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Cost-effectiveness of telehealth-delivered diet and exercise interventions: A systematic review

Running head: Costs of telehealth lifestyle interventions

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Abstract

Objectives: Telehealth is a promising tool for delivering lifestyle interventions in the management of health conditions. However, limited evidence exists regarding the cost-effectiveness of these interventions. This systematic review aimed to evaluate the current literature reporting on the cost-effectiveness of telehealth-delivered diet and/or exercise interventions.

Methods: Four electronic databases (PubMed, CENTRAL, CINAHL and Embase) were searched for published literature from database inception to November 2020. This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the ISPOR Criteria for Cost-Effectiveness Review Outcomes (CiCERO) Checklist. The quality of reporting was assessed using the CHEERS checklist. The extracted data were grouped into subcategories according to telehealth modality, organised into tables and reported narratively.

Results: Twenty-four studies of controlled trials (11 combined diet and exercise, 9 exercise-only and 4 diet-only telehealth-delivered interventions) were included for data extraction and quality assessment. Interventions were reported as cost-effective in twelve studies (50%), five (21%) reported inconclusive results, and seven (29%) reported that the interventions were not cost-effective. Telephone interventions were applied in eight studies (33%), seven studies (29%) used internet interventions, six studies (25%) used a combination of internet and telephone interventions, and three studies (13%) evaluated mHealth interventions. Quality of study reporting varied with between 54% to 92% of CHEERS items reported.

Conclusions: This review suggests that telehealth-delivered lifestyle interventions can be cost-effective compared to traditional care. There is a need for further investigations that employ rigorous methodology and economic reporting, including appropriate decision analytical models and longer timeframes.

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Introduction

Global healthcare costs are rising, driven by an ageing population, increasing incidence of chronic disease, and costly medical interventions [1]. The Organisation for Economic Co-operation and Development (OECD) projects global health spending to reach 10.2% of Gross Domestic Product (GDP) by 2030. Healthcare expenditure in Australia has almost doubled from 2010 to 2017, driving a search for cost-reduction strategies while maintaining the same quality of care [2]. Additionally, the novel coronavirus (COVID-19) pandemic has led to sweeping reform across the healthcare sector and has challenged systems to look for scalable and cost-effective alternatives to delivering effective care [3, 4].

There is increasing interest in telehealth technology as a means of delivering affordable interventions for individuals with chronic disease [5] and to reduce strain on healthcare systems. Telehealth is defined as the use of information and communication technology to deliver health services, information, and facilitate monitoring at a distance [6]. These services include lifestyle modifications such as through diet and exercise, which are often an important component of individuals' treatment and management plans and are considered essential for minimising complications and optimising an individual's quality of life [7]. Diet and exercise interventions delivered via telehealth modalities such as web and telephone [8-11] have been shown to be effective across primary and secondary prevention contexts. However, treatment plans for health conditions can be complex, involving intensive patient self-management and are notorious for high patient burden and poor adherence [12]. Regular engagement with treating health professionals and ongoing monitoring are recommended to achieve long-term behaviour change, and the use of telehealth modalities in these cases have been proven beneficial for patients experiencing barriers to access, including those in isolation[13].

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Telehealth has been proposed as a promising tool to encourage self-management and long-term behaviour change in patients, yet its widespread adoption has not yet occurred. High-quality cost-effectiveness evidence is needed to help define the appropriate deployment and scope of telehealth in various settings. Investment in telehealth thus far has been rationalised due to the costs saved from secondary healthcare use or avoidance of emergency hospital care[14]. However, the evidence for the cost-effectiveness of telehealth services is varied [15], and measuring its economic impact is a complex process. Systematic reviews of telemedicine cost-effectiveness studies found that they were either not well-designed [16] or failed to address cost-effectiveness for specific populations[17]. To date, and to the best of our knowledge, no systematic review has been published that summarises economic evaluations for telehealth-delivered diet or exercise interventions for the treatment of health conditions. Therefore, this systematic review aims to summarise and analyse the current evidence for the cost-effectiveness of diet and/or exercise interventions delivered via telehealth.

Methods

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline (Appendix 1, Supplementary material)[18] and ISPOR Criteria for Cost-Effectiveness Review Outcomes (CiCERO) Checklist (Appendix 2, Supplementary material) [19]. The study protocol was registered on PROSPERO (CRD42021224078).

Search Strategy

Structured searches were performed in MEDLINE (via PubMed), The Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL (via EBSCO) and Embase, from the

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inception of each database to November 2, 2020 (Appendix 3). The search strategy comprised of three stages: (i) An initial limited search of MEDLINE to identify relevant keywords and controlled vocabulary from National Library of Medicine's Medical Subject Headings (MeSH) terms in four domains: telehealth, exercise and/or dietary interventions, and cost-effectiveness analysis; (ii) Pilot searches were undertaken for each domain and combined concepts to ensure the sensitivity and specificity of the search; (iii) The selected terms and their synonyms were translated for respective databases using Polyglot [20] and were used in an extensive literature search. (iv) Unstructured searches were also conducted in EconLit, Centre of Reviews and Dissemination (CRD), and the Cost-Effectiveness Analysis Registry (CEA) (Appendix 3)

Eligibility Criteria

Studies were selected according to criteria based on the Population, Intervention, Comparator, Outcome(s) of interest, and Study design (PICOS) framework (Table 1).

Following the structured database searches, LL imported identified articles into Endnote X9 reference management software [21], conducted deduplication using the Endnote duplication tool, and imported the resulting set into Covidence for screening. References retrieved from the additional unstructured economic database searches were managed and screened in Endnote only. Two reviewers (LL, HS, HM or JK) independently screened the titles and abstracts of retrieved articles in duplicate to identify studies which potentially met eligibility criteria. Full texts were independently reviewed by two of the same four authors. Any discrepancies were resolved by consensus or a third reviewer.

Data extraction

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Data extraction and assessment of reporting quality of articles followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement [22], using a standardised data extraction form developed in Microsoft Excel (2016, Microsoft Corp., Redmond, WA, USA). The statement consists of 24 items that assesses articles on six main categories: (i) title and abstract, (ii) introduction, (iii) methods, (iv) results, (v) discussion, and (vi) funding and conflict of interest. Data extracted included country, study design, duration, sample size, participant characteristics (health condition, age, and gender), intervention and comparator details, and time horizon. LL independently extracted data from the 23 studies. DE independently extracted data from five studies and the results were compared and then the remaining were cross-checked by DE. Any discrepancies were resolved by discussion. If any information were missing or unclear, an attempt to contact authors of the study was made through email, with a follow-up email sent after one week. If authors did not provide the requested information, the study would be excluded.

Data analysis

Meta-analysis was not possible due to the heterogeneity of the intervention groups included (diet, exercise, or combined therapy), populations, and methodologies used for economic analyses. Therefore, a combination of narrative synthesis and simple descriptive statistics (percentages, means and standard deviations) were used to present the date relating to the economic findings and the assessment of the quality of economic reporting of the studies including tables based on recommendations of the CHEERS checklist. Studies were assessed as meeting or not meeting a CHEERS criteria element only if that criterion was considered relevant to the study.

Results

Search results and study quality

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A total of 10,158 articles were identified (Figure 1). Following deduplication, the titles and abstracts of 7843 articles were screened, with 7445 deemed irrelevant and 398 progressing to full-text review. After review, 374 articles were excluded, leaving 24 studies for data extraction and quality assessment.

Study and sample characteristics

The general characteristics of the included articles are summarised in Appendix 4 (Supplementary material). The studies were conducted exclusively in high-income countries: these were Australia (n=8, 33%) [8, 23-29] the Netherlands (n=6, 25%) [30-36], the United Kingdom (n=5, 21%) [37-41], Belgium (n=1, 4%) [42], Hong Kong (n=1, 4%) [43], the United States (n=1, 4%) [44], Korea (n=1, 4%) [45] and New Zealand (n=1, 4%) [46]. Duration of the studies ranged from 12 weeks to four years. Mean participant age ranged from 34 to 75.8 years in the intervention group and 32 to 73.5 years in the control group. No studies were conducted in children. The most common primary conditions were high BMI (n=8, 33%) [23, 25, 30, 36-38, 41, 43, 45], non-acute cardiac conditions such as coronary artery disease or chronic heart failure (n=7, 29%) [24, 26, 28, 32, 34, 40, 42, 47], and T2DM (n=2, 8%) [8, 44].

Description of telehealth and comparator interventions

Eight studies (33%) used telephone-based interventions aimed at supporting participant self-management and involved periodic consultations with trained professionals oradvocates, and/or automated text messaging. Six of the eight telephone-based studies individualised these communications using data reported by patients to their clinicians [8, 23, 25, 29, 34, 44], while others provided generalised educational information [27] or regular automated text messages [41]. Seven studies (29%) used internet-based interventions that varied in design. These included the delivery of online educational seminars [43], use of informational websites [45], internet applications consisting of online activity modules [31], and the use of online videoconferencing rehabilitation sessions [28]. Two studies employed websites with diet or exercise programmes that were individualised according to patient preference or progress [38, 39]. Six studies (25%) used a combination of internet- and telephone-based interventions [24, 26, 30, 36, 37, 40, 46]. Two studies (13%) evaluated mHealth interventions, where participants were provided heart rate (HR) monitors [32] or motion sensors associated with an internet service [42]. Several interventions also included other modalities (in addition to telehealth or mHealth) for content delivery, such as printed material [25, 28, 29, 34] or face-to-face sessions (that were not the predominant delivery mode) [27, 37, 41]. Comparator groups to which intervention costs and effects were compared included usual care or current practice (n=15, 62%), educational information control (n=6, 25%), waitlist control (n=2, 8%), or face-to-face visits at a public health centre (n=1, 4%).

Description of economic evaluation

The types of economic evaluation in the included studies were cost-effectiveness analyses (CEA); cost-utility analyses (CUA), and cost-benefit analyses (CBA) (Appendix 5, Supplementary material). The costs and resource use of the interventions and control varied according to the perspective taken for the analysis. Seventeen studies (71%) were analysed using within-trial CUA [23, 24, 27, 28, 31-34, 36-42, 46], four used within-trial CEA (17%) [30, 43-45], and one study each used modelled CUA (4%) [8], modelled CEA (4%) [25], and CBA combined with CEA (4%) [26].

Despite the CHEERS statement strongly recommending that studies provide a figure to show model structure, only one study did so [8]. Eleven (46%) adopted a health providers' perspective and eight studies (33%) adopted a societal perspective, and five (21%) did not

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clearly report their perspectives. Eighteen studies (75%) used quality-adjusted life years (QALYs) as a measure of preference-based outcomes. Intervention costs were estimated from trial data, micro-costed (direct costing of every input consumed in the intervention [48]), or from self-report by participants, (e.g., number of physiotherapy sessions [31]). Instruments used to calculate health utility scores included the EuroQol-5D (EQ-5D) [49] and the 36-item Short Form Survey (SF-36) [50]. Studies using CEA measured benefits in natural units related to changes in health outcomes or changes related to diet and exercise (e.g., percentage weight loss [43] or self-rated physical disability [33]). Twelve studies (50%) reported QALYs in addition to natural units. The heterogeneity of natural units used for outcome measures selected in the CEAs, study setting, different perspectives, and variations in intervention design limited comparability of results between these studies.

Reporting of costs and effectiveness

Overall, over 50% of telehealth-delivered diet and/or exercise interventions (12 studies) reported results as cost effective[8, 25-29, 32, 34, 40-44], five (21%) reporting inconclusive results [30, 36-39], and seven (29%) reporting that the interventions were not cost-effective[23, 24, 30, 31, 33, 41, 47] (Table 2 and Figure 2). Varying willingness-to-pay (WTP) thresholds were applied, and six studies did not state their thresholds. Suman et al. [33] and Kraal et al. [32] presented cost-effectiveness results graphically, making it difficult to determine precise incremental cost-effectiveness ratios. One study had different demographics for the intervention and comparator groups, with participants in the intervention group being younger and more likely to be employed [25].

While the types of costs included varied depending on study setting and perspective, key inputs for cost analysis typically included medication costs, healthcare system-related costs,

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and costs related to productivity losses (e.g., absenteeism). All studies except one [25] described the approach used to estimate unit costs and cost calculations. Sixteen studies clearly reported incremental cost-effectiveness ratios (ICERs) as an economic evaluation outcome, with 11stating the WTP threshold used. ICERs varied widely from being cost saving [8, 42, 44] to AUD$58,182 per QALY [23]. An economic evaluation conducted alongside the Telerehab III clinical trial in Belgium [42] found that the addition of a cardiac telerehabilitation programme to usual centre-based cardiac rehabilitation was more effective than usual rehabilitation alone with an ICER of -€21,707 per QALY. Another Australian trial-based analysis[28] evaluating a home-based telerehabilitation program for stable chronic heart failure compared to usual care concluded that the telerehabilitation program was cost-effective at a WTP threshold of $50,000 (ICER: -$82,536 per QALY gained. Conversely, a study from the Netherlands [36] targeted at participants with BMI ≥25 kg/m^2 found that referral to a telephone-based diet and exercise counselling was not cost-effective at a WTP of €20,000 per QALY (€245,243 per QALY). Email counselling showed promising results (€1337 per QALY), although definitive conclusions could not be drawn due to high dropout rates, with 45% of participants dropping out after two years [36].

Cost-effectiveness according to telehealth modality

Of the 12 studies reporting cost-effectiveness, four assessed solely telephone interventions [8, 29, 30, 44], three internet interventions [28, 31, 43], three a combination of internet and telephone [26, 37, 40], and two using mHealth [32, 42] (Figure 2). Three assessed only dietary interventions [29, 43, 44], four assessed only exercise [26, 28, 32, 37], and five assessed a combination of diet and exercise [8, 25, 30, 40, 42]. Of the four studies with inconclusive results, one assessed a dietary intervention [34], one an exercise intervention [39], and two assessed a combination of diet and exercise [27, 36]. Of

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eight studies reporting non-cost effectiveness, three assessed exercise only [31, 33, 46], and five assessed a combination [23, 24, 30, 38, 41, 45].

Quality assessment

Figure 3 provides a graphical summary of the CHEERS quality assessment results of the 24 included studies. The results of study-level quality assessment (Appendix 6 Supplementary material) ranged from 54% to 92% of items reported out of 24. The top 25% of studies in this range found mixed results [23, 25, 27, 31, 36, 40], with no specific telehealth modality (internet, phone, or combination) or intervention (diet, exercise, or combination) emerging as cost-effective or not cost-effective. Results were often contradictory, and authors noted limitations such as missing outcome data [27, 33, 36, 37] and short durations [28, 30, 45].

Twelve elements were consistently reported (Figure 3) with 95% or more of studies reporting these elements. Only two studies estimating costs and effects over a >12-month time horizon reported discount rates for economic evaluations. One study applied a 3% discount rate [8], and the other applied a rate of 4% and 1.5% in two sensitivity analyses [36]. Six studies stated that a discount rate was not applied due to having a time horizon of 12 months or less (26%), and 13 studies did not report any discount rate (57%), and while not disclosed, is likely due to the same reason. The item that least complied with CHEERS was reporting the choice of decision-analytic model and model assumptions, compliant only in two out of 24 studies.

Discussion

This systematic review sought to summarise and critically appraise existing economic evidence for telehealth-delivered diet and exercise interventions. We identified 24 studies conducted across a variety of health conditions including overweight populations, non-acute

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cardiac conditions, T2DM and chronic kidney disease. The findings will be of interest to researchers and policymakers seeking cost-effective interventions which are just as, or more effective than face-to-face individual or group interventions. This review is a timely analysis, considering the context of the COVID-19 pandemic and systemic healthcare inequalities that necessitate policies supporting continued adoption and integration of telehealth technologies for remote delivery of health services [51]. Nineteen of the included studies (79%) were funded by a public organisation, showing that the public sector has a strong interest in telehealth. While there are no other existing reviews on the cost-effectiveness of telehealth-delivered interventions, a review evaluating telemedicine in general clinical practice also found mixed results regarding cost-effectiveness, largely due to a paucity of methodologically-sound studies with generalisable conclusions [52].

The results show good evidence suggesting that telehealth diet and exercise interventions can be cost-effective, with 12 out of 24 studies (50%) concluding that their telehealth intervention was cost-effective compared to the comparator group. There is most evidence to support cost-effectiveness of telephone-based interventions, possibly due to well-established infrastructure and hence less set up costs, compared to mHealth interventions utilising more novel technologies. However, some uncertainty remains due to heterogeneity across study cohorts, interventions, and settings. Inputs with the greatest influence on ICER estimates were variations in costs included and the perspectives adopted. While Chung et al.[43] and McConnon et al.[38] found that telehealth interventions were not cost-effective in the short term due to initial set-up costs, several studies demonstrate that costs will be offset in the medium to long-term or through implementation of the intervention on a broader scale [9]. With several studies indicating that long-term nutrition interventions are more effective[53, 54], health economic evaluations should be of sufficient duration to measure true costs and health

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outcomes. For example, Rollo et al. [55] compared the theoretical costs of a face-to-face weight-management program compared to telehealth using mHealth technologies, and found that while establishment costs were higher for mHealth, total costs per patient over 12 months was higher for in-person delivery when establishment costs were excluded.

These findings should be interpreted with caution given the heterogeneity across intervention methodology and settings of included reviews. Only seven studies (29%) attempted to explore the level of use necessary for telehealth interventions to compare favourably with conventional healthcare. This highlights the need for more research into the cost-effectiveness of telehealth-delivered diet and exercise interventions for the prevention and treatment of diverse health conditions given the growing interest in the use of technology in healthcare [10, 56-60]. The addition of economic analyses as an adjunct to clinical trials have been associated with various issues, including an increased likelihood that economic findings will be statistically underpowered [61]. These issues can be addressed through careful trial design and implementation requiring close collaboration with health economists [62, 63]. All included studies were conducted in high-income countries, and yet telehealth presents exciting opportunities to address access and equity issues in lower income countries and low-resource settings [64].

The main shortcomings in economic reporting quality as assessed by the CHEERS statement were reporting of type of decision-analytic model used, model assumptions, lack of reporting on characterising heterogeneity and time horizons. Intervention effect and sustainability are key factors affecting the cost-effectiveness of telehealth interventions, especially given the potential cost-savings of these delivery modes compared with face-to-face modes. Analytic time horizons and implementation periods should also be long enough to avoid curtailing the

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assessment and interpretation of intervention results [65]. Twenty-two studies (92%) had a time horizon of two years or less, producing costs and benefits that may not reflect true values that arise once the service is established and operating over a longer duration. Twenty-three studies (96%) used the clinical evidence generated by a RCT, which provide reliable and rigorous datasets. However, a potential drawback is that their highly controlled settings may not reflect routine clinical practice. It is also difficult to generalise the results of individual cost-effectiveness studies due to regional variations in aspects of telehealth systems and evaluations conducted in specific contexts. This emphasises the importance of evaluating the local applicability of telehealth interventions to support generating generalisable messages.

While rigorous and standardised approaches were employed to summarise and present data on the cost-effectiveness of telehealth interventions from existing literature, several limitations of this work should be noted. Studies reported in languages other than English and studies with unavailable full text were excluded, which may introduce bias in the estimates of effect [66]. We also found that all the economic evaluations were targeted to adults only, making it impossible to generalise results to younger populations. There is scope for more studies targeted at wider population groups including children and adolescents requiring healthcare interventions. No studies implemented evaluations longer than two years or long-term economic modelling. Future studies should conform to CHEERS statement reporting guidelines to demonstrate methodological rigor, apply longer time horizons over two years, and use decision-analytic modelling to compare the cost-effectiveness of multiple treatment strategies (conducted alongside clinical trials). The use of modelling will also assist with establishing the long-term effect and cost-effect of diet and exercise telehealth interventions. Finally, all of the included studies were conducted before the COVID-19 pandemic.

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Conclusions

Diet and/or exercise interventions delivered via telehealth have the potential to improve the management of health conditions. We found that a significant proportion of studies (50%) were cost-effective and 29% were not. However, there were unclear results in 21% of studies which reduces the confidence in the existing evidence-base to conclude that the use of telehealth is cost-effective for the delivery of diet and exercise interventions over traditional care. There is a need for further investigations that employ rigorous methodology and economic reporting, and which improve generalisability by expanding targeted population demographics, locations, appropriate decision analytical models and longer timeframes. Health economists should be involved at all stages of trial design and implementation. Such economic evaluations can positively influence policy decisions, practice changes and adoption for improved management of various health conditions.

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Table 1. PICOS eligibility criteria

Criteria	Include	Exclude
Participants	Individuals (adults and/or children) with at least one health condition or a BMI >25kg/m².(or BMI> 23 for Asian populations).	Studies conducted in animals.
Interventions	Telehealth was defined as any technology used to deliver an intervention, such as video, internet or telephone-based, or remote monitoring. Lifestyle interventions that predominantly use either single or multifactorial telehealth diet and/or exercise strategies.	Studies on interventions that were not focused on diet and/or exercise e.g., pharmaceutical, or simple remote physiological monitoring e.g., oxygen saturation or blood glucose levels.
Control / Comparator	Usual care (as defined by authors of included studies), educational information or waitlist control, or no intervention or face-to-face education.	Studies with no control group or which compared telehealth to another intervention.
Outcomes	Outcomes of interest were any economic analysis in the form of cost-analysis or cost-utility analysis.	Studies reporting simple costs without analysis.
Study Design	Eligible studies were RCTs cluster RCTs, non-randomized controlled trials, and quasi-RCTs. No date restrictions were applied. Only studies published in the English language were considered.	Systematic reviews, narrative reviews, protocols, conference abstracts, studies published in languages other than English.

Abbreviations: BMI, body mass index; RCT, randomised controlled trial

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Table 2. Cost-effectiveness outcomes, N=24

Author, year	Perspective	Condition	Intervention	WTP used	Analysis/main findings		Author's conclusion
					Base case analysis	**Sensitivity analysis**	
Chung et al, 2015	Health service	BMI>23 (based on WHO criteria for Asian population)	Internet diet intervention	Not clearly stated	24-week ICER: $24.87/kg weight loss, $31.81/kg fat loss	NR	The face-to-face dietetics model is more cost-effective than the teledietetics model in short-term weight reduction. However, the teledietetics model is more cost-effective in the long-term.
Delahanty et al., 2020	Health service and patient	Type 2 Diabetes Mellitus	Telephone diet intervention	Not clearly stated	Incremental cost/kg lost: In-person was $321 and $483 for telephone LI. Cost/% weight loss was $296 for in-person and $432 for telephone LI.	SA 1: The exact number of days from enrolment at time of measurement was explored as a continuous variable and estimated the responses at months 6 and 12. A slightly smaller intervention effect at 6 months but a slightly larger intervention effect at 12 months. SA 2: Limited to research data only (excluding data obtained from clinical care), and data within a narrower visit window only (excluding data collected outside of a 2-month window of target follow-up date).	In-person and telephone LI had reasonable cost-effectiveness from the health system perspective. This study likely reflected real-world MNT utilization and underestimated the effectiveness of optimal and adequately covered MNT. If lifestyle intervention had also required co-pays, it likely would have reduced participation rates and influenced the outcome.

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						- Completers had higher mean weight loss than non-completers in both intervention arms. When time-to-weight measurement was considered as a continuous variable, a slightly smaller intervention effect was observed at 6 months but a slightly larger intervention effect at 12 months.	
Frederix et al, 2015	Societal and patient	CAD or CHF	mHealth diet and exercise intervention	Not clearly stated	Incremental cost: €–564.40 Incremental health gain: 0.026 QALYs ICER: €–21,707/QALY	Not clear. The study did not report findings from either one way and probabilistic sensitivity analysis.	Addition of cardiac telerehabilitation to conventional centre-based cardiac rehabilitation is more effective and efficient than centre-based cardiac rehabilitation alone.
Graves et al, 2009	Health service	T2DM	Telephone diet and exercise intervention	$64,000/ QALY	ICER: $78,489/QALY	NR	Telephone counselling shows higher efficacy and cost-effectiveness over Real Control. Assumptions about the positive effects being achieved and maintained in broad-reach public health programs can be supported.
Gussenhoven et al, 2013	Dutch company perspective	BMI≥25	Telephone diet and exercise intervention	€0 and €1500 per extra kg body	Incremental costs were €59/ kg body weight lost based on GLPDs, and €267 based on NLPDs	SA1: Indirect costs were valued using the self-reported income of the participants and missing data were imputed	The study does not provide evidence that distance lifestyle counselling by phone or Inter-net is cost-effective for weight loss among overweight employees.

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				weight loss		SA2: The main analysis was repeated using only the complete cases (i.e., complete costs and bodyweight data) - Results were more in favour of the interventions than the multiply imputed analyses, but also showed no statistically significant differences in costs and effects.	Firm conclusions cannot be drawn because of the large amount of missing data. Nonetheless, the intervention does show some promise.
Hwang et al, 2019	Health service	Stable chronic heart failure (CHF)	Internet exercise intervention	$50,000-$60,000 per QALY	ICER: -$4157/QALY	SA 1: healthcare costs estimated based on the number of exercise programs required if there were full attendances - $1478 in IG and $2243 in CG, leading to non-significant difference of -$765 SA 2: Healthcare costs expanded from hospital readmissions related to heart failure to all-causes - $6625 in IG and $11,077 in CG, leading to non-significant difference of -$4452	Telerehabilitation appears to be a cost-saving intervention for the healthcare provider. Note that the analysis was conducted from healthcare provider perspective and not societal, and thereby disregarded patient transportation costs and time incurred by CG.
Kloek et al, 2018	Society and health service (secondary)	Osteoarthritis (OA) of the hip	Internet exercise intervention	€10,000 from societal and €80,000 from health	ICER: €52,900/QALY	SA 1: performed by using total costs data of complete cases with follow-up-data at each time-point that additionally completed all questionnaires. - Results showed significant higher costs in the e-Exercise group compared to	e-Exercise cannot be seen as cost-effective in comparison with usual physiotherapy from both a societal and a healthcare perspective. From both perspectives, no significant differences were seen in total

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				service perspective		usual physiotherapy, but no significant differences in effects. SA 2: Per-protocol analyses, performed by comparing total costs of patients from the e-Exercise group that completed≥8 modules (out of 12) with the entire usual physiotherapy group. - Results were in line with those of the main analysis	costs and effects. The decision about which intervention to use should be based on the preferences of the patient and the physiotherapist.
Kraal et al, 2017	Society	Acute coronary syndrome Post-percutaneous coronary intervention Post-coronary artery bypass grafting	mHealth exercise intervention	€20,000-€40,000/ QALY	Not specified – diagram available	SA 1: Primary outcomes were compared between 'as treated' groups - no significant change in PAL after the three-month rehabilitation period among patients in the centre-based group (p=0.51). All other results were similar to the intention-to-treat analysis. SA 2: presenteeism was also included in the societal perspective	Home-based CR has the potential to increase overall participation in exercise-based CR, especially for cardiac patients with the ambition to return to work quickly or with transportation difficulties. In addition, home-based CR appears to have lower societal costs and to be more cost-effective than centre-based CR. Therefore, we conclude that home-based training with telemonitoring guidance is a useful alternative to conventional centre-based training for young and motivated low-to-moderate cardiac risk patients entering CR.

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Little et al, 2017	NHS and Personal Social Services	BMI≥30 (or ≥28 with additional risk factors)	Internet and telephone exercise intervention	£100/kg lost (NICE)	FG vs CG: ICER= £18/kg lost RG vs CG: ICER= –£25/kg lost	SA 1: complete cases SA 2: cost per percentage achieving weight loss of>5% from baseline SA 3: excluding hospital costs Increasing the cost of face-to-face contacts in RG would make little difference, as the mean number of such contacts was only 0.10. Similarly, as the mean number of telephone calls was almost the same in each group (mean of 0.81 and 0.74 in the FG and RG, respectively), adjusting their unit cost would make little difference to the difference in cost between interventions. The main difference between the two groups was the use of e-mails, with a mean number of 0.92 in FG and 2.0 in RG. The mean cost in RG would rise to that of FG only if e-mails cost the same as face-to-face contacts.	Overall, both interventions were cost-effective in terms of weight loss, but less so in terms of incremental cost per QALY. This was the case for the base-case analyses of cost per kilogram lost and per QALY and showed little variation in other analyses. The cost per kilogram lost is highly likely to be below NICE's threshold of £100 per kilogram lost, but this conclusion is limited by a lack of data on the maintenance of weight loss beyond 12 months
Maddison et al, 2015	NR	Diagnosis of IHD	Internet and telephone exercise intervention	$20,000 and $50,000/ QALY	ICER: $28,768/QALY ICER/MET-hour of walking and leisure activity a week were $48 and $74 respectively	NR	A mobile phone intervention was not effective at increasing exercise capacity over and above usual care. Positive effects were found for physical activity in favour of the intervention, which

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							was likely to be cost-effective, and may have potential to augment existing CR services.
McConnon et al, 2007	Society	BMI≥ 30	Internet diet and exercise intervention	£20,000–£30,000 per QALY	ICER: £39,248/QALY	NR	In terms of cost-effectiveness, the Internet-based support in this trial does not seem to fall within accepted standards for the ICER. This is mainly due to the high fixed cost of setting up and running the program (£771 per participant in the Internet group), which made it substantially more costly than the usual care group to set up. However, as the intervention is Internet-based, its use by a larger pool of participants could improve cost-effectiveness
O'Brien, et al, 2018	Society and health service (secondary)	Complaint of knee osteoarthritis is pain >3 months; and BMI ≥27 and <40	Telephone diet and exercise intervention	Cost-effectiveness acceptability curves used to assess	Societal ICER: $581,82/QALY Health service ICER: $387,820/QALY	SA 1: Per-protocol sensitivity analysis from the societal perspective that included only participants that completed at least six telephone GHS coaching calls in the intervention group (n= 20 participants). For QALYs, the probability of cost-effectiveness was 0.63 at a WTP of	Findings suggest that referral to a telephone-based weight management and healthy lifestyle service is not cost-effective compared with usual care for overweight and obese patients with knee osteoarthritis. These findings apply to QALYs, knee

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				different WTP values		$0/QALY gained. For QALYs the probability of cost-effectiveness remained about the same irrespective of the WTP	pain intensity, disability, weight, or BMI, from the societal and health service system perspectives.
Paul et al, 2019	NR	Multiple sclerosis	Internet exercise intervention	Not clearly stated.	NR	NR	The estimated differences in costs and QALYs between groups were small and further research to reduce the uncertainty associated with these estimates would be beneficial.
Salisbury et al, 2016	NHS	Risk of having a cardiac event in the next 10 years of ≥20%, and ≥1 modifiable risk factors (systolic blood pressure ≥140 mmHg, body mass	Internet and telephone diet and exercise intervention	£20,000-£30,000 per QALY	ICER= £10,859/QALY	SA 1: Complete case analysis was conducted as a check on the base case imputed cost-effectiveness analysis. SA 2: Base case (imputed) results were assessed for their sensitivity to self-reported use of secondary care in order to assess the effect of rare but expensive events and to address potential recall bias or misclassification of resource use.	The results suggest that healthcare delivery systems based on telehealth may be associated with some benefits, although these should not be assumed. The study demonstrated the feasibility of delivering an intervention on a wide scale at relatively low cost and using non-clinically trained health advisors supported by computerised algorithms.

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		index ≥30, being a current smoker, or any combination of these)					
Sniehotta et al, 2019	NR	BMI≥30 in the 24 months preceding trial entry and had lost ≥5% body weight in the preceding 12 months to recruitment.	Telephone diet and exercise intervention	£20,000 to £30,000 per QALY	Incremental cost: £131/participant (ICER not clearly reported)	Sensitivity analyses accounted for a potential effect for reductions in salary costs associated with the delivery of the intervention.	No evidence that the intervention was cost-effective.
Suman et al, 2019	Society	Diagnosis of non-specific	Internet exercise intervention	€10,000 and €80,000	Inadequately reported - no numbers provided, only the diagram scatterplot that indicated	Sensitivity analysis performed: Only patients with complete data on all measurement points were included	A multifaceted eHealth strategy was not effective in improving patients' back pain beliefs or in decreasing disability and

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		lower-back pain		per QALY	that intervention was more cost-effective than UC.	Results of the sensitivity analysis differed extensively from those of the main analysis (adjusted cost difference €1780 per patient; 95% CI €−1298 to 6945; adjusted effect difference −0.002; 95% CI −0.079 to 0.075), suggesting that the 'missingness' of data is likely related to various observed factors.	absenteeism but showed promising cost- utility results based on QALYs.
Turkstra et al, 2013	Australian government	CHD	Internet and telephone diet and exercise intervention	Not clearly stated.	ICER: $85,423/QALY	NR	The intervention was not a cost-effective intervention in the short-term compared to UC. There was no significant improvement in utility, and it resulted in significantly increased costs. However, while we have not assessed this in the current study, higher cost may result in future cost-savings as patients are potentially better monitored, and therefore it could be suggested that health problems may be identified at an earlier stage resulting in better health outcomes.

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van Keulen et al, 2011	Health service	Hypertension	Telephone diet intervention	€2,851 and €8,200 per QALY	TPC vs TMI ICER: €160/QALY TPC vs CG ICER: €2,867/QALY	NR	For low society's willingness to pay, the control group was most cost-effective for the number of QALYs experienced over 73 weeks. This also applied to the increase in the number of guidelines met at lower ceiling ratios, whereas at higher ceiling ratios, TPC had a higher probability of being more cost-effective than the TMI, combined or control conditions. This also seemed to apply for QALYs experienced over 73 weeks. More research is needed on the long-term efficacy of both TPC and TMI, as well as on how to increase their cost-effectiveness.
Joo et al, 2010	Not clearly stated	BMI≥25 kg/m^2	Internet diet and exercise intervention	For per-protocol, WTP (SD): V-type= $70.62 (79.40)	NR	NR	The cost-effectiveness of the visiting type short-duration obesity control programme offered by a public health centre was higher than a remote type programme.

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				R-type= $20.65 (22.26)			
van Wier et al, 2012	Society	BMI≥25	Internet and telephone diet and exercise intervention	€20,000 per QALY	PG vs CG ICER: €1009/kg weight loss IG vs CG ICER: €16/kg weight loss PG vs CG ICUR: €245,243/QALY IG vs CG ICUR: €1337/QALY	SA 1: Costs for the second year were discounted with 4% and QALYs achieved in this year were discounted with 1.5%, according to Dutch guidelines Results were comparable with main analysis SA 2: restricted to participants with complete cost and effect data, i.e., complete case analysis An ICER of €-62 and an ICUR of€-27,908, as compared with self-help, were found. The probability that the internet intervention was cost-effective at a WTP of €0/kg weight loss was 57% and reached a maximum of 89% at a WTP of €550.The probability of its cost-utility was 86% at €20,000/QALY. SA 3: Done from the perspective of a Dutch company, with a WTP of €0 for all health effects. Results like main analysis for PG. Results of the internet group showed a saving of €149 Euros. At	The lifestyle program with phone counselling was not proven to be cost effective. The program with e-mail counselling showed some promising results but its cost-effectiveness was uncertain. Due to high loss to follow-up firm conclusions cannot be drawn. Future economic evaluations of weight control interventions should ensure that dropout is limited.

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						a WTP of €0 per unit of health effect, the likelihood that the intervention was cost-effective was 66 % for both weight loss and QALYs gained SA 4: QALYs were estimated using the UK EQ-5D tariff The ICUR in the phone group was €52,496, which was lower than in the main analysis. The probability of cost-utility at €20,000/QALY was 8%. Similarly, the ICUR of the internet group was lower, €702. The probability of cost-utility was 71% at €20,000/QALY	
Whelan et al, 2016	Health service	BMI≥25	Telephone diet and exercise intervention	NR	The cost per healthy life-year gained was $33,000 for TP and $85,000 for CG.	A sensitivity analysis using multiple imputation was performed to evaluate the sensitivity of conclusions to assumptions regarding missing data.	The telephone-based weight loss program was a feasible, effective and cost-effective service delivery option when evaluated in a real-world hospital outpatient setting. Additionally, the telephone-delivered program may be a suitable alternative service delivery option to the existing group-based program.
Whittaker et	Health service and patient	Patients referred for cardiac	Internet and telephone	NR	NR	NR	Cardiac rehabilitation by telehealth offers obvious advantages, at least to the group

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al, 2014		rehabilitation	exercise intervention				of patients who were able and willing to enter the study. There is enough evidence to suggest that a telehealth option should be available to all patients who are eligible for cardiac rehabilitation, although the hospital option should continue to be available for those who prefer an in-person service
Williams et al, 2019	Society and health service (secondary)	Lower back pain and BMI ≥27kg and <40 kg/m	Telephone diet and exercise intervention	$0 and $67,000 per QALY	ICER: −$31,087/QALY	SA 1: One participant with very high absenteeism costs was excluded. The total cost difference was -$8 when outlier was removed For QALYs, the probability of cost-effectiveness was 0.51 The probability of cost- effectiveness increased to 0.90 at a WTP of $47,000/QALY and reached a maximum of 0.92 at a WTP of $77,000/QALY. SA 2: Exclusion of intervention participants who did not have reasonable adherence, defined as not attending the clinical consultation and receiving <6 GHS health coaching calls Total cost difference was -$74	The intervention seems to be cost-effective for QALYs from the societal perspective but not from the healthcare perspective. Variability found in the sensitivity analyses findings should be considered in the decision to utilize this intervention.

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						For QALYs, the probability of cost-effectiveness was 0.54 The probability of cost-effectiveness increased to 0.90 at a WTP of $72,000/QALY and reached a maximum of 0.91 at a WTP of $86,000/QALY.	

Abbreviations: WTP, willingness-to-pay; ICER, incremental cost-effectiveness ratio; SA, sensitivity analysis; BMI, body mass index; RCT, randomised controlled trial; UC, usual care; NR, not reported; QALY, quality-adjusted life years

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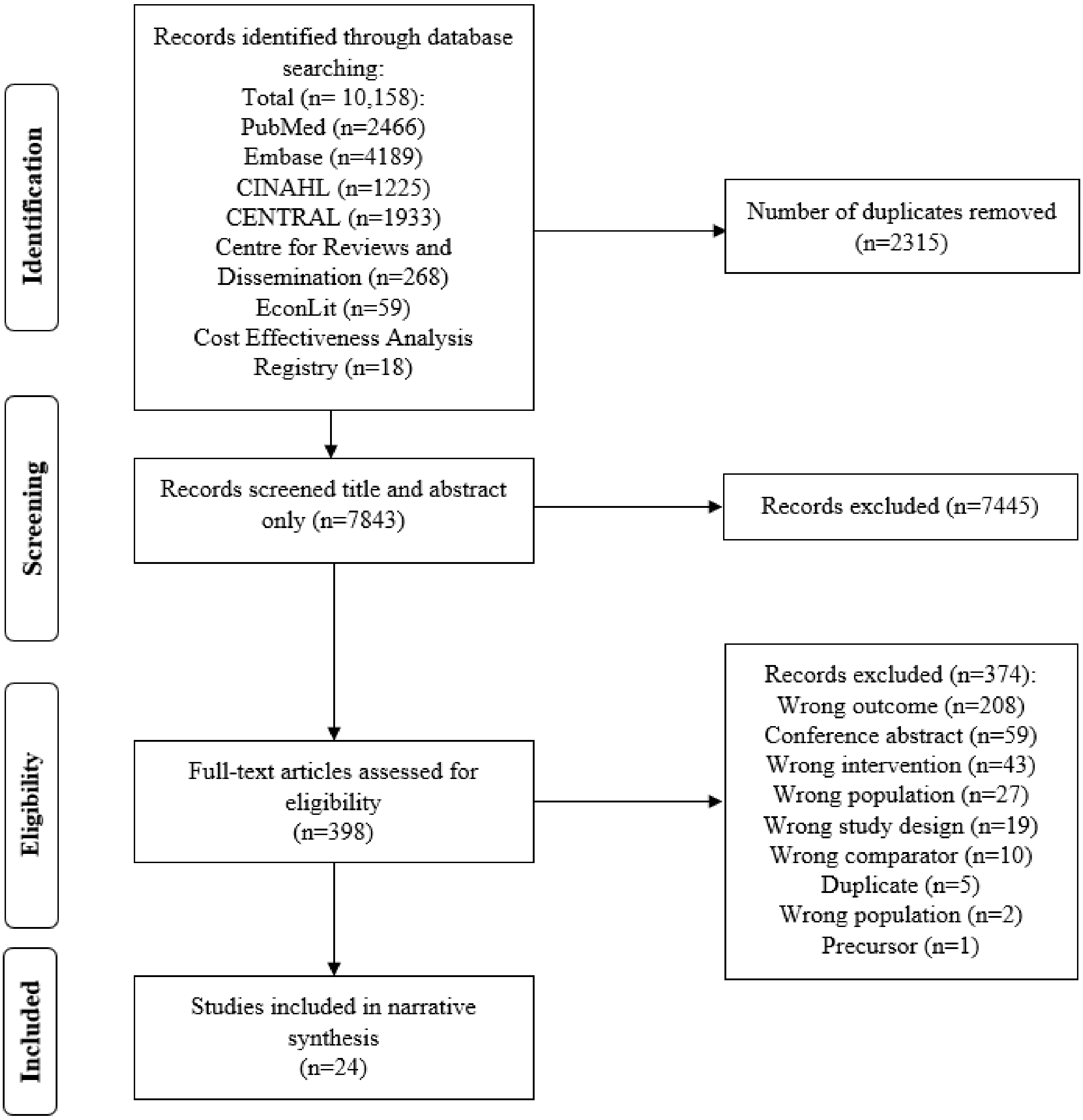

Figure 1: PRISMA flowchart of the search results and included studies

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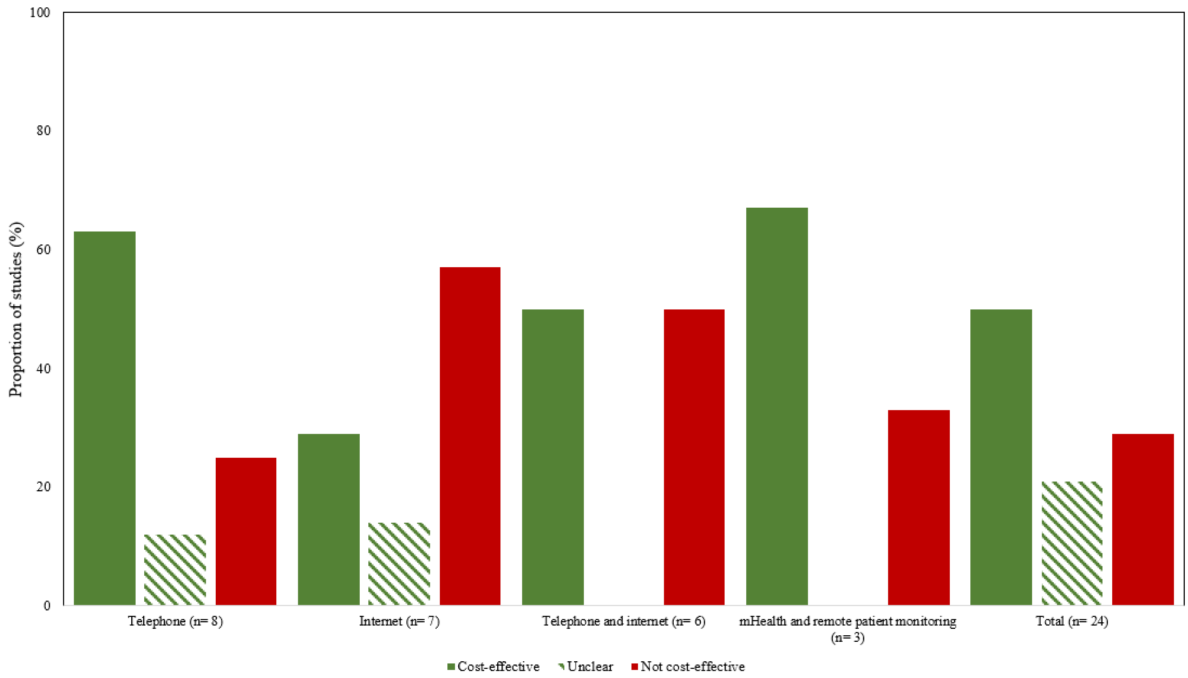

Figure 2: Cost-effectiveness results from included studies, broken down according to telehealth modality and data presented as the proportion of studies

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Figure 3: Diagrammatic summary of CHEERS assessment results (N=24)

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Supplementary Material

Appendix 1: Completed PRISMA Checklist

Appendix 2: Completed ISPOR CiCERO Checklist

Appendix 3: Structured database systematic search strategies

Appendix 4: General characteristics of included studies, N=24

Appendix 5: Reporting of costs and effectiveness, N=24

Appendix 6: Study-level quality assessment using CHEERS checklist divided across two tables for display of all included studies

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