baroni, Andrea; Lamberti, Nicola; Brondi, Laura; Da Roit, Marco; Pizzongolo, Laura Di Marco; Basaglia, Nino; Manfredini, Fabio Combining a supervised and home-based task-oriented circuit training improves walking endurance in patients with multiple sclerosis. The MS_TOCT randomized-controlled trial. Mult Scler Relat Disord. 2022;60():103721. doi:10.1016/j.msard.2022.103721
167	Takemura, S.; Yoshimasu, K.; Fukumoto, J.; Mure, K.; Nishio, N.; Kishida, K.; Yano, F.; Mitani, T.; Takeshita, T.; Miyashita, K. Safety and adherence of Umezu polyphenols in the Japanese plum (Prunus mume) in a 12-week double-blind randomized placebo-controlled pilot trial to evaluate antihypertensive effects. Environ Health Prev Med. 2014;19(6):444-51. doi:10.1007/s12199-014-0404-8	Takemura, Shigeki; Yoshimasu, Kouichi; Tsuno, Kanami; Kuroda, Mototsugu; Kishida, Kunihiro; Mitani, Takahiko; Miyashita, Kazuhisa Potential hypotensive effects of Umezu polyphenols: a 14-week community-based, double-masked and placebo-controlled trial. Blood Press Monit. 2020;25(6):355-358. doi:10.1097/MBP.0000000000000476
168	Weinstock, J.; Capizzi, J.; Weber, S. M.; Pescatello, L. S.; Petry, N. M. Exercise as an intervention for sedentary hazardous drinking college students: A pilot study. Ment Health Phys Act. 2014;7(1):55-62. doi:10.1016/j.mhpa.2014.02.002	Weinstock, Jeremiah; Petry, Nancy M.; Pescatello, Linda S.; Henderson, Craig E. Sedentary college student drinkers can start exercising and reduce drinking after intervention. Psychol Addict Behav. 2016;30(8):791-801. doi:10.1037/adb0000207
169	Wells, R. E.; Burch, R.; Paulsen, R. H.; Wayne, P. M.; Houle, T. T.; Loder, E. Meditation for migraines: a pilot randomized controlled trial. Headache. 2014;54(9):1484-95. doi:10.1111/head.12420	Wells, Rebecca Erwin; O'Connell, Nathaniel; Pierce, Charles R.; Estave, Paige; Penzien, Donald B.; Loder, Elizabeth; Zeidan, Fadel; Houle, Timothy T. Effectiveness of Mindfulness Meditation vs Headache Education for Adults With Migraine: A Randomized Clinical Trial. JAMA Intern Med. 2021;181(3):317-328. doi:10.1001/jamainternmed.2020.7090
170	Wilhelm, S.; Phillips, K. A.; Didie, E.; Buhlmann, U.; Greenberg, J. L.; Fama, J. M.; Keshaviah, A.; Steketee, G. Modular cognitive-behavioral therapy for body dysmorphic disorder: a randomized controlled trial. Behav Ther. 2014;45(3):314-27. doi:10.1016/j.beth.2013.12.007	Wilhelm, Sabine; Phillips, Katharine A.; Greenberg, Jennifer L.; O'Keefe, Sheila M.; Hoeppner, Susanne S.; Keshaviah, Aparna; Sarvode-Mothi, Suraj; Schoenfeld, David A. Efficacy and Posttreatment Effects of Therapist-Delivered Cognitive Behavioral Therapy vs Supportive Psychotherapy for Adults With Body Dysmorphic Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2019;76(4):363-373. doi:10.1001/jamapsychiatry.2018.4156
171	Wu, L.; Zhang, A. L.; Di, Y. M.; Shergis, J. L.; Chen, Y.; Guo, X.; Wen, Z.; Thien, F.; Worsnop, C.; Lin, L.; Xue, C. C. Panax ginseng therapy for chronic obstructive pulmonary disease: a clinical trial protocol and pilot study. Chin Med. 2014;9():20. doi:10.1186/1749-8546-9-20	Chen, Yuanbin; Lin, Lin; Wu, Lei; Xu, Yinji; Shergis, Johannah L.; Zhang, Anthony L.; Wen, Zehuai; Worsnop, Christopher; Da Costa, Cliff; Thien, Frank; Xue, Charlie C. Effect of Panax Ginseng (G115) Capsules versus Placebo on Acute Exacerbations in Patients with Moderate to Very Severe COPD: A Randomized Controlled Trial. Int J Chron Obstruct Pulmon Dis. 2020;15():671-680. doi:10.2147/COPD.S236425
172	PARITY Investigators Prophylactic antibiotic regimens in tumour surgery (PARITY): a pilot multicentre randomised controlled trial.	Prophylactic Antibiotic Regimens in Tumor Surgery (PARITY) Investigators; Ghert, Michelle; Schneider, Patricia; Guyatt, Gordon; Thabane,

	Bone Joint Res. 2015;4(9):154-162. doi:10.1302/2046-3758.49.2000482	Lehana; Vélez, Roberto; O'Shea, Timothy; Randall, R. Lor; Turcotte, Robert; Wilson, David; Wunder, Jay S.; Baptista, André Mathias; Cheng, Edward Y.; Doung, Yee-Cheen; Ferguson, Peter C.; Giglio, Victoria; Hayden, James; Heels-Ansdell, Diane; Khan, Shah Alam; Sampath Kumar, Venkatesan; McKay, Paula; Miller, Benjamin; van de Sande, Michiel; Zumárraga, Juan P.; Bhandari, Mohit Comparison of Prophylactic Intravenous Antibiotic Regimens After Endoprosthetic Reconstruction for Lower Extremity Bone Tumors: A Randomized Clinical Trial. JAMA Oncol. 2022;8(3):345-353. doi:10.1001/jamaoncol.2021.6628
173	Akard, T. F.; Dietrich, M. S.; Friedman, D. L.; Hinds, P. S.; Given, B.; Wray, S.; Gilmer, M. J. Digital storytelling: an innovative legacy-making intervention for children with cancer. Pediatr Blood Cancer. 2015;62(4):658-65. doi:10.1002/pbc.25337	Akard, Terrah Foster; Dietrich, Mary S.; Friedman, Debra L.; Wray, Sarah; Gerhardt, Cynthia A.; Hendricks-Ferguson, Verna; Hinds, Pamela S.; Rhoten, Bethany; Gilmer, Mary Jo Randomized Clinical Trial of a Legacy Intervention for Quality of Life in Children with Advanced Cancer. J Palliat Med. 2021;24(5):680-688. doi:10.1089/jpm.2020.0139
174	Bonell, C.; Fletcher, A.; Fitzgerald-Yau, N.; Hale, D.; Allen, E.; Elbourne, D.; Jones, R.; Bond, L.; Wiggins, M.; Miners, A.; Legood, R.; Scott, S.; Christie, D.; Viner, R. Initiating change locally in bullying and aggression through the school environment (INCLUSIVE): a pilot randomised controlled trial. Health Technol Assess. 2015;19(53):1-109, vii. doi:10.3310/hta19530	Bonell, Chris; Allen, Elizabeth; Warren, Emily; McGowan, Jennifer; Bevilacqua, Leonardo; Jamal, Farah; Legood, Rosa; Wiggins, Meg; Opondo, Charles; Mathiot, Anne; Sturgess, Jo; Fletcher, Adam; Sadique, Zia; Elbourne, Diana; Christie, Deborah; Bond, Lyndal; Scott, Stephen; Viner, Russell M. Effects of the Learning Together intervention on bullying and aggression in English secondary schools (INCLUSIVE): a cluster randomised controlled trial. Lancet. 2018;392(10163):2452-2464. doi:10.1016/S0140-6736(18)31782-3
175	Carrico, A. W.; Gómez, W.; Siever, M. D.; Discepola, M. V.; Dilworth, S. E.; Moskowitz, J. T. Pilot randomized controlled trial of an integrative intervention with methamphetamine-using men who have sex with men. Arch Sex Behav. 2015;44(7):1861-7. doi:10.1007/s10508-015-0505-5	Carrico, Adam W.; Neilands, Torsten B.; Dilworth, Samantha E.; Evans, Jennifer L.; Gómez, Walter; Jain, Jennifer P.; Gandhi, Monica; Shoptaw, Steven; Horvath, Keith J.; Coffin, Lara; Discepola, Michael V.; Andrews, Rick; Woods, William J.; Feaster, Daniel J.; Moskowitz, Judith T. Randomized controlled trial of a positive affect intervention to reduce HIV viral load among sexual minority men who use methamphetamine. J Int AIDS Soc. 2019;22(12):e25436. doi:10.1002/jia2.25436
176	Causarano, N.; Platt, J.; Baxter, N. N.; Bagher, S.; Jones, J. M.; Metcalfe, K. A.; Hofer, S. O.; O'Neill, A. C.; Cheng, T.; Starenkyj, E.; Zhong, T. Pre-consultation educational group intervention to improve shared decision-making for postmastectomy breast reconstruction: a pilot randomized controlled trial. Support Care Cancer. 2015;23(5):1365-75. doi:10.1007/s00520-014-2479-6	Zhong, Toni; Quong, Whitney L.; Cheng, Terry; Kerrebijn, Isabel; Butler, Kate; Hofer, Stefan O. P.; O'Neill, Anne C.; Cil, Tulin D.; Metcalfe, Kelly A. Preconsultation Educational Group Intervention Can Address the Knowledge Gap in Postmastectomy Breast Reconstruction. Ann Plast Surg. 2021;86(6):695-700. doi:10.1097/SAP.0000000000002603

177	Charvet, L. E.; Shaw, M. T.; Haider, L.; Melville, P.; Krupp, L. B. Remotely-delivered cognitive remediation in multiple sclerosis (MS): protocol and results from a pilot study. Mult Scler J Exp Transl Clin. 2015;1():2055217315609620. doi:10.1177/2055217315609629	Charvet, Leigh E.; Yang, Jie; Shaw, Michael T.; Sherman, Kathleen; Haider, Lamia; Xu, Jianjin; Krupp, Lauren B. Cognitive function in multiple sclerosis improves with telerehabilitation: Results from a randomized controlled trial. PLoS One. 2017;12(5):e0177177. doi:10.1371/journal.pone.0177177
178	Leff, Julian; Williams, Geoffrey; Huckvale, Mark A.; Arbuthnot, Maurice; Leff, Alex P. Computer-assisted therapy for medication-resistant auditory hallucinations: proof-of-concept study. Br J Psychiatry. 2013;202():428-433. doi:10.1192/bjp.bp.112.124883	Craig, Tom Kj; Rus-Calafell, Mar; Ward, Thomas; Leff, Julian P.; Huckvale, Mark; Howarth, Elizabeth; Emsley, Richard; Garety, Philippa A. AVATAR therapy for auditory verbal hallucinations in people with psychosis: a single-blind, randomised controlled trial. Lancet Psychiatry. 2018;5(1):31-40. doi:10.1016/S2215-0366(17)30427-3
179	Daley, A. J.; Jolly, K.; Jebb, S. A.; Lewis, A. L.; Clifford, S.; Roalfe, A. K.; Kenyon, S.; Aveyard, P. Feasibility and acceptability of regular weighing, setting weight gain limits and providing feedback by community midwives to prevent excess weight gain during pregnancy: randomised controlled trial and qualitative study. BMC Obes. 2015;2():35. doi:10.1186/s40608-015-0061-5	Daley, Amanda; Jolly, Kate; Jebb, Susan A.; Roalfe, Andrea; Mackilllop, Lucy; Lewis, Amanda; Clifford, Sue; Usman, Muhammad; Ohadike, Corah; Kenyon, Sara; MacArthur, Christine; Aveyard, Paul Effectiveness of a behavioural intervention involving regular weighing and feedback by community midwives within routine antenatal care to prevent excessive gestational weight gain: POPS2 randomised controlled trial. BMJ Open. 2019;9(9):e030174. doi:10.1136/bmjopen-2019-030174
180	das Nair, Roshan; Lincoln, Nadina B. Evaluation of rehabilitation of memory in neurological disabilities (ReMiND): a randomized controlled trial. Clin Rehabil. 2012;26(10):894-903. doi:10.1177/0269215511435424	das Nair, Roshan; Bradshaw, Lucy E.; Day, Florence Ec; Drummond, Avril; Harris, Shaun Rs; Fitzsimmons, Deborah; Montgomery, Alan A.; Newby, Gavin; Sackley, Catherine; Lincoln, Nadina B. Clinical and cost effectiveness of memory rehabilitation following traumatic brain injury: a pragmatic cluster randomized controlled trial. Clin Rehabil. 2019;33(7):1171-1184. doi:10.1177/0269215519840069
181	Dodds, S. E.; Pace, T. W.; Bell, M. L.; Fiero, M.; Negi, L. T.; Raison, C. L.; Weihs, K. L. Feasibility of Cognitively-Based Compassion Training (CBCT) for breast cancer survivors: a randomized, wait list controlled pilot study. Support Care Cancer. 2015;23(12):3599-608. doi:10.1007/s00520-015-2888-1	Gonzalez-Hernandez, Edgar; Romero, Rocio; Campos, Daniel; Burychka, Diana; Diego-Pedro, Rebeca; Baños, Rosa; Negi, Lobsang Tenzin; Cebolla, Ausiàs Cognitively-Based Compassion Training (CBCT®) in Breast Cancer Survivors: A Randomized Clinical Trial Study. Integr Cancer Ther. 2018;17(3):684-696. doi:10.1177/1534735418772095
182	Gilbody, S.; Peckham, E.; Man, M. S.; Mitchell, N.; Li, J.; Becque, T.; Hewitt, C.; Knowles, S.; Bradshaw, T.; Planner, C.; Parrott, S.; Michie, S.; Shepherd, C. Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2015;2(5):395-402. doi:10.1016/s2215-0366(15)00091-7	Gilbody, Simon; Peckham, Emily; Bailey, Della; Arundel, Catherine; Heron, Paul; Crosland, Suzanne; Fairhurst, Caroline; Hewitt, Catherine; Li, Jinshuo; Parrott, Steve; Bradshaw, Tim; Horspool, Michelle; Hughes, Elizabeth; Hughes, Tom; Ker, Suzy; Leahy, Moira; McCloud, Tayla; Osborn, David; Reilly, Joe; Steare, Thomas; Ballantyne, Emma; Bidwell, Polly; Bonner, Sue; Brennan, Diane; Callen, Tracy; Carey, Alex; Colbeck, Charlotte; Coton, Debbie; Donaldson, Emma; Evans, Kimberley; Herlihy, Hannah; Khan, Wajid; Nyathi, Lizwi; Nyamadzawo,

		Elizabeth; Oldknow, Helen; Phiri, Peter; Rathod, Shanaya; Rea, Jamie; Romain-Hooper, Crystal-Bella; Smith, Kaye; Stribling, Alison; Vickers, Carinna Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 2019;6(5):379-390. doi:10.1016/S2215-0366(19)30047-1
183	Chaboyer, Wendy; Anderson, Vinah; Webster, Joan; Sneddon, Anne; Thalib, Lukman; Gillespie, Brigid M. Negative Pressure Wound Therapy on Surgical Site Infections in Women Undergoing Elective Caesarean Sections: A Pilot RCT. Healthcare (Basel). 2014;2(4):417-428. doi:10.3390/healthcare2040417	Gillespie, Brigid M.; Webster, Joan; Ellwood, David; Thalib, Lukman; Whitty, Jennifer A.; Mahomed, Kassam; Clifton, Vicki; Kumar, Sailesh; Wagner, Adam; Kang, Evelyn; Chaboyer, Wendy Closed incision negative pressure wound therapy versus standard dressings in obese women undergoing caesarean section: multicentre parallel group randomised controlled trial. BMJ. 2021;373():n893. doi:10.1136/bmj.n893
184	Goldstein, L. H.; Chalder, T.; Chigwedere, C.; Khondoker, M. R.; Moriarty, J.; Toone, B. K.; Mellers, J. D. C. Cognitive-behavioral therapy for psychogenic nonepileptic seizures: a pilot RCT. Neurology. 2010;74(24):1986-1994. doi:10.1212/WNL.0b013e3181e39658	Goldstein, Laura H.; Robinson, Emily J.; Mellers, John D. C.; Stone, Jon; Carson, Alan; Reuber, Markus; Medford, Nick; McCrone, Paul; Murray, Joanna; Richardson, Mark P.; Pilecka, Izabela; Eastwood, Carole; Moore, Michele; Mosweu, Iris; Perdue, Iain; Landau, Sabine; Chalder, Trudie; CODES study group Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multicentre, randomised controlled trial. Lancet Psychiatry. 2020;7(6):491-505. doi:10.1016/S2215-0366(20)30128-0
185	Lood, Q.; Gustafsson, S.; Dahlin Ivanoff, S. Bridging barriers to health promotion: a feasibility pilot study of the 'Promoting Aging Migrants' Capabilities study'. J Eval Clin Pract. 2015;21(4):604-13. doi:10.1111/jep.12345	Arola, L. A.; Barenfeld, E.; Dahlin-Ivanoff, S.; Häggblom-Kronlöf, G. Distribution and evaluation of sense of coherence among older immigrants before and after a health promotion intervention - results from the RCT study promoting aging migrants' capability. Clin Interv Aging. 2018;13():2317-2328. doi:10.2147/CIA.S177791
186	McClay, C. A.; Collins, K.; Matthews, L.; Haig, C.; McConnachie, A.; Morrison, J.; Lynch, P.; Waters, L.; Day, I.; McAnee, G.; Williams, C. A community-based pilot randomised controlled study of life skills classes for individuals with low mood and depression. BMC Psychiatry. 2015;15():17. doi:10.1186/s12888-015-0384-2	Williams, Christopher; McClay, Carrie-Anne; Matthews, Lynsay; McConnachie, Alex; Haig, Caroline; Walker, Andrew; Morrison, Jill Community-based group guided self-help intervention for low mood and stress: randomised controlled trial. Br J Psychiatry. 2018;212(2):88-95. doi:10.1192/bjp.2017.18
187	Nadkarni, A.; Velleman, R.; Dabholkar, H.; Shinde, S.; Bhat, B.; McCambridge, J.; Murthy, P.; Wilson, T.; Weobong, B.; Patel, V. The systematic development and pilot randomized evaluation of counselling for alcohol problems, a lay counselor-delivered psychological treatment for harmful drinking in primary care in India: the PREMIUM study. Alcohol Clin Exp Res. 2015;39(3):522-31. doi:10.1111/acer.12653	Nadkarni, Abhijit; Weobong, Benedict; Weiss, Helen A.; McCambridge, Jim; Bhat, Bhargav; Katti, Basavaraj; Murthy, Pratima; King, Michael; McDaid, David; Park, A.-La; Wilson, G. Terence; Kirkwood, Betty; Fairburn, Christopher G.; Velleman, Richard; Patel, Vikram Counselling for Alcohol Problems (CAP), a lay counsellor-delivered brief psychological treatment for harmful drinking in men, in primary care in India: a randomised controlled trial. Lancet. 2017;389(10065):186-195. doi:10.1016/S0140-6736(16)31590-2

188	Norris, E.; Shelton, N.; Dunsmuir, S.; Duke-Williams, O.; Stamatakis, E. Virtual field trips as physically active lessons for children: a pilot study. BMC Public Health. 2015;15():366. doi:10.1186/s12889-015-1706-5	Norris, Emma; Dunsmuir, Sandra; Duke-Williams, Oliver; Stamatakis, Emmanuel; Shelton, Nicola Physically Active Lessons Improve Lesson Activity and On-Task Behavior: A Cluster-Randomized Controlled Trial of the "Virtual Traveller" Intervention. Health Educ Behav. 2018;45(6):945-956. doi:10.1177/1090198118762106
189	Pandian, J. D.; Felix, C.; Kaur, P.; Sharma, D.; Julia, L.; Toor, G.; Arora, R.; Gandhi, D. B.; Verma, S. J.; Anderson, C. S.; Langhorne, P.; Murthy, G. V.; Hackett, M. L.; Maulik, P. K.; Alim, M.; Harvey, L. A.; Jan, S.; Walker, M.; Forster, A.; Lindley, R. FAmily-Led RehabiliTaTion aftEr Stroke in INDia: the ATTEND pilot study. Int J Stroke. 2015;10(4):609-14. doi:10.1111/ijs.12475	ATTEND Collaborative Group Family-led rehabilitation after stroke in India (ATTEND): a randomised controlled trial. Lancet. 2017;390(10094):588-599. doi:10.1016/S0140-6736(17)31447-2
190	Redeker, N. S.; Jeon, S.; Andrews, L.; Cline, J.; Jacoby, D.; Mohsenin, V. Feasibility and Efficacy of a Self-Management Intervention for Insomnia in Stable Heart Failure. J Clin Sleep Med. 2015;11(10):1109-19. doi:10.5664/jcsm.5082	Redeker, Nancy S.; Yaggi, Henry Klar; Jacoby, Daniel; Hollenbeak, Christopher S.; Breazeale, Stephen; Conley, Samantha; Hwang, Youri; Iennaco, Joanne; Linsky, Sarah; Nwanaji-Enwerem, Uzoji; O'Connell, Meghan; Jeon, Sangchoon Cognitive behavioral therapy for insomnia has sustained effects on insomnia, fatigue, and function among people with chronic heart failure and insomnia: the HeartSleep Study. Sleep. 2022;45(1):zsab252. doi:10.1093/sleep/zsab252
191	Seebacher, B.; Kuisma, R.; Glynn, A.; Berger, T. Exploring cued and non-cued motor imagery interventions in people with multiple sclerosis: a randomised feasibility trial and reliability study. Arch Physiother. 2018;8():6. doi:10.1186/s40945-018-0045-0	Seebacher, Barbara; Kuisma, Raija; Glynn, Angela; Berger, Thomas The effect of rhythmic-cued motor imagery on walking, fatigue and quality of life in people with multiple sclerosis: A randomised controlled trial. Mult Scler. 2017;23(2):286-296. doi:10.1177/1352458516644058
192	Singh, R. H.; Espey, E.; Carr, S.; Pereda, B.; Ogburn, T.; Leeman, L. Nitrous oxide for pain management of first trimester surgical abortion -- a randomized controlled pilot study. Contraception. 2015;91(2):164-6. doi:10.1016/j.contraception.2014.09.013	Singh, Rameet H.; Montoya, Maria; Espey, Eve; Leeman, Lawrence Nitrous oxide versus oral sedation for pain management of first-trimester surgical abortion - a randomized study. Contraception. 2017;96(2):118-123. doi:10.1016/j.contraception.2017.06.003
193	Visser, A.; van Laarhoven, H. W.; Govaert, P. H.; Schlooz, M. S.; Jansen, L.; van Dalen, T.; Prins, J. B. Group medical consultations in the follow-up of breast cancer: a randomized feasibility study. J Cancer Surviv. 2015;9(3):450-61. doi:10.1007/s11764-014-0421-z	Visser, Annemiek; Prins, Judith B.; Jansen, Lisette; Radema, Sandra A.; Schlooz, Margrethe S.; van Dalen, Thijs; van Laarhoven, Hanneke W. M. Group medical consultations (GMCs) and tablet-based online support group sessions in the follow-up of breast cancer: A multicenter randomized controlled trial. Breast. 2018;40():181-188. doi:10.1016/j.breast.2018.05.012
194	Wang, C.; Bickmore, T.; Bowen, D. J.; Norkunas, T.; Campion, M.; Cabral, H.; Winter, M.; Paasche-Orlow, M. Acceptability and feasibility of a virtual counselor (VICKY) to collect family health histories. Genet Med.	Wang, Catharine; Paasche-Orlow, Michael K.; Bowen, Deborah J.; Cabral, Howard; Winter, Michael R.; Norkunas Cunningham, Tricia; Trevino-Talbot, Michelle; Toledo, Diana M.; Cortes, Dharma E.; Campion, MaryAnn; Bickmore, Timothy Utility of a virtual counselor

	2015;17(10):822-30. doi:10.1038/gim.2014.198	(VICKY) to collect family health histories among vulnerable patient populations: A randomized controlled trial. Patient Educ Couns. 2021;104(5):979-988. doi:10.1016/j.pec.2021.02.034
195	Yehuda, R.; Bierer, L. M.; Pratchett, L. C.; Lehrner, A.; Koch, E. C.; Van Manen, J. A.; Flory, J. D.; Makotkine, I.; Hildebrandt, T. Cortisol augmentation of a psychological treatment for warfighters with posttraumatic stress disorder: Randomized trial showing improved treatment retention and outcome. Psychoneuroendocrinology. 2015;51():589-97. doi:10.1016/j.psyneuen.2014.08.004	Lehrner, Amy; Hildebrandt, Tom; Bierer, Linda M.; Flory, Janine D.; Bader, Heather N.; Makotkine, Iouri; Yehuda, Rachel A randomized, double-blind, placebo-controlled trial of hydrocortisone augmentation of Prolonged Exposure for PTSD in U.S. combat veterans. Behav Res Ther. 2021;144():103924. doi:10.1016/j.brat.2021.103924
196	Zou, C.; Yang, L.; Wu, Y.; Su, G.; Chen, S.; Guo, X.; Wu, X.; Liu, X.; Lin, Q. Auricular acupressure on specific points for hemodialysis patients with insomnia: a pilot randomized controlled trial. PLoS One. 2015;10(4):e0122724. doi:10.1371/journal.pone.0122724	Wu, Yuchi; Yang, Lihong; Zhong, Zhicong; Wu, Xiuqing; He, Zhiren; Ma, Hongyan; Cai, Cun; Li, Yin; Wu, Xufang; Fu, Bo; Chen, Xiaoling; Wang, Lixin; Zhao, Daixin; Meng, Xiangxin; Qi, Airong; Yang, Aicheng; Li, Lingli; Liu, Xusheng; Zou, Chuan; Lin, Qizhan Auricular Acupressure for Hemodialysis Patients with Insomnia: A Multicenter Double-Blind Randomized Sham-Controlled Trial. J Integr Complement Med. 2022;28(4):339-348. doi:10.1089/jicm.2021.0332
197	Benger, J.; Coates, D.; Davies, S.; Greenwood, R.; Nolan, J.; Rhys, M.; Thomas, M.; Voss, S. Randomised comparison of the effectiveness of the laryngeal mask airway supreme, i-gel and current practice in the initial airway management of out of hospital cardiac arrest: a feasibility study. Br J Anaesth. 2016;116(2):262-8. doi:10.1093/bja/aev477	Benger, Jonathan R.; Kirby, Kim; Black, Sarah; Brett, Stephen J.; Clout, Madeleine; Lazaroo, Michelle J.; Nolan, Jerry P.; Reeves, Barnaby C.; Robinson, Maria; Scott, Lauren J.; Smartt, Helena; South, Adrian; Stokes, Elizabeth A.; Taylor, Jodi; Thomas, Matthew; Voss, Sarah; Wordsworth, Sarah; Rogers, Chris A. Effect of a Strategy of a Supraglottic Airway Device vs Tracheal Intubation During Out-of-Hospital Cardiac Arrest on Functional Outcome: The AIRWAYS-2 Randomized Clinical Trial. JAMA. 2018;320(8):779-791. doi:10.1001/jama.2018.11597
198	Breitenstein, S. M.; Fogg, L.; Ocampo, E. V.; Acosta, D. I.; Gross, D. Parent Use and Efficacy of a Self-Administered, Tablet-Based Parent Training Intervention: A Randomized Controlled Trial. JMIR Mhealth Uhealth. 2016;4(2):e36. doi:10.2196/mhealth.5202	Breitenstein, Susan M.; Fehrenbacher, Caitlin; Holod, Alicia F.; Schoeny, Michael E. A Randomized Trial of Digitally Delivered, Self-Administered Parent Training in Primary Care: Effects on Parenting and Child Behavior. J Pediatr. 2021;231():207-214.e4. doi:10.1016/j.jpeds.2020.12.016
199	Calear, A. L.; Christensen, H.; Brewer, J.; Mackinnon, A.; Griffiths, K. M. A pilot randomized controlled trial of the e-couch anxiety and worry program in schools. Internet Interv. 2016;6():44931. doi:10.1016/j.invent.2016.08.003	Calear, Alison L.; Batterham, Philip J.; Poyser, Carmel T.; Mackinnon, Andrew J.; Griffiths, Kathleen M.; Christensen, Helen Cluster randomised controlled trial of the e-couch Anxiety and Worry program in schools. J Affect Disord. 2016;196():210-217. doi:10.1016/j.jad.2016.02.049
200	Cardel, M. I.; Johnson, S. L.; Beck, J.; Dhurandhar, E.; Keita, A. D.; Tomczik, A. C.; Pavela, G.; Huo, T.; Janicke, D. M.; Muller, K.; Piff, P. K.; Peters, J. C.; Hill, J. O.; Allison, D. B. The effects of experimentally	Cardel, Michelle I.; Pavela, Greg; Janicke, David; Huo, Tianyao; Miller, Darci; Lee, Alexandra M.; Gurka, Matthew J.; Dhurandhar, Emily; Peters, John C.; Caldwell, Ann E.; Krause, Eric; Fernandez, Alicia; Allison, David B.

	manipulated social status on acute eating behavior: A randomized, crossover pilot study. Physiol Behav. 2016;162():93-101. doi:10.1016/j.physbeh.2016.04.024	Experimentally Manipulated Low Social Status and Food Insecurity Alter Eating Behavior Among Adolescents: A Randomized Controlled Trial. Obesity (Silver Spring). 2020;28(11):2010-2019. doi:10.1002/oby.23002
201	Chowdhary, N.; Anand, A.; Dimidjian, S.; Shinde, S.; Weobong, B.; Balaji, M.; Hollon, S. D.; Rahman, A.; Wilson, G. T.; Verdeli, H.; Araya, R.; King, M.; Jordans, M. J.; Fairburn, C.; Kirkwood, B.; Patel, V. The Healthy Activity Program lay counsellor delivered treatment for severe depression in India: systematic development and randomised evaluation. Br J Psychiatry. 2016;208(4):381-8. doi:10.1192/bjp.bp.114.161075	Patel, Vikram; Weobong, Benedict; Weiss, Helen A.; Anand, Arpita; Bhat, Bhargav; Katti, Basavraj; Dimidjian, Sona; Araya, Ricardo; Hollon, Steve D.; King, Michael; Vijayakumar, Lakshmi; Park, A.-La; McDaid, David; Wilson, Terry; Velleman, Richard; Kirkwood, Betty R.; Fairburn, Christopher G. The Healthy Activity Program (HAP), a lay counsellor-delivered brief psychological treatment for severe depression, in primary care in India: a randomised controlled trial. Lancet. 2017;389(10065):176-185. doi:10.1016/S0140-6736(16)31589-6
202	Davis, J. S.; Sud, A.; O'Sullivan, M. V. N.; Robinson, J. O.; Ferguson, P. E.; Foo, H.; van Hal, S. J.; Ralph, A. P.; Howden, B. P.; Binks, P. M.; Kirby, A.; Tong, S. Y. C.; Tong, S.; Davis, J.; Binks, P.; Majumdar, S.; Ralph, A.; Baird, R.; Gordon, C.; Jeremiah, C.; Leung, G.; Brischetto, A.; Crowe, A.; Dakh, F.; Whykes, K.; Kirkwood, M.; Menon, M.; Somerville, L.; Subedi, S.; Owen, S.; O'Sullivan, M.; Liu, E.; Zhou, F.; Robinson, O.; Coombs, G.; Ferguson, P.; Pollet, S.; Van Hal, S.; Davis, R. Combination of Vancomycin and β-Lactam Therapy for Methicillin-Resistant Staphylococcus aureus Bacteremia: A Pilot Multicenter Randomized Controlled Trial. Clin Infect Dis. 2016;62(2):173-180. doi:10.1093/cid/civ808	Tong, Steven Y. C.; Lye, David C.; Yahav, Dafna; Sud, Archana; Robinson, J. Owen; Nelson, Jane; Archuleta, Sophia; Roberts, Matthew A.; Cass, Alan; Paterson, David L.; Foo, Hong; Paul, Mical; Guy, Stephen D.; Tramontana, Adrian R.; Walls, Genevieve B.; McBride, Stephen; Bak, Narin; Ghosh, Niladri; Rogers, Benjamin A.; Ralph, Anna P.; Davies, Jane; Ferguson, Patricia E.; Dotel, Ravindra; McKew, Genevieve L.; Gray, Timothy J.; Holmes, Natasha E.; Smith, Simon; Warner, Morgyn S.; Kalimuddin, Shirin; Young, Barnaby E.; Runnegar, Naomi; Andresen, David N.; Anagnostou, Nicholas A.; Johnson, Sandra A.; Chatfield, Mark D.; Cheng, Allen C.; Fowler, Vance G.; Howden, Benjamin P.; Meagher, Niamh; Price, David J.; van Hal, Sebastiaan J.; O'Sullivan, Matthew V. N.; Davis, Joshua S.; Australasian Society for Infectious Diseases Clinical Research Network Effect of Vancomycin or Daptomycin With vs Without an Antistaphylococcal β-Lactam on Mortality, Bacteremia, Relapse, or Treatment Failure in Patients With MRSA Bacteremia: A Randomized Clinical Trial. JAMA. 2020;323(6):527-537. doi:10.1001/jama.2020.0103
203	DeVan, A. E.; Johnson, L. C.; Brooks, F. A.; Evans, T. D.; Justice, J. N.; Cruickshank-Quinn, C.; Reisdorph, N.; Bryan, N. S.; McQueen, M. B.; Santos-Parker, J. R.; Chonchol, M. B.; Bassett, C. J.; Sindler, A. L.; Giordano, T.; Seals, D. R. Effects of sodium nitrite supplementation on vascular function and related small metabolite signatures in middle-aged and older adults. J Appl Physiol (1985). 2016;120(4):416-25. doi:10.1152/japplphysiol.00879.2015	Rossman, Matthew J.; Gioscia-Ryan, Rachel A.; Santos-Parker, Jessica R.; Ziemba, Brian P.; Lubieniecki, Kara L.; Johnson, Lawrence C.; Poliektov, Natalie E.; Bispham, Nina Z.; Woodward, Kayla A.; Nagy, Erzsebet E.; Bryan, Nathan S.; Reisz, Julie A.; D'Alessandro, Angelo; Chonchol, Michel; Sindler, Amy L.; Seals, Douglas R. Inorganic Nitrite Supplementation Improves Endothelial Function With Aging: Translational Evidence for Suppression of Mitochondria-Derived Oxidative Stress. Hypertension. 2021;77(4):1212-1222. doi:10.1161/HYPERTENSIONAHA.120.16175

204	Domek, G. J.; Contreras-Roldan, I. L.; O'Leary, S. T.; Bull, S.; Furniss, A.; Kempe, A.; Asturias, E. J. SMS text message reminders to improve infant vaccination coverage in Guatemala: A pilot randomized controlled trial. Vaccine. 2016;34(21):2437-2443. doi:10.1016/j.vaccine.2016.03.065	Domek, Gretchen J.; Contreras-Roldan, Ingrid L.; Bull, Sheana; O'Leary, Sean T.; Bolaños Ventura, Guillermo Antonio; Bronsert, Michael; Kempe, Allison; Asturias, Edwin J. Text message reminders to improve infant immunization in Guatemala: A randomized clinical trial. Vaccine. 2019;37(42):6192-6200. doi:10.1016/j.vaccine.2019.08.046
205	Foster, B. A.; Aquino, C. A.; Gil, M.; Gelfond, J. A.; Hale, D. E. A Pilot Study of Parent Mentors for Early Childhood Obesity. J Obes. 2016;2016():2609504. doi:10.1155/2016/2609504	Foster, Byron A.; Weinstein, Kelsey; Padilla, Thalia; Martinez, Cynthia; Angeles-Ramos, Diana Growing Healthy Together: A Randomized Clinical Trial Using Parent Mentors for Early Childhood Obesity in Low-Income, Latino Families. Child Obes. 2022;18(3):168-177. doi:10.1089/chi.2021.0165
206	Griffin, X. L.; Parsons, N.; McArthur, J.; Achten, J.; Costa, M. L. The Warwick Hip Trauma Evaluation One: a randomised pilot trial comparing the X-Bolt Dynamic Hip Plating System with sliding hip screw fixation in complex extracapsular hip fractures: WHiTE (One). Bone Joint J. 2016;98-b(5):686-9. doi:10.1302/0301-620x.98b5.37350	Griffin, Xavier L.; Achten, Juul; O'Connor, Heather Marie; Cook, Jonathan A.; Costa, Matt L.; WHiTE Four Investigators Effect on health-related quality of life of the X-Bolt dynamic plating system versus the sliding hip screw for the fixation of trochanteric fractures of the hip in adults: the WHiTE Four randomized clinical trial. Bone Joint J. 2021;103-B(2):256-263. doi:10.1302/0301-620X.103B.BJJ-2020-1404.R1
207	Kidger, J.; Stone, T.; Tilling, K.; Brockman, R.; Campbell, R.; Ford, T.; Hollingworth, W.; King, M.; Araya, R.; Gunnell, D. A pilot cluster randomised controlled trial of a support and training intervention to improve the mental health of secondary school teachers and students - the WISE (Wellbeing in Secondary Education) study. BMC Public Health. 2016;16(1):1060. doi:10.1186/s12889-016-3737-y	Kidger, Judi; Turner, Nicholas; Hollingworth, William; Evans, Rhiannon; Bell, Sarah; Brockman, Rowan; Copeland, Lauren; Fisher, Harriet; Harding, Sarah; Powell, Jillian; Araya, Ricardo; Campbell, Rona; Ford, Tamsin; Gunnell, David; Murphy, Simon; Morris, Richard An intervention to improve teacher well-being support and training to support students in UK high schools (the WISE study): A cluster randomised controlled trial. PLoS Med. 2021;18(11):e1003847. doi:10.1371/journal.pmed.1003847
208	Lewis, S. C.; Bhattacharya, S.; Wu, O.; Vincent, K.; Jack, S. A.; Critchley, H. O.; Porter, M. A.; Cranley, D.; Wilson, J. A.; Horne, A. W. Gabapentin for the Management of Chronic Pelvic Pain in Women (GaPP1): A Pilot Randomised Controlled Trial. PLoS One. 2016;11(4):e0153037. doi:10.1371/journal.pone.0153037	Horne, Andrew W.; Vincent, Katy; Hewitt, Catherine A.; Middleton, Lee J.; Koscielniak, Magda; Szubert, Wojciech; Doust, Ann M.; Daniels, Jane P.; GaPP2 collaborative Gabapentin for chronic pelvic pain in women (GaPP2): a multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2020;396(10255):909-917. doi:10.1016/S0140-6736(20)31693-7
209	Milgrom, J.; Danaher, B. G.; Gemmill, A. W.; Holt, C.; Holt, C. J.; Seeley, J. R.; Tyler, M. S.; Ross, J.; Ericksen, J. Internet Cognitive Behavioral Therapy for Women With Postnatal Depression: A Randomized Controlled Trial of MumMoodBooster. J Med Internet Res. 2016;18(3):e54. doi:10.2196/jmir.4993	Milgrom, Jeannette; Danaher, Brian G.; Seeley, John R.; Holt, Christopher J.; Holt, Charlene; Ericksen, Jennifer; Tyler, Milagra S.; Gau, Jeff M.; Gemmill, Alan W. Internet and Face-to-face Cognitive Behavioral Therapy for Postnatal Depression Compared With Treatment as Usual: Randomized Controlled Trial of MumMoodBooster. J Med Internet Res. 2021;23(12):e17185. doi:10.2196/17185
210	Morgan, A. J.; Rapee, R. M.; Bayer, J. K. Prevention and early intervention of anxiety	Morgan, Amy J.; Rapee, Ronald M.; Salim, Agus; Goharpey, Nahal; Tamir, Elli; McLellan, Lauren

	problems in young children: A pilot evaluation of Cool Little Kids Online. Internet Interv. 2016;4():105-112. doi:10.1016/j.invent.2016.05.001	F.; Bayer, Jordana K. Internet-Delivered Parenting Program for Prevention and Early Intervention of Anxiety Problems in Young Children: Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2017;56(5):417-425.e1. doi:10.1016/j.jaac.2017.02.010
211	Muth, C.; Harder, S.; Uhlmann, L.; Rochon, J.; Fullerton, B.; Güthlin, C.; Erler, A.; Beyer, M.; van den Akker, M.; Perera, R.; Knottnerus, A.; Valderas, J. M.; Gerlach, F. M.; Haefeli, W. E. Pilot study to test the feasibility of a trial design and complex intervention on PRIoritising MUltimedication in Multimorbidity in general practices (PRIMUMpilot). BMJ Open. 2016;6(7):e011613. doi:10.1136/bmjopen-2016-011613	Muth, Christiane; Uhlmann, Lorenz; Haefeli, Walter E.; Rochon, Justine; van den Akker, Marjan; Perera, Rafael; Güthlin, Corina; Beyer, Martin; Oswald, Frank; Valderas, Jose Maria; Knottnerus, J. André; Gerlach, Ferdinand M.; Harder, Sebastian Effectiveness of a complex intervention on Prioritising Multimedication in Multimorbidity (PRIMUM) in primary care: results of a pragmatic cluster randomised controlled trial. BMJ Open. 2018;8(2):e017740. doi:10.1136/bmjopen-2017-017740
212	Pears, S.; Bijker, M.; Morton, K.; Vasconcelos, J.; Parker, R. A.; Westgate, K.; Brage, S.; Wilson, E.; Prevost, A. T.; Kinmonth, A. L.; Griffin, S.; Sutton, S.; Hardeman, W. A randomised controlled trial of three very brief interventions for physical activity in primary care. BMC Public Health. 2016;16(1):1033. doi:10.1186/s12889-016-3684-7	Hardeman, Wendy; Mitchell, Joanna; Pears, Sally; Van Emmenis, Miranda; Theil, Florence; Gc, Vijay S.; Vasconcelos, Joana C.; Westgate, Kate; Brage, Søren; Suhrcke, Marc; Griffin, Simon J.; Kinmonth, Ann Louise; Wilson, Edward C. F.; Prevost, A. Toby; Sutton, Stephen; VBI Research Team Evaluation of a very brief pedometer-based physical activity intervention delivered in NHS Health Checks in England: The VBI randomised controlled trial. PLoS Med. 2020;17(3):e1003046. doi:10.1371/journal.pmed.1003046
213	Scheller, Christian; Richter, Hans-Peter; Engelhardt, Martin; Köenig, Ralph; Antoniadis, Gregor The influence of prophylactic vasoactive treatment on cochlear and facial nerve functions after vestibular schwannoma surgery: a prospective and open-label randomized pilot study. Neurosurgery. 2007;61(1):92-97; discussion 97-98. doi:10.1227/01.neu.0000279728.98273.51	Scheller, Christian; Wienke, Andreas; Tatagiba, Marcos; Gharabaghi, Alireza; Ramina, Kristofer F.; Ganslandt, Oliver; Bischoff, Barbara; Zenk, Johannes; Engelhorn, Tobias; Matthies, Cordula; Westermaier, Thomas; Antoniadis, Gregor; Pedro, Maria Teresa; Rohde, Veit; von Eckardstein, Kajetan; Kretschmer, Thomas; Kornhuber, Malte; Steighardt, Jörg; Richter, Michael; Barker, Fred G.; Strauss, Christian Prophylactic nimodipine treatment for cochlear and facial nerve preservation after vestibular schwannoma surgery: a randomized multicenter Phase III trial. J Neurosurg. 2016;124(3):657-664. doi:10.3171/2015.1.JNS142001
214	Aharonovich, Efrat; Greenstein, Eliana; O'Leary, Ann; Johnston, Barbara; Seol, Simone G.; Hasin, Deborah S. HealthCall: technology-based extension of motivational interviewing to reduce non-injection drug use in HIV primary care patients - a pilot study. AIDS Care. 2012;24(12):1461-1469. doi:10.1080/09540121.2012.663882	Aharonovich, Efrat; Sarvet, Aaron; Stohl, Malki; DesJarlais, Don; Tross, Susan; Hurst, Teresa; Urbina, Antonio; Hasin, Deborah Reducing non-injection drug use in HIV primary care: A randomized trial of brief motivational interviewing, with and without HealthCall, a technology-based enhancement. J Subst Abuse Treat. 2017;74():71-79. doi:10.1016/j.jsat.2016.12.009
215	Anthenelli, Robert M.; Blom, Thomas J.; McElroy, Susan L.; Keck, Paul E. Preliminary evidence for gender-specific effects of topiramate as a potential aid to	Anthenelli, Robert M.; Heffner, Jaimee L.; Wong, Esther; Tibbs, Jessie; Russell, Katie; Isgro, Melodie; Dinh, Elizabeth; Wehrle, Chris; Worley, Matthew J.; Doran, Neal A Randomized Trial

	smoking cessation. Addiction. 2008;103(4):687-694. doi:10.1111/j.1360-0443.2008.02148.x	Evaluating Whether Topiramate Aids Smoking Cessation and Prevents Alcohol Relapse in Recovering Alcohol-Dependent Men. Alcohol Clin Exp Res. 2017;41(1):197-206. doi:10.1111/acer.13279
216	Artz, N.; Dixon, S.; Wylde, V.; Marques, E.; Beswick, A. D.; Lenguerrand, E.; Blom, A. W.; Gooberman-Hill, R. Comparison of group-based outpatient physiotherapy with usual care after total knee replacement: a feasibility study for a randomized controlled trial. Clin Rehabil. 2017;31(4):487-499. doi:10.1177/0269215516642503	Lenguerrand, Erik; Artz, Neil; Marques, Elsa; Sanderson, Emily; Lewis, Kristina; Murray, James; Parwez, Tarique; Bertram, Wendy; Beswick, Andrew D.; Burston, Amanda; Gooberman-Hill, Rachael; Blom, Ashley W.; Wylde, Vikki Effect of Group-Based Outpatient Physical Therapy on Function After Total Knee Replacement: Results From a Multicenter Randomized Controlled Trial. Arthritis Care Res (Hoboken). 2020;72(6):768-777. doi:10.1002/acr.23909
217	Bouma, G.; de Hosson, L. D.; van Woerkom, C. E.; van Essen, H.; de Bock, G. H.; Admiraal, J. M.; Reyners, A. K. L.; Walenkamp, A. M. E. Web-based information and support for patients with a newly diagnosed neuroendocrine tumor: a feasibility study. Support Care Cancer. 2017;25(7):2075-2083. doi:10.1007/s00520-017-3598-7	de Hosson, L. D.; Bouma, G.; Stelwagen, J.; van Essen, H.; de Bock, G. H.; de Groot, D. J. A.; de Vries, E. G. E.; Walenkamp, A. M. E. Web-based personalised information and support for patients with a neuroendocrine tumour: randomised controlled trial. Orphanet J Rare Dis. 2019;14(1):60. doi:10.1186/s13023-019-1035-3
218	Burke, L. E.; Zheng, Y.; Ma, Q.; Mancino, J.; Loar, I.; Music, E.; Styn, M.; Ewing, L.; French, B.; Sieworek, D.; Smailagic, A.; Sereika, S. M. The SMARTER pilot study: Testing feasibility of real-time feedback for dietary self-monitoring. Prev Med Rep. 2017;6():278-285. doi:10.1016/j.pmedr.2017.03.017	Burke, Lora E.; Sereika, Susan M.; Parmanto, Bambang; Bizhanova, Zhadyra; Kariuki, Jacob K.; Cheng, Jessica; Beatrice, Britney; Loar, India; Pulantara, I. Wayan; Wang, Yuhan; Cedillo, Maribel; Conroy, Molly B. Effect of tailored, daily feedback with lifestyle self-monitoring on weight loss: The SMARTER randomized clinical trial. Obesity (Silver Spring). 2022;30(1):75-84. doi:10.1002/oby.23321
219	Chow, E. P.; Howden, B. P.; Walker, S.; Lee, D.; Bradshaw, C. S.; Chen, M. Y.; Snow, A.; Cook, S.; Fehler, G.; Fairley, C. K. Antiseptic mouthwash against pharyngeal Neisseria gonorrhoeae: a randomised controlled trial and an in vitro study. Sex Transm Infect. 2017;93(2):88-93. doi:10.1136/sextrans-2016-052753	Chow, Eric P. F.; Williamson, Deborah A.; Hocking, Jane S.; Law, Matthew G.; Maddaford, Kate; Bradshaw, Catriona S.; McNulty, Anna; Templeton, David J.; Moore, Richard; Murray, Gerald L.; Danielewski, Jennifer A.; Wigan, Rebecca; Chen, Marcus Y.; Guy, Rebecca J.; Zhang, Lei; Donovan, Basil; Grulich, Andrew E.; Kaldor, John M.; Whiley, David M.; Cornelisse, Vincent J.; Howden, Benjamin P.; Lewis, David A.; Read, Tim R. H.; Fairley, Christopher K. Antiseptic mouthwash for gonorrhoea prevention (OMEGA): a randomised, double-blind, parallel-group, multicentre trial. Lancet Infect Dis. 2021;21(5):647-656. doi:10.1016/S1473-3099(20)30704-0
220	Cook, R. L.; Weber, K. M.; Mai, D.; Thoma, K.; Hu, X.; Brumback, B.; Karki, M.; Bryant, K.; Rathore, M.; Young, M.; Cohen, M. Acceptability and feasibility of a randomized clinical trial of oral naltrexone vs. placebo for women living with HIV infection: Study design challenges and pilot study results.	Cook, Robert L.; Zhou, Zhi; Miguez, Maria Jose; Quiros, Clery; Espinoza, Luis; Lewis, John E.; Brumback, Babette; Bryant, Kendall Reduction in Drinking was Associated With Improved Clinical Outcomes in Women With HIV Infection and Unhealthy Alcohol Use: Results From a Randomized Clinical Trial of Oral Naltrexone

	Contemp Clin Trials. 2017;60():72-77. doi:10.1016/j.cct.2017.06.012	Versus Placebo. Alcohol Clin Exp Res. 2019;43(8):1790-1800. doi:10.1111/acer.14130
221	Ehling, R.; Edlinger, M.; Hermann, K.; Dröge, K.; Seidinger, Y.; Miller, U.; Alber, H. F.; Brenneis, C. Successful long-term management of spasticity in patients with multiple sclerosis using a software application (APP): A pilot study. Mult Scler Relat Disord. 2017;17():15-21. doi:10.1016/j.msard.2017.06.013	Ehling, Rainer; Seebacher, Barbara; Harsányi, Andrea; Ganzbiller, Nicole; Papez, Stephanie; Haider, Bernhard; Hoertenhuber, Doris; Kranz, Gottfried; Tarasiewicz, Roland; Spatt, Josef; Moser, Hermann; Klein, Wolfhard; Barth, Cosmas; Kubik, Wolfgang; Kronberger, Eva; Winkler, Andreas; Brenneis, Christian Successful long-term management of spasticity in people with multiple sclerosis using a software application: Results from a randomized, controlled, multicenter study. Eur J Neurol. 2022;29(6):1697-1707. doi:10.1111/ene.15271
222	Hossain, M. S.; Harvey, L. A.; Rahman, M. A.; Bowden, J. L.; Islam, M. S.; Taylor, V.; Muldoon, S.; Herbert, R. D. A pilot randomised trial of community-based care following discharge from hospital with a recent spinal cord injury in Bangladesh. Clin Rehabil. 2017;31(6):781-789. doi:10.1177/0269215516654207	Hossain, Mohammad Sohrab; Harvey, Lisa A.; Islam, Md Shofiqul; Rahman, Md Akhlasur; Muldoon, Stephen; Biering-Sorensen, Fin; Jan, Stephen; Liu, Hueiming; Li, Qiang; Cameron, Ian D.; Taylor, Valerie; Lindley, Richard I.; Billot, Laurent; Herbert, Robert D. A community-based intervention to prevent serious complications and death 2 years after discharge in people with spinal cord injury in Bangladesh (CIVIC): a randomised trial. Spinal Cord. 2021;59(6):649-658. doi:10.1038/s41393-020-00546-9
223	Jacq, O.; Arnulf, I.; Similowski, T.; Attali, V. Upper airway stabilization by osteopathic manipulation of the sphenopalatine ganglion versus sham manipulation in OSAS patients: a proof-of-concept, randomized, crossover, double-blind, controlled study. BMC Complement Altern Med. 2017;17(1):546. doi:10.1186/s12906-017-2053-0	Attali, Valérie; Jacq, Olivier; Martin, Karine; Arnulf, Isabelle; Similowski, Thomas Osteopathic Manipulation of the Sphenopalatine Ganglia Versus Sham Manipulation, in Obstructive Sleep Apnoea Syndrom: A Randomised Controlled Trial. J Clin Med. 2021;11(1):99. doi:10.3390/jcm11010099
224	Kauer, S. D.; Buhagiar, K.; Blake, V.; Cotton, S.; Sanci, L. Facilitating mental health help-seeking by young adults with a dedicated online program: a feasibility study of Link. BMJ Open. 2017;7(7):e015303. doi:10.1136/bmjopen-2016-015303	Sanci, Lena; Kauer, Sylvia; Thuraisingam, Sharmala; Davidson, Sandra; Duncan, Ann-Maree; Chondros, Patty; Mihalopoulos, Cathrine; Buhagiar, Kerrie Effectiveness of a Mental Health Service Navigation Website (Link) for Young Adults: Randomized Controlled Trial. JMIR Ment Health. 2019;6(10):e13189. doi:10.2196/13189
225	Korthuis, P. T.; Lum, P. J.; Vergara-Rodriguez, P.; Ahamad, K.; Wood, E.; Kunkel, L. E.; Oden, N. L.; Lindblad, R.; Sorensen, J. L.; Arenas, V.; Ha, D.; Mandler, R. N.; McCarty, D. Feasibility and safety of extended-release naltrexone treatment of opioid and alcohol use disorder in HIV clinics: a pilot/feasibility randomized trial. Addiction. 2017;112(6):1036-1044. doi:10.1111/add.13753	Korthuis, P. Todd; Cook, Ryan R.; Lum, Paula J.; Waddell, Elizabeth Needham; Tookes, Hansel; Vergara-Rodriguez, Pamela; Kunkel, Lynn E.; Lucas, Gregory M.; Rodriguez, Allan E.; Bielavitz, Sarann; Fanucchi, Laura C.; Hoffman, Kim A.; Bachrach, Ken; Payne, Elizabeth H.; Collins, Julia A.; Matthews, Abigail; Oden, Neal; Jacobs, Petra; Jelstrom, Eve; Sorensen, James L.; McCarty, Dennis HIV clinic-based extended-release naltrexone versus treatment as usual for people with HIV and opioid use disorder: a non-blinded, randomized non-inferiority trial. Addiction. 2022;117(7):1961-1971. doi:10.1111/add.15836

226	Madurasinghe, V. W.; Sohanpal, R.; James, W.; Steed, L.; Eldridge, S.; Taylor, S.; Griffiths, C.; Walton, R. Smoking treatment optimisation in pharmacies (STOP): a cluster randomised pilot trial of a training intervention. Pilot Feasibility Stud. 2017;3():1. doi:10.1186/s40814-016-0120-9	Jumbe, Sandra; Madurasinghe, Vichithranie W.; James, Wai Yee; Houlihan, Colin; Jumbe, Samantha L.; Yau, Tammy; Tomini, Florian; Eldridge, Sandra; Mihaylova, Borislava; Steed, Liz; Sohanpal, Ratna; Attar, Darush; Taylor, Stephanie J. C.; Griffiths, Chris; Walton, Robert STOP- a training intervention to optimise treatment for smoking cessation in community pharmacies: cluster randomised controlled trial. BMC Med. 2022;20(1):212. doi:10.1186/s12916-022-02412-2
227	McInnes, N.; Smith, A.; Otto, R.; Vandermey, J.; Punthakee, Z.; Sherifali, D.; Balasubramanian, K.; Hall, S.; Gerstein, H. C. Piloting a Remission Strategy in Type 2 Diabetes: Results of a Randomized Controlled Trial. J Clin Endocrinol Metab. 2017;102(5):1596-1605. doi:10.1210/jc.2016-3373	McInnes, Natalia; Hall, Stephanie; Sultan, Farah; Aronson, Ronnie; Hramiak, Irene; Harris, Stewart; Sigal, Ronald J.; Woo, Vincent; Liu, Yan Yun; Gerstein, Hertzel C. Remission of Type 2 Diabetes Following a Short-term Intervention With Insulin Glargine, Metformin, and Dapagliflozin. J Clin Endocrinol Metab. 2020;105(8):dgaa248. doi:10.1210/clinem/dgaa248
228	Ou-Yang, J.; He, B.; Rong, X.; Bei, C. H. Can inactive blood donors be re-recruited? A stratified randomised pilot study. Transfus Med. 2017;27(6):421-427. doi:10.1111/tme.12436	Ou-Yang, Jian; Bei, Chun-Hua; Liang, Hua-Qin; He, Bo; Chen, Jin-Yan; Fu, Yong-Shui Effective methods for reactivating inactive blood donors: a stratified randomised controlled study. BMC Public Health. 2020;20(1):475. doi:10.1186/s12889-020-08594-9
229	Rafiq, R.; Prins, H. J.; Boersma, W. G.; Daniels, J. M.; den Heijer, M.; Lips, P.; de Jongh, R. T. Effects of daily vitamin D supplementation on respiratory muscle strength and physical performance in vitamin D-deficient COPD patients: a pilot trial. Int J Chron Obstruct Pulmon Dis. 2017;12():2583-2592. doi:10.2147/copd.S132117	Rafiq, Rachida; Aleva, Floor E.; Schrumpf, Jasmijn A.; Daniels, Johannes M.; Bet, Pierre M.; Boersma, Wim G.; Bresser, Paul; Spanbroek, Michiel; Lips, Paul; van den Broek, Tim J.; Keijser, Bart J. F.; van der Ven, André J. A. M.; Hiemstra, Pieter S.; den Heijer, Martin; de Jongh, Renate T.; PRECOVID-study group Vitamin D supplementation in chronic obstructive pulmonary disease patients with low serum vitamin D: a randomized controlled trial. Am J Clin Nutr. 2022;116(2):491-499. doi:10.1093/ajcn/nqac083
230	Reeves, G. R.; Whellan, D. J.; O'Connor, C. M.; Duncan, P.; Eggebeen, J. D.; Morgan, T. M.; Hewston, L. A.; Pastva, A.; Patel, M. J.; Kitzman, D. W. A Novel Rehabilitation Intervention for Older Patients With Acute Decompensated Heart Failure: The REHAB-HF Pilot Study. JACC Heart Fail. 2017;5(5):359-366. doi:10.1016/j.jchf.2016.12.019	Kitzman, Dalane W.; Whellan, David J.; Duncan, Pamela; Pastva, Amy M.; Mentz, Robert J.; Reeves, Gordon R.; Nelson, M. Benjamin; Chen, Haiying; Upadhya, Bharathi; Reed, Shelby D.; Espeland, Mark A.; Hewston, LeighAnn; O'Connor, Christopher M. Physical Rehabilitation for Older Patients Hospitalized for Heart Failure. N Engl J Med. 2021;385(3):203-216. doi:10.1056/NEJMoa2026141
231	Lim, Kyeong-Tae; Hwang, Eui-Hyoung; Cho, Jae-Heung; Jung, Jae-Young; Kim, Koh-Woon; Ha, In-Hyuk; Kim, Me-Riong; Nam, Kibong; Lee A, Min Ho; Lee, Jun-Hwan; Kim, Namkwen; Shin, Byung-Cheul Comparative effectiveness of Chuna manual therapy versus conventional usual care for non-acute low back pain: a pilot randomized controlled	Park, Sun-Young; Hwang, Eui-Hyoung; Cho, Jae-Heung; Kim, Koh-Woon; Ha, In-Hyuk; Kim, Me-Riong; Nam, Kibong; Lee, Min Ho; Lee, Jun-Hwan; Kim, Namkwen; Shin, Byung-Cheul Comparative Effectiveness of Chuna Manipulative Therapy for Non-Acute Lower Back Pain: A Multi-Center, Pragmatic, Randomized Controlled Trial. J Clin Med. 2020;9(1):E144. doi:10.3390/jcm9010144

	trial. Trials. 2019;20(1):216. doi:10.1186/s13063-019-3302-y	
232	Smit, A. K.; Espinoza, D.; Newson, A. J.; Morton, R. L.; Fenton, G.; Freeman, L.; Dunlop, K.; Butow, P. N.; Law, M. H.; Kimlin, M. G.; Keogh, L. A.; Dobbinson, S. J.; Kirk, J.; Kanetsky, P. A.; Mann, G. J.; Cust, A. E. A Pilot Randomized Controlled Trial of the Feasibility, Acceptability, and Impact of Giving Information on Personalized Genomic Risk of Melanoma to the Public. Cancer Epidemiol Biomarkers Prev. 2017;26(2):212-221. doi:10.1158/1055-9965.Epi-16-0395	Smit, Amelia K.; Allen, Martin; Beswick, Brooke; Butow, Phyllis; Dawkins, Hugh; Dobbinson, Suzanne J.; Dunlop, Kate L.; Espinoza, David; Fenton, Georgina; Kanetsky, Peter A.; Keogh, Louise; Kimlin, Michael G.; Kirk, Judy; Law, Matthew H.; Lo, Serigne; Low, Cynthia; Mann, Graham J.; Reyes-Marcelino, Gillian; Morton, Rachael L.; Newson, Ainsley J.; Savard, Jacqueline; Trevena, Lyndal; Wordsworth, Sarah; Cust, Anne E. Impact of personal genomic risk information on melanoma prevention behaviors and psychological outcomes: a randomized controlled trial. Genet Med. 2021;23(12):2394-2403. doi:10.1038/s41436-021-01292-w
233	Vázquez, F. L.; Torres, Á; Otero, P.; Blanco, V.; Díaz, O.; Estévez, L. E. Analysis of the components of a cognitive-behavioral intervention administered via conference call for preventing depression among non-professional caregivers: a pilot study. Aging Ment Health. 2017;21(9):938-946. doi:10.1080/13607863.2016.1181714	Vázquez, Fernando L.; López, Lara; Torres, Ángela J.; Otero, Patricia; Blanco, Vanessa; Díaz, Olga; Páramo, Mario Analysis of the Components of a Cognitive-Behavioral Intervention for the prevention of Depression Administered via Conference Call to Nonprofessional Caregivers: A Randomized Controlled Trial. Int J Environ Res Public Health. 2020;17(6):E2067. doi:10.3390/ijerph17062067
234	Buyse, Gunnar M.; Goemans, Nathalie; van den Hauwe, Marleen; Thijs, Daisy; de Groot, Imelda J. M.; Schara, Ulrike; Ceulemans, Berten; Meier, Thomas; Mertens, Luc Idebenone as a novel, therapeutic approach for Duchenne muscular dystrophy: results from a 12 month, double-blind, randomized placebo-controlled trial. Neuromuscul Disord. 2011;21(6):396-405. doi:10.1016/j.nmd.2011.02.016	Buyse, Gunnar M.; Voit, Thomas; Schara, Ulrike; Straathof, Chiara S. M.; D'Angelo, M. Grazia; Bernert, Günther; Cuisset, Jean-Marie; Finkel, Richard S.; Goemans, Nathalie; McDonald, Craig M.; Rummey, Christian; Meier, Thomas; DELOS Study Group Efficacy of idebenone on respiratory function in patients with Duchenne muscular dystrophy not using glucocorticoids (DELOS): a double-blind randomised placebo-controlled phase 3 trial. Lancet. 2015;385(9979):1748-1757. doi:10.1016/S0140-6736(15)60025-3
235	Guo, Y.; Xu, Z.; Qiao, J.; Hong, Y. A.; Zhang, H.; Zeng, C.; Cai, W.; Li, L.; Liu, C. Development and Feasibility Testing of an mHealth (Text Message and WeChat) Intervention to Improve the Medication Adherence and Quality of Life of People Living with HIV in China: Pilot Randomized Controlled Trial. JMIR Mhealth Uhealth. 2018;6(9):e10274. doi:10.2196/10274	Guo, Yan; Hong, Y. Alicia; Cai, Weiping; Li, Linghua; Hao, Yuantao; Qiao, Jiaying; Xu, Zhimeng; Zhang, Hanxi; Zeng, Chengbo; Liu, Cong; Li, Yiran; Zhu, Mengting; Zeng, Yu; Penedo, Frank J. Effect of a WeChat-Based Intervention (Run4Love) on Depressive Symptoms Among People Living With HIV in China: A Randomized Controlled Trial. J Med Internet Res. 2020;22(2):e16715. doi:10.2196/16715
236	Hei, S. V.; McKinstry, S.; Bardsley, G.; Weatherall, M.; Beasley, R.; Fingleton, J. Randomised controlled trial of rhinothermy for treatment of the common cold: a feasibility study. BMJ Open. 2018;8(3):e019350. doi:10.1136/bmjopen-2017-019350	Bird, Grace; Braithwaite, Irene; Harper, James; Koorevaar, Iris; van den Berg, Marthe; Maijers, Ingrid; Kearns, Nethmi; Dilcher, Meik; Jennings, Lance; Fingleton, James; Shortt, Nick; Weatherall, Mark; Beasley, Richard Rhinothermy delivered by nasal high flow therapy in the treatment of the common cold: a randomised controlled trial. BMJ Open.

		2021;11(11):e047760. doi:10.1136/bmjopen-2020-047760
237	Lannin, N. A.; Ada, L.; Levy, T.; English, C.; Ratcliffe, J.; Sindhusake, D.; Crotty, M. Intensive therapy after botulinum toxin in adults with spasticity after stroke versus botulinum toxin alone or therapy alone: a pilot, feasibility randomized trial. Pilot Feasibility Stud. 2018;4():82. doi:10.1186/s40814-018-0276-6	Lannin, Natasha A.; Ada, Louise; English, Coralie; Ratcliffe, Julie; Faux, Steven G.; Palit, Mithu; Gonzalez, Senen; Olver, John; Cameron, Ian; Crotty, Maria; InTENSE Trial Group Effect of Additional Rehabilitation After Botulinum Toxin-A on Upper Limb Activity in Chronic Stroke: The InTENSE Trial. Stroke. 2020;51(2):556-562. doi:10.1161/STROKEAHA.119.027602
238	Laufs, U.; Griese-Mammen, N.; Krueger, K.; Wachter, A.; Anker, S. D.; Koehler, F.; Rettig-Ewen, V.; Botermann, L.; Strauch, D.; Trenk, D.; Böhm, M.; Schulz, M. PHARMacy-based interdisciplinary program for patients with Chronic Heart Failure (PHARM-CHF): rationale and design of a randomized controlled trial, and results of the pilot study. Eur J Heart Fail. 2018;20(9):1350-1359. doi:10.1002/ejhf.1213	Schulz, Martin; Griese-Mammen, Nina; Anker, Stefan D.; Koehler, Friedrich; Ihle, Peter; Ruckes, Christian; Schumacher, Pia M.; Trenk, Dietmar; Böhm, Michael; Laufs, Ulrich; PHARM-CHF Investigators Pharmacy-based interdisciplinary intervention for patients with chronic heart failure: results of the PHARM-CHF randomized controlled trial. Eur J Heart Fail. 2019;21(8):1012-1021. doi:10.1002/ejhf.1503
239	Lennox, C.; Kirkpatrick, T.; Taylor, R. S.; Todd, R.; Greenwood, C.; Haddad, M.; Stevenson, C.; Stewart, A.; Shenton, D.; Carroll, L.; Brand, S. L.; Quinn, C.; Anderson, R.; Maguire, M.; Harris, T.; Shaw, J.; Byng, R. Pilot randomised controlled trial of the ENGAGER collaborative care intervention for prisoners with common mental health problems, near to and after release. Pilot Feasibility Stud. 2018;4():15. doi:10.1186/s40814-017-0163-6	Byng, Richard; Kirkpatrick, Tim; Lennox, Charlotte; Warren, Fiona C.; Anderson, Rob; Brand, Sarah Louise; Callaghan, Lynne; Carroll, Lauren; Durcan, Graham; Gill, Laura; Goodier, Sara; Graham, Jonathan; Greer, Rebecca; Haddad, Mark; Harris, Tirril; Henley, William; Hunter, Rachael; Leonard, Sarah; Maguire, Mike; Michie, Susan; Owens, Christabel; Pearson, Mark; Quinn, Cath; Rybczynska-Bunt, Sarah; Stevenson, Caroline; Stewart, Amy; Stirzaker, Alex; Todd, Roxanne; Walter, Florian; Weston, Lauren; Wright, Nat; Taylor, Rod S.; Shaw, Jenny Evaluation of a complex intervention for prisoners with common mental health problems, near to and after release: the Engager randomised controlled trial. Br J Psychiatry. 2022;():44935. doi:10.1192/bjp.2022.93
240	Locke, S. R.; Bourne, J. E.; Beauchamp, M. R.; Little, J. P.; Barry, J.; Singer, J.; Jung, M. E. High-Intensity Interval or Continuous Moderate Exercise: A 24-Week Pilot Trial. Med Sci Sports Exerc. 2018;50(10):2067-2075. doi:10.1249/mss.0000000000001668	Jung, M. E.; Locke, S. R.; Bourne, J. E.; Beauchamp, M. R.; Lee, T.; Singer, J.; MacPherson, M.; Barry, J.; Jones, C.; Little, J. P. Cardiorespiratory fitness and accelerometer-determined physical activity following one year of free-living high-intensity interval training and moderate-intensity continuous training: a randomized trial. Int J Behav Nutr Phys Act. 2020;17(1):25. doi:10.1186/s12966-020-00933-8
241	Pfaeffli Dale, Leila; Whittaker, Robyn; Jiang, Yannan; Stewart, Ralph; Rolleston, Anna; Maddison, Ralph Text Message and Internet Support for Coronary Heart Disease Self-Management: Results From the Text4Heart Randomized Controlled Trial. J Med Internet Res. 2015;17(10):e237. doi:10.2196/jmir.4944	Maddison, Ralph; Jiang, Yannan; Stewart, Ralph; Scott, Tony; Kerr, Andrew; Whittaker, Robyn; Benatar, Jocelyn; Rolleston, Anna; Estabrooks, Paul; Dale, Leila An Intervention to Improve Medication Adherence in People With Heart Disease (Text4HeartII): Randomized Controlled Trial. JMIR Mhealth Uhealth. 2021;9(6):e24952. doi:10.2196/24952

242	Lewis, Catrin E.; Farewell, Daniel; Groves, Vicky; Kitchiner, Neil J.; Roberts, Neil P.; Vick, Tracey; Bisson, Jonathan I. Internet-based guided self-help for posttraumatic stress disorder (PTSD): Randomized controlled trial. Depress Anxiety. 2017;34(6):555-565. doi:10.1002/da.22645	Bisson, Jonathan I.; Ariti, Cono; Cullen, Katherine; Kitchiner, Neil; Lewis, Catrin; Roberts, Neil P.; Simon, Natalie; Smallman, Kim; Addison, Katy; Bell, Vicky; Brookes-Howell, Lucy; Cosgrove, Sarah; Ehlers, Anke; Fitzsimmons, Deborah; Foscarini-Craggs, Paula; Harris, Shaun R. S.; Kelson, Mark; Lovell, Karina; McKenna, Maureen; McNamara, Rachel; Nollett, Claire; Pickles, Tim; Williams-Thomas, Rhys Guided, internet based, cognitive behavioural therapy for post-traumatic stress disorder: pragmatic, multicentre, randomised controlled non-inferiority trial (RAPID). BMJ. 2022;377():e069405. doi:10.1136/bmj-2021-069405
243	Ramnarayan, P.; Lister, P.; Dominguez, T.; Habibi, P.; Edmonds, N.; Canter, R. R.; Wulff, J.; Harrison, D. A.; Mouncey, P. M.; Peters, M. J. FIRST-line support for Assistance in Breathing in Children (FIRST-ABC): a multicentre pilot randomised controlled trial of high-flow nasal cannula therapy versus continuous positive airway pressure in paediatric critical care. Crit Care. 2018;22(1):144. doi:10.1186/s13054-018-2080-3	Ramnarayan, Padmanabhan; Richards-Belle, Alvin; Drikite, Laura; Saull, Michelle; Orzechowska, Izabella; Darnell, Robert; Sadique, Zia; Lester, Julie; Morris, Kevin P.; Tume, Lyvonne N.; Davis, Peter J.; Peters, Mark J.; Feltbower, Richard G.; Grieve, Richard; Thomas, Karen; Mouncey, Paul R.; Harrison, David A.; Rowan, Kathryn M.; FIRST-ABC Step-Up RCT Investigators and the Paediatric Critical Care Society Study Group Effect of High-Flow Nasal Cannula Therapy vs Continuous Positive Airway Pressure Therapy on Liberation From Respiratory Support in Acutely Ill Children Admitted to Pediatric Critical Care Units: A Randomized Clinical Trial. JAMA. 2022;328(2):162-172. doi:10.1001/jama.2022.9615
244	Retnakaran, R.; Choi, H.; Ye, C.; Kramer, C. K.; Zinman, B. Two-year trial of intermittent insulin therapy vs metformin for the preservation of β-cell function after initial short-term intensive insulin induction in early type 2 diabetes. Diabetes Obes Metab. 2018;20(6):1399-1407. doi:10.1111/dom.13236	Retnakaran, Ravi; Emery, Alexandra; Ye, Chang; Harris, Stewart B.; Reichert, Sonja M.; McInnes, Natalia; Gerstein, Hertzel C.; Thorpe, Kevin E.; Kramer, Caroline K.; Zinman, Bernard Short-term intensive insulin as induction and maintenance therapy for the preservation of beta-cell function in early type 2 diabetes (RESET-IT Main): A 2-year randomized controlled trial. Diabetes Obes Metab. 2021;23(8):1926-1935. doi:10.1111/dom.14421
245	Seebacher, B.; Kuisma, R.; Glynn, A.; Berger, T. Rhythmic cued motor imagery and walking in people with multiple sclerosis: a randomised controlled feasibility study. Pilot Feasibility Stud. 2015;1():25. doi:10.1186/s40814-015-0021-3	Seebacher, Barbara; Kuisma, Raija; Glynn, Angela; Berger, Thomas Effects and mechanisms of differently cued and non-cued motor imagery in people with multiple sclerosis: A randomised controlled trial. Mult Scler. 2019;25(12):1593-1604. doi:10.1177/1352458518795332
246	Heo, In; Hwang, Man-Suk; Hwang, Eui-Hyoung; Cho, Jae-Heung; Ha, In-Hyuk; Shin, Kyung-Min; Lee, Jun-Hwan; Kim, Nam-Kwen; Son, Dong-Wuk; Shin, Byung-Cheul Electroacupuncture as a complement to usual care for patients with non-acute low back pain after back surgery: a pilot randomised controlled trial. BMJ Open.	Heo, In; Shin, Byung-Cheul; Cho, Jae-Heung; Ha, In-Hyuk; Hwang, Eui-Hyoung; Lee, Jun-Hwan; Kim, Koh-Woon; Kim, Me-Riong; Jung, So-Young; Kwon, Ojin; Kim, Nam-Kwen; Son, Dong-Wuk; Shin, Kyung-Min Multicentre randomised controlled clinical trial of electroacupuncture with usual care for patients with non-acute pain after back surgery. Br J

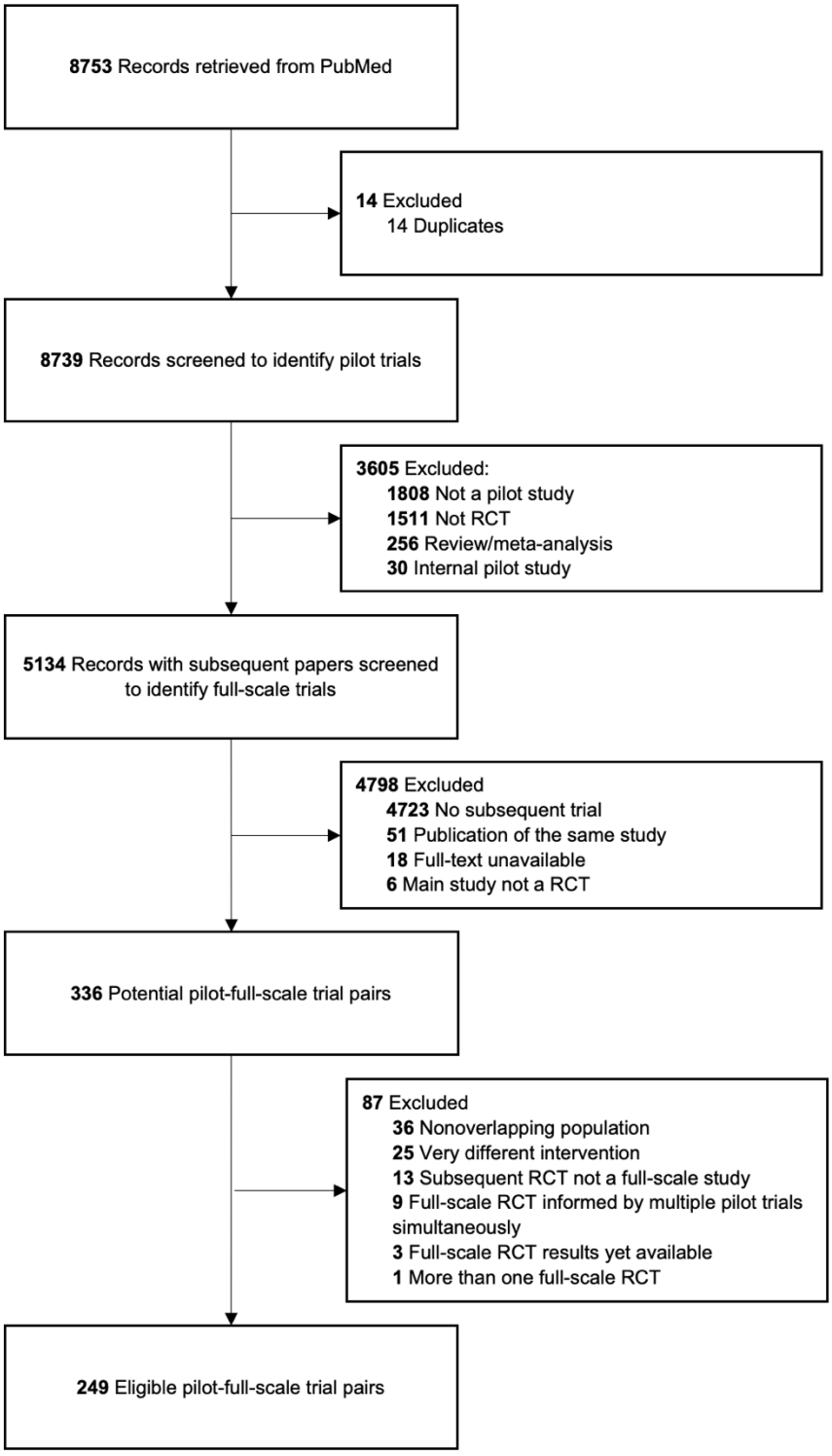
	2018;8(5):e018464. doi:10.1136/bmjopen-2017-018464	Anaesth. 2021;126(3):692-699. doi:10.1016/j.bja.2020.10.038
247	Njuguna, Irene N.; Wagner, Anjuli D.; Omondi, Vincent O.; Otieno, Verlinda A.; Neary, Jillian; Bosire, Rose; Babigumira, Joseph B.; Levin, Carol; Maleche-Obimbo, Elizabeth; Wamalwa, Dalton C.; John-Stewart, Grace; Slyker, Jennifer Financial Incentives for Pediatric HIV Testing in Kenya. Pediatr Infect Dis J. 2018;37(11):1142-1144. doi:10.1097/INF.0000000000002035	Njuguna, Irene N.; Wagner, Anjuli D.; Neary, Jillian; Omondi, Vincent O.; Otieno, Verlinda A.; Orimba, Anita; Mugo, Cyrus; Babigumira, Joseph B.; Levin, Carol; Richardson, Barbra A.; Maleche-Obimbo, Elizabeth; Wamalwa, Dalton C.; John-Stewart, Grace; Slyker, Jennifer Financial incentives to increase pediatric HIV testing: a randomized trial. AIDS. 2021;35(1):125-130. doi:10.1097/QAD.0000000000002720
248	Lo, C.; Hales, S.; Chiu, A.; Panday, T.; Malfitano, C.; Jung, J.; Rydall, A.; Li, M.; Nissim, R.; Zimmermann, C.; Rodin, G. Managing Cancer And Living Meaningfully (CALM): randomised feasibility trial in patients with advanced cancer. BMJ Support Palliat Care. 2019;9(2):209-218. doi:10.1136/bmjspcare-2015-000866	Rodin, Gary; Lo, Christopher; Rydall, Anne; Shnall, Joanna; Malfitano, Carmine; Chiu, Aubrey; Panday, Tania; Watt, Sarah; An, Ekaterina; Nissim, Rinat; Li, Madeline; Zimmermann, Camilla; Hales, Sarah Managing Cancer and Living Meaningfully (CALM): A Randomized Controlled Trial of a Psychological Intervention for Patients With Advanced Cancer. J Clin Oncol. 2018;36(23):2422-2432. doi:10.1200/JCO.2017.77.1097

Appendix B: Supplementary Materials for Paper 2

eTable 1. Search Strategy

#1	"Pilot Projects"[Mesh] OR "Feasibility Studies"[Mesh]
#2	(Feasib*[Title/Abstract] OR pilot[Title/Abstract]) AND (study[Title/Abstract] OR trial[Title/Abstract])
#3	#1 OR #2
#4	retention[Title/Abstract] OR attrition[Title/Abstract] OR recruitment[Title/Abstract] OR randomization[Title/Abstract] OR participation[Title/Abstract] OR adherence[Title/Abstract] OR compliance[Title/Abstract] OR acceptability[Title/Abstract] OR completion[Title/Abstract] OR attendance[Title/Abstract]
#5	randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] NOT (animals [mh] NOT humans [mh])
#6	random*[Title/Abstract]
#7	#5 AND #6
#8	#3 AND # 4 AND #7

eFigure 1. Flowchart of Study Selection Process



eTable 2. Complete list of diseases

Disease	Freq.	Percent
mental health	34	13.65
addiction	24	9.64
oncology	21	8.43
physical activity	14	5.62
obesity	13	5.22
pain	12	4.82
HIV	11	4.42
stroke	11	4.42
orthopedics	10	4.02
aging	7	2.81
diabetes	7	2.81
heart disease	7	2.81
multiple sclerosis	6	2.41
diet	5	2.01
healthcare	5	2.01
obstetric	5	2.01
sleep	5	2.01
developmental	4	1.61
transplantation	4	1.61
acute respiratory infection	3	1.2
critical care	3	1.2
neuropathy	3	1.2
parenting	3	1.2
renal	3	1.2
chronic obstructive pulmonary disease	2	0.8
dementia	2	0.8
hypertension	2	0.8
metabolic	2	0.8
Duchenne Muscular Dystrophy	1	0.4
acute lung injury	1	0.4
asthma	1	0.4
auditory hallucination	1	0.4
bacteremia	1	0.4
Barrett esophagus	1	0.4
blood donation	1	0.4
chronic fatigue syndrome	1	0.4
cystic fibrosis	1	0.4

diarrhea	1	0.4
domestic violence	1	0.4
gonorrhoeae	1	0.4
irritable bowel syndrome	1	0.4
otitis media prophylaxis	1	0.4
Parkinson	1	0.4
seizure	1	0.4
spinal cord injury	1	0.4
tuberculosis	1	0.4
urinary tract infection	1	0.4
vaccination	1	0.4
vitiligo	1	0.4
Total	249	100

Supplemental text. Missing data description

Information on successful screening probability, enrollment rate, and retention probability was available in 183, 177, and 238 pairs of pilot and full-scale trials, respectively. The primary source of this missing data was the pilot trials. Specifically, successful screening probability was not reported in 57 pilot trials and 30 full-scale trials. Enrollment rate was omitted in 69 pilot trials and 20 full-scale trials, while retention probability was not reported in 11 pilot and 11 full-scale trials. Comparison of pilot and full-scale trial characteristics between pairs with and without missing data is available in eTable 3 and eTable 4.

Pilot trials from pairs with unavailable data on successful screening probability were less likely to have more than two arms (8% vs 19%, P=.035), while tending to have larger average sample sizes (212±554 vs 88±93, P=.004) (eTable 3). No significant between-group differences were found in relation to the full-scale trials' characteristics (eTable 4).

Regarding the enrollment rate, pilot trials in pairs lacking data on this metric more commonly examined interventions for obesity or physical activity (18% vs 8%, P=.047), were less frequently published post-2015 (14% vs 35%, P=0.003), and were less likely to use masking (33% vs 49%, P=.028) (eTable 3). The full-scale trials from pairs lacking data on the enrollment rate were also less frequently published after 2015 (18% vs 32%, P=.031), had a higher likelihood of being cluster-randomized trials (25% vs 12%, P=.010), were less frequently multicenter (38% vs 60%, P<.001), and had smaller median sample sizes (203 vs 290, P=.024) (eTable 4).

Pilot trials in pairs missing data on retention probability had larger median sample sizes (479 vs 104, P<.001) and longer median follow-up lengths (182 vs 91 days, P=.038) (eTable 3). Similarly, full-scale trials in pairs missing data on retention probability also had larger median sample sizes (600 vs 264, P=.016) and longer median follow-up lengths (365 vs 182 days, P=.019) (eTable 4).

eTable 3. Comparison of pilot trial characteristics between pairs with and without missing data on feasibility parameters [a]

	No. (%)								
	Successful screening probability			Enrollment rate per week			Retention probability		
	Non-missing (n=183)	Missing (n=66)	P-value	Non-missing (n=177)	Missing (n=72)	P-value	Non-missing (n=238)	Missing (n=11)	P-value
Disease [b]			0.45			**0.047**			0.33
Addiction	19 (10)	5 (8)		**19 (11)**	**5 (7)**		23 (10)	1 (9)	
Mental health	26 (14)	8 (12)		**23 (13)**	**11 (15)**		34 (14)	0 (0)	
Obesity & physical activity	21 (11)	6 (9)		**14 (8)**	**13 (18)**		25 (11)	2 (18)	
Oncology	12 (7)	9 (14)		19 (11)	2 (3)		19 (8)	2 (18)	
Other	105 (57)	38 (58)		102 (58)	41 (57)		137 (58)	6 (55)	
Intervention			0.15			0.11			0.51
Behavioral	131 (72)	41 (62)		117 (66)	55 (76)		163 (68)	9 (82)	
Pharmaceutical & other	52 (28)	25 (38)		60 (34)	17 (24)		75 (32)	2 (18)	
Publication year			0.32			**0.003**			0.93
2004-2009	50 (27)	24 (36)		**46 (26)**	**28 (39)**		70 (29)	4 (36)	
2010-2014	80 (44)	23 (35)		**69 (39)**	**34 (47)**		99 (42)	4 (36)	
2015-2019	53 (29)	19 (29)		**62 (35)**	**10 (14)**		69 (29)	3 (27)	
Funding source			0.75			0.22			0.45
Non-industry	161 (88)	59 (89)		160 (90)	60 (83)		211 (89)	9 (82)	
Industry	4 (2)	2 (3)		4 (2)	2 (3)		6 (3)	0 (0)	
None or not reported	18 (10)	5 (8)		13 (7)	10 (14)		21 (9)	2 (18)	
Cluster randomization			0.40			0.78			0.17
No	172 (94)	60 (91)		164 (93)	68 (94)		223 (94)	9 (82)	
Yes	11 (6)	6 (9)		13 (7)	4 (6)		15 (6)	2 (18)	
No. of sites			0.92			0.093			0.73
Single center	137 (75)	49 (74)		127 (72)	59 (82)		177 (74)	9 (82)	
Multicenter	46 (25)	17 (26)		50 (28)	13 (18)		61 (26)	2 (18)	
No. of arms			**0.035**			0.30			0.68
2	**149 (81)**	**61 (92)**		152 (86)	58 (81)		201 (84)	9 (82)	
>2	**34 (19)**	**5 (8)**		25 (14)	14 (19)		37 (16)	2 (18)	
Sample size									
Mean (SD)	**88 (93)**	**212 (554)**	**0.004**	143 (351)	67 (60)	0.072	**104 (213)**	**479 (1002)**	**<0.001**
Median (IQR)	56 (34, 100)	49 (28, 100)	0.35	60 (32, 115)	48 (30, 82)	0.11	52 (31, 100)	66 (33, 355)	0.32
Masking used			0.96			**0.028**			0.36
No	102 (56)	37 (56)		**91 (51)**	**48 (67)**		131 (55)	8 (73)	

Yes	81 (44)	29 (44)		**86 (49)**	**24 (33)**		107 (45)	3 (27)	
Primary length of follow-up (days)									
Mean (SD)	158 (236)	187 (240)	0.39	178 (263)	136 (152)	0.21	163 (240)	220 (144)	0.44
Median (IQR)	91 (45, 182)	91 (30, 274)	0.87	91 (61, 182)	91 (14, 182)	0.22	**91 (42, 182)**	**182 (91, 365)**	**0.038**
Intervention efficacy			0.13			0.78			0.31
Not statistically significant	81 (44)	28 (42)		79 (45)	30 (42)		106 (45)	3 (27)	
Statistically significant	72 (39)	20 (30)		63 (36)	29 (40)		88 (37)	4 (36)	
Not evaluated	30 (16)	18 (27)		35 (20)	13 (18)		44 (18)	4 (36)	

Abbreviations: SD, standard deviation; IQR, interquartile range.

[a] P values are derived from Student's t tests for means, Wilcoxon rank-sum tests for medians, Pearson's Chi-squared tests for frequencies if all cell counts exceed 5 or Fisher's Exact tests if at least one cell count is less than 5. Bold text indicates P<.05.

[b] The diseases listed represent the top four most frequently occurring within the dataset. All other disease types are grouped under the category labeled as "other." A complete list of diseases is available in eTable 2 in Appendix B.

eTable 4. Comparison of full-scale trial characteristics between pairs with and without missing data on feasibility parameters [a]

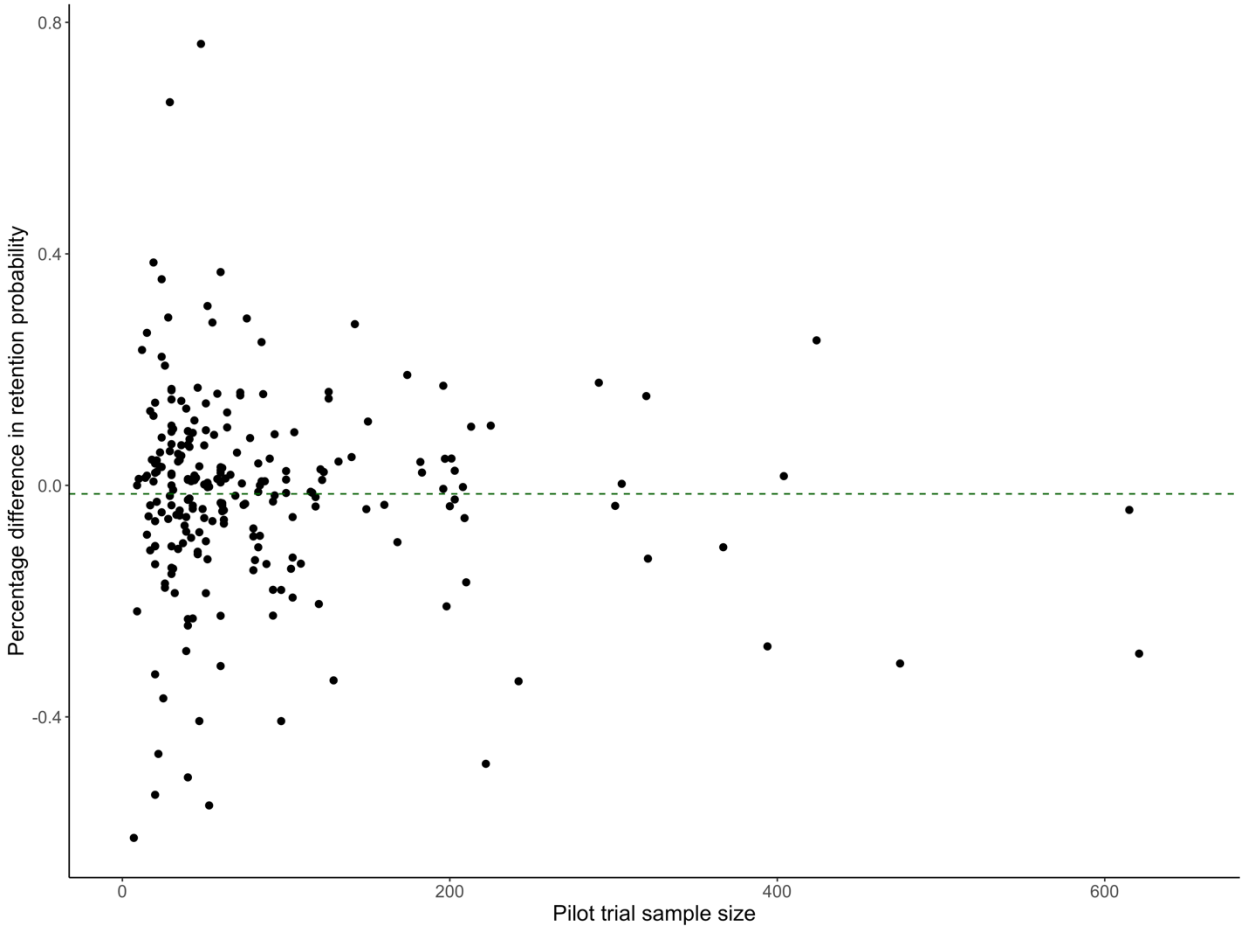
	No. (%)								
	Successful screening probability			Enrollment rate per week			Retention probability		
	Non-missing (n=183)	Missing (n=66)	P-value	Non-missing (n=183)	Missing (n=66)	P-value	Non-missing (n=183)	Missing (n=66)	P-value
Publication year			0.61			**0.031**			0.51
2004-2009	4 (2)	2 (3)		**2 (1)**	**4 (6)**		6 (3)	0 (0)	
2010-2014	34 (19)	17 (26)		**33 (19)**	**18 (25)**		47 (20)	4 (36)	
2015-2019	93 (51)	30 (45)		**86 (49)**	**37 (51)**		119 (50)	4 (36)	
2020-2022	52 (28)	17 (26)		**56 (32)**	**13 (18)**		66 (28)	3 (27)	
Funding source			0.45			0.55			0.34
Non-industry	171 (93)	59 (89)		165 (93)	65 (90)		220 (92)	10 (91)	
Industry	7 (4)	5 (8)		7 (4)	5 (7)		12 (5)	0 (0)	
None or not reported	5 (3)	2 (3)		5 (3)	2 (3)		6 (3)	1 (9)	
Cluster randomization			0.29			**0.010**			0.075
No	157 (86)	53 (80)		**156 (88)**	**54 (75)**		203 (85)	7 (64)	
Yes	26 (14)	13 (20)		**21 (12)**	**18 (25)**		35 (15)	4 (36)	
No. of sites			0.47			**<0.001**			0.96
Single center	82 (45)	33 (50)		**70 (40)**	**45 (62)**		110 (46)	5 (45)	
Multicenter	101 (55)	33 (50)		**107 (60)**	**27 (38)**		128 (54)	6 (55)	
No. of arms			0.60			0.51			0.075
2	153 (84)	57 (86)		151 (85)	59 (82)		203 (85)	7 (64)	
>2	30 (16)	9 (14)		26 (15)	13 (18)		35 (15)	4 (36)	
Sample size									
Mean (SD)	935 (2562)	1800 (6750)	0.14	1470 (4833)	414 (574)	0.066	**842 (2005)**	**8145 (16364)**	**<0.001**
Median (IQR)	269 (140, 560)	256 (150, 861)	0.43	**290 (150, 697)**	**203 (132, 373)**	**0.024**	**264 (140, 599)**	**600 (250, 11880)**	**0.016**
Masking used			0.22			0.082			0.062
No	62 (34)	28 (42)		58 (33)	32 (44)		83 (35)	7 (64)	
Yes	121 (66)	38 (58)		119 (67)	40 (56)		155 (65)	4 (36)	
Primary length of follow-up (days)									
Mean (SD)	330 (465)	295 (304)	0.56	342 (482)	270 (243)	0.23	**307 (377)**	**616 (1032)**	**0.019**
Median (IQR)	210 (91, 365)	182 (90, 365)	0.62	182 (91, 365)	182 (91, 365)	0.57	182 (91, 365)	365 (84, 548)	0.26

Intervention efficacy		0.55		0.082		**0.043**
Not statistically significant	84 (46)	35 (53)	90 (51)	29 (40)	**115 (48)**	**4 (36)**
Statistically significant	98 (54)	31 (47)	87 (49)	42 (58)	**123 (52)**	**6 (55)**
Not evaluated	1 (1)	0 (0)	0 (0)	1 (1)	**0 (0)**	**1 (9)**

Abbreviations: SD, standard deviation; IQR, interquartile range.

[a] P values are derived from Student's t tests for means, Wilcoxon rank-sum tests for medians, Pearson's Chi-squared tests for frequencies if all cell counts exceed 5 or Fisher's Exact tests if at least one cell count is less than 5. Bold text indicates P<.05.

eFigure 2. Scatterplot of percentage difference in retention probability versus pilot trial sample size



Appendix C: Supplementary Materials for Paper 3

eTable 1. Search Strategy

#1	"Pilot Projects"[Mesh] OR "Feasibility Studies"[Mesh]
#2	(Feasib*[Title/Abstract] OR pilot[Title/Abstract]) AND (study[Title/Abstract] OR trial[Title/Abstract])
#3	#1 OR #2
#4	retention[Title/Abstract] OR attrition[Title/Abstract] OR recruitment[Title/Abstract] OR randomization[Title/Abstract] OR participation[Title/Abstract] OR adherence[Title/Abstract] OR compliance[Title/Abstract] OR acceptability[Title/Abstract] OR completion[Title/Abstract] OR attendance[Title/Abstract]
#5	randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] NOT (animals [mh] NOT humans [mh])
#6	random*[Title/Abstract]
#7	#5 AND #6
#8	#3 AND # 4 AND #7

eTable 2. Study selection criteria

Meta-analysis ID	# all	# eligible	# included	Criteria used to define similar trials	Further exclusion reasons
Ma 2022	6	6	2	all	3 pilot, 1 nonrct
Liu 2021	7	2	2	Figure 4. BPI pain-related interference. 1.1.1 TA vs SA, Body acupuncture and auricular acupuncture	
Dalla Via 2018	12	4	4	Fig3 bone mineral density between the exercise and control groups at a lumbar spine, breast cancer	
Azarpazhooh 2016	5	3	3	Analysis 4.1. Comparison 4 Xylitol syrup versus control for younger children unable to chew, Outcome 1 Final diagnosis of at least one episode of AOM.	
Ramamoorthi 2019	14	4	2	outcome: glucose	1 nonrct, 1 same pub
Jefferson 2020	78	6	6	Analysis 1.1. Comparison 1: Randomised trials: medical/surgical masks versus no masks, Outcome 1: Viral illness, 1.1.2 Laboratory-confirmed influenza	
Petrucci 2021	16	3	2	Figure 6. Disability: MBSR versus control.	1 pilot
Wayne 2018	15	4	4	Table 1 breast, RCT, FACT, quality of life, figure 2E	
Naqvi 2020	15	14	9	Analysis 1.1.	3 pilot, 2 no fulltext
Grant 2017	9	9	2	all	6 pilot, 1 no fulltext
Whittaker 2016	12	12	6	Analysis 1.1.	3 pilot, 2 ongoing, 1 with a pilot study
Walker 2020	26	6	4	Analysis 1.4. Comparison 1: UDCA versus placebo, Outcome 4: Stillbirth	1 pilot, 1 no fulltext
Laurenzi 2021	30	12	5	Viral load (n = 12)	7 pilot
Mead 2017	70	15	9	Analysis 1.15. Comparison 1 Behaviour-changing interventions versus no treatment/usual care, Outcome 15 Change in BMI z score - type of control. 1.15.1 No treatment	3 pilot, 1 nonrct, 1 no fulltext, 1 with a pilot study
Grimmett 2019	27	4	3	Table 1 Measure of physical activity: Actirgraph	1 pilot

Lewis 2022	77	5	4	eFigure 7. Proportion of Time at Target Sedation Forest Plot (%)	1 pilot
Smith 2018	64	5	3	Analysis 1.1. Comparison 1 Acupuncture versus no treatment/waitlist/TAU, Outcome 1Severity of depression at the end of treatment. 1.1.1 Manual acupuncture	1 pilot, 1 no fulltext
Storebø 2020	75	3	3	Analysis 8.1. Comparison 8: Systems training for emotional predictability and problem solving (STEPPS) vs TAU, Outcome 1: Primary: BPD symptom severity (continuous), at end of treatment, 8.1.1 End of treatment	
Sherrington 2019	108	8	6	1.5.2 Not group exercise, 1.3.2 Age 75+, 1.4.1 Health professional delivering intervention, 12.2.1 Balance and functional exercises vs control, outcome: rate of fall	2 pilot
Huang 2013	8	3	2	outcome: Figure 6a Adherence to antidepressant medication and oral hypoglycemic agent, primary care setting	1 pilot
Légaré 2018	87	3	2	Analysis 4.19 Comparison 4 Group 4: Interventions targeting patients compared to other interventions targeting patients, Outcome 19 Adherence (categorical).	1 nonrct
Coxeter 2015	9	8	6	Analysis 1.1. Comparison 1Shared decision making versus usual care (control), Outcome 1 Antibiotics prescribed, dispensed or decision to use (short-term, index consultation to ≤ 6 weeks).	1 pilot, 1 no fulltext
Shi 2020	26	2	2	kidney, immunosuppressive medication adherence rate	
Turrini 2019	26	12	8	fig2, appendix, PTSD, post-treatment, adult, formal diagnosis	4 pilot
Williams 2020	75	15	11	Analysis 2.4. Comparison 2: Cognitive behavioural vs treatment as usual, Outcome 4: Pain follow-up	1 no fulltext, 4 with a pilot study
Carandini 2018	6	4	2	fig 2, outcome: mortality or disability	3 pilot
Danon 2022	40	3	2	intervention: relaxation, pain was studied in a cluster syndrome and	1 pilot

				measured by visual analog scale or numerical pain rating scale	
Moullaali 2022	16	9	8	primary outcome: mRS, population: Mixed stroke & prehospital	1 pilot
Jackson 2022	21	5	4	Analysis 2.1. Comparison 2: Acceptance and commitment therapy (ACT), Outcome 1: ACTvs matched-intensity smoking cessation treatment	1 pilot
Ma 2017	54	2	2	White, male	
Abbott 2019	7	2	2	rct, fig3 agitation	
Wu 2022	23	5	5	Diet+PA vs clt,obese	
Lou 2017	12	4	3	figure3a 1.6.1 operative management, Tibia	1 pilot
Rankin 2018	32	11	9	Analysis 1.5. Comparison 1 Postintervention analysis, Outcome 5The proportion of patients with one or more potentially inappropriate medications	2 pilot
Smith 2017	7	2	2	Figure 4 Forest plot of exercises into pain versus pain-free exercises—short term, Physiotherapy and home setting	
Aemaz 2022	10	6	2	figure 2 headache frequency	4 pilot
Fraguas 2021	69	23	20	universal intervention, primary school, outcome: overall bullying	1 pilot, 2 no fulltext
Blackburn 2020	62	3	3	Behavioural intervention, inactive control, sedentary outcome: sedentary behavior, setting: school	
van Agteren 2021	393	8	6	outcome: Warwick–Edinburgh Mental Wellbeing Scale (WEMWBS), "Multi-theoretical interventions"	2 pilot
Connolly 2021	19	3	3	depression	
Ye 2021	14	5	3	figure 5 3.1.1 methicillin-resistant S. aureus bacteraemia (MRSAB)	2 pilot
Fan 2021	4	4	2	all	2 pilot
Lau 2021	25	8	5	figure 4, postnatal, community setting, anxiety symptoms for digital psychotherapeutic intervention and comparators, CBT	2 pilot, 1 no fulltext
Smith 2021	22	2	2	All outpatients (S3 Table)	

Marcum 2021	40	7	5	intervention: Pharmaceutical care, outcome: Pharmacy refills	1 pilot, 1 no fulltext
Zhu 2020	18	8	6	CLBP, Intermediate-term effects (6 to 7 months)	2 pilot
Neil-Sztramko 2021	89	6	3	Analysis 1.3. 1.3.1 Before and after school programmes	3 pilot

Bibliography

1. Moore TJ, Zhang H, Anderson G, Alexander GC. Estimated Costs of Pivotal Trials for Novel Therapeutic Agents Approved by the US Food and Drug Administration, 2015-2016. *JAMA Intern Med*. 2018;178(11):1451-1457. doi:10.1001/jamainternmed.2018.3931

2. Mullard A. How much do phase III trials cost? *Nat Rev Drug Discov*. 2018;17(11):777-777. doi:10.1038/nrd.2018.198

3. Moore TJ, Heyward J, Anderson G, Alexander GC. Variation in the estimated costs of pivotal clinical benefit trials supporting the US approval of new therapeutic agents, 2015-2017: a cross-sectional study. *BMJ Open*. 2020;10(6):e038863. doi:10.1136/bmjopen-2020-038863

4. G G, Jl M, Ag G, Cl M. Assessment of Trends in the Design, Accrual, and Completion of Trials Registered in ClinicalTrials.gov by Sponsor Type, 2000-2019. *JAMA Netw Open*. 2020;3(8). doi:10.1001/jamanetworkopen.2020.14682

5. Parkinson B, Meacock R, Sutton M, et al. Designing and using incentives to support recruitment and retention in clinical trials: a scoping review and a checklist for design. *Trials*. 2019;20(1):1-14. doi:10.1186/s13063-019-3710-z

6. Cutler DM, Everett W. Thinking Outside the Pillbox — Medication Adherence as a Priority for Health Care Reform. *N Engl J Med*. 2010;362(17):1553-1555. doi:10.1056/NEJMp1002305

7. Kearney A, Ashford PA, Butlin L, et al. Developing an online, searchable database to systematically map and organise current literature on retention research (ORRCA2): *Clin Trials*. Published online October 24, 2021. doi:10.1177/17407745211053803

8. Moroshko I, Brennan L, O'Brien P. Predictors of dropout in weight loss interventions: a systematic review of the literature. *Obes Rev*. 2011;12(11):912-934. doi:10.1111/j.1467-789X.2011.00915.x

9. Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters. *Biostatistics*. 2019;20(2):273-286. doi:10.1093/biostatistics/kxx069

10. Hay M, Thomas DW, Craighead JL, Economides C, Rosenthal J. Clinical development success rates for investigational drugs. *Nat Biotechnol*. 2014;32(1):40-51. doi:10.1038/nbt.2786

11. Tay-Teo K, Ilbawi A, Hill SR. Comparison of Sales Income and Research and Development Costs for FDA-Approved Cancer Drugs Sold by Originator Drug Companies. *JAMA Netw Open*. 2019;2(1):e186875. doi:10.1001/jamanetworkopen.2018.6875

12. Everitt BS. *Medical Statistics from A to Z: A Guide for Clinicians and Medical Students*. 2nd ed. Cambridge University Press; 2006. doi:10.1017/CBO9780511544453

13. Arnold DM, Burns KEA, Adhikari NKJ, et al. The design and interpretation of pilot trials in clinical research in critical care. *Crit Care Med*. 2009;37(1 Suppl):S69-74. doi:10.1097/CCM.0b013e3181920e33

14. Kistin C, Silverstein M. Pilot Studies: A Critical but Potentially Misused Component of Interventional Research. *JAMA*. 2015;314(15):1561-1562. doi:10.1001/jama.2015.10962

15. Beets MW, Weaver RG, Ioannidis JPA, et al. Identification and evaluation of risk of generalizability biases in pilot versus efficacy/effectiveness trials: a systematic review and meta-analysis. *Int J Behav Nutr Phys Act*. 2020;17(1):19. doi:10.1186/s12966-020-0918-y

16. Malmqvist J, Hellberg K, Möllås G, Rose R, Shevlin M. Conducting the Pilot Study: A Neglected Part of the Research Process? Methodological Findings Supporting the Importance of Piloting in Qualitative Research Studies. *Int J Qual Methods*. 2019;18:1609406919878341. doi:10.1177/1609406919878341

17. Lancaster GA. Pilot and feasibility studies come of age! *Pilot Feasibility Stud*. 2015;1(1):1-4. doi:10.1186/2055-5784-1-1

18. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ*. 2016;355:i5239. doi:10.1136/bmj.i5239

19. Lancaster GA, Thabane L. Guidelines for reporting non-randomised pilot and feasibility studies. *Pilot Feasibility Stud*. 2019;5(1):1-6. doi:10.1186/s40814-019-0499-1

20. Arain M, Campbell MJ, Cooper CL, Lancaster GA. What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Med Res Methodol*. 2010;10:67. doi:10.1186/1471-2288-10-67

21. Kannan S, Gowri S. Pilot studies: Are they appropriately reported? *Perspect Clin Res*. 2015;6(4):207-210. doi:10.4103/2229-3485.167097

22. Whitehead AL, Julious SA. Pilot Studies in Clinical Research. In: *Wiley StatsRef: Statistics Reference Online*. John Wiley & Sons, Ltd; 2020:1-8. doi:10.1002/9781118445112.stat08205

23. Sim J. Should treatment effects be estimated in pilot and feasibility studies? *Pilot Feasibility Stud*. 2019;5(1):107. doi:10.1186/s40814-019-0493-7

24. Beets MW, von Klinggraeff L, Weaver RG, Armstrong B, Burkart S. Small studies, big decisions: the role of pilot/feasibility studies in incremental science and premature scale-up of behavioral interventions. *Pilot Feasibility Stud*. 2021;7(1):173. doi:10.1186/s40814-021-00909-w

25. Leon AC, Davis LL, Kraemer HC. The Role and Interpretation of Pilot Studies in Clinical Research. *J Psychiatr Res*. 2011;45(5):626-629. doi:10.1016/j.jpsychires.2010.10.008

26. Cooper CL, Whitehead A, Pottrill E, Julious SA, Walters SJ. Are pilot trials useful for predicting randomisation and attrition rates in definitive studies: A review of publicly funded trials. *Clin Trials*. 2018;15(2):189-196. doi:10.1177/1740774517752113

27. Beets MW, von Klinggraeff L, Burkart S, et al. Impact of risk of generalizability biases in adult obesity interventions: A meta-epidemiological review and meta-analysis. *Obes Rev*. 2022;23(2):e13369. doi:10.1111/obr.13369

28. Bhatt A. Quality of clinical trials: A moving target. *Perspect Clin Res*. 2011;2(4):124-128. doi:10.4103/2229-3485.86880

29. Vinkers CH, Lamberink HJ, Tijdink JK, et al. The methodological quality of 176,620 randomized controlled trials published between 1966 and 2018 reveals a positive trend but also an urgent need for improvement. *PLOS Biol*. 2021;19(4):e3001162. doi:10.1371/journal.pbio.3001162

30. Yordanov Y, Dechartres A, Porcher R, Boutron I, Altman DG, Ravaud P. Avoidable waste of research related to inadequate methods in clinical trials. *BMJ*. 2015;350:h809. doi:10.1136/bmj.h809

31. Meeker-O'Connell A, Glessner C. Clinical trial quality: From supervision to collaboration and beyond. *Clin Trials*. 2018;15(1_suppl):23-26. doi:10.1177/1740774518755056

32. Meeker-O'Connell A, Glessner C, Behm M, et al. Enhancing clinical evidence by proactively building quality into clinical trials. *Clin Trials*. 2016;13(4):439-444. doi:10.1177/1740774516643491

33. Treweek S, Pitkethly M, Cook J, et al. Strategies to improve recruitment to randomised trials. *Cochrane Database Syst Rev*. 2018;2(2):MR000013. doi:10.1002/14651858.MR000013.pub6

34. Gillies K, Kearney A, Keenan C, et al. Strategies to improve retention in randomised trials. *Cochrane Database Syst Rev*. 2021;(3). doi:10.1002/14651858.MR000032.pub3

35. Lancaster GA, Dodd S, Williamson PR. Design and analysis of pilot studies: recommendations for good practice. *J Eval Clin Pract*. 2004;10(2):307-312. doi:10.1111/j..2002.384.doc.x

36. Moore CG, Carter RE, Nietert PJ, Stewart PW. Recommendations for Planning Pilot Studies in Clinical and Translational Research. *Clin Transl Sci*. 2011;4(5):332-337. doi:10.1111/j.1752-8062.2011.00347.x

37. Psioda MA, Soukup M, Ibrahim JG. A practical Bayesian adaptive design incorporating data from historical controls. *Stat Med*. 2018;37(27):4054-4070. doi:10.1002/sim.7897

38. Puffer S, Torgerson D, Watson J. Evidence for risk of bias in cluster randomised trials: review of recent trials published in three general medical journals. *BMJ*. 2003;327(7418):785-789.

39. Easter C, Thompson JA, Eldridge S, Taljaard M, Hemming K. Cluster randomized trials of individual-level interventions were at high risk of bias. *J Clin Epidemiol*. 2021;138:49-59. doi:10.1016/j.jclinepi.2021.06.021