Norwegian Institute of Public Health

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REPORT

OVERVIEW OF OVERVIEWS:
Managing chronic illnesses with remote patient monitoring in primary health care

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Key messages

Remote patient monitoring (RPM) allows for the real-time transmission of health data, evaluation of this data, and appropriate follow-up. This allows providers to monitor the health status of chronically ill patients and quickly adjust treatment regimes, without requiring that patients continually visit providers' offices.

We summarized systematic reviews of a specific type of RPM that the Norwegian Directorate of Health is most interested in: RPM that is occurring in primary health services, in which provider feedback is included, and not including technologies based on internet, mobile, or tablet applications.

We included 11 randomized controlled trials of patients with diabetes and/or hypertension, from four systematic reviews. Patients were on average in their 50s, 60s, or 70s, and roughly one to two of every 20 patients had at least one additional multi-morbidity.

Based on summaries of each outcome and our assessment of the certainty of the evidence, we have drawn the following conclusions:

- RPM probably makes little to no difference on HbA1c in diabetic patients (types I and II) and on systolic blood pressure in hypertensive patients.
- RPM probably has a small negative effect on the physical component of health-related quality of life.
- RPM may make little to no difference to diastolic blood pressure, cholesterol, number of patients needing hospitalizations or emergency stays, and the mental health component of health-related quality of life.

The specific type of RPM we examined in this review does not appear commonly implemented among people with chronic conditions other than diabetes or hypertension. Evidence of its clinical and health care utilization effectiveness is weak.

Title:
Managing chronic illnesses with remote patient monitoring in primary health care: an overview of overviews

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Type of publication:
Overview of systematic reviews
A review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.

Doesn't answer everything:
- Patient or provider experiences with remote patient monitoring
- Health economic evaluation

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Executive summary (English)

Background

The proportion of Norwegians with chronic conditions is increasing, as is the amount of years they will survive with these conditions. The health care system must move away from a curative perspective and towards a chronic care model: how best can it help patients manage daily life with one or more chronic conditions? How can patients maintain optimal functioning and as good a quality of life for as many years as possible?

Ideally, patient data could be collected unobtrusively and sent frequently to providers, to allow for continuous monitoring and the provision of care before patients' conditions deteriorate. One technique is remote patient monitoring (RPM), a broad term referring to the remote transmission and evaluation of patient data that provides health personnel with real-time or frequently collected information about a patient's health condition. This broad term has been fine-tuned by the Norwegian Directorate of Health for this review to refer to interventions occurring within the primary health services and requiring the involvement of providers (as opposed to fully-automated processes).

Evidence of the efficacy of RPM and related strategies has increased significantly, yet we do not know whether previous strategies describe the specific type of RPM in which the Directorate is most interested. A systematic review that assesses both the evidence and the types of strategies used is therefore needed.

Objective

This overview of systematic reviews sought to measure the effectiveness of RPM on clinical and health care utilization outcomes among chronic disease patients.

Method

We conducted an overview of systematic reviews. We systematically searched the literature for systematic reviews and overviews that conducted their own searches in 2015 or more recently. Reviews of randomized controlled trials (RCTs) that included adult patients with cardiovascular disease, diabetes, hypertension, chronic lung diseases, cancer, mental disorders, chronic musculoskeletal disorders, osteoporosis, or impaired vision/hearing were included if they examined the effectiveness of RPM according to our definition of RPM, and reported

clinical or health utilization outcomes. Two researchers screened 3373 records at the title and abstract level, and included reviews that contained at least one RCT that met the inclusion criteria. As all systematic reviews included both RCTs that were eligible for our review and RCTs that were ineligible, we included only eligible RCTs from the systematic reviews for further inclusion. We summarized results and displayed these in forest plots, but we conducted no meta-analyses, as our overview of systematic reviews was not a comprehensive identification of all existing RCTs. Our certainty in the primary outcomes was assessed using the Grading of Recommendations Assessment, Development, and Evaluation approach (GRADE).

Results

We included four systematic reviews that together reported on 11 RCTs that met our definition of RPM. Only patients with diabetes (types I and II) and/or hypertension were captured by these RCTs, with average ages from 51 to 73 years. Roughly one to two of every twenty patients had a multi-morbidity, among the RCTs that reported these.

The RCTs lasted from 6 to 12 months, and while all met our definition of RPM, they were heterogeneous with regards to how data was transmitted (from commercial telehealth units to patients' existing landlines) and who assessed it (providers, monitoring centers, or the devices themselves). In most cases, patients were only followed up with if data values were of concern, so that patients without an assessed need for further medical attention would not be contacted by providers. It was difficult to determine whether the follow-up they received was akin to usual care or was more enhanced, because most RCTs scarcely described usual care. In the most conservative interpretation, RPM patients received the same follow-up as usual care patients but more often (if needed); in the most generous interpretation, RPM patients received not only more contact with providers but also enhanced treatment.

Among our eight primary outcomes, only three were affected by RPM. RPM probably makes little to no difference on HbA1c levels in diabetic patients. Similarly, RPM probably leads to a slight reduction in systolic blood pressure, with questionable clinical meaningfulness. RPM probably has a small negative effect on the physical component of health-related quality of life; the clinical significance of this reduction is again uncertain. We have low confidence in the findings that RPM makes no difference to the remaining five primary outcomes: diastolic blood pressure, cholesterol, number of patients needing hospitalizations or emergency stays, the mental health component of health-related quality of life, and Hospital Anxiety and Depression Scale scores. RPM also showed no effect in 22 of the remaining 23 outcomes.

Discussion

Many of our findings are consistent with reviews of other, broader definitions of RPM. The clinically insignificant reduction to HbA1c may be explained by our

RCTs mainly utilizing single-component interventions instead of multi-component interventions. However, if RPM itself is more of a mechanism to facilitate contact with providers at the cusp of patient deterioration, it may be that increased contact is insufficient. Patients with diabetes and/or hypertension may need treatment that focuses on behavioral change in order to improve clinical outcomes such as HbA1c, blood pressure, and cholesterol, and increased contact may not be enough to change behavior.

One identified gap in the research is an understanding of why RPM has a *negative* effect on quality on life, a finding that has also been reported by previous reviews. Qualitative methods are likely the best tools to explore this question. Other research gaps include the effects of RPM on patients with both chronic physical conditions and psychiatric conditions, who are most often excluded from clinical trials, and the effects of RPM on patients with impaired vision/hearing. The inherent innovative nature of technologies included in RPM, and particularly their ability to be tailored to patients' capacities and limitations, make RPM seem uniquely able to address the needs of these patient groups – yet we found no RCTs including these patients.

Conclusion

The type of RPM examined in this review is neither particularly commonly implemented nor particularly effective for patients with diabetes and/or hypertension.

Hovedbudskap

Medisinsk avstandsoppfølging muliggjør oversendelse av pasientdata i sanntid, evaluering av data og tilpasset oppfølging. Med denne typen oppfølging kan helsepersonell overvåke helsetilstanden til pasienter med kroniske lidelser og justere behandlingen raskere, uten å møte pasienten ansikt til ansikt.

Vi oppsummerte systematiske kunnskapsoversikter om en spesifikk type avstandsoppfølging valgt av Helsedirektoratet. Avstandsoppfølgingen skulle skje i primærhelsetjenesten, inkludere oppfølging gitt av helsepersonell og kunne ikke inkludere bruk av internett-, mobiltelefon- eller nettbrettapplikasjoner.

Vi inkluderte 11 randomiserte kontrollerte studier av pasienter som hadde diabetes eller høyt blodtrykk, fra fire systematiske oversikter. De fleste av pasientene var i 50-, 60- eller 70-årene, og omtrent 5-10 % av pasientene hadde også andre sykdommer.

Basert på vår narrative oppsummering og vurdering av tillit til resultatene, har vi konkludert med følgende: Sammenlignet med kontroll er det med medisinsk avstandsoppfølging

- trolig en liten bedring på HbA1c og systolisk blodtrykk.
- trolig en liten reduksjon i den fysiske helsekomponenten av helserelatert livskvalitet.
- muligens liten eller ingen forskjell når det gjelder diastolisk blodtrykk, kolesterol, antall pasienter som trenger sykehusinnleggelse eller akuttopphold, og den psykiske helsekomponenten av helserelatert livskvalitet.

Den typen medisinsk avstandsoppfølging som vi oppsummerer i denne oversikten implementeres i liten grad blant personer med kroniske lidelser, bortsett fra diabetes og høyt blodtrykk. Dokumentasjonsgrunnlaget for effekten av slik avstandsoppfølging på kliniske utfall og bruk av helsetjenester er begrenset.

Tittel:

Oppfølging av kroniske sykdommer med medisinsk avstandsoppfølging i primærhelsetjenesten: en oversikt over oversikter

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Publikasjonstype:

Systematisk oversikt

En systematisk oversikt er resultatet av å
- innhente
- kritisk vurdere og
- sammenfatte

relevante forskningsresultater ved hjelp av forhåndsdefinerte og eksplisitte metoder.

Svarer ikke på alt:

- Pasienters eller helsepersonell sine erfaringer med avstandsoppfølging
- Helse økonomisk analyse

Hvem står bak denne publikasjonen?

Folkehelseinstituttet har gjennomført oppdraget etter forespørsel fra Helsedirektoratet.

Når ble litteratursøket utført?

Søk etter studier ble avsluttet mai 2019.

Eksterne fagfeller:

Kari Dyb, Forsker, Nasjonalt senter for e-helseforskning

Line Melby, Førsteamanuensis, Norges teknisk-naturvitenskapelige universitet

Sammendrag

Innledning

Andelen nordmenn med kroniske lidelser øker, og samtidig øker antall pasienter som lever med disse lidelsene. Helsevesenet må bevege seg bort fra et kurativt perspektiv og mot en mer helhetlig modell med behandling og omsorg: hvordan kan helsevesenet best hjelpe pasienter å håndtere dagliglivet med en eller flere kroniske lidelser? Hvordan kan pasienters optimale funksjonsnivå opprettholdes, og hvordan kan man oppnå så god livskvalitet som mulig i så mange år som mulig?

Ideelt sett kunne pasientdata diskret samles inn og hyppig oversendes til helsepersonell, for på den måten å muliggjøre kontinuerlig overvåking og justering av behandlingen før pasientens tilstand forverres. Én slik metode er medisinsk avstandsoppfølging (Engelsk: remote patient monitoring, «RPM»). RPM er et bredt begrep som refererer til overvåking og vurdering av pasientdata som skjer over avstand, og som gir helsepersonell sanntids- eller hyppig informasjon om pasientens symptomer og helsetilstand. Dette brede begrepet har for denne oversikten blitt spesifisert av Helsedirektoratet til å referere til tiltak som skjer innen primærhelsetjenesten og som inkluderer helsepersonell (i motsetning til helautomatiske tiltak).

Det har vært en dramatisk økning i forskning om RPM og lignende tiltak, men det er uklart om tidligere tiltak har operert med den samme forståelsen av RPM som Helsedirektoratet er interessert i. Det er derfor nødvendig med en systematisk oversikt som vurderer både effektene av RPM og hvilke typer RPM som brukes.

Hensikt

Hensikten med denne systematiske oversikten var å undersøke effektene av RPM på kliniske utfall og på bruk av helsetjenester blant pasienter med kroniske lidelser.

Metode

Vi utførte en oversikt over systematiske oversikter. Vi søkte i flere litteraturdatabaser etter systematiske oversikter og etter oversikter over oversikter. De kunne ikke ha litteratursøk senere enn 2015. Oversiktene måtte inkludere randomiserte kontrollerte studier (RCTer) hvor pasientene var voksne med hjerte- og karsykdommer, diabetes, høyt blodtrykk, kroniske lungesykdommer, kreft, psykiske lidelser, kroniske muskel- og skjelettplager, osteoporose eller nedsatt syn/hørsel. De måtte videre måle effekten av RPM slik vi definerte det og rapportere utfall som enten var kliniske eller som omhandlet bruk av helsetjenester. To forskere vurderte 3373 titler og sammendrag fra litteratursøkene. De inkluderte oversikter som hadde minst én RCT som undersøkte RPM som definert ovenfor. Alle oversiktene inkluderte imidlertid både RCTer som beskrev RPM i henhold til vår definisjon og RCTer som beskrev andre typer av RPM. Vi oppsummerte resultatene fra RCTene som undersøkte RPM i henhold til vår definisjon narrativt. Vi viste også resultatene i forest plots, men vi utførte ingen metaanalyser, pga. at vår oversikt over systematiske oversikter ikke var en uttømmende identifisering av alle eksisterende RCTer. Vi vurderte tillit til resultatene ved bruk av Grading of Recommendations Assessment, Development and Evaluation (GRADE), for åtte primærutfall.

Resultater

Vi inkluderte fire systematiske oversikter som til sammen rapporterte resultatene fra elleve RCTer som undersøkte RPM i henhold til vår definisjon. Kun pasienter med diabetes og/eller høyt blodtrykk var inkludert i disse RCTene. Gjennomsnittsalderen deres var fra 51 til 73 år. I RCTene som rapporterte om komorbiditet var omtrent 5-10 % av pasienter multisyke.

RCTene hadde 6-12 måneders oppfølging, men selv om alle undersøkte RPM i henhold til vår definisjon, var de nokså heterogene med hensyn til hvordan data ble overført (fra kommersielle telemedisinenheter til pasienters vanlige telefoner) og hvem som vurderte informasjonen (helsepersonell, telemedisinsenter eller selve enhetene). I de fleste tilfellene ble pasientene fulgt opp kun hvis de hadde bekymringsfulle helsedata. De fleste RCTene beskrev i liten grad hva vanlig oppfølging var. Det var derfor vanskelig å avgjøre hvorvidt oppfølgingen pasientene mottok var lik vanlig oppfølging eller om den var mer omfattende eller forbedret. Med utgangspunkt i en konservativ tolkning fikk RPM-pasientene den samme oppfølgingen som pasientene i kontrollgruppene, men hyppigere (om nødvendig); og med en rausere tolkning mottok RPM-pasienter ikke bare hyppigere oppfølging, men også forbedret behandling.

Resultatene viste at RPM hadde en effekt på kun tre av åtte primærutfall. RPM utgjør sannsynligvis liten eller ingen forskjell på HbA1c - en statistisk signifikant, men ingen klinisk signifikant reduksjon ble rapportert av RPM-pasientene. Tilsvarende fører RPM trolig til en svak reduksjon i systolisk blodtrykk, med tvilsom klinisk betydning. RPM har trolig en liten negativ effekt på den fysiske helsekomponenten av helserelatert livskvalitet; den kliniske betydningen av denne negative effekten er også usikker. Vi har lav tillit til de resterende utfallene, nemlig at RPM har ingen effekt på diastolisk blodtrykk, kolesterol, antall pasienter som trenger sykehusinnleggelse eller akuttopphold, den psykiske helsekomponenten av helserelatert livskvalitet og Hospital Anxiety and Depression Scale skåre. RPM viste heller ingen effekt når det gjelder 22 av 23 andre utfall, og en negativ effekt på vekt.

Diskusjon

Mange av funnene våre stemmer overens med oversikter som har undersøkt andre eller bredere typer RPM. Det er mulig at den klinisk ubetydelige reduksjonen på HbA1c kan forklares med at våre inkluderte RCTer hovedsakelig brukte kun én komponent (f.eks. SMS) i stedet for flere komponenter (f.eks. nettbrett og SMS sammen). Hvis RPM forstås mer som en metode som gjør det mulig å ha hyppigere kontakt med helsepersonell idet pasientens helse er i ferd med å forverres, så kan det bety at hyppigere kontakt er utilstrekkelig. Pasienter med diabetes eller høyt blodtrykk kan ha behov for behandling som fokuserer på atferdsendring for å forbedre kliniske utfall som HbA1c, blodtrykk og kolesterol, og hyppigere kontakt er kanskje ikke nok til å endre atferd.

Et identifisert behov for forskning er hvorfor RPM har en negativ påvirkning på livskvalitet. Dette er et funn som er rapportert av flere tidligere oversikter. Kvalitative metoder er sannsynligvis de beste verktøyene for å utforske dette spørsmålet. Andre behov for forskning inkluderer effekten av RPM på pasienter med både kroniske fysiske lidelser og psykiske lidelser, som ofte er ekskluderte fra kliniske studier, og effekten av RPM på pasienter med nedsatt syn/hørsel. De iboende innovative egenskapene til RPM, og spesielt muligheten til å skreddersy teknologien til pasientenes kapasiteter og begrensninger, gjør at RPM er unikt egnet til å imøtekomme behovene til disse pasientgruppene - men vi fant likevel ingen RCTer som inkluderte disse pasientene.

Konklusjon

Vi konkluderer med at den typen RPM som vi undersøkte i denne oversikten hverken er hyppig implementert eller effektiv for pasienter med diabetes eller høyt blodtrykk.

Preface

The Norwegian Directorate of Health commissioned a systematic review of overviews of the effectiveness of remote patient monitoring on clinical and health utilization outcomes of patients with chronic conditions.

We assisted the Directorate to develop a specific definition of remote patient monitoring, one that captured only the types of interventions currently of interest in the Norwegian primary health care system. This systematic review therefore provides the Directorate with evidence regarding the most relevant remote patient monitoring strategies, and findings can be used to inform recommendations and further pilot tests of remote patient monitoring in Norway.

The project group consisted of:

- Project coordinator: Ashley Elizabeth Muller (AEM), researcher, Norwegian Institute of Public Health
- Other members: Rigmor C Berg (RCB), Sari Susanna Ormstad (SSO), Patricia Sofia Jacobsen Jardim (PSJJ), Trine Bjerke Johansen (TBJ), Hong Lien Nguyen (HLN), Tonje Lehne Refsdal (TLR), and Alexandra Pirnat (AP)

All authors and peer reviewers filled out a form to document potential conflicts of interest, and none were declared.

The authors thank the three members of the reference group, Undine Knarvik (Norwegian Centre for E-Health Research), Gustavo Toshiaki (Oslo Metropolitan University) and Inger-Alice Naley Ås (Sørlandet Hospital), for their conversations and feedback. Their expertise regarding health technology uptake and the significance of population ageing to health services, as well as their clinical perspectives on the implementation of monitoring and mechanisms behind uptake, were instrumental in writing the discussion.

Kåre Birger Hagen	Rigmor C Berg	Ashley Elizabeth Muller
Research director	*Department director*	*Project leader*

Introduction

Longevity continues to increase worldwide and in Norway, with Norwegians gaining nearly two years in life expectancy between 2005 and 2015 alone (1). However, not all of these years are healthy. The average sixty-year-old Norwegian can expect to live another twenty-two years, but ten of those years will be burdened by morbidity from chronic diseases (1). The health care system faces the challenge not of curing chronic diseases as people age, but of managing them: preventing the impairment of functioning and helping people maintain as good a quality of life for as many years as possible (2, 3).

Regular assessments of chronic diseases are crucial to monitor treatment progress, prevent deterioration, and prevent the development of additional diseases, injuries, and complications (4). Frequent assessments increase accuracy and allow for individualization of treatment decisions. In the absence of real-time data, neither patients nor providers may be aware of the need for additional health services until after patients' deterioration.

At the same time, face-to-face meetings with health care providers can be burdensome for both the patient and the provider, and are often not prioritized for lower risk patients, or not possible for patients in geographically remote areas, with mobility restrictions, or with low resources. The benefits of receiving real-time patient data must be balanced with the burden of frequent assessments (5, 6).

The amount of preventable hospitalizations among chronically ill Norwegians increased by 5% from 2014 to 2017 (7). Given this trend along with the increasing prevalence of chronic conditions in the Norwegian population, it is not feasible to expect that specialist health care providers will be able to provide the type of frequent, preventative, and non-acute monitoring that many patients could benefit from. The Norwegian Directorate of Health has suggested that proper follow-up of these patients by their general practitioners could help prevent overuse of specialist health services (7).

One solution is for patients to be able to transmit health data without seeing providers, and for this data to be sent and evaluated often enough to initiate interventions or treatment adjustments before the patient's health status becomes acute. Strategies that allow patients to remain at home while they transmit data and receive follow-up services can be collectively referred to as remote patient monitoring (RPM).

The Norwegian government has prioritized piloting RPM as well as other types of chronic care and care coordination programs within the municipal health services (see (8-10)). Anchoring RPM within municipal health services will enable the co-location of patients and their care, namely, at home. Two parliamentary white papers, *Tomorrow's care services* (3) and *Primary health care in the future* (9), describe the logic behind RPM: If patients are able to remain living at home with well-managed disabilities, unnecessary and resource-intensive hospitalizations and specialist health care utilization will be prevented (3). Allowing patients to remain living at home is also expected to help allow them to be active participants in the social activities and networks they find meaningful (3, 9). Finally, as the WHO has highlighted (11), engaging patients in collecting and sending their own data – situating them and their knowledge at the center of health services – should increase patient empowerment, and the empowerment of chronically ill people is an explicit goal of *Tomorrow's care services* (3).

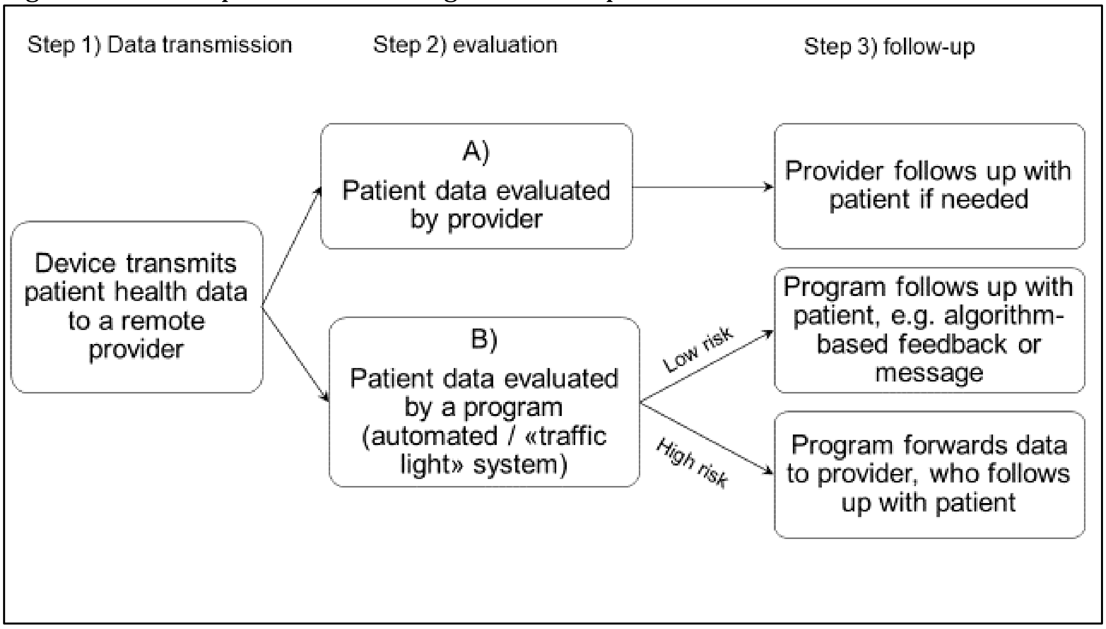
What is remote patient monitoring?

No generally accepted definition of the term RPM exists, and the terms telemedicine, telehealth, and eHealth are often used interchangeably. For example, three recent Cochrane Reviews (considered the highest methodological quality systematic reviews) use different terms for similar interventions: In Kew et al., *remote monitoring* refers to interventions that allow patients to share data using information and communication technologies and health care providers to respond, and is situated as "a form of 'telehealth', otherwise referred to as 'telecare', 'digital health', 'mHealth' [mobile Health] or 'telemedicine'" (12). McLean et al. write that "telemedicine" implies health care is being delivered, and instead uses *telehealthcare* to mean the electronic transfer of patient data and the receipt of provider feedback (13). In Flodgren et al., *interactive telemedicine* specifically means providers respond to patient data transmission in real time, while *remote monitoring* services also include provider feedback, but not in real time (14). Despite the difference in terms, these reviews focused on similar interventions that aimed at replacing costly and burdensome face-to-face care, allowing patients to remain at home, enabling early detection of condition exacerbation, and involving patients more in their own care.

Remote patient monitoring in a Norwegian context

As no generally accepted definition of RPM exists, for this commissioned review, the Norwegian Directorate of Health has developed a specific definition of RPM that is most relevant to the Norwegian context (15). This definition includes three steps, as displayed in Figure 1.

Figure 1. Remote patient monitoring in three steps



The first step is data transmission. The patient either answers questions about their own health condition using a digital device, and/or takes measurements of metabolic data related to their diagnosis using digital devices. This health data is then transmitted to a provider. In step two, data evaluation, the patient's data is received and evaluated by the provider (alternative A). In alternative B, the assessment is automated (i.e. evaluated by a program), and the program forwards data it evaluates as high-risk to health care providers for further follow-up. In the third and final step, follow-up, a provider follows up with the patient if the patient's health data indicates a concern.

Welfare technology such as RPM cannot preclude person-to-person care and closeness, the parliamentary white paper *Tomorrow's care services* (3) is careful to specify. Thus in this definition, fully automatic interventions that exclude the possibility of health personnel's involvement in either data evaluation or follow-up are not of interest.

Previous research

There exist numerous overviews of systematic reviews of interventions defined so broadly as to make their relevance to this review's definition of RPM, and therefore to Norway, unclear. For example, when defined as any method of patient data sent remotely, a recent overview of 19 systematic reviews of the effect on heart failure outcomes concluded that *remote monitoring devices* reduce mortality; however, mobile phone applications that did not involve providers – which fall outside of our definition of RPM – were included (16). Another overview of four systematic reviews of *telehealth for monitoring* patients with diabetes reported a modest effect on glycated hemoglobin levels, but fully automated programs were again included, again not meeting our definition (17). Patients with chronic obstructive pulmonary disease (COPD) were the population of interest in Murphy et al.'s overview of overviews (18), and identified four systematic reviews of *telemonitoring, telehealth, or telemedicine*. This broad category included health care and education provided remotely, and therefore the positive effects on hospitalization, and unclear effects on quality of life, cannot be safely interpreted as applicable to the RPM prioritized in Norway.

Why do we need this review?

As summarized above, RPM is of clear political and policy interest to Norway, yet whether the particular types of RPM implemented in previous studies are relevant to Norway is unclear. The Directorate of Health needs knowledge of the effectiveness and cost utility of RPM, and particularly which patient group may benefit most.

Research question

What is the effectiveness of remote patient monitoring on chronically ill patients' clinical outcomes and health care utilization?

Method

We conducted this overview of systematic reviews according to the methods described in the handbook "Slik oppsummerer vi forskning", prepared by the Norwegian Knowledge Centre for the Health Services (19). A protocol reviewed and approved by the project team and commissioner was published prior to beginning the review (https://www.fhi.no/globalassets/dokumenterfiler/prosjekter/121-med-avstandoppfolg-protokoll-v10-rb.pdf). Modifications that have been made during the process are presented at the end of this chapter.

Inclusion criteria

We searched for and included reviews according to the inclusion criteria in Table 1.

Table 1 Inclusion criteria

Population:	Persons who are 18 years or older; persons who have cardiovascular disease, diabetes, hypertension, chronic lung diseases, cancer, mental disorders, chronic musculoskeletal disorders, osteoporosis, or impaired vision/hearing; and persons who are neither in the very early nor very acute phase of these conditions.[1]
Intervention:	RPM according to the Health Directorate's definition, as defined above; RPM provided in the primary health care services; RPM involving phones, mobile phones, videos, and portable/implantable devices; data sent at least twice per year.
Comparison:	Standard care that does not involve RPM; other type of RPM.
Outcome:	Primary outcomes: mental health (symptoms or diagnoses); diagnosis-specific physical health; physical functioning level; quality of life; consumption of health services (hospital admissions, emergency care, number of bed-days, outpatient consultations, nursing home stays, home care [both home nursing and practical assistance], and general practitioner consultations); or health services costs.

[1] Target patients of this review are those falling in groups 3 and 4 according to the Scottish Centre for Telehealth & Telecare's report "A National Service Model for Home and Mobile Health Monitoring," published in Nov. 2016.

	Secondary outcomes: employment; education; social health (isolation, loneliness); patient experiences; or health literacy. Other secondary outcomes were considered if they were similar to the aforementioned secondary outcomes.
Language:	No language exclusions a priori, but publications in languages that neither the project staff nor colleagues at NIPH speak were not included.
Years	Search conducted in 2015 or more recently.
Study design	Systematic reviews and overviews of systematic reviews.

Systematic reviews and overviews of systematic reviews were eligible if the search was conducted latest 2015, while also assessed to be of high methodological quality. A systematic review shall contain:

- a clearly stated set of objectives with pre-defined eligibility criteria for studies;
- an explicit and reproducible methodology;
- a systematic search that attempts to identify all studies meeting the eligibility criteria;
- an assessment of the validity of the included studies, for example through the assessment of risk of bias;
- a systematic synthesis and presentation of the characteristics and findings of the included studies (19).

Exclusion criteria

We excluded reviews if participants were reported to have reduced cognitive function, as they may not be able to report their own health outcomes. Reviews utilizing internet-based RPM or RPM executed through mobile applications on phones or tablets were also excluded. Finally, reviews that explicitly excluded Norway or the part of the world in which Norway is located, e.g. studies of low- and middle-income countries, were also excluded.

Literature search

An information specialist (LN) developed and conducted systematic searches for literature in the following databases: MEDLINE, Embase, PsycINFO, Epistemonikos, Cochrane Library: Cochrane Database of Systematic Reviews, and Web of Science.

Before the searches were conducted, the search strategies were peer reviewed by a second information specialist (TLR) using the PRESS checklist (20). We employed both subject headings (e.g. MeSH terms in MEDLINE) and free text terms characterizing the intervention and population. The complete search strategies, information about database versions and providers, search dates, and number of hits in each database, can be found in the search strategy in Appendix 1. Search strategy.

Study selection

Two researchers (AEM/RCB/AP) independently assessed all titles and abstracts from the systematic literature search for eligibility using Rayyan (21). Full-text publications were retrieved when one or both researcher(s) judged the review to likely meet the inclusion criteria. Full-text publications were then read by two researchers independently (AEM, RCB/AP/SSO/TBJ/PSJJ) using Covidence (22), with final inclusion based on consensus by the two researchers. As anticipated in the protocol, few of the overviews or systematic reviews read in full-text described interventions thoroughly enough for us to determine eligibility. Therefore, when reading a systematic review, we retrieved each included primary study and assessed its eligibility after reading in full-text. This was a time consuming, but necessary step as our review's RPM definition was distinct. If a systematic review included at least one RCT that met our inclusion criteria, the entire systematic review was included in our review (see below for further details). When reading an overview of systematic reviews, we did not proceed to primary studies, but read the full-text of each included systematic review. If any single systematic review met our criteria, we included the entire review. Appendix Table 2.1 contains a list of reviews excluded after full-text review.

Assessment of included systematic reviews and their overlap

After a review was read in full-text and determined to meet our definition of RPM and the other inclusion criteria, we assessed its methodological quality using the NIPH's checklist for systematic reviews (Appendix Table 3.2). Two authors (AEM, SSO/TBJ/PSJJ) independently assessed methodological quality and met to discuss conflicts. Any disagreements were resolved through discussion. Only systematic reviews rated as having high methodological quality were included in our review; in practice, this required that a review met all items on the checklist.

One author (AEM) then mapped all RCTs captured in each systematic review to determine overlap. We extracted data only from the RCTs that met inclusion criteria.

Assessing risk of bias in included RCTs

We extracted and presented systematic review authors' own risk of bias assessments of included RCTs. All the reviews with relevant RCTs used the Cochrane Risk of Bias Tool. Bias was assessed as low, unclear or high in the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. In one of these systematic reviews (23), the authors modified this tool slightly by not reporting blinding of participants and personnel and other biases and instead reporting funding as a separate (risk of bias) criterion. We chose to report systematic review authors' judgement on funding as part of the assessment of other biases, as presented in

Figure 3. We used Review Manager 5.3 (24) to create a risk of bias assessment table and graph for the included RCTs.

Data extraction

Two levels of data extraction occurred. From the systematic reviews, we extracted the number of included RCTs that met our inclusion criteria as well as risk of bias of each eligible RCT. We extracted most data from the RCTs themselves, as most systematic reviews did not sufficiently report findings or characteristics. This data included country, setting, information about participants (inclusion and exclusion criteria, number of participants in each group, baseline characteristics), intervention characteristics, comparator(s), and outcomes assessed. One author (AEM) extracted data and another author (SSO) double-checked data extraction for accuracy and completeness. Covidence software was used for data extraction (22).

Analyses

As neither entire overviews of systematic reviews nor systematic reviews met our inclusion criteria, it was necessary to summarize the data from the relevant RCTs the reviews contained. Interventions lasted six months (four RCTs), nine months (three RCTs), or twelve months (four RCTs). When an RCT measured an outcome at multiple time points, the last measurement was used. In one RCT (25), data was collected three months after the completion of the intervention; the remainder of the RCTs collected outcome data at intervention completion. Data for one outcome, HbA1c, was only available as adjusted for baseline values in both Dario et al. (26) and Egede et al. (27), and was presented alongside the remaining RCTs' unadjusted outcomes.

We presented normally distributed results for each outcome in a forest plot and reported raw mean differences, standardized mean differences, odds ratios, or rate ratios; non-normally distributed outcomes were reported as medians. As this review is an overview of systematic reviews, we summarized data from RCTs that were identified within the systematic reviews we searched for – we did not search for RCTs directly. A meta-analysis is therefore inappropriate, as it implies the synthesis of all relevant RCTs, which our methodology does not guarantee. Accordingly, we did not produce the summary statistic within forest plots or report these summary statistics in the summary of findings table. Studies were presented in forest plots in order of effect size, to aid interpretation. Forest plots were created using Review Manager 5.3 (24).

One RCT (28) contained more than two arms: usual care, high-intensity RPM, and low-intensity RPM. The high-intensity RPM differed only from the low-intensity arm in that the former included automated messages that were more tailored to each patient, compared to the latter. We analyzed only data from the high-intensity arm, as dividing this RPM into two comparisons would have duplicated the usual care group's data.

Missing data

Several RCTs failed to report standard deviations. For the purposes of visualizing outcomes in forest plots, we used standard deviations from RCTs with the most similar patient population. Wakefield et al.'s (28) missing systolic blood pressure standard deviations were borrowed from Magid et al. (29), due to both patient populations coming from the United States and having co-occurring hypertensive and diabetic patients. Schillinger et al.'s (25) standard deviations were used for Carter et al.'s (30) blood pressure and BMI outcomes, due to both patient groups being American, obese, urban, and with ethnic minorities overrepresented.

Assessment of certainty of the evidence

We assessed the certainty of the evidence for each of the seven primary outcomes using GRADE (Grading of Recommendations Assessment, Development, and Evaluation). GRADE is a method for assessing the certainty of the evidence in systematic reviews, and can be used even when meta-analytic pooled effect estimates are not available (31). An assessment for each primary outcome is conducted using five criteria: i) systematic review authors' assessment of RCT methodological quality (risk of bias), ii) degree of inconsistency, iii) indirectness, iv) imprecision, and v) publication bias. We specified in the protocol that we would use systematic review authors' own GRADE assessments, but as we included only individual RCTs from each systematic review, this was not possible.

GRADE has four levels of certainty, as displayed in Table 2.

Table 2 Explanation of GRADE certainty levels

Certainty	Symbol	Interpretation
High certainty	⊕⊕⊕⊕	Further research is very unlikely to change our confidence in the estimate of effect
Moderate certainty	⊕⊕⊕◯	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low certainty	⊕⊕◯◯	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low certainty	⊕◯◯◯	We are very uncertain about the estimate

The GRADE assessments were conducted using the software GRADEpro (32).

Ethics

We did not assess ethical considerations in this systematic review.

Modifications to the protocol

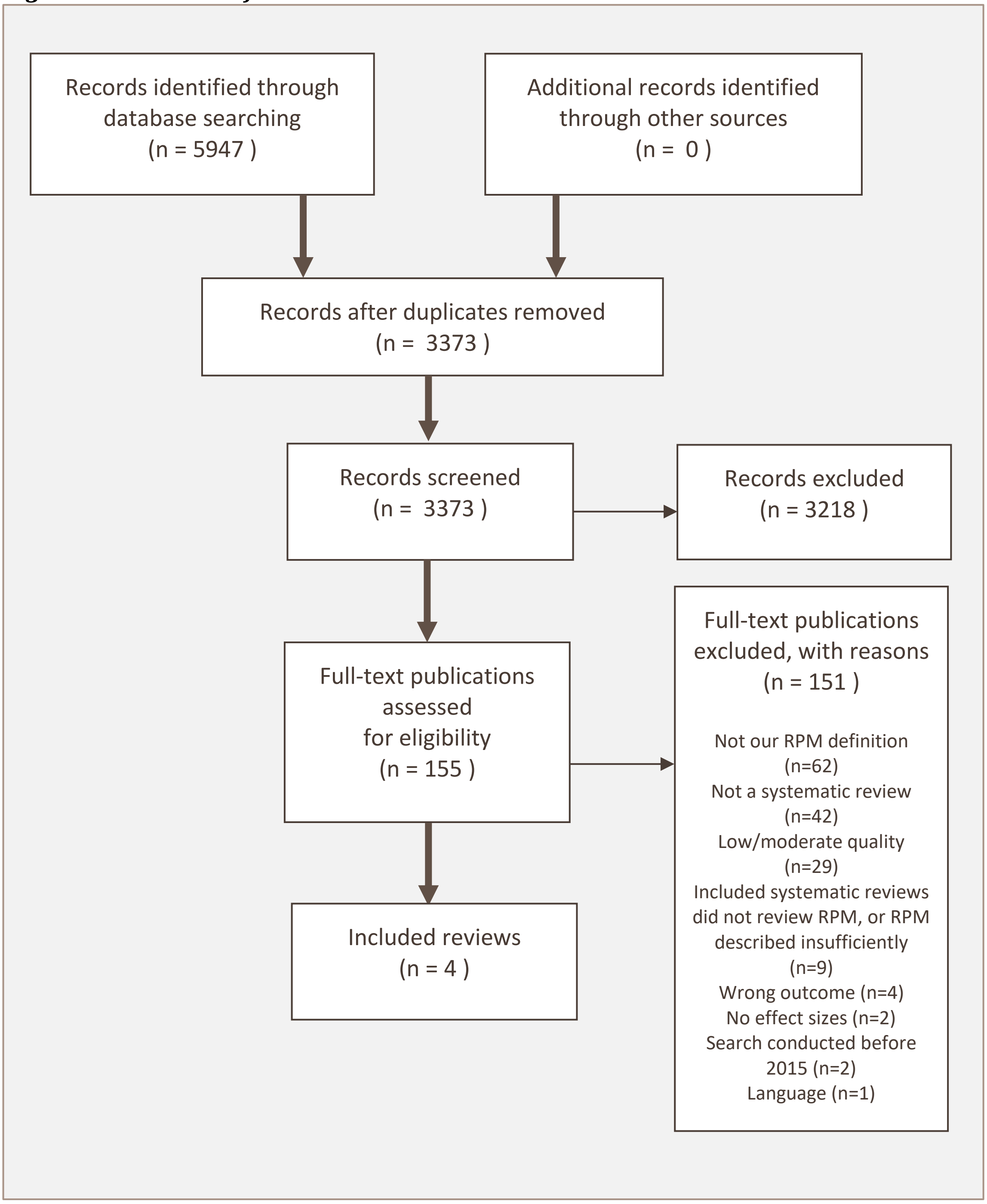
During our full-text review of RCTs, we decided to include patients with hypertension, although they were not one of the eight original chronic condition groups specified in the project plan. This was decided in cooperation with the commissioner due to the overlap between diabetes and hypertension among many of the included RCTs' patients, and because hypertension is a common comorbidity with many of the other chronic conditions of interest. Thus, we did not exclude any systematic reviews based on including hypertensive patients. The only practical consequence of this protocol modification was to allow the inclusion of one RCT (29), which recruited hypertensive patients, of whom nearly half also had either diabetes or renal disease.

Results

Results of the literature search

The literature search resulted in 5947 records, as exhibited in Figure 2. After de-duplication, we screened 3373 records at the title and abstract level, and we read 155 publications in full-text. We excluded 151 publications after full-text review, most commonly for not reporting on RPM as defined by the Directorate of Health, not meeting the criteria for systematic reviews, or not being of high methodological quality. We included four systematic reviews in this report: Bittner et al. (33), Faruque et al. (23), Kebede et al. (34) and Posadzki et al. (35). Appendix Table 2.1 lists all publications excluded after full-text review, with reasons for exclusion and chronic disease category.

Figure 2 Flow chart of search results



Description of the included systematic reviews (N=4)

The four included systematic reviews searched for randomized controlled studies (RCTs), cluster RCTs, quasi-RCTs, controlled before-and-after studies, and interrupted time series studies of different types of remote communication or health care delivery. Every review defined their intervention of interest differently and with a slightly different name, as displayed in Table 3. Bittner et al. (33) searched for *telerehabilitation* services, explicitly including remote monitoring within this definition, for patients with impaired vision. Faruque et al. (23) searched broadly for *telemedicine* interventions, defined as all electronic forms of communication, among diabetes patients. Kebede et al. (34) focused on diabetes type 2 patients using *digital interventions*, meaning any technology-based intervention. Posadzki et al. (35) searched for *eHealth* (electronic health) interventions among patients with long-term conditions. Faruque et al. (23) excluded studies that involved patients with gestational diabetes, and Kebede et al. (34) excluded studies with diabetes type 1 patients. Aside from this, there were no other disease-related exclusion criteria specified by the systematic reviews.

Table 3 Description of included systematic reviews

Systematic review	Search date	RCTs*	Description of RPM, in the authors' words / interventions of interest	Chronic disease
Bittner et al. (33)	June 2015	0 included in this review; 0 analyzed by the authors.	Telerehabilitation: rehabilitation services delivered via information and communication technologies, and including monitoring and clinical evaluation services.	Low vision
Faruque et al. (23)	Nov. 2015	7 included in this review, out of 111 analyzed by the authors: Carter et al. (30), Nicolucci et al. (36), Rodriguez-Idigoraz et al. (37), Schilinger et al. (25), Steventon et al. (38), Stone et al. (39), Wakefield et al (28).	Telemedicine: all electronic forms of communication between provider and patient (telephone, smartphone application, email, text messaging, web portal, "smart" device or glucometer).	Diabetes type 1 or 2
Kebede et al. (34)	June 2017	3 included in this review, out of 21 analyzed by the authors: Dario et al. (26), Egede et al. (27), Wild et al (40).	Digital interventions: technology based, such as m-health interventions, web-based interventions, interventions delivered through the use of a personal digital assistant, a tablet, a computer, the Internet, telemedicine, videoconferencing, telehealth, or other forms of e-health.	Diabetes type 2
Posadzki et al. (35)	June 2015	1 included in this review, out of 132 analyzed by the authors: Magid et al. (29)	eHealth interventions: interventions that use devices featuring interactive wireless communication capability, operating web-based applications and with high portability (such as smartphone, computer and personal digital assistance tools), or interventions comprising self-care, self-management, self-care behavioral change or education dissemination.	Any long-term condition
* We included and extracted data only from the RCTs that met our inclusion criteria.				

Descriptions of the included RCTs from the reviews (n=11)

With the exception of Bittner, a review that found no relevant studies, these reviews' interventions of interest were defined far more broadly than relevant for this overview, and therefore the RCTs they analyzed also reported on a far wider array of interventions. Altogether, only eleven RCTs implemented an intervention that met our definition of RPM (see *Remote patient monitoring in a Norwegian context*). None of these RCTs occurred in more than one of the included reviews (Appendix Table 3.3). Seven RCTs involved diabetes type 2 patients (25-27, 30, 37, 38, 40), one RCT included both type 1 and 2 diabetes patients (39), two RCTs included patients with both hypertension and diabetes (28, 36), and one RCT included only hypertensive patients (29).

Multi-morbidities

Six RCTs reported on participants' co-/multi-morbidities in their descriptions, revealing an inadvertent overlap of morbidities between some of the participants in the RCTs. For example, while two RCTs explicitly targeted patients with co-occurring diabetes and hypertension (28, 36), a majority of one of the diabetes RCTs' patients also had hypertension (37), and nearly half of the hypertension RCT's patients also had either diabetes or renal disease (29).

Other included RCTs reported similar prevalence of other multi-morbidities. About four of ten patients in Rodriguez-Idigoras et al. (37) and Nicolucci et al. (36) reported dyslipidemia. Chronic obstructive pulmonary disease was reported by 6.3-14.2% in Dario et al. (26), Steventon et al. (38), and Stone et al. (39), and heart failure by 3.6-16.1% in Steventon et al. (38), Stone et al. (39), and Nicolucci et al. (36). Stroke was reported by 2.4-4.7% of the patients in Dario et al. (26) and Nicolucci et al. (36).

Given these similarities in multi-morbidities, all eleven RCTs could be grouped together as involving "diabetes and/or hypertension" patients. Appendix Table 3.4 provides further details of the patients included in each RCT, including multi-morbidities.

It is worth noting that psychiatric multi-morbidities were not reported by any of the RCTs. They were exclusion factors of five RCTs in some manner, such as "reliance on psychotropic medication" (30), "mental conditions, depression, or high anxiety;… abuse of drugs or alcohol" (36), "alcohol or drug abuse/dependency, active psychosis or acute mental disorder," (27), "psychotic illness," (25), and "psychosis" (28).

Descriptions of the various types of RPM used in the included RCTs

According to our definition, RPM referred to the three steps of digital data transmission, evaluation, and follow-up. There were a variety of devices used to transmit data, three methods of data evaluation, and some variation in the method of follow-up response given to patients, as summarized in Table 4. Each step is described below.

Step 1: Data transmission

In all RCTs, patients collected and transmitted up to three biometric measurements: blood glucose (23, 25-28, 30, 33-40), blood pressure (25, 27-30, 36, 38-40), and weight (30, 36, 39, 40). Seven RCTs utilized telehealth devices that transmitted patient data measured from standard instruments such as glucometers; three RCTs utilized telephones, either patients' existing phones or those provided to them (25, 29, 37); and one RCT provided a laptop with peripheral equipment (30). Frequency of patient data transmission varied from three times a day to twice a month, with two RCTs individualizing frequency according to clinical histories, and two not specifying frequencies.

Step 2: Data evaluation

Patient data was then evaluated either manually (five RCTs), automatically by a monitoring center (four RCTs), or automatically by the RPM device itself (two RCTs). A traffic light system – in which data values in particular ranges were pre-programmed to be expressed in colors, and particular colors would trigger particularly responses – was specifically mentioned by one RCT using a monitoring center and one in which the device evaluated the data.

Step 3: Follow-up response

This step refers to how providers followed up with patients in response to the evaluation of their data. Follow up was individualized medical care such as medication adjustment, discussion of adherence, counselling on behavioral changes such as diet, smoking, weight management, and physical activity, and support for other conditions. Care was often described as focusing on helping patients self-manage their conditions. It was difficult to determine whether the follow-up described in each RCT differed from the care normally provided to patients – that is, whether RPM was providing patients with enhanced care – or whether RPM was simply facilitating more frequent usual care.

In about half of the RCTs, patients were only followed up with by providers if their data had been evaluated (manually or automatically) as concerning (26, 29, 37, 38, 40). In one RCT, patients received scheduled follow-up regardless of data values (30). In other RCTs, patients received both scheduled follow-up and follow-up indicated by concerning data (36, 39). Finally, in some RCTs patients received automated responses if data was not of concern, and personal follow-up if data was concerning (25, 28).

In two of the four RCTs using monitoring centers, concerning data was transmitted by the centers to the patients' health care providers; in the third RCT, the monitoring center contacted the patient directly; and in the fourth RCT, the center contacted both providers and patients. In both of the RCTs in which data was evaluated by the RPM device itself, the patient received an automated response even if the data was not of concern, and the device alerted providers if data was concerning.

Table 4. Description of RPM implemented in the included RCTs

Author	Chronic disease	Data transmission	Data evaluation	Follow-up response
Carter et al. (30)	Diabetes type 2	Weight and blood pressure sent 1/week and blood glucose sent 3/day; using a laptop that was equipped with a wireless scale, a blood pressure cuff, and a glucometer	Manual review by telehealth nurse.	Nurse discussed data and behavior change strategies with patient over video conference during biweekly, 30-minute calls. Additional support/contact: health education videos and online resources, and a social networking module that allowed patients to contact each other.
Dario et al. (26)	Diabetes type 2	Blood glucose measured (frequency not reported) with a glucometer connected to a telecare device that sent data to an eHealth center	Alerts automatically generated by eHealth center if data values crossed pre-specified thresholds.	If automatic alert was generated, eHealth staff contacted clinician. Clinician took subsequent action according to normal protocols and contacted patients by telephone or other unspecified methods. If an emergency, eHealth center contacted next of kin and emergency department. Clinicians had access to a portal with patient data.
Egede et al. (27)	Diabetes type 2	Blood glucose and blood pressure sent 1/day, using a commercial telehealth device that uploaded blood glucose and blood pressure to a central server	Manual review by nurse case manager	If necessary, nurse contacted patients by telephone to make weekly or biweekly medication adjustments. Additional contact: Nurse case managers made weekly reminder calls to upload data.
Magid et al. (29)	Hypertension	Blood pressure sent 1/week over the patient's usual telephone, using an interactive voice response phone system	Manual review by pharmacist	If data values exceeded guideline-recommended treatment goals, pharmacists contacted patients to review medication adherence, adjust medications, and provide counselling on healthy therapeutic lifestyle changes, using the interactive voice response system or telephone. Pharmacists contacted GP in the case of medication adjustments.
Nicolucci et al. (36)	Diabetes type 2 and hypertensive	Blood glucose, blood pressure, and weight sent 2/month, using a weight scale, glucometer, and a	Alerts automatically generated by telehealth center if data values concerning	Telehealth center nurses forwarded alerts to GPs, who contacted patients. Alerts could also be sent to patients. GPs and patients had access to all patient data collected by the telehealth center.

	(>130/80 mmHg)	sphygmomanometer, respectively, connected via Bluetooth to a device that transmitted data in real-time to a telehealth center.		Additional support/contact: Telehealth nurses contacted patients monthly to discuss results and barriers to compliance, using text messages, e-mail, or telephone.
Rodriguez-Idigoras et al. (37)	Diabetes type 2	Blood glucose measured using a glucometer and sent via patient's usual telephone to a call center; no required frequency reported, but actual frequency was an average of 7/months	Alarms automatically generated by call center if data values outside normal range.	Call center staff contacted GP and patient by telephone. Unspecified "standard protocols" were followed.
Schillinger et al. (25)	Diabetes type 2	Blood glucose and blood pressure sent 1/week, using telephone touchpads during an automated telephone call	Evaluated by an automated telephone support system	The telephone system either immediately responded with a narrated health education message, or the system alerted a nurse, and the nurse contacted the patient.
Steventon et al. (38)	Diabetes type 2	Blood glucose and blood pressure sent up to 5/week, with the frequency adjusted according to participants' individual clinical histories, using a freestanding telehealth unit or a television set top box that connected to a blood pressure monitor and glucometer or to weighing scales / pulse oximeters	Traffic light system: automatic evaluation at monitoring center	If "red", monitoring center staff reviewed data 1/day and contacted the patient for further evaluation, to offer disease management advice, or to give referrals. Contact was made using the telehealth unit or other unspecified methods.
Stone et al. (39)	Diabetes type 1 or 2	Blood glucose, blood pressure, and weight sent 1/day, using a commercial home telemonitoring device that transmitted measurements to a central server	Traffic light system: automatic evaluation by the device	If "red", nurse contacted patients and adjusted medication, over the telephone or using the home monitoring system. Additional support: monthly calls to provide individualized self-management counseling tailored to specific issues, based on data values.
Wakefield et al. (28)	Diabetes type 2 and hypertension	Blood glucose and blood pressure sent 1/day, using a commercial home telehealth device that sent and received data through the patient's landline	Manual review by nurse, 1/day	Tailored, automated responses sent based on data. Nurses reviewed data daily and contacted the patients if necessary. Additional support: daily prompts to enter data and educational content, sent through the telehealth device. Educational content was interactive, and patients received automated response that confirmed or corrected their answers.

Wild et al. (40)	Diabetes type 2	Blood glucose sent at least 2/week, and blood pressure, and weight sent at least 1/week; using Bluetooth-enabled blood pressure, blood glucose, and weight monitors that transmitted data via a supplied modem	Manual review by primary care nurse or family practice clinician, recommended 1/week.	Provider changed treatment if necessary to comport with national guidelines for diabetes and hypertension management if necessary, and provided advice on lifestyle modification, information about medication effects; the method of communicating back to the patient was not specified.

Usual care as a comparator

In all RCTs, participants were recruited from existing general practitioner lists, healthcare networks, or other patient pools, indicating that they had already some minimum amount of contact or usual care with the primary health services.

However, the usual care described in nine RCTs appeared to be quite minimal, such as an educational pamphlet, encouragement to contact providers, or yearly review of health status (27-30, 36, 37, 40). This was also the case for the two RCTs that specified that they compared RPM adjunct to usual care, with usual care alone (25, 38).

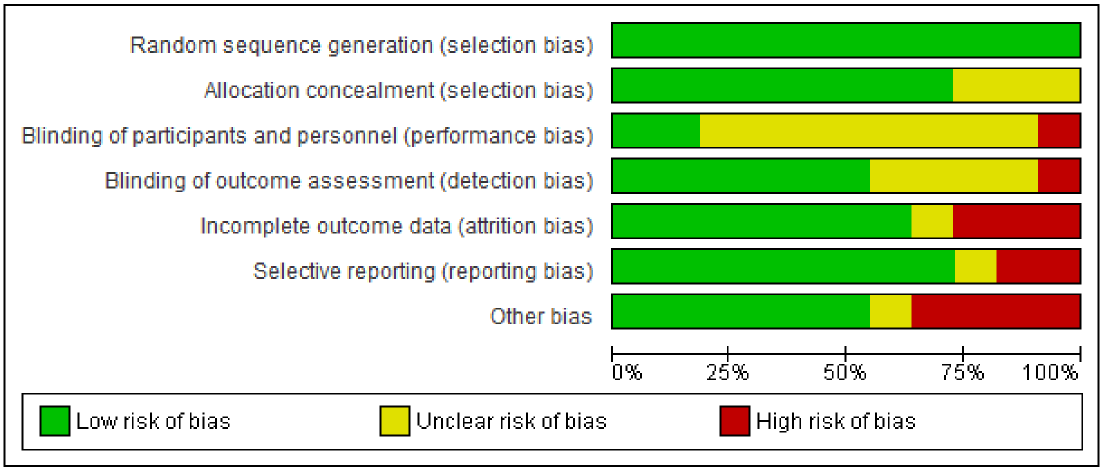
In the remaining two RCTs, usual care contained the same self-monitoring that the RPM group conducted, but without the benefit of digital transmission of this data or guaranteed provider knowledge of health status (26, 39). In Dario et al., patients in usual care were supposed to measure HbA1c and bring paper logs to providers (26). In Stone et al., usual care patients were supposed to measure HbA1c, blood pressure, and weight daily, and discuss these with diabetes nurse educators over the phone once per month (39). Neither of these RCTs reported the actual frequency of self-monitoring, making it difficult to conclude the extent to which usual care in these RCTs differs from usual care in the remaining RCTs.

Self-monitoring may have been practiced by patients in usual care in Rodriguez-Idigoras et al. and Schillinger et al. (25, 37). Six months' self-monitoring was an inclusion criterion for Rodriguez-Idigoras et al., in order to recruit among patients already capable of complying with a monitoring regime, although there was no mention of the usual care group being expected to continue. Schillinger et al. specified that if usual care patients were already self-monitoring when enrolled in the RCT, they were encouraged to continue doing so; no estimates were provided of how common this was. In both cases, as in Dario et al. and Stone et al., any self-monitoring conducted by usual care patients would not have been digitally transmitted or evaluated by providers.

Risk of bias in the RCTs

The review authors' own judgment of each risk of bias domain is presented as percentages across all 11 included RCTs in Figure 3. The majority of the RCTs were assessed as having low risk of selection bias. All studies reported adequate procedures for randomization, and most studies (75%) reported adequate procedures for allocation concealment. The majority of the RCTs were assessed as having unclear risk of performance bias. In many instances, this was due to non-reporting of blinding of participants and personnel. The majority of studies also had a low risk of reporting bias (75%), attrition bias (60%), detection bias (55%), and other biases (55%).

Figure 3 Risk of bias graph



In Figure 4 we present the review authors' judgements about each risk of bias domain for each included RCT separately. Wild et al. (40) and Stone et al. (39)were rated with the lowest risks of bias across all domains; Wild et al. with low risk in all domains, and Stone et al. with unclear risk regarding blinding of participants and personnel. Most RCTs had low risk of bias in the majority of domains. Only one – Dario et al. (26) – had three domains with high risk of bias; the remaining RCTs had no more than one domain each at high risk.

Figure 4 Risk of bias summary

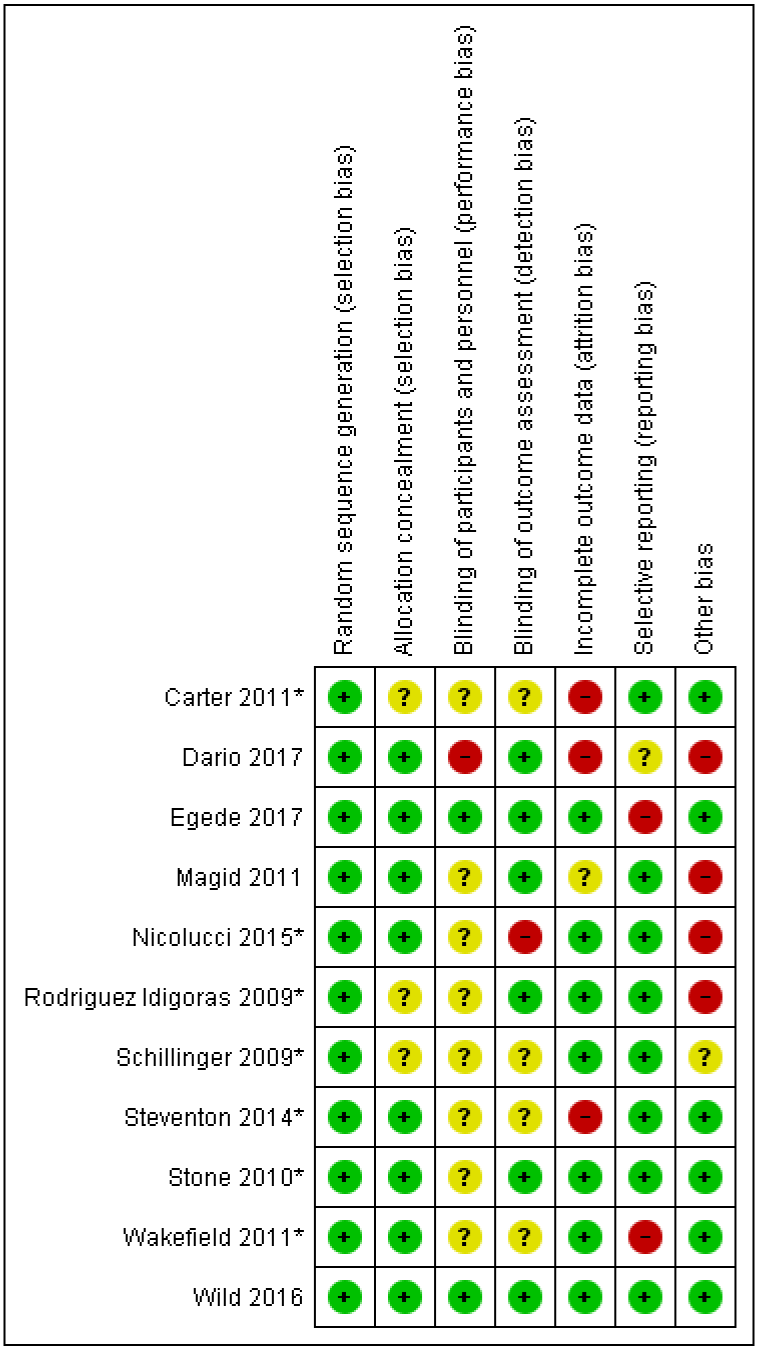


*Figure caption: Review authors' own judgements about each risk of bias item for each included study. *Assessment of other biases is based on funding only.*

Effects of RPM on patients with diabetes and/or hypertension

In this section, each of the subsections include a narrative summary of the findings for an outcome, as well as a presentation of the results by means of forest plots. In addition, we give results of the GRADE assessment (our evaluation of the certainty of the evidence) for each outcome. Due to the large number of included outcomes, eight outcomes considered the primary outcomes were assessed with GRADE. These outcomes were selected in consultation with the commissioner. Table 5 provides an overview of the conducted GRADE assessments, and further details can be found in Appendix Table 4.5.

Table 5 Summary of findings table: RPM compared to usual care for chronic disease

Outcomes	Effect	№ of participants (studies)	Certainty of the evidence (GRADE)
HbA1c [%]	Most studies showed a reduction, from 0.23% lower to 1.08% lower. However, only four exceeded the suggested minimum clinically importance difference of ≥0.5% [2]. RPM probably slightly reduces Hba1C.	2235 (10 RCTs)	⊕⊕⊕◯ MODERATE [a]
Systolic blood pressure [mmHg]	No studies showed a statistically significant effect, but tended to benefit RPM. RPM probably leads to a slight reduction.	1407 (7 RCTs)	⊕⊕⊕◯ MODERATE [a]
Diastolic blood pressure [mmHg]	No studies showed an effect. RPM may make no difference.	1207 (6 RCTs)	⊕⊕◯◯ LOW [b,c]
Total cholesterol	No studies showed an effect. RPM may make no difference	664 (3 RCTs)	⊕⊕◯◯ LOW [c,d,]
Patients with hospitalizations or ER visits, all-cause	No effect. RPM may make no difference.	249 (1 RCT)	⊕⊕◯◯ LOW [e,f]
Quality of life (SF-12/SF-36), mental health component	Two studies showed no effect, and one showed a small benefit to usual care patients. RPM may make no difference.	698 (3 RCTs)	⊕⊕◯◯ LOW [d,g]
Quality of life (SF-12/SF-36), physical health component	Usual care reported higher scores, with a small effect size. RPM probably harms this outcome.	698 (3 RCTs)	⊕⊕⊕◯ MODERATE [g]
Hospital Anxiety and Depression Scale total score	No effect. RPM may make no difference.	257 (1 RCT)	⊕⊕◯◯ LOW [f,h]

[2] As suggested by the National Institute for Health and Care Excellence (2013) and the Dutch College of General Practictioners (see Lenters-Westra et al., 2014). See also Little and Rohlfing (2013) and Wilding et al. (2018).

Outcomes	Effect	№ of participants (studies)	Certainty of the evidence (GRADE)

a. In four RCTs, patients differed significantly from the Norwegian patient population (e.g. American war veterans, urban poor, only men)
b. In two RCTs, patients differed significantly from the Norwegian patient population (e.g. American war veterans, urban poor, only men)
c. Effect estimates favor both RPM and usual care.
d. Wide confidence intervals, with studies showing both a moderately negative effect and a moderately positive effect
e. Likely bias related to study funding
f. One study
g. Performance bias, detection bias, attrition bias, and other bias.
h. Wide confidence interval and small number of participants.

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

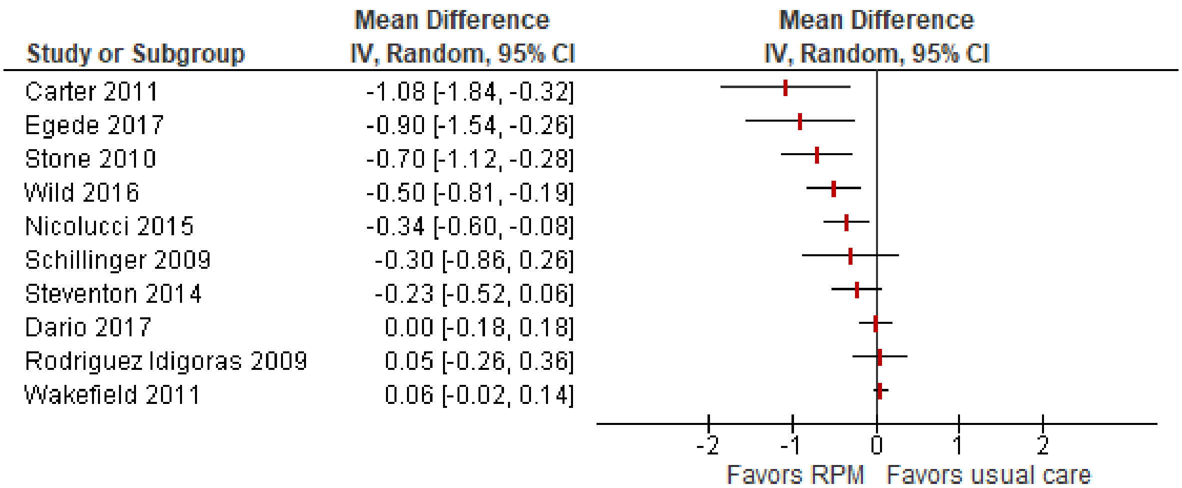
Forest plots in this section omit group sizes and raw data values, such as mean values for RPM and usual care groups, for ease of reading. These numbers are instead displayed in extended forest plots in Appendix 5, Figures 1-25. In every forest plot, the colored notch indicates the value of the statistic measuring the difference between the RPM and usual care group per RCT, and the horizontal line around that notch represents the 95% confidence interval. If a confidence interval crosses the vertical line between *Favors RPM* and *Favors usual care*, we cannot be sure that the outcome was reported or achieved significantly different by the RPM and the usual care groups. As all RCTs randomized their participants, we assume that a difference between the groups by the end of the intervention is due to RPM itself; if there is no difference, we conclude that RPM did not have an effect on this outcome.

Outcome 1: HbA1c

HbA1c (glycated haemoglobin) is a diagnostic test that reflects average plasma glucoses over the past eight to twelve weeks. No precise cut-off has been established, but values ≥7.0% are typically considered indicative of diabetes (41). RCTs in this review included patients with HbA1c ≥7.0%, ≥7.5%, or ≥8.0%.

Among the ten RCTs that reported HbA1c, there appeared to be a small pooled reduction among the RPM group by the end of interventions (Figure 5). With three exceptions that reported either no difference or a slight benefit to usual care patients (26, 28, 37), the RPM patients in the RCTs reported an average of 0.23-1.08% lower HbA1c scores than the usual care groups. However, only in four studies was this reduction above the suggested threshold for clinical meaningfulness, ≥0.5% (see (42-44)). Moreover, due to the high amount of heterogeneity among the studies and uncertainty about the applicability of the findings (four RCTs were conducted in with patients significantly different from Norwegian patients, namely American patients who were veterans, African-Americans, or utilizing "safety net" health clinics reserved for the lowest-income people), we have low confidence in this finding. The true effect of RPM on HbA1c relative to usual care may be substantially different from this estimate.

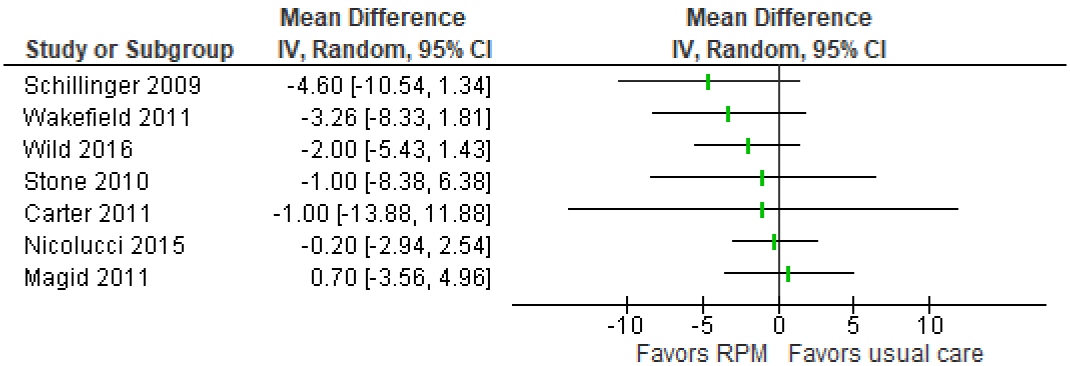
Figure 5 Forest plot of HbA1c



Outcomes 2 and 3: Blood pressure

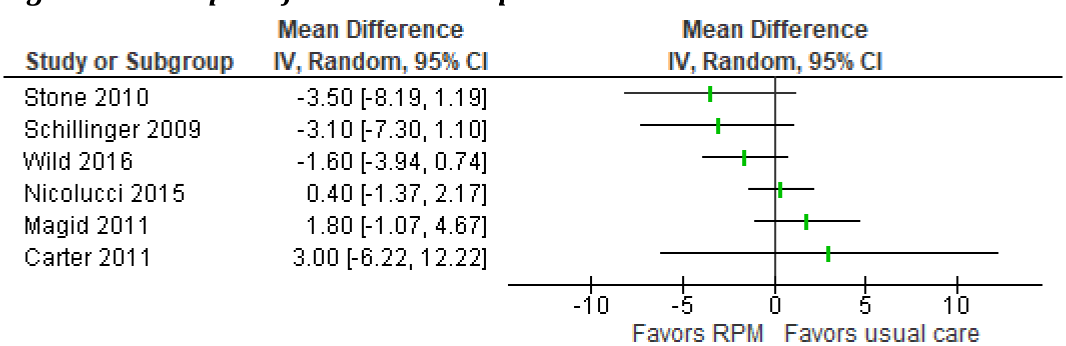
Systolic blood pressure was measured by seven studies, with no differences between the RPM and usual care patients overall (Figure 6). Studies reported mean values both above and below NICE's recommended target of 135/85 (45), and these values are shown in Appendix Figure 2. Due to the consistency of each RCTs' estimates, it is likely that the true effect of RPM on systolic blood pressure is close to the estimates we see here, namely, a small reduction. The sole reason for uncertainty in this finding is that the four RCTs from the U.S. reduce the direct applicability of the setting and patient population to Norway.

Figure 6 Forest plot of systolic blood pressure



Diastolic blood pressure was measured by six studies, again with no mean differences between the RPM and usual care patients (Figure 7). In all studies, mean diastolic values were below NICE's recommended target of 135/85 (45); see Appendix Figure 3 for values. We are not confident that the true effect of RPM on diastolic blood pressure is close to the effect estimates we see here, both because of moderate heterogeneity and effect estimates spread widely and in directions that favor both RPM and usual care.

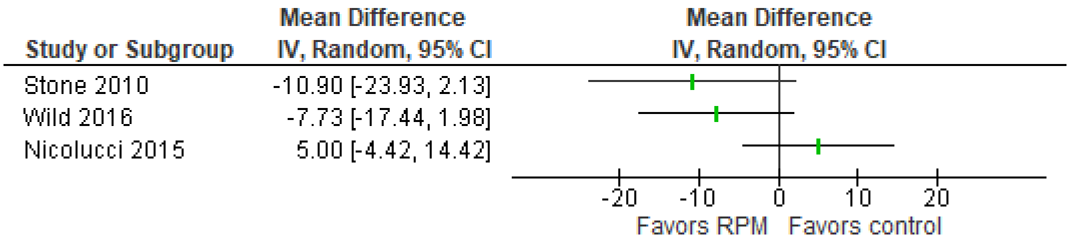
Figure 7 Forest plot of diastolic blood pressure



Outcome 4: Cholesterol

Total cholesterol was measured by three studies. None of the studies reported a mean difference between the RPM and usual care patients (Figure 8). We have low confidence in this finding, given large heterogeneity and individual effect estimates that show not only opposite findings, but findings with almost no overlap with one another. RPM's true effect on cholesterol is unlikely to be close to the estimates we see here.

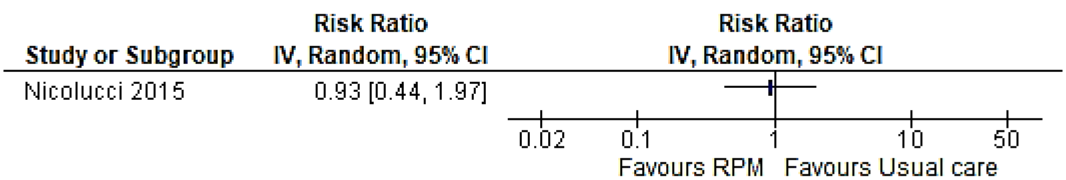
Figure 8 Forest plot of cholesterol



Outcome 5: Patients with hospitalizations or emergency stays

One study reported the amount of patients who had a hospitalization or an emergency room visit during the course of the intervention, with no difference between the two groups. As this finding drew from only one RCT, which was also judged to have a high risk of bias due to commercial funding, we are not confident that the true effect of RPM on this outcome is close to the estimate presented here.

Figure 9 Forest plot of patients with hospitalizations or emergency stays



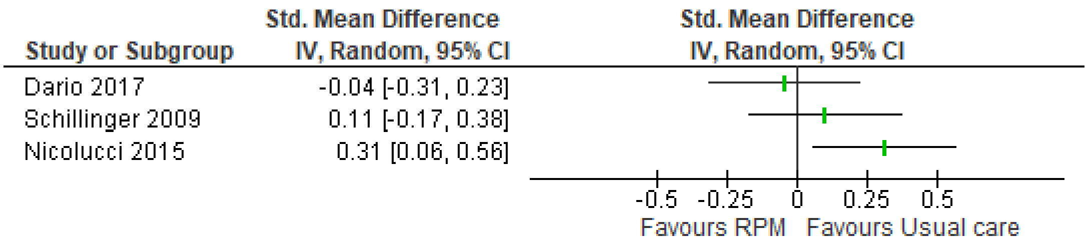
Outcomes 6 and 7: Health-related quality of life

Health-related quality of life (HRQOL) was one of the few patient-reported outcomes. HRQOL instruments measure the impacts of health status on one's subjective evaluation of their quality of life (46). Generic HRQOL instruments produce scores that can be compared across disease groups and to healthy populations. Overall quality of life and HRQOL have become established outcome measures of chronic disease treatment, as enhancing and maintaining patients' daily functioning with a disease – which can only be assessed by patients themselves – have become central indicators of clinical success.

The Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) and its abbreviated 12-item version (SF-12) are some of the most commonly used generic HRQOL instruments (47, 48). Both instruments produce two overall domains scores, referred to as mental and physical component summaries, on the same scale (0-100). Neither of these scores have established minimum important differences for people with diabetes and/or hypertension, therefore effect sizes are presented as standardized mean differences, rather than mean differences.

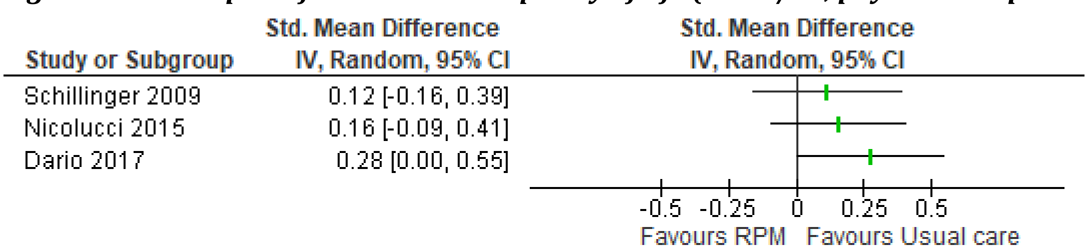
The standardized mean difference of HRQOL in the mental component summary of the SF-12 or SF-36 was no different for the RPM or usual care patients in three studies (Figure 10). We have low certainty in this finding, primarily due to wide- and varying confidence intervals between the three RCTs, and risks of bias identified by the systematic review authors. RPM may in fact have an effect on this component, potentially negatively.

Figure 10 Forest plot of health-related quality of life (SF-12/36, mental component summary)



In the physical component summary of the same instrument, the usual care group reported slightly higher mean HRQOL than the RPM group (a small effect size), as displayed in Figure 11. In this component, the three studies' effect studies agreed more with one another, but our certainty was still downgraded due to potential biases. We are moderately certain that this small effect size is similar to the true effect of RPM on the physical health component of HRQOL; that is, that RPM has a small negative impact on physical HRQOL.

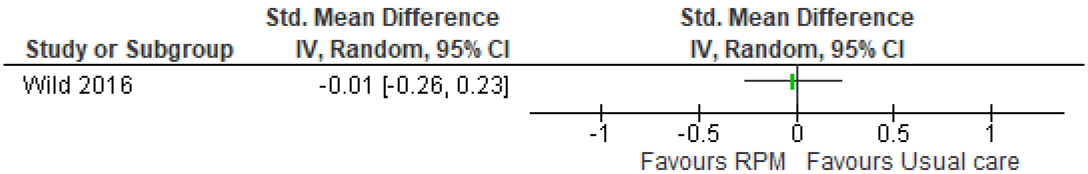
Figure 11 Forest plot of health-related quality of life (SF-12/36, physical component summary)



Outcome 8: Hospital Anxiety and Depression Scale total score

One study reported the total score from the Hospital Anxiety and Depression Scale (HADS), with no difference between the RPM and usual care patients. Standardized mean differences are again reported, due to a lack of an established minimum clinically important difference of the HADS in this population (Figure 12). As only one RCT reported this outcome, with a relatively small number of participants and therefore wide confidence intervals of the effect estimate, it is unlikely that this effect estimate mirrors the true effect of RPM on the HADS total score.

Figure 12 Forest plot of mental health symptoms (total HADS score)



Additional outcomes

Twenty-two of 23 additional outcomes, reported by one to two RCTs each, showed no effect of RPM. The following table displays their categorization into several biometric, patient-reported, health care utilization groups. As with the primary outcomes, extended forest plots in Appendix 5, Figures 8-25 include group sizes and raw data columns. We did not assess the certainty of the evidence using a GRADE assessment of these additional outcomes.

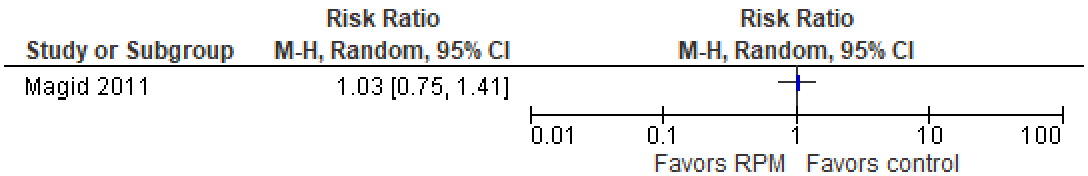
Table 6 Categorization of additional outcomes

Biometric	• achievement of normal blood pressure • achievement of target HbA1c • daytime ambulatory systolic blood pressure • daytime ambulatory diastolic blood pressure • weight • body mass index
Patient-reported	• overall health-related quality of life • diabetes knowledge
Mental health symptoms	• HADS anxiety subscale • HADS depression subscale
General practitioner utilization	• contact with general practitioner • practice nurse visits • primary care physician encounters with procedures
Emergency care utilization	• amount of emergency department visits
Hospital services utilization	• all-cause hospitalization • all-cause emergency hospitalization • bed days for all-cause hospitalization • bed days for diabetes-related hospitalized patients
Outpatient and specialist services utilization	• patients who visited a specialist • amount of outpatient visits
Home care services utilization	• patients with home visits
Cost and cost-effectiveness	• start-up, ongoing, and total costs • costs per quality-adjusted life year gained

- ***Biometric***

In addition to reporting on the effect of RPM on systolic and diastolic blood pressure, Magid et al. (29) reported the amount of patients who achieved "normal" blood pressure, corresponding to <140/90mmHg for those without co-morbid diabetes and/or renal disease, and <130/90mmHg for those with one or both of these comorbidities. The odds ratio of achieving this dichotomous outcome indicates no difference between the RPM and usual care group (Figure 13).

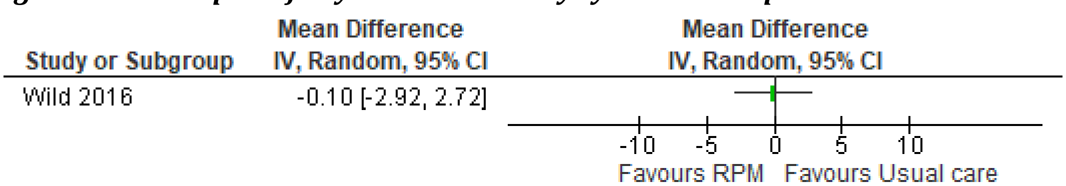
Figure 13 Forest plot of normal blood pressure achievement



Similarly, the amounts of patients who achieved target HbA1c goals were reported by two RCTs (in addition to both reporting effects on % HbA1c), although defined slightly differently. Nicolucci et al.'s (36) target HbA1c was <7%, and measured at the end of the intervention. Steventon et al.'s (38) target was <7.5%, and achieved at any point during the intervention. The trend in both RCTs was for a larger proportion of the RPM group to achieve HbA1c targets, but these differences were not statistically significant.

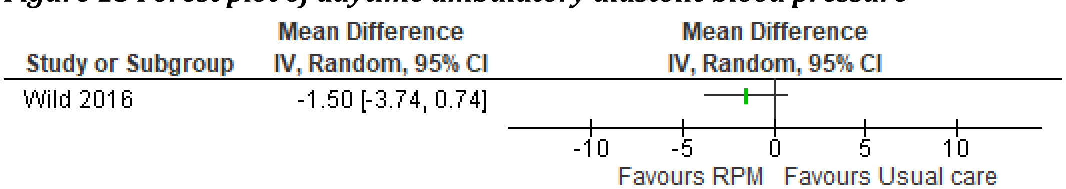
Wild et al. (40) reported daytime ambulatory systolic blood pressure, and found no difference between the two groups (Figure 14).

Figure 14 Forest plot of daytime ambulatory systolic blood pressure



Neither was there a difference in this RCT in daytime ambulatory diastolic blood pressure (Figure 15).

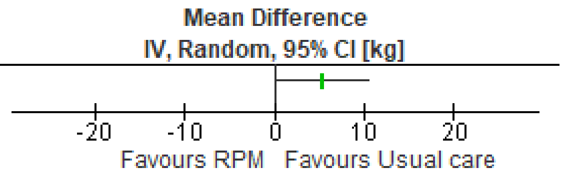
Figure 15 Forest plot of daytime ambulatory diastolic blood pressure



The usual care group weighed 5.40 kg less at the end of the intervention in Wild et al. (40), with a range of 0.42 kg less to 10.38 kg less (Figure 16).

Figure 16 Forest plot of weight

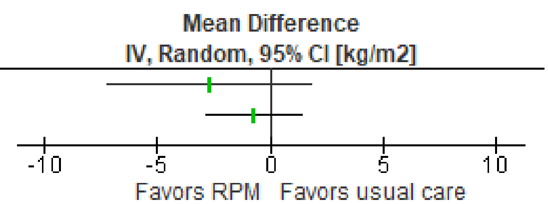
Study or Subgroup	Mean Difference IV, Random, 95% CI [kg]
Wild 2016	5.40 [0.42, 10.38]



However, this finding was not replicated by two different RCTs that measured body mass index. Neither reported a mean difference between the RPM and usual care groups, although the trend in both was for the RPM group to have a lower body mass index (Figure 17).

Figure 17 Forest plot of body mass index

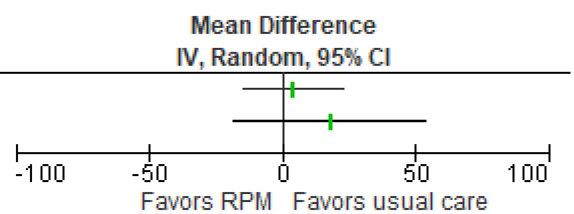
Study or Subgroup	Mean Difference IV, Random, 95% CI [kg/m2]
Carter 2011	-2.70 [-7.20, 1.80]
Schillinger 2009	-0.70 [-2.80, 1.40]



Triglyceride levels were reported by two studies, with no mean differences between the RPM and usual care groups (Figure 18).

Figure 18 Forest plot of triglyceride levels

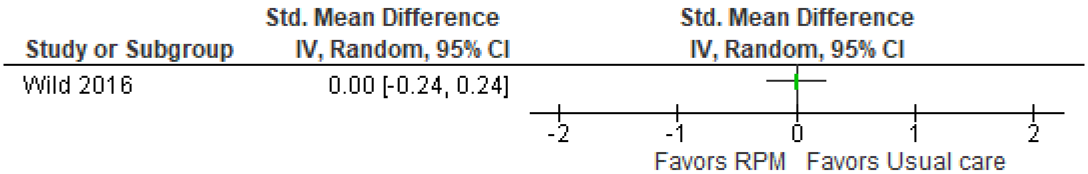
Study or Subgroup	Mean Difference IV, Random, 95% CI
Nicolucci 2015	4.00 [-14.90, 22.90]
Stone 2010	18.00 [-18.10, 54.10]



- ***Patient-reported***

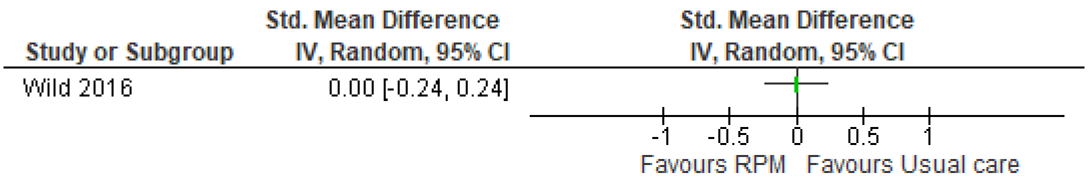
Overall health-related quality of life was also measured by one RCT with the EQ-5D. Mean scores were nearly identical between the RPM and usual care patients, with a standardized mean difference of 0 (Figure 19).

Figure 19 Forest plot of health-related quality of life (EQ-5D)



Wild et al. (40) also administered part of a diabetes knowledge test (49) after the intervention, and found no difference in scores (Figure 20).

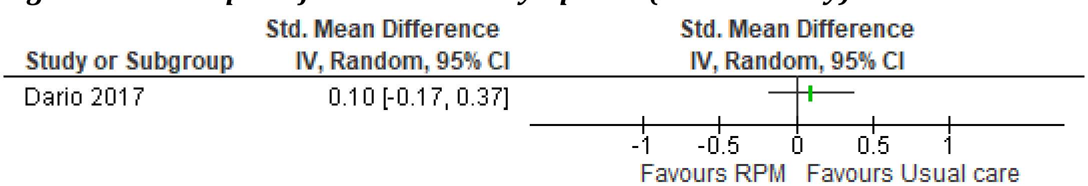
Figure 20 Forest plot of diabetes knowledge



- ***Mental health symptoms***

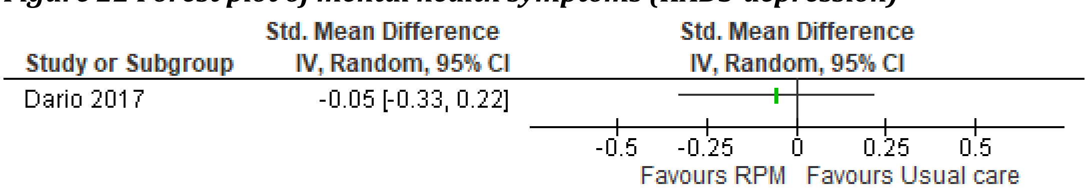
One RCT reported the anxiety subscale and the depression subscale of the HADS, instead of the total score. There was no difference between the RPM and usual care patients on the anxiety subscale (Figure 21).

Figure 21 Forest plot of mental health symptoms (HADS-anxiety)



Neither was there a difference on the depression subscale (Figure 22).

Figure 22 Forest plot of mental health symptoms (HADS-depression)

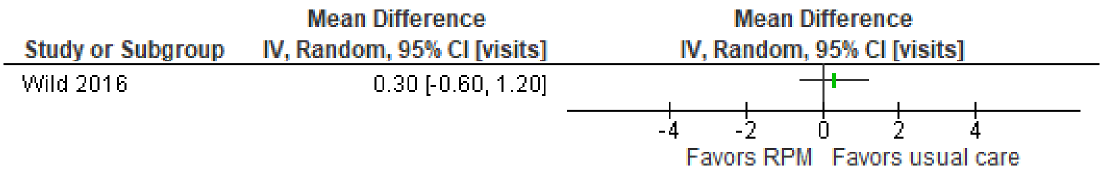


- ***General practitioner utilization***

Contact with general practitioners was reported in three different ways by two RCTs, with no differences between the RPM and usual care groups.

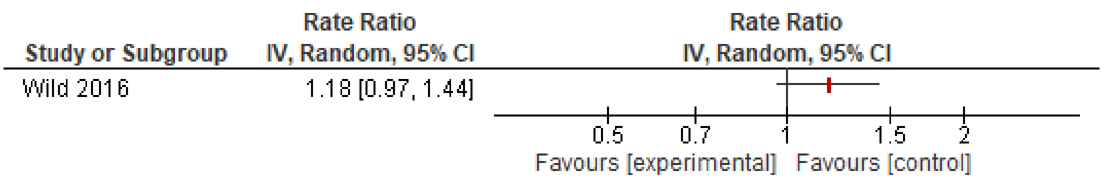
One RCT reported that the usual care group attended an average of 0.3 more visits than the RPM group, but with confidence intervals extending to 0.6 fewer visits to 1.2 more visits (Figure 23).

Figure 23 Forest plot of general practitioner visits



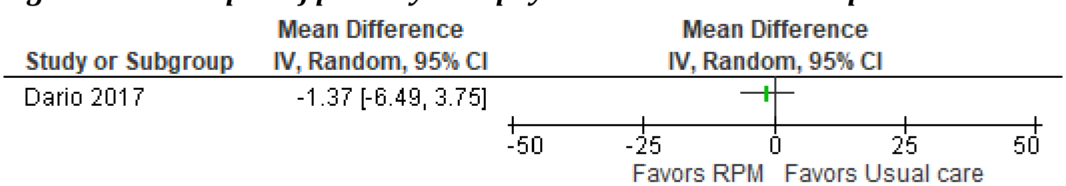
This RCT also reported no difference in the amount of patients with practice nurse visits between RPM and usual care, which were low enough in both groups to correspond to less than 1 out of 1000 patients (Figure 24).

Figure 24 Forest plot of practice nurse visits



A second RCT reported primary care physician encounters with procedures, with no difference between the groups (Figure 25).

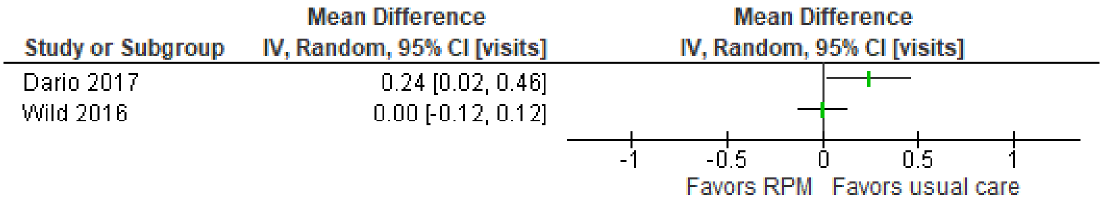
Figure 25 Forest plot of primary care physician encounters with procedures



- ***Emergency care utilization***

Two RCTs reported the amount of emergency department visits per person, which were on average less than one visit in both groups. In Dario et al. (26), the usual care group reported 0.24 more visits (0.02 more to 0.48 more); Wild et al. (40) reported no difference between the two (Figure 26).

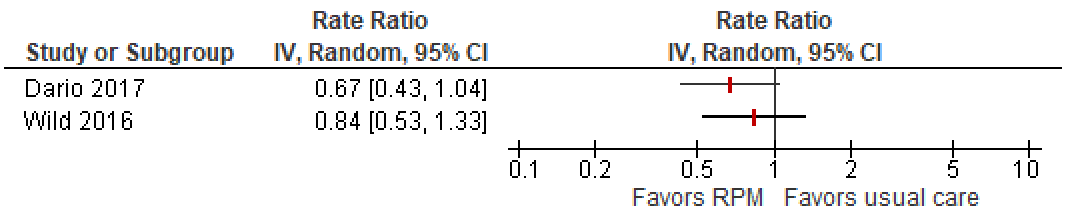
Figure 26 Forest plot of emergency department visits per person



- ***Hospital services utilization***

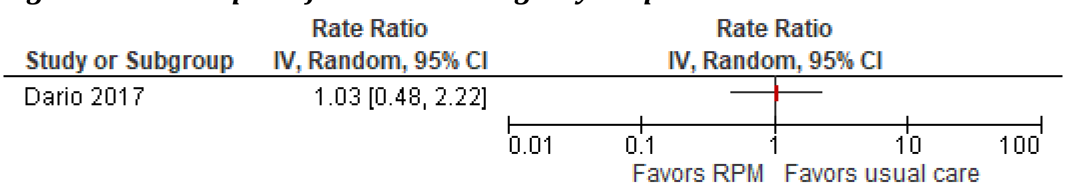
Two studies reported all-cause hospitalization/hospital attendance. Neither reported a difference between the RPM and usual care groups, although there was a trend towards fewer hospitalizations in the RPM group (Figure 27).

Figure 27 Forest plot of all-cause hospitalization/hospital attendance



The amount of all-cause emergency hospitalizations was additionally reported by one RCT, again with no differences (Figure 28).

Figure 28 Forest plot of all-cause emergency hospitalizations



Among the few patients hospitalized for all-cause reasons in Dario et al. (26), bed days were non-normally distributed, with no difference between the median days in each group: 13 days in the RPM group (interquartile range 1.5-23), and 9 days in the usual care group (interquartile range 2–23.25). Median bed days for patients hospitalized for diabetes-related causes were also similar between the two groups: 14 days in the RPM group (interquartile range 9.25–35.75), and 9 days in the usual care group (interquartile range 4-20).

- ***Outpatient and specialist services utilization***

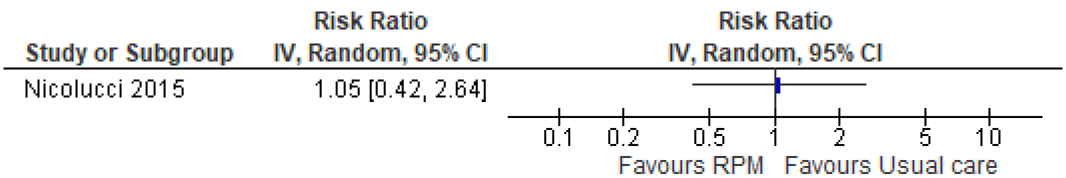
Two outpatient-related outcomes were reported in two RCTs. Nicolucci et al. (36) reported the amount of patients who visited a specialist. 46.4% of patients receiving RPM attended a specialist appointment during the course of the RCT, compared to 64.4% of usual care patients. This corresponds to 180 per 1000 fewer RPM patients than usual care patients (from 377 fewer to 58 fewer).

Dario et al. (26) reported no difference in the median amount of outpatient visits (rather than the amount of patients with a visit) to a diabetologist with a procedure: 1 visit in the RPM group (inter-quartile range 0-3), compared to the usual care group's median of 3 (interquartile range 1-4).

• ***Home care services utilization***

Nicolucci et al. (36) also reported on the patients who received a home visit during the RCT, with no difference between the two groups (3 per 1000 more in RPM, with a range of 39 fewer to 109 more). Figure 29 shows the risk ratio for this outcome.

Figure 29 Forest plot of patients with home visits



• ***Cost and cost-effectiveness***

Cost effectiveness was reported by Schillinger et al. (25, 50). Start-up costs were 394 USD and ongo-ing costs were 388 USD, for a total of 782 USD per RPM patient. RPM was associated with a gain of 0.012 quality-adjusted life years, relative to usual care. Accounting for the total cost per patient of RPM, the cost of RPM was 65,167 USD per quality-adjusted life year gained.

Discussion

Key findings summary

This overview of systematic reviews sought to assess the effectiveness of remote patient monitoring (RPM) on chronically ill patients' clinical outcomes and health care utilization. RPM of interest was defined as a process beginning with a device that sent any biometric or other patient data remotely; the evaluation of data; and a provider responding to the patient if necessary. Excluded therefore were fully-automated processes that excluded provider evaluation or response, as were processes occurring purely over the internet or on mobile or tablet applications. Data evaluation – the first point of provider contact – must have also occurred with primary health services for an RPM intervention to be included.

After assessment of 155 systematic reviews and their approximately 3,500 RCTs, only four high-quality reviews met our criteria. And of these four reviews' 176 included RCTs, only eleven reported on interventions that met our definition of RPM. An immediate conclusion to draw from the eligibility determination process is that the type of RPM of interest to the Norwegian Directorate of Health is not widely implemented.

Even comporting to our stringent definition of RPM, the RCTs reported a variety of practices. Data was transmitted most often by telehealth devices, but also by patients simply using the keypads of their landline telephones. Data was evaluated by staff at telemonitoring centers, by the device itself, or by providers manually. In most cases, patients were only followed up with if their data was assessed as concerning, usually by telephone. In addition to follow-up triggered by concerning data, two RCTs provided automated follow-up between once per day and once per week, and one reported scheduled follow-up once per month. Follow-up was often described as counselling to improve self-management, but it was difficult to determine how different this follow-up was from providers' usual care. The RPM conducted by these RCTs could therefore refer to more frequent monitoring and more frequent *enhanced* care, compared to usual care, or only to more frequent monitoring and more frequent usual care.

Patients in these eleven RCTs were adults with diabetes and/or hypertension, with mean ages from 51 to 73. Additional multi-morbidities such as chronic obstructive pulmonary disease, heart failure, and stroke were reported by roughly one to two out of every twenty patients across the RCTs. Psychiatric comorbidities were not measured by any RCT, and were often exclusion criteria.

We summarized results from 31 outcomes (8 primary and 23 secondary), and RPM appeared to effect only four of these 31 outcomes. Two effects were positive, and two were negative.

RPM probably benefited patients in only two primary outcomes, HbA1c and systolic blood pressure, but the benefits reported were not large enough to meet typical clinical goals. In another primary outcome, *usual care patients* benefited more than RPM patients: the physical health component of health-related quality of life. However, the effect that usual care patients reported was again small; it is difficult to say with any certainty that RPM patients noticed or appreciated being "worse off" than usual care patients.

Otherwise, RPM appeared to have no effect on the remaining five primary outcomes (diastolic blood pressure, cholesterol, the mental health component of health-related quality of life, the number of patients with a hospitalization or emergency room visit, and Hospital Anxiety and Depression Scale scores), and no effect on 22 of 23 secondary outcomes. The one secondary outcome it did effect, weight, showed RPM patients reported a mean weight gain of 5.4kg compared to usual care patients.

Quality of the evidence

Our eligibility requirement of high methodological quality for systematic reviews enables us to trust the findings of our four included reviews. Specifically, we are confident that each review conducted a sufficiently thorough search for RCTs, and therefore that their lists of included RCTs that we assessed for further eligibility were comprehensive, and we are confident that their assessments of each RCT's risk of bias are correct.

Overall, these RCTs utilized adequate randomization and had no risks of selection bias. Most were unable to blind participants or personnel, which is not unexpected, and likely does not impact the measurement of biometric outcomes. The most concerning risks across the studies were the presence of attrition bias and other biases, typically related to being funded by commercial telehealth actors.

We nevertheless had low confidence in most of our findings, after evaluating each outcome using the GRADE methodology. This was often due to a combination of attrition bias (most studies did not report on patients who had dropped out, and those who remained had quite positive outcomes), heterogeneous effect estimates, and only indirect applicability of an RCT's setting and patient population to Norway. An example of indirectness is that four RCTs were conducted in the United States, and with specific patient populations, such as veterans, African-Americans, only men, obese, and the urban poor. The remaining studies in Italy, Spain, and the United Kingdom were evaluated as more applicable to Norway.

This means that we are not certain that the "true" effect of RPM on five of our outcomes is, in fact, no effect. The three exceptions are HbA1c (it is likely that RPM has a slight positive effect), systolic blood pressure (it is likely that RPM has a slight positive effect), and the physical health component of health-related quality of life (it is likely that the true effect of RPM is a small negative one). These findings and others are discussed below in *Consistency with other reviews.*

Strengths and weaknesses

A strength of this overview is the definition of RPM developed in collaboration with the commissioner. While the specificity of the definition required screening of approximately 3,500 RCTs included in 155 systematic reviews, a time-consuming practice atypical of an overview of systematic reviews, it has also ensured that the interventions summarized in this overview are highly relevant to Norway. Even working within this specific definition, the interventions managed to involve a variety of actors, data transmission methods, data evaluation methods, and response options. Each of these can be used as possible design options as the commissioner moves forward with national RPM recommendations.

We utilized an exhaustive search strategy that allowed us to capture interventions that were not called RPM but nevertheless met our definition. For example, the RCTs used terms such as *telehealth, home telehealth, teleassistance, telemonitoring, home telemonitoring, supported telemonitoring, remote monitoring, home measurement reporting, self-management support,* and *provider-assisted telehealth self-management*. In describing these interventions and others, the four included systematic reviews called these interventions *telerehabilitation, telemedicine, digital interventions*, and *eHealth interventions.* With our exhaustive search strategy, it is unlikely that we failed to identify systematic reviews that had captured interventions of interest to us.

These RCTs are additionally relevant because of our use of time as an eligibility criterion. We included only systematic reviews with a search conducted in 2015 or more recently, in order to exclude the most outdated technologies. Nevertheless, any RCTs published after the most recent search (June 2017 by Kebede et al. (34)) would not be captured by our included systematic reviews. The decision to search for systematic reviews and not for RCTs was a pragmatic one, given the limited amount of time to complete this review and the vast amount of studies published each year, but we recognize that the risk of not capturing the most recent RCTs is a limitation to our review.

Our inclusion of only high-quality systematic reviews was necessary in order to trust (among other issues) their risk of bias evaluations of individual RCTs. While this resulted in discarding several systematic reviews that may have included otherwise eligible RCTs, it was another necessary choice given the vast amount of studies and the limited amount of time to complete this review. If the commissioner is interested at a later time point in examining lower quality systematic reviews, Appendix Table 2.1 indicates these.

We were analytically limited by the methodological choices of both the included systematic reviews and RCTs. For example, two of the RCTs did not report standard deviations. We borrowed standard deviations from the RCTs with the most common patient populations, and while this was only for the purposes of displaying outcomes in forest plots, borrowing standard deviations may have made confidence intervals appear artificially narrower, lending a false precision. One review (34) reported HbA1c outcomes adjusted for baseline values, and unadjusted values were not reported by the RCTs themselves (26, 27). There is conflicting evidence as to whether adjusting for baseline values appropriately reduces heterogeneity or contributes to confounding, that is, whether it inflates or deflates effect sizes (see for example (51, 52)). This is less of a problem in this overview, as we did not calculate summary effect sizes, but is worth keeping in mind when viewing the HbA1c forest plot that eight of ten RCTs' effect estimates were not adjusted for baseline values, and two were.

Despite our inclusion of only high-quality systematic reviews, we cannot exclude the possibility that these reviews' own limitations have influenced our findings. For example, it is possible that they failed to identify relevant RCTs. This is unlikely, however, as all reviews utilized broad definitions of RPM and several included more than one hundred studies. Another potential limitation of systematic reviews – incorrect data extraction – is unlikely to be replicated here, as we often extracted data directly from the RCTs themselves.

Diversity in outcome reporting was unfortunately common, and prevented the pooling of many health service utilization outcomes. For example, several RCTs reported overlapping outcomes: patients with hospitalization or emergency room stays, amount of emergency department visits, and all-cause emergency hospitalization were reported as three distinct outcomes, but were likely a phenomenon that could have been defined more narrowly and measured similarly. When possible, the use of a standard, clearly defined set of outcome measures among RCTs in different settings will clearly benefit future systematic reviews.

Generalizability of findings

Overall completeness and relevance of evidence from systematic review

The goal of this overview was to identify and synthesize types of RPM that were generalizable to Norway, and by extension, to any other country or setting interested in the same type of RPM. Due to the specificity of our definition of RPM, we are confident that that these eleven RCTs have implemented interventions similar to what the commissioner was interested in.

These interventions, however, were conducted in primary care settings that may be less generalizable to Norway. Our confidence in the applicability of the majority of the American RCTs was down-graded due to the RCTs variously drawing patients from health clinics reserved for the lowest-income residents (typically indicating unemployment or precarious employment), and/or including only African-Americans or war veterans, with the latter two categories comprised of people with poorer health and less access to care compared to Americans in general.

We did not down-grade either of the British RCTs, with the logic that the United Kingdom's publicly funded health care system provides similar primary care services as Norway. Neither did we down-grade the remaining Spanish or Italian RCTs, although these settings were scarcely described.

The patients of the eleven included RCTs are unfortunately only a small sample of the patients in whom the commissioner was interested. We cannot speak to whether RPM would result in the same negative impact on health-related quality of life, for example, among patients with cardiovascular disease, chronic lung diseases, cancer, mental disorders, chronic musculoskeletal disorders, osteoporosis, and/or impaired vision or hearing – all of which were populations for whom we searched.

Consistency with other reviews

There are no high-quality systematic reviews utilizing a similar definition of RPM with which to compare our findings. We can only compare our findings to recent systematic reviews with meta-analyses that included more broadly defined RPM interventions – such as those utilizing internet-based technologies, fully automated programs without provider input, and interventions organized in specialist health services – as well as to meta-analyses that were part of systematic reviews of less than high methodological quality. Overall, our findings comported with previous reviews, such as small benefits to HbA1c, small harms to health-related quality of life, and no effect on remaining clinical outcomes.

HbA1c

At first glance, the literature appears to show solid positive effects of RPM on diabetic patients' HbA1c. (We use a ≥0.5% to indicate clinical meaningfulness, to aid interpretation of these meta-analyses.) Faruque et al., using a broad definition of RPM that included any form of remote communication or data transmission between patients and providers, reported clinically meaningful reductions in HbA1c across 111 studies, -0.57% (23). So et al. used a similarly broad definition but looked only at primary care settings, and reported a nearly identical reduction across seven studies, -0.61% (53). However, both meta-analyses contained large amounts of unexplained heterogeneity.

Looking then at reviews that parsed RPM into distinct sub-types, a technique to explore and explain heterogeneity, the specifics of RPM appear to impact the effect it has on HbA1c. Reviews that operated with more specific definitions of RPM have tended to report more modest impacts of RPM, as we see in this review. RPM that used automated telephone services resulted in a non-meaningful reduction in HbA1c (35). Kebede et al. included diabetes type 1 patients and compared text-messaged based RPM, RPM in which patients communicated with providers, and web-based RPM delivered through PDA, tablet, computer, or smartphones, and reported reductions in HbA1c only for the latter category, around the threshold of being clinically meaningful, -0.41% (34). Shen et al. (diabetes type 2) further differentiated website-only interventions from those that used only mobile technologies, and from those that used both mobile and website components. While their meta-analysis found all three types had positive effects, only combined interventions exceeded the threshold for clinically meaningful change, –0.77% (54). The authors further conducted a subgroup analysis of interventions that provided manual feedback versus automated feedback, and found no difference in effect size.

RPM using combination mobile-and-website components and RPM using online components were more effective than other single-component technologies, such as text-messaging, automated telephone, website, or mobile technologies. Our included RCTs might have been collectively less effective because they utilized single-component technologies.

Blood pressure

Our finding of little or no effect of RPM on blood pressure of patients with diabetes and/or hypertension contributes to a mixed body of evidence. Posadzki et al. also found that RPM with automated telephone services had no effect on hypertensive patients (35), and Lee et al. found that broadly-defined telemedicine on diabetes type 1 patients of all ages also had no effect (55). However, Duan et al. reported a positive effect of home blood pressure monitoring on hypertensive patients (56). Similarly, Flodgren et al. found that interactive telemedicine and self-management reduced blood pressure among diabetes types 1 and 2 patients of all ages (14), as did self-management among hypertension patients in other reviews (57, 58).

Ma et al. speculate that RPM's positive effect on blood pressure only arises if medications are adjusted appropriately, and if patients then adhere to new medication regimes (57). In this explanation, RPM facilitates only one of three necessary steps, namely, provider knowledge of patient condition. The remaining two steps – provider adjustment of medication and patient adherence to medication – are required for effectiveness, but are not guaranteed by RPM itself. Duan et al. also argue that medication adherence is the decisive factor behind RPM effectiveness, and suggest that additional support such as education or counselling will not increase effectiveness if a minimum level of medication adherence does not exist (56). The reason for the lack of meaningful effect of RPM on blood pressure in our review may therefore be due to insufficient patient behavior change, which is not necessarily the goal of a monitoring program.

Cholesterol

We found no effect of RPM on total cholesterol levels, as reported by other meta-analyses. Ma et al.'s meta-analysis of three eHealth interventions among hypertensive patients, including self-management and provider feedback, similarly reported no effect on cholesterol (57). Posadzki et al., looking at patients with hypercholesterolaemia, reported no effect across two studies (35). Gandhi et al. also pooled two studies of patients with cardiovascular disease and reported no effect (59). Interestingly, none of these authors discussed this lack of efficacy. The medical counselling and support provided in RPM may be insufficient to effect total cholesterol levels, if they are insufficient in effecting exercise, dietary, and smoking modifications, in addition to improving statin adherence. One large study of statin adherence among more than 22,000 Australians found that not only was attrition common – more than half discontinued in the first year of prescribing – but prescription by a general practitioner instead a specialist and the presence of diabetes independently increased the risk for attrition (60). The RPM interventions in this review, by including patients with diabetes and being treated within primary health services, may have captured a particular subgroup for which extra support is needed.

Patients with hospitalizations or emergency room visits, all-cause

Meta-analyses of specific healthcare utilization outcomes are rare, likely due to the difficulties in comparing these outcomes across settings, and there is little summarized evidence to which we can compare our results.

Among other patient groups, recent systematic reviews have tended to use narrative syntheses, not meta-analysis, and to conclude that evidence of efficacy regarding hospitalization is insufficient. This has been reported, for example, among heart failure patients in Bashi et al.'s overview of systematic reviews (61), and among mixed patient groups in Kalenkesh et al. (62) and Vegesna et al. (63). Sul et al. conducted a meta-analysis of hospitalizations and reported no difference among COPD patients, but with a moderate amount of unexplained heterogeneity in the model that suggests a meta-analysis was not appropriate until intervention differences had been further explored (64).

Hospitalization and emergency room utilization among patients with diabetes and/or patients would be triggered by a significant deterioration in health condition. The duration of our included RCTs – from six to twelve months – is likely too short a period to allow for such deterioration, which may explain why this outcome was only reported by one RCT.

Health-related quality of life

We found a small negative effect of RPM on the physical health component of health-related quality of life, and no effect on the mental health component. Neither diabetes-specific quality of life nor health-related quality of life have been found to be effected by RPM among patients with diabetes (14, 23, 65) or hypertension (56, 57). If it is reasonable to expect that RPM will not improve quality of life, but that it should at the very least not *lower* HRQOL when compared to usual care, that is, face-to-face contact with health care providers, then this finding can be viewed positively.

However, improving HRQOL is a goal of chronic disease treatment in general, not simply maintaining HRQOL. Our findings are aligned with the literature, but are nevertheless disappointing. It is concerning that HRQOL is consistently measured by RCTs despite a similarly consistent lack of effect, or as we found, even a slight negative effect. Several questions beg answers: are RPM interventions being developed with quality of life in mind? Is quality of life an outcome taken seriously in these trials, or is it being measured habitually, to check the box of patient-reported outcomes? As HRQOL is by definition patient-reported, patient input in developing, modifying, and improving RPM may be key to improving this outcome.

Depression

Depression is not a commonly measured outcome among RPM trials patients with diabetes and/or hypertension. Posadzki et al.'s review reported a slight decrease in depressive symptoms among patients with hypertension as a result of automated telephone programs (35). More research has been conducted among patients with comorbid depression and diabetes, with little effectiveness shown (66). There is a clear need for effective strategies: a review of 20 studies concluded that not only do diabetic patients have increased risks of depression and impaired quality of life, but their effects are likely multiplicative, and contribute to worse functioning over time (67) .

Implication of results on practice

The type of RPM we analyzed does not appear particularly effective. Given that RPM defined more broadly has been reported to have positive effects on HbA1c and, in some cases, blood pressure among people with diabetes and/or hypertension, it may be that our selection or definition of RPM have captured the types that are least effective. The three characteristics of our definition were the requirement that providers be involved (i.e. not fully automated), that the process occurs within primary health services, and that data transmission not occur via web, mobile, or tablet applications. If the commissioner nonetheless considers this exact type of RPM to be most relevant to Norway, then further development – rather than immediate implementation as is – would be advantageous. User testing should be conducted and patient groups involved in implementation and evaluation, to maximize potential for modification and ultimately efficacy. Patients may have preferences as to the frequency of feedback from providers, the content of such feedback, and even the method of contact. Pekmezaris et al. provide one example of a participatory approach to designing an RPM program for heart failure patients (68), while Ware et al. describe suggestions made by patients for program modification after conclusion (69).

Monitoring itself, even including frequent feedback on health status, may not be sufficient to enact the behavior change often needed in these two disease groups, such as medication, diet, and physical activity modification. RPM is perhaps better conceptualized as a data transmission and feedback system, and additional, targeted support integrated within feedback – such as behavioral change counselling, review of barriers to medication compliance, dis/satisfaction with the intervention itself – may be needed to actually ensure behavior modifications. For conditions in which adhering to provider feedback is acceptable and easy for patients, for example, instructions to adjust the dose of a well-tolerated medication, or a new appointment with a specialist on a day that was already planned to be spent at a hospital, feedback alone may be effective. For diabetes and/or hypertension, it appears that patients may need to be supported in adhering to provider feedback.

It is unsurprising that the impaired vision/hearing systematic review was an empty review, as this was an exclusion criteria for many of our identified RCTs – despite the fact that impaired vision and hearing are conditions that will only increase with age, along with other chronic diseases. In a longitudinal Icelandic population study, 42% of adults over 67 had impaired vision and/or hearing, which increased mortality risk even after adjusting for covariates such as age and other chronic diseases (70). There is both potential and need to tailor RPM to people with impaired vision/hearing, particularly if they have other chronic conditions, or conditions that limit mobility and utilization of in-person health services. RPM technologies should be developed following universal design principles to be suitable for people with disabilities. Doing so many allow for the inclusion of other under-represented populations, such as people with cognitive impairments (71), as well as older patients, who may have the most to gain from attention in the design phase to vision, hearing, and cognitive impairments (72, 73) .

Need for further research

While physical multi-morbidities were reported by many RCTs, most excluded based on psychiatric multi-morbidity. Excluding patients on the basis of psychiatric multi-morbidities is, unfortunately, standard practice in clinical trials; investigators often assume that these potential patients will struggle more with treatment adherence than other patients. However, a recent systematic review of technology-assisted interventions for people with severe mental illness reported "concerning" levels of attrition (>20%) among less than 10% of trials (74) – while an earlier review of RCTs published in four top medical journals reported that 18% of trials have attrition levels >20% (75). Assuming that patients with mental health problems will not comply may be selling them short. Excluding patients who use any type of psychotropic medicine, or those with anxiety, depression, alcohol, and/or substance problems, belies the prevalence of these conditions among people with diabetes and/or hypertension. A range of estimates point towards higher prevalence of depression (76) and anxiety (77) among people with diabetes, while substance use disorders and other mental illnesses increase the risk of both diabetes and hypertension (78, 79). We encourage the inclusion of people with comorbid mental health problems in future trials of RPM for chronic physical conditions, and the inclusion of people with other cognitive impairments.

Qualitative methods are an important tool to understand why patient-reported outcomes such as health-related quality of life were not improved by RPM. Previous qualitative studies have reported conflicting experiences, such as patients who feel empowered and confident through handling their own data, while others are made anxious by frequent measurements and discouraged that they will be able to change their health status (80, 81). Future research can recruit among trial participants and explore the experiences of participants receiving RPM compared to usual care, and potentially identify particular groups who would benefit from additional or different support.

One such qualitative study was conducted among the patients and providers in Wild et al.'s RCT (82). A key finding was that the burden of RPM was experienced quite differently between these two groups. RPM was seen as convenient and sensible by patients, while providers felt RPM was an additional burden to their workload, and could not imagine RPM being a scalable intervention, given the amount of time they were required to spend providing feedback to the data transmitted. The lack of efficacy seen in our review may be in part explained by difficulties in implementation from the provider side, and such difficulties may best be explored through qualitative methods.

Potential topics for future commissioned systematic reviews

- RPM implemented within specialist health services, over the internet, or without provider input (i.e. fully automated) – our list of excluded studies contains those that we identified after full-text screening.
- RPM for patients with dementia, Alzheimers, or other neurodegenerative diseases.
- RPM for people in institutional settings that are not healthcare-related, such as prisons or community living programs for people with developmental disabilities.
- Patient and provider experiences of RPM development, organization, or implementation.

Conclusion

In this comprehensive overview of four systematic reviews, we aimed to assess the effectiveness of a specific type of remote patient monitoring (RPM) on clinical and health care utilization outcomes for chronic disease patients. This specific type of RPM was implemented in eleven randomized controlled trials (RCTs) of patients with diabetes and/or hypertension, and it had little to no effectiveness on the majority of outcomes compared to usual care. RPM patients experienced a small, clinically non-meaningful reduction in HbA1c (we have moderate certainty in this finding), and likely a similarly small reduction in systolic blood pressure (moderate certainty). Usual care patients reported an improvement in the physical health component of health-related quality of life, but the effect size was very small (moderate certainty). We have low certainty that RPM also did not impact diastolic blood pressure, cholesterol, patients with hospitalizations or emergency stays, or the mental health component of health-related quality of life. In the remaining 23 secondary outcomes in which we did not assess our certainty in, RPM had no effect in 22 of them, and a negative effect in one, weight.

The slight benefit of RPM to HbA1c and systolic blood pressure, and the negative effect of RPM on one type of health-related quality of life, have both been reported in previous reviews utilizing different or broader definitions of RPM. These somewhat disappointing results may be because RPM facilitates data transmission, analysis, and feedback, but does not necessarily assist patients in making or sustaining the medication, diet, or physical activity change that are often necessary for these conditions. RPM could be seen as a bridge to necessary further support, but not superior by itself to usual care. More complex RPM interventions may be required to support such complicated behavioral change, such as interventions combining multiple components, or perhaps involving specialists from the beginning.

More complex interventions are on the horizon. With machine learning and artificial intelligence (AI), the potential of RPM is unlimited. Such enhanced RPM strategies can collect and analyze massive amounts of real-time data, genomic information, and other risk factors, and they have the potential to increase accuracy and speed of clinical decision-making and follow-up. While AI-aided RPM strategies would likely not fall under our definition of RPM, this overview has, at the very least, pointed to the patient groups and outcomes not currently being effectively served, and that could be targets of RPM strategies of the future.

Appendices

Appendix 1. Search strategy

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to May 21, 2019
Dato: 22.05.2019
Treff: 1352

Searches Results
1 Telemedicine/ 19411
2 Telerehabilitation/ 245
3 Telenursing/ 199
4 Remote Consultation/ 4542
5 or/1-4 23509
6 exp Telecommunications/ 84877
7 (care or healthcare).hw. 1179219
8 6 and 7 14549
9 (telecare or telecheck* or teleconsult* or telefollow* or telehealth* or telehome* or telemanag* or telemedicine or telemental* or telemonitor* or telenursing* or telepatient* or telepsych* or tele-rehab* or telereport* or telesupport*).ti,ab,kf. 16721
10 ((tele or telemedical* or tele medical*) adj (care or checkup* or check up* or consult* or fol-lowup* or follow up* or health* or home* or manag* or medicine* or mental or monitor* or nurs-ing* or patient* or psych* or rehab* or report* or support*)).ti,ab,kf. 837
11 (ecare or econsult* or ehealth or emedicine or emental* or enursing* or erehab* or mcare or mconsult* or mhealth or mmedicine or mmental* or mnurs*).ti,ab,kf. 6002
12 ((e or m or mobile or digital) adj (care or consult* or health* or medicine* or mental* or nurs-ing* or rehab*)).ti,ab,kf. 7806
13 (remote adj2 (care or checkup* or check up* or consult* or followup* or follow up* or health* or home* or manag* or medicine* or mental or monitor* or nursing or patient* or psych* or rehab* or self)).ti,ab,kf. 5456

14 5 or 8 or 9 or 10 or 11 or 12 or 13 46223
15 Meta-Analysis/ 101020
16 Meta-Analysis as Topic/ 16935
17 Systematic Reviews as Topic/ 2257
18 Systematic Review.pt. 106708
19 ((systematic* adj2 (overview or review* or search*)) or meta anal* or metaanal* or meta regression* or meta review* or umbrella review* or "overview of reviews" or "review of reviews" or (evidence* adj2 synth*) or synthesis review*).ti,ab,kf. 256235
20 Review.pt. and (pubmed or medline).ab. 120264
21 or/15-20 325341
22 14 and 21 2050
23 exp animals/ not humans.sh. 4581973
24 (news or editorial or comment).pt. 1300176
25 22 not (23 or 24) 2033
26 limit 25 to yr="2015-Current" 1354
27 remove duplicates from 26 1352

Database: (OVID) Embase 1974 to 2019 May 21
Dato: 22.05.2019
Treff: 713

Searches Results
1 *telemedicine/ 11894
2 *telehealth/ 2600
3 *teleconsultation/ 2826
4 *telepsychiatry/ 340
5 *telerehabilitation/ 316
6 *telenursing/ 151
7 or/1-6 17846
8 exp *telecommunication/ 29287
9 exp *health care delivery/ 624637
10 8 and 9 21385
11 (telecare or telecheck* or teleconsult* or telefollow* or telehealth* or telehome* or telemanag* or telemedicine or telemental* or telemonitor* or telenurs* or telepatient* or telepsych* or telerehab* or telereport* or telesupport*).ti,ab,kw. 22356
12 ((tele or telemedical* or tele medical*) adj (care* or checkup* or check up* or consult* or followup* or follow up* or health* or home* or manag* or medicine* or mental or monitor* or nurs* or patient* or psych* or rehab* or report* or support*)).ti,ab,kw. 1545
13 (ecare or econsult* or ehealth or emedicine or emental* or enurs* or erehab* or mcare or mconsult* or mhealth or mnurse or mcare or mnursing or mconsult* or mmedicine or mmental* or mnurs*).ti,ab,kw. 5998

14 ((e or m or mobile or digital) adj (care or consult* or health* or medicine* or mental* or nurs* or rehab*)).ti,ab,kw. 9438
15 (remote adj2 (care* or checkup* or check up* or consult* or followup* or follow up* or health* or home* or manag* or medicine* or mental or monitor* or nursing or patient* or psych* or rehab* or self)).ti,ab,kw. 8446
16 7 or 10 or 11 or 12 or 13 or 14 or 15 47982
17 Meta Analysis/ 162846
18 Systematic Review/ 204735
19 ((systematic* adj2 (overview or review* or search*)) or meta anal* or metaanal* or meta regression* or meta review* or umbrella review* or "overview of reviews" or "review of reviews" or (evidence* adj2 synth*) or synthesis review*).ti,ab,kw. 328748
20 (review and (pubmed or medline)).ti,ab. 158206
21 or/17-20 443237
22 16 and 21 2228
23 (exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/) not (human/ or normal human/ or human cell/) 6195378
24 (news or editorial or comment).pt. 601134
25 22 not (23 or 24) 2223
26 limit 25 to yr="2015-current" 1479
27 limit 26 to embase 719
28 remove duplicates from 27 713

Database: (OVID) PsycINFO 1806 to May Week 2 2019
Dato: 22.05.2019
Treff: 344

Searches Results
1 telemedicine/ 4751
2 exp internet/ 28372
3 exp TELECOMMUNICATIONS MEDIA/ 12461
4 2 or 3 40381
5 exp health care delivery/36915
6 4 and 5 1032
7 (telecare or telecheck* or teleconsult* or telefollow* or telehealth* or telehome* or telemanag* or telemedicine or telemental* or telemonitor* or telenurs* or telepatient* or telepsych* or telerehab* or telereport* or telesupport*).ti,ab,id. 3874
8 ((tele or telemedical* or tele medical*) adj (care* or checkup* or check up* or consult* or followup* or follow up* or health* or home* or manag* or medicine* or mental or monitor* or nurs* or patient* or psych* or rehab* or report* or support*)).ti,ab,id. 192

9 (ecare or econsult* or ehealth or emedicine or emental* or enurs* or erehab* or mcare or mconsult* or mhealth or mnurse or mcare or mnursing or mconsult* or mmedicine or mmental* or mnurs*).ti,ab,id. 1417
10 ((e or m or mobile or digital) adj (care or consult* or health* or medicine* or mental* or nurs* or rehab*)).ti,ab,id. 2020
11 (remote adj2 (care* or checkup* or check up* or consult* or followup* or follow up* or health* or home* or manag* or medicine* or mental or monitor* or nursing or patient* or psych* or rehab* or self)).ti,ab,id. 761
12 1 or 6 or 7 or 8 or 9 or 10 or 11 8541
13 Meta Analysis/ 4417
14 Systematic Review.md. 21348
15 ((systematic* adj2 (overview or review* or search*)) or meta anal* or metaanal* or meta regression* or meta review* or umbrella review* or "overview of reviews" or "review of reviews" or (evidence* adj2 synth*) or synthesis review*).ti,ab,id. 57176
16 (review and (pubmed or medline)).ti,ab. 15784
17 or/13-16 65050
18 12 and 17 541
19 limit 18 to yr="2015-current" 344
20 remove duplicates from 19 344

Database: Epistemonikos
Dato: 22.05.2019
Treff: 1418 (Broad synthesis 33, Structured summary 5, Systematic review 1380)

[Title/Abstract:] (telecare or telecheck* or teleconsult* or telefollow* or telehealth* or telehome* or telemanag* or telemedic* or telemental* or telemonitor* or telenursing* or telepatient* or telepsych* or telerehab* or telereport* or telesupport* or tele-care or tele-check* or tele-consult* or tele-follow* or tele-health* or tele-home* or tele-manag* or tele-medic* or tele-mental* or tele-monitor* or tele-nursing* or tele-patient* or tele-psych* or tele-rehab* or tele-report* or tele-support* or ecare or econsult* or ehealth or emedicine or emental* or enurs* or erehab* or mcare or mconsult* or mhealth* or mmedicine or mmental* or mnursing* or e-care or e-consult* or e-health or e-medicine or e-mental* or e-nurs* or e-rehab* or m-care or m-consult* or m-health* or m-medicine or m-mental* or m-nursing* or "mobile care" or "mobile consultation" or "mobile consultations" or "mobile health" or "mobile healthcare" or "mobile medicine" or "mobile mental“ or "mobile nursing" or "mobile rehabilitation" or "mobile rehabilitations" or "digital care" or "digital consultation" or "digital consultations" or "digital health" or "digital healthcare" or "digital medicine" or "digital mental" or "digital nursing" or "digital rehabilitation" or "digital rehabilitations")
OR
[Title/Abstract:] (remote) AND (care* OR checkup* OR check-up* OR "check up" OR "check ups" OR consult* OR followup* OR follow-up* OR "follow up" OR "follow ups" OR health* OR home* OR

manag* OR medicine* OR mental OR monitor* OR nursing OR patient* OR psych* OR rehab* OR self-*)

Database: Cochrane Library (Wiley)
Dato: 22.05.2019
Treff: 681

ID Search Hits
#1 MeSH descriptor: [Telemedicine] this term only 1666
#2 MeSH descriptor: [Telerehabilitation] this term only 76
#3 MeSH descriptor: [Telenursing] this term only 28
#4 MeSH descriptor: [Remote Consultation] this term only 350
#5 {or #1-#4} 2083
#6 MeSH descriptor: [Telecommunications] explode all trees 5541
#7 MeSH descriptor: [Delivery of Health Care] explode all trees 42729
#8 #6 and #7 3336
#9 (telecare or telecheck* or teleconsult* or telefollow* or telehealth* or telehome* or telemanag* or telemedicine or telemental* or telemonitor* or telenursing* or telepatient* or telepsych* or tele-rehab* or telereport* or telesupport*):ti,ab 3163
#10 ((tele or telemedical* or tele-medical*) NEXT (care or checkup* or check-up* or consult* or followup* or follow-up* or health* or home* or manag* or medicine* or mental or monitor* or nurs-ing* or patient* or psych* or rehab* or report* or support*)):ti,ab 386
#11 (ecare or econsult* or ehealth or emedicine or emental* or enursing* or erehab* or mcare or mconsult* or mhealth or mmedicine or mmental* or mnurs*):ti,ab 1445
#12 (e-care or e-consult* or e-health or e-medicine or e-mental* or e-nurs* or e-rehab* or m-care or m-consult* or m-health* or m-medicine or m-mental* or m-nursing*):ti,ab2678
#13 (remote NEAR/2 (care* or checkup* or check-up* or consult* or followup* or follow-up* or health* or home* or manag* or medicine* or mental or monitor* or nursing or patient* or psych* or rehab* or self)):ti,ab 920
#14 {or #5, #8-#13} with Cochrane Library publication date Between Jan 2015 and May 2019, in Cochrane Reviews

Database: Web Of Science Core Collection [SCI-EXPANDED & SSCI] (Clarivate)
Dato: 22.05.2019
Treff: 681

1 TOPIC: (telecare or telecheck* or teleconsult* or telefollow* or telehealth* or telehome* or te-lemanag* or telemedicine or telemental* or telemonitor* or telenursing* or telepatient* or telepsych* or telerehab* or telereport* or telesupport*) 19,466

2 TOPIC: (((tele or telemedical* or tele-medical*) NEAR/0 (care or checkup* or check-up* or consult* or followup* or follow-up* or health* or home* or manag* or medicine* or mental or monitor* or nursing* or patient* or psych* or rehab* or report* or support*))) 1,069
3 TOPIC: ((ecare or econsult* or ehealth or emedicine or emental* or enursing* or erehab* or mcare or mconsult* or mhealth or mmedicine or mmental* or mnurs*)) 5,956
4 TOPIC: (e-care or e-consult* or e-health or e-medicine or e-mental* or e-nurs* or e-rehab* or m-care or m-consult* or m-health* or m-medicine or m-mental* or m-nursing*) 4,987
5 TOPIC: ((remote NEAR/1 (care* or checkup* or check-up* or consult* or followup* or follow-up* or health* or home* or manag* or medicine* or mental or monitor* or nursing or patient* or psych* or rehab* or self))) 8,044
6 TOPIC: (((systematic* NEAR/2 (overview or review* or search*)) or meta-anal* or metaanal* or meta-regression* or meta-review* or umbrella-review* or "overview of reviews" or "review of reviews" or (evidence* NEAR/1 synth*) or synthesis-review*)) 449,422
7 #5 OR #4 OR #3 OR #2 OR #1 35,408
8 #7 AND #6 1,639 [Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=2015-2019]

Appendix 2. Excluded reviews

Systematic reviews excluded after full-text assessment are listed alphabetically, along with the reason for their exclusion and the chronic disease group of interest.

Appendix Table 2.1

Systematic review	Reason for exclusion	Chronic disease
Adamson PB, Ginn G, Anker SD, Bourge RC, Abraham WT. Remote haemodynamic-guided care for patients with chronic heart failure: a meta-analysis of completed trials. Eur J Heart Fail 2017;19(3):426-33.	Not RPM (Specialist health services)	heart failure
Agboola SO, Ju W, Elfiky A, Kvedar JC, Jethwani K. The effect of technology-based interventions on pain, depression, and quality of life in patients with cancer: a systematic review of randomized controlled trials. J Med Internet Res 2015;17(3):e65.	Not RPM (Interventions; or in specialist health services)	cancer
Agostini M, Moja L, Banzi R, Pistotti V, Tonin P, Venneri A, et al. Telerehabilitation and recovery of motor function: a systematic review and meta-analysis. J Telemed Telecare 2015;21(4):202-13.	Not RPM (exercise monitoring; internet-based)	multiple
Aminov A, Rogers JM, Middleton S, Caeyenberghs K, Wilson PH. What do randomized controlled trials say about virtual rehabilitation in stroke? A systematic literature review and meta-analysis of upper-limb and cognitive outcomes. Journal of NeuroEngineering and Rehabilitation 2018;15(1):1-24.	Not RPM (exercise monitoring)	stroke

Arambepola C, Ricci-Cabello I, Manikavasagam P, Roberts N, French DP, Farmer A. The impact of automated brief messages promoting lifestyle changes delivered via mobile devices to people with type 2 diabetes: a systematic literature review and meta-analysis of controlled trials. J Med Internet Res 2016;18(4):e86.	Not RPM (No provider input in monitoring)	diabetes
Aronow WS, Shamliyan TA. Comparative effectiveness of disease management with information communication technology for preventing hospitalization and readmission in adults with chronic congestive heart failure. J Am Med Dir Assoc 2018;19(6):472-9.	Low/moderate methodological quality	chronic heart failure
Bashi N, Karunanithi M, Fatehi F, Ding H, Walters D. Remote monitoring of patients with heart failure: an overview of systematic reviews. J Med Internet Res 2017;19(1):e18.	No included systematic reviews meet our definition	heart failure
Batsis JA, DiMilia PR, Seo LM, Fortuna KL, Kennedy MA, Blunt HB, et al. Effectiveness of ambulatory telemedicine care in older adults: a systematic review. J Am Geriatr Soc 2019;67(8):1737-49.	Not RPM (Interventions)	multiple
Bauce K, Fahs DB, Batten J, Whittemore R. Videoconferencing for management of heart failure an integrative review. J Gerontol Nurs 2018; 44(4):45-52.	Not systematic review	heart failure
Bhavnani S, Waalen J, Srivastava A, Heywood JT. Which patients? Which devices? Mhealth monitoring with wearable and implantable devices in heart failure: meta analyses of randomized trails. J Am Coll Cardiol 2015;65 (Supplement):A1030.	Not systematic review	heart failure
Bush ML, Thompson R, Irungu C, Ayugi J. The role of telemedicine in auditory rehabilitation: a systematic review. Otol Neurotol 2016;37(10):1466-74.	Not RPM (Specialist health services)	impaired hearing
Cajita MI, Gleason KT, Han HR. A systematic review of mHealth-based heart failure interventions. J Cardiovasc Nurs 2016;31(3):E10-22.	Low/moderate methodological quality	heart failure
Carbo A, Gupta M, Tamariz L, Palacio A, Levis S, Nemeth Z, et al. Mobile technologies for managing heart failure: a systematic review and meta-analysis. Telemed J E Health 2018;24(02):958-68.	Low/moderate methodological quality	heart failure
Chan C, Yamabayashi C, Syed N, Kirkham A, Camp PG. Exercise telemonitoring and telerehabilitation compared with traditional cardiac and pulmonary rehabilitation: a systematic review and meta-analysis. Physiother Can 2016;68(3):242-51.	Not RPM (exercise monitoring)	cardiovascular disease, chronic obstructive pulmonary disease
Chandak A, Joshi A. Self-management of hypertension using technology enabled interventions in primary care settings. Technol Health Care 2015;23(2):119-28.	Not systematic review	hypertension
Chen J, Jin W, Zhang XX, Xu W, Liu XN, Ren CC. Telerehabilitation approaches for stroke patients: systematic review and meta-analysis of randomized controlled trials. J Stroke Cerebrovasc Dis 2015;24(12):2660-8.	Not RPM (exercise monitoring)	stroke
Chen YY, Guan BS, Li ZK, Li XY. Effect of telehealth intervention on breast cancer patients' quality of life and psychological outcomes: a meta-analysis. J Telemed Telecare 2018;24(3):157-67.	Not RPM (Interventions)	cancer
Chongmelaxme B, Lee S, Dhippayom T, Saokaew S, Chaiyakunapruk N, Dilokthornsakul P. The effects of telemedicine on asthma control and patients' quality of life in adults: a systematic review and meta-analysis. J Allergy Clin Immunol Pract 2019;7(1):199-16.	Low/moderate methodological quality	asthma
Clark RA. Telehealth in the elderly with chronic heart failure: what is the evidence? Stud Health Technol Inform 2018;246(Jan):18-23.	Not systematic review	chronic heart failure

Conway N, Webster C, Smith B, Wake D. eHealth and the use of individually tailored information: a systematic review. Health Inform J 2017;23(3):218-33.	Not RPM (No provider input in monitoring)	multiple
Cottrell MA, Galea OA, O'Leary SP, Hill AJ, Russell TG. Real-time telerehabilitation for the treatment of musculoskeletal conditions is effective and comparable to standard practice: a systematic review and meta-analysis. Clin Rehabil 2017;31(5):625-38.	Not RPM (exercise monitoring)	musculoskeletal
Cristo Dd, Nascimento NPd, Dias AS, Sachetti A. Telerehabilitation for cardiac patients: systematic review. Int j cardiovasc sci (Impr) 2018;31(4):443-50.	Not RPM (exercise monitoring)	cardiovascular disease
Cruz JPdS. Self-management in the rehabilitation of patients with chronic obstructive pulmonary disease: the role of telemonitoring and physical activity. Dissertation Abstracts International Section C: Worldwide 2018;75(1-C):No Pagination Specified.	Low/moderate methodological quality	chronic obstructive pulmonary disease
Da Silva RH, Moore SA, Price CI. Self-directed therapy programmes for arm rehabilitation after stroke: a systematic review. Clin Rehabil 2018;32(10):1412-1.	Not RPM (exercise monitoring)	stroke
de la Torre-Diez I, Lopez-Coronado M, Vaca C, Aguado JS, de Castro C. Cost-utility and cost-effectiveness studies of telemedicine, electronic, and mobile health systems in the literature: a systematic review. Telemed J E Health 2015;21(2):81-5.	Not systematic review	multiple
Delgoshaei B, Mobinizadeh M, Mojdekar R, Afzal E, Arabloo J, Mohamadi E. Telemedicine: a systematic review of economic evaluations. Med J Islam Repub Iran 2017;(20 Dec).	Not systematic review	multiple
Devi R, Singh SJ, Powell J, Fulton EA, Igbinedion E, Rees K. Internet-based interventions for the secondary prevention of coronary heart disease. Cochrane Database of Systematic Reviews 2015;(12):CD009386.	Not RPM (Internet-based)	coronary heart disease
Diedrich L, Dockweiler C, Kupitz A, Hornberg C. Telemonitoring in heart failure: update on health-related and economic implications. Herz 2018;43(4):298-09.	Low/moderate methodological quality	heart failure
Dikoudi A, Sourtzi P. Εκπαιδευτικές παρεμβάσεις με τη χρήση Τηλεϊατρικής στο Σακχαρώδη Διαβήτη τύ-που II και οι επιπτώσεις τους στο γλυκαιμι-κό έλεγχο. Nursing Care & Research / Nosileia kai Ereuna 2017;9(48):144-68 [in greek].	Language	diabetes
Dobson R, Whittaker R, Pfaeffli Dale L, Maddison R. The effectiveness of text message-based self-management interventions for poorly-controlled diabetes: a systematic review. Digit Health 2017;3(Nov):1-12.	Not RPM (No provider input in monitoring)	diabetes
Duan Y, Xie Z, Dong F, Wu Z, Lin Z, Sun N, et al. Effectiveness of home blood pressure telemonitoring: a systematic review and meta-analysis of randomised controlled studies. J Hum Hypertens 2017;31(7):427-37.	Low/moderate methodological quality	hypertension
Duan YX, Xie ZQ. Effectiveness of home blodd presuure telemonitoring: a systematic review and meta-analysis of randomized controlled studies. J Hypertens 2018;31(7):427-437.	Not systematic review	hypertension
Duke DC, Barry S, Wagner DV, Speight J, Choudhary P, Harris MA. Distal technologies and type 1 diabetes management. Lancet Diabetes Endocrinol 2018;6(2):143-56.	Not systematic review	diabetes
Emtekaer Haesum LK, Ehlers L, Hejlesen O K. Influence of health literacy on outcomes using telehomecare technology: a systematic review. HEALTH EDUC J 2016;75(1):72-83.	Wrong outcome	multiple
Escriva Boulley G, Leroy T, Bernetiere C, Paquienseguy F, Desfriches-Doria O, Preau M. Digital health interventions to help living with cancer: a systematic review of participants' engagement and psychosocial effects. Psychooncology 2018;27(12):2677-86.	Not RPM (No provider input in monitoring; specialist health services)	cancer

Flodgren G, Rachas A, Farmer AJ, Inzitari M, Shepperd S. Interactive telemedicine: effects on professional practice and health care outcomes. Cochrane Database of Systematic Reviews 2015;(9):CD002098.	Search before 2015	multiple
Fridriksdottir N, Gunnarsdottir S, Zoega S, Ingadottir B, Hafsteinsdottir EJG. Effects of web-based interventions on cancer patients' symptoms: review of randomized trials. Support Care Cancer 2018;26(2):337-51.	Not RPM (Specialist health services; or internet-based)	cancer
Gandhi S, Chen S, Hong L, Sun K, Gong E, Li C, et al. Effect of mobile health interventions on the secondary prevention of cardiovascular disease: systematic review and meta-analysis. Can J Cardiol 2017;33(2):219-31.	Not RPM (Specialist health services; no provider input; mobile applications; or internet-based)	cardiovascular disease
Garabedian LF, Ross-Degnan D, Wharam JF. Mobile phone and smartphone technologies for diabetes care and self-management. Curr Diabetes Rep 2015;15(12):109.	Not systematic review	diabetes
Gordon LAN. Assessment of smart watches for management of non-communicable diseases in the ageing population: a systematic review. Geriatr 2018;3(3):56.	Not systematic review	multiple
Gregersen TL, Green A, Frausing E, Ringbaek T, Brondum E, Suppli UC. Do telemedical interventions improve quality of life in patients with COPD? A systematic review. Int J Chron Obstruct Pulmon Dis 2016;11(Apr):809-22.	Not systematic review	chronic obstructive pulmonary disease
Grona SL, Bath B, Busch A, Rotter T, Trask C, Harrison E. Use of videoconferencing for physical therapy in people with musculoskeletal conditions: a systematic review. J Telemed Telecare 2018;24(5):341-55.	Not RPM (exercise monitoring)	musculoskeletal
Gu X, Zhu Y, Zhang Y, Sun L, Bao ZY, Shen JH, et al. Effect of telehealth interventions on major cardiovascular outcomes: a metaanalysis of randomized controlled trials. J Geriatr Cardiol. 2017;14(8):501-8.	Low/moderate methodological quality	cardiovascular disease
Hall AK, Cole-Lewis H, Bernhardt JM. Mobile text messaging for health: a systematic review of reviews. Annu Rev Public Health. 2015;18(36):393-415.	Not RPM (Interventions)	multiple
Hamine S, Gerth-Guyette E, Faulx D, Green BB, Ginsburg AS. Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. J Med Internet Res 2015;17(2):e52.	Not systematic review	multiple
Hanlon P, Daines L, Campbell C, McKinstry B, Weller D, Pinnock H. Telehealth interventions to support self-management of long-term conditions: a systematic metareview of diabetes, heart failure, asthma, chronic obstructive pulmonary disease, and cancer. J Med Internet Res 2017;19(5):e172.	Included systematic reviews not described enough to assess eligibility	multiple
Harerimana B, Forchuk C, O'Regan T. The use of technology for mental healthcare delivery among older adults with depressive symptoms: a systematic literature review. Int J Ment Health Nurs 2019;28(3):657-70.	Not RPM (Interventions)	psychiatric
Health Quality Ontario. Remote monitoring of implantable cardioverter-defibrillators, cardiac resynchronization therapy and permanent pacemakers: a health technology assessment. Ont Health Technol Assess Ser 2018;18(7):1-199.	Not RPM (Specialist health services)	heart failure, abnormal heart rate or rhythm
Heitkemper EM, Mamykina L, Travers J, Smaldone A. Do health information technology self-management interventions improve glycemic control in medically underserved adults with diabetes? A systematic review and meta-analysis. J Am Med Inform Assoc 2017;24(5):1024-35.	Low/moderate methodological quality	diabetes
Honarvar B, Salehi F, Shaygani F, Hajebrahimi M, Homayounfar R, Dehghan S, et al. Opportunities and threats of electronic health in management of diabetes	Included systematic reviews not described	diabetes

mellitus: an umbrella review of systematic review and meta-analysis studies. Shiraz E Medical Journal 2019;20(1).	enough to assess eligibility	
Hong Y, Lee SH. Effectiveness of tele-monitoring by patient severity and intervention type in chronic obstructive pulmonary disease patients: a systematic review and meta-analysis. Int J Nurs Stud 2019;92(apr):1-15.	Low/moderate methodological quality	chronic obstructive pulmonary disease
Hu Y, Wen X, Wang F, Yang D, Liu S, Li P, et al. Effect of telemedicine intervention on hypoglycaemia in diabetes patients: a systematic review and meta-analysis of randomised controlled trials. J Telemed Telecare 2019;25(7):402-13.	Low/moderate methodological quality	diabetes
Huang JW, Lin YY, Wu NY. The effectiveness of telemedicine on body mass index: a systematic review and meta-analysis. J Telemed Telecare 2019;25(7):389-1.	Low/moderate methodological quality	multiple
Huang K, Liu W, He D, Huang B, Xiao D, Peng Y, et al. Telehealth interventions versus center-based cardiac rehabilitation of coronary artery disease: A systematic review and meta-analysis. Eur J Prev Cardiolog 2015;22(8):959-71.	Not RPM (exercise monitoring)	coronary artery disease
Huang Z, Tao H, Meng Q, Jing L. Effects of telecare intervention on glycemic control in type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials. Eur J Endocrinol. 2015; 172(3):93-101.	Search before 2015	diabetes
Inglis SC, Clark RA, Dierckx R, Prieto-Merino D, Cleland JG. Structured telephone support or non-invasive telemonitoring for patients with heart failure. Cochrane Database Syst Rev. 2015;(10):CD007228.	Low/moderate methodological quality	heart failure
Inglis SC, Conway A, Cleland JG, Clark RA. Is age a factor in the success or failure of remote monitoring in heart failure? Telemonitoring and structured telephone support in elderly heart failure patients. Eur J Cardiovasc Nurs 2015;14(3):248-55.	Not systematic review	heart failure
Jayakody A, Bryant J, Carey M, Hobden B, Dodd N, Sanson-Fisher R. Effectiveness of interventions utilising telephone follow up in reducing hospital readmission within 30 days for individuals with chronic disease: a systematic review. BMC Health Serv Res 2016;16(1):403.	Not RPM (Interventions; or in specialist health services)	multiple
Jin K, Khonsari S, Gallagher R, Gallagher P, Clark AM, Freedman B, et al. Telehealth interventions for the secondary prevention of coronary heart disease: a systematic review and meta-analysis. Eur J Cardiovasc Nurs 2019;18(4):260-71.	Not RPM (Interventions; in specialist health services; no provider input; or internet-based)	coronary heart disease
Kalankesh LR, Pourasghar F, Nicholson L, Ahmadi S, Hosseini M. Effect of telehealth interventions on hospitalization indicators: a systematic review. Perspect 2016;13(Fall).	Not systematic review	multiple
Kew KM, Cates CJ. Home telemonitoring and remote feedback between clinic visits for asthma. Cochrane Database of Systematic Reviews 2016;(8):CD011714.	Not RPM (Specialist health services)	asthma
Kew KM, Cates CJ. Remote versus face-to-face check-ups for asthma. Cochrane Database of Systematic Reviews 2016;4:CD011715.	Not RPM (Specialist health services; children; internet-based)	asthma
Kidholm K, Dahl Kristensen MB. Review of high quality economic evaluations of telemedicine. International Journal of Integrated Care (IJIC) 2016;16(5 Supplement):1-2.	Not systematic review	multiple
Kim Y, Park JE, Lee BW, Jung CH, Park DA. Comparative effectiveness of telemonitoring versus usual care for type 2 diabetes: a systematic review and meta-analysis. J Telemed Telecare 2018;25(10):587-1.	Low/moderate methodological quality	diabetes

Kitsiou S, Pare G, Jaana M, Gerber B. Effectiveness of mHealth interventions for patients with diabetes: an overview of systematic reviews. PLoS ONE 2017;12(3).	Included systematic reviews not described enough to assess eligibility	diabetes
Kitsiou S, Pare G, Jaana M. Effects of home telemonitoring interventions on patients with chronic heart failure: an overview of systematic reviews. J Med Internet Res 2015;17(3).	No included systematic reviews meet our definition	diabetes
Klersy C, Boriani G, De Silvestri A, Mairesse GH, Braunschweig F, Scotti V, et al. Effect of telemonitoring of cardiac implantable electronic devices on healthcare utilization: a meta-analysis of randomized controlled trials in patients with heart failure. Eur J Heart Fail 2016;18(2):195-204.	Not RPM (Specialist health services)	heart failure
Knox L, Rahman RJ, Beedie C. Quality of life in patients receiving telemedicine enhanced chronic heart failure disease management: A meta-analysis. J Telemed Telecare 2017;23(7):639-49.	Low/moderate methodological quality	chronic heart failure
Koblauch H, Reinhardt SM, Lissau W, Jensen PL. The effect of telepsychiatric modalities on reduction of readmissions in psychiatric settings: a systematic review. J Telemed Telecare 2018;24(1):31-6.	Not systematic review	psychiatric
Kotb A, Cameron C, Hsieh S, Wells G. Comparative effectiveness of different forms of telemedicine for individuals with heart failure (HF): a systematic review and network meta-analysis. PLoS ONE 2015;10(2).	No included systematic reviews meet our definition	heart failure
Kraft P, Hillmann S, Rucker V, Heuschmann PU. Telemedical strategies for the improvement of secondary prevention in patients with cerebrovascular events-A systematic review and meta-analysis. Int j 2017;12(6):597-605.	Not RPM (Interventions; specialist health services; or internet-based)	stroke
Kruse C, Pesek B, Anderson M, Brennan K, Comfort H. Telemonitoring to manage chronic obstructive pulmonary disease: systematic literature review. JMIR Med Inform 2019;7(1).	Not systematic review	chronic obstructive pulmonary disease
Kruse CS, Soma M, Pulluri D, Nemali NT, Brooks M. The effectiveness of telemedicine in the management of chronic heart disease - a systematic review. JRSM Open 2017;8(3).	Not systematic review	chronic heart disease
Larson JL, Rosen AB, Wilson FA. The effect of telehealth interventions on quality of life of cancer patients: a systematic review and meta-analysis. Telemed J E Health.2018;24(6):397-405.	Not RPM (Specialist health services)	cancer
Lawes-Wickwar S, McBain H, Mulligan K. Application and effectiveness of telehealth to support severe mental illness management: systematic review. JMIR Ment Health 2018;5(4):e62.	Not RPM (Interventions)	psychiatric
Lee JY, Lee SWH. Telemedicine cost-effectiveness for diabetes management: a systematic review. diabetes Technol Ther 2018;20(7):492-00.	Low/moderate methodological quality	diabetes
Lee PA, Greenfield G, Pappas Y. The impact of telehealth remote patient monitoring on glycemic control in type 2 diabetes: a systematic review and meta-analysis of systematic reviews of randomised controlled trials. BMC Health Serv Res 2018;18(1):495.	Low/moderate methodological quality	diabetes
Lee SWH, Chan CKY, Chua SS, Chaiyakunapruk N. Comparative effectiveness of telemedicine strategies on type 2 diabetes management: a systematic review and network meta-analysis. Sci Rep 2017;7(1).	Not systematic review	diabetes
Lee SWH, Ooi L, Lai YK. Telemedicine for the management of glycemic control and clinical outcomes of type 1 diabetes mellitus: a systematic review and meta-analysis of randomized controlled studies. Front Pharmacol 2017;30(8):330.	Not RPM (Specialist health services)	diabetes

Lieber BA, Taylor B, Appelboom G, Prasad K, Bruce S, Yang A, et al. Meta-analysis of telemonitoring to improve HbA1c levels: promise for stroke survivors. J Clin Neurosci 2015;22(5):807-11.	Not systematic review	stroke
Lin MH, Yuan WL, Huang TC, Zhang HF, Mai JT, Wang JF. Clinical effectiveness of telemedicine for chronic heart failure: a systematic review and meta-analysis. J Investig Med 2017;65(5):899-11.	Low/moderate methodological quality	chronic heart failure
Liu L, Stroulia E, Nikolaidis I, Miguel-Cruz A, Rios Rincon A. Smart homes and home health monitoring technologies for older adults: a systematic review. Int J Med Inf 2016;91(Jul):44-59.	Wrong outcome	multiple
Liu P, Li G, Jiang S, Liu Y, Leng M, Zhao J, et al. The effect of smart homes on older adults with chronic conditions: A systematic review and meta-analysis. Geriatr Nurs 2019;40(5):522-30.	Low/moderate methodological quality	multiple
Long G. Impact of Home Telemonitoring on 30-Day Hospital readmission rates for patients with heart failure: a systematic review. MEDSURG Nursing 2017;26(5):337-43.	Not systematic review	heart failure
Loo Gee B, Griffiths KM, Gulliver A. Effectiveness of mobile technologies delivering Ecological Momentary Interventions for stress and anxiety: a systematic review. J Am Med Inform Assoc 2016;23(1):221-9.	Not RPM (Interventions)	psychiatric
Lopez-Villegas A, Catalan-Matamoros D, Martin-Saborido C, Villegas-Tripiana I, Robles-Musso E. A systematic review of economic evaluations of pacemaker telemonitoring systems. Rev Esp Cardiol (Engl) 2016;69(2):125-33.	Not RPM (Specialist health services)	cardiovascular disease
Lundell S, Holmner A, Rehn B, Nyberg A, Wadell K. Telehealthcare in COPD: a systematic review and meta-analysis on physical outcomes and dyspnea. Respir Med 2015;109(1):11-26.	Not RPM (Interventions)	chronic obstructive pulmonary disease
Ma Y, Cheng HY, Cheng L, Sit JWH. The effectiveness of electronic health interventions on blood pressure control, self-care behavioural outcomes and psychosocial well-being in patients with hypertension: a systematic review and meta-analysis. Int J Nurs Stud 2019;92(apr):27-46.	Low/moderate methodological quality	hypertension
Mani S, Sharma S, Omar B, Paungmali A, Joseph L. Validity and reliability of internet-based physiotherapy assessment for musculoskeletal disorders: a systematic review. J Telemed Telecare 2017;23(3):379-91.	Not RPM (exercise monitoring)	musculoskeletal
Marcolino MS, Oliveira JAQ, D'Agostino M, Ribeiro AL, Alkmim MBM, Novillo-Ortiz D. The impact of mHealth interventions: systematic review of systematic reviews. JMIR Mhealth Uhealth 2018;6(1):e23.	No included systematic reviews meet our definition	multiple
McCabe C, McCann M, Brady AM. Computer and mobile technology interventions for self-management in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017;5:CD011425.	Not RPM (No provider input in monitoring)	chronic obstructive pulmonary disease
McLean G, Murray E, Band R, Moffat KR, Hanlon P, Bruton A, et al. Interactive digital interventions to promote self-management in adults with asthma: systematic review and meta-analysis. BMC polm 2016;16(1).	Not RPM (No provider input)	asthma
Michaud TL, Zhou J, McCarthy MA, Siahpush M, Su D. Costs of home-based telemedicine programs: a systematic review. Int J Technol Assess Health Care 2018;34(4):410-8.	Not systematic review	multiple
Miller L, Schuz B, Walters J, Walters EH. Mobile Technology interventions for asthma self-management: systematic review and meta-analysis. JMIR Mhealth Uhealth 2017;5(5).	Not RPM (No provider input in monitoring)	asthma

Murphy LA, Harrington P, Taylor SJ, Teljeur C, Smith SM, Pinnock H, et al. Clinical-effectiveness of self-management interventions in chronic obstructive pulmonary disease: an overview of reviews. Chron 2017;14(3):276-88.	Included systematic reviews not described enough to assess eligibility	chronic obstructive pulmonary disease
Mushcab H, Kernohan WG, Wallace J, Martin S. Web-based remote monitoring systems for self-managing type 2 diabetes: a systematic review. Diabetes Technol Ther 2015;17(7):498-509.	Not systematic review	diabetes
O'Brien KM, Hodder RK, Wiggers J, Williams A, Campbell E, Wolfenden L, et al. Effectiveness of telephone-based interventions for managing osteoarthritis and spinal pain: a systematic review and meta-analysis. Peerj 2018;6:e5846.	Not RPM (Interventions)	osteoporosis
O'Connor M, Munnelly A, Whelan R, McHugh L. The efficacy and acceptability of third-wave behavioral and cognitive eHealth treatments: a systematic review and meta-analysis of randomized controlled trials. Behav 2018;49(3):459-75.	Not RPM (Interventions)	multiple
Palm U, Kumpf U, Behler N, Wulf L, Kirsch B, Worsching J, et al. Home use, remotely supervised, and remotely controlled transcranial direct current stimulation: a systematic review of the available evidence. Neuromodulation 2018;21(4):323-33.	Not systematic review	psychiatric
Pandor A, Gomersall T, Stevens JW, Wong R. Remote monitoring strategies for patients with stable heart failure: a systematic review and network meta-analysis.Value Health 2015;18(3).	Not systematic review	heart failure
Park DA, Yun JE, Park JE. Comparative safety and effectiveness of telemonitoring intervention versus usual care for heart failure: A systematic review and meta-analysis. Value Health 2016;19(7).	Not systematic review	heart failure
Parthiban N, Esterman A, Mahajan R, Twomey DJ, Pathak RK, Lau DH, et al. Remote monitoring of implantable cardioverter-defibrillators: a systematic review and meta-analysis of clinical outcomes. J Am Coll Cardiol 2015;65(24):2591-600.	Not systematic review	diabetes
Pedone C, Lelli D. Systematic review of telemonitoring in COPD: an update. Pneumonol Alergol Pol 2015;83(6):476-84.	Not systematic review	chronic obstructive pulmonary disease
Pekmezaris R, Tortez L, Williams M, Patel V, Makaryus A, Zeltser R, et al. Home telemonitoring in heart failure: a systematic review and meta-analysis. Health Aff (Millwood) 2018;37(12):1983-9.	Not systematic review	chronic obstructive pulmonary disease
Peretz D, Arnaert A, Ponzoni NN. Determining the cost of implementing and operating a remote patient monitoring programme for the elderly with chronic conditions: a systematic review of economic evaluations. J Telemed Telecare 2018;24(1):13-21.	Not systematic review	multiple
Pfaeffli Dale L, Dobson R, Whittaker R, Maddison R. The effectiveness of mobile-health behaviour change interventions for cardiovascular disease self-management: a systematic review. Eur J Prev Cardiolog 2016;23(8):801-17.	Not RPM (Specialist health services; no provider input; or internet-based)	multiple
Piga M, Cangemi I, Mathieu A, Cauli A. Telemedicine for patients with rheumatic diseases: systematic review and proposal for research agenda. Semin Arthritis Rheum 2017;47(1):121-8.	Not RPM (Specialist health services)	rheumatic diseases
Porter J, Huggins CE, Truby H, Collins J. The Effect of using mobile technology-based methods that record food or nutrient intake on diabetes control and nutrition outcomes: a systematic review. Nutrients 2016;8(12):815.	Not RPM (No provider input)	musculoskeletal

Queiros A, Alvarelhao J, Cerqueira M, Silva AG, Santos M, Rocha NP. Remote care technology: a systematic overview. Stud Health Technol Inform 2017;242:111-8.	Not systematic review	diabetes
Queiros A, Alvarelhao J, Cerqueira M, Silva AG, Santos M, Rocha NP. Remote Care Technology: A Systematic Overview. Stud Health Technol Inform 2017;242:111-8.	Not systematic review	multiple
Rawstorn JC, Gant N, Direito A, Beckmann C, Maddison R. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. Heart 2016;102(15):1183-92.	Not RPM (exercise monitoring)	multiple
Rintala A, Paivarinne V, Hakala S, Paltamaa J, Heinonen A, Karvanen J, et al. Effectiveness of technology-based distance physical rehabilitation interventions for improving physical functioning in stroke: a systematic review and meta-analysis of randomized controlled trials. Arch Phys Med Rehabil 2019;100(7):1339-58.	Not RPM (exercise monitoring)	multiple
Rush KL, Howlett L, Munro A, Burton L. Videoconference compared to telephone in healthcare delivery: A systematic review. Int J Med Inf 2018;118(oct):44-53.	Wrong outcome	stroke
Saeed N, Manzoor M, Khosravi P. An exploration of usability issues in telecare monitoring systems and possible solutions: a systematic literature review. Disabil 2019;Feb 22 [Epub ahead of print]	Wrong outcome	multiple
Sandran N, Hillier S, Hordacre B. Strategies to implement and monitor in-home transcranial electrical stimulation in neurological and psychiatric patient populations: a systematic review. J Neuroengineering Rehabil 2019;16(1):58.	Not RPM (Device fitting/monitoring)	multiple
Santiago de Araújo Pio C, Chaves GS, Davies P, Taylor RS, Grace SL. Interventions to promote patient utilisation of cardiac rehabilitation. The Cochrane database of systematic reviews 2019;2:CD007131.	Wrong outcome	psychiatric
Sarfo FS, Ulasavets U, Opare-Sem OK, Ovbiagele B. Tele-rehabilitation after stroke: an updated systematic review of the literature. J Stroke Cerebrovasc Dis 2018;27(9):2306-18.	Not systematic review	stroke
Schroder J, van Criekinge T, Embrechts E, Celis X, Van Schuppen J, Truijen S, et al. Combining the benefits of tele-rehabilitation and virtual reality-based balance training: a systematic review on feasibility and effectiveness. Disabil 2019;14(1):2-11.	Not RPM (exercise monitoring)	stroke
Seiler A, Klaas V, Troster G, Fagundes CP. eHealth and mHealth interventions in the treatment of fatigued cancer survivors: a systematic review and meta-analysis. Psychooncology 2017;26(9):1239-53.	Not RPM (Interventions)	stroke
Seppala J, De Vita I, Jamsa T, Miettunen J, Isohanni M, Rubinstein K, et al. Mobile phone and wearable sensor-based mHealth approaches for psychiatric disorders and symptoms: systematic review. JMIR Ment Health 2019;6(2).	Not systematic review	cancer
Shahaj O, Denneny D, Schwappach A, Pearce G, Epiphaniou E, Parke HL, et al. Supporting self-management for people with hypertension: a meta-review of quantitative and qualitative systematic reviews. J Hypertens 2019;37(2):264-79.	No included systematic reviews meet our definition	psychiatric
Shen Y, Wang FB, Zhang X, Zhu XR, Sun QD, Fisher E, et al. Effectiveness of internet-based interventions on glycemic control in patients with type 2 diabetes: meta-analysis of randomized controlled trials. J Med Internet Res 2018;20(5): e172.	Low/moderate methodological quality	diabetes
Shigekawa E, Fix M, Corbett G, Roby DH, Coffman J. The current state of telehealth evidence: a rapid review. Health Aff (Millwood) 2018;37(12):1975-82.	Not systematic review	hypertension

Singh TP, Vangaveti VN, Kennedy RL, Malabu UH. Role of telehealth in diabetic foot ulcer management -a systematic review. Aust J Rural Health 2016;24(4):224-9.	Not systematic review	multiple
Slev VN, Mistiaen P, Pasman HR, Verdonck-de Leeuw IM, van Uden-Kraan CF, Francke AL. Effects of eHealth for patients and informal caregivers confronted with cancer: a meta-review. Int J Med Inf 2016;87:54-67.	Not RPM (Interventions; not remote; or in specialist health services)	diabetes
So CF, Chung J. Telehealth for diabetes self-management in primary healthcare - a systematic review and meta-analysis. J Telemed Telecare 2018; 24(5):356-64.	Low/moderate methodological quality	diabetes
Su D, McBride C, Zhou J, Kelley MS. Does nutritional counseling in telemedicine improve treatment outcomes for diabetes? A systematic review and meta-analysis of results from 92 studies. J Telemed Telecare 2016;22(6):333-47.	Not systematic review	cancer
Su D, Zhou J, Kelley MS, Michaud TL, Siahpush M, Kim J, et al. Does telemedicine improve treatment outcomes for diabetes? A meta-analysis of results from 55 randomized controlled trials. Diabetes Res Clin Pract 2016;116 (jun):136-48.	Low/moderate methodological quality	diabetes
Suh SR, Lee MK. Effects of nurse-led telephone-based supportive interventions for patients with cancer: a meta-analysis. Oncol Nurs Forum 2017;44(4):168-84.	Not RPM (Specialist health services)	diabetes
Sul AR, Lyu DH, Park DA. Effectiveness of telemonitoring versus usual care for chronic obstructive pulmonary disease: a systematic review and meta-analysis. J Telemed Telecare 2018 Dec 12:[Epub ahead of print].	Low/moderate methodological quality	chronic obstructive pulmonary disease
Tao KFM, Brennan-Jones CG, Capobianco-Fava DM, Jayakody DMP, Friedland PL, Swanepoel D, et al. Teleaudiology services for rehabilitation with hearing aids in adults: a systematic review. J Speech Lang Hear Res 2018;61(7):1831-49.	Not RPM (Device fitting/monitoring)	cancer
Tchero H, Kangambega P, Briatte C, Brunet-Houdard S, Retali GR, Rusch E. Clinical effectiveness of telemedicine in diabetes mellitus: a meta-analysis of 42 randomized controlled trials. Telemed J E Health 2019;25(7):569-83.	Low/moderate methodological quality	diabetes
Tchero H, Noubou L, Becsangele B, Mukisi-Mukaza M, Retali GR, Rusch E. Telemedicine in diabetic foot care: a systematic literature review of interventions and meta-analysis of controlled trials. Int 2017;16(4):274-83.	Not RPM (Specialist health services)	impaired hearing
Tchero H, Tabue Teguo M, Lannuzel A, Rusch E. Telerehabilitation for stroke survivors: systematic review and meta-analysis. J Med Internet Res 2018;20(10):e10867.	Not RPM (exercise monitoring; interventions)	stroke
Triberti S, Savioni L, Sebri V, Pravettoni G. eHealth for improving quality of life in breast cancer patients: A systematic review. Cancer Treat Rev 2019;74(Mar):1-14.	Not RPM (Interventions; or in specialist health services)	diabetes
Tse G, Chan C, Gong M, Meng L, Zhang J, Su XL, et al. Telemonitoring and hemodynamic monitoring to reduce hospitalization rates in heart failure: a systematic review and meta-analysis of randomized controlled trials and real-world studies. J Geriatr Cardiol;15(4):298-09.	Low/moderate methodological quality	heart failure
Unni E, Gabriel S, Ariely R. A review of the use and effectiveness of digital health technologies in patients with asthma. Ann Allergy Asthma Immunol 2018;121(6):680-91.	Not systematic review	cancer
Valenzuela Espinoza A, Steurbaut S, Dupont A, Cornu P, van Hooff RJ, Brouns R, et al. Health economic evaluations of digital health interventions for secondary prevention in stroke patients: a systematic review. Cerebrovasc 2019;9(1):1-8.	Not systematic review	asthma

Vargas G, Cajita MI, Whitehouse E, Han HR. Use of short messaging service for hypertension management a systematic review. J Cardiovasc Nurs 2017;32(3):260-70.	Low/moderate methodological quality	hypertension
Vegesna A, Tran M, Angelaccio M, Arcona S. Remote patient monitoring via non-invasive digital technologies: a systematic review. Telemedicine Journal & E-Health 2017;23(1):3-17.	No effect sizes	stroke
Wang X, Shu W, Du J, Du M, Wang P, Xue M, et al. Mobile health in the management of type 1 diabetes: a systematic review and meta-analysis. BMC Endocr Disord 2019;19(1):21.	Not RPM (Specialist health services)	diabetes
Wang Y, Xue H, Huang Y, Huang L, Zhang D. A systematic review of application and effectiveness of mHealth interventions for obesity and diabetes treatment and self-management. Adv Nutr (Bethesda) 2017;8(3):449-62.	Not systematic review	multiple
Wei J, Zheng H, Wang L, Wang Q, Wei F, Bai L. Effects of telephone call intervention on cardiovascular risk factors in type 2 diabetes mellitus: A meta-analysis. J Telemed Telecare 2017: 25(2):93-105.	Not RPM (Interventions)	diabetes
Yang Q, Van Stee SK. The Comparative Effectiveness of Mobile Phone Interventions in Improving Health Outcomes: Meta-Analytic Review. JMIR Mhealth Uhealth 2019;7(4):e11244.	Not systematic review	diabetes
Yang S, Jiang Q, Li H. The role of telenursing in the management of diabetes: a systematic review and meta-analysis. Public health nursing: 36(4):575-586.	Not RPM (Specialist health services)	diabetes
Yasmin F, Banu B, Zakir SM, Sauerborn R, Ali L, Souares A. Positive influence of short message service and voice call interventions on adherence and health outcomes in case of chronic disease care: a systematic review. BMC Med Inf Decis Mak 2016;16(Apr):46.	Not systematic review	multiple
Yoshida Y, Boren SA, Soares J, Popescu M, Nielson SD, Simoes EJ. Effect of health information technologies on glycemic control among patients with type 2 diabetes. Curr Diabetes Rep 2018;18(12):11.	Low/moderate methodological quality	diabetes
Yun JE, Park JE, Park HY, Lee HY, Park DA. Comparative effectiveness of telemonitoring versus usual care for heart failure: a systematic review and meta-analysis. J Card Fail 2018;24(1):19-28.	Low/moderate methodological quality	heart failure
Zhang Q, Zhang L, Yin R, Fu T, Chen H, Shen B. Effectiveness of telephone-based interventions on health-related quality of life and prognostic outcomes in breast cancer patients and survivors: a meta-analysis. Eur J Cancer Care (Engl) 2018;27(1):1-10.	Not RPM (Interventions; not remote; or inspecialist health services)	multiple
Zhao J, Zhai YK, Zhu WJ, Sun DX. Effectiveness of telemedicine for controlling asthma symptoms: a systematic review and meta-analysis. Telemed J E Health. Health 2015;21(6):484-92.	Not RPM (Interventions; specialist health services; no provider input; or internet-based)	cancer
Ντικούδη Α, Σουρτζή Π. Εκπαιδευτικές Παρεμβάσεις στον Σακχαρώδη Διαβήτη Τύπου 2 με τη Χρήση Τηλεϊατρικής: Οι Επιδράσεις τους στην Αυτοδιαχείριση της Νόσου και στην Ποιότητα Ζωής των Ασθενών. Nosileftiki 2017;56(3):187-200 [in greek].	No effect sizes	asthma

Appendix 3. Characteristics of included systematic reviews and RCTs

We used NIPH's checklist of systematic reviews to evaluate the included review' methodological quality. One question (9) regarding the authors' conclusions was not possible to answer, as review authors did not discuss individual RCTs, leaving eight questions and a summary evaluation.

1. Do the authors clearly describe the methods they used to identify primary studies?
2. Was the literature search conducted satisfactory/thorough?
3. Do the authors describe which criteria they used to determine which studies to include (study design, participants, intervention, outcome)?
4. Were attempts made to reduce systematic bias during the study selection phase (explicit inclusion/exclusion criteria, selection made by multiple independent persons)?
5. Were criteria to assess the internal validity of studies clearly described?
6. Was the validity of the studies evaluated (either during inclusion or analysis of primary studies) using relevant criteria?
7. Are the methods used when the results were summarized clearly described?
8. Were the results of the studies properly summarized?

Appendix Table 3.2 Evaluation of the included reviews' methodological quality

Review	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Summary**
Bittner et al. 2015	Yes	Yes	Yes	Yes	Yes	N/A	Yes	N/A	High
Faruque et al. 2017	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Kebede et al. 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Posadzki et al. 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High

Appendix Table 3.3 RCTs mapped to systematic reviews

	Systematic review			
RCT	Bittner et al. 2015	Faruque et al. 2017	Kebede et al. 2018	Posadzki et al. 2016
Carter et al. 2011		X		
Dario et al. 2017			X	
Egede et al. 2017			X	
Magid et al. 2011				X
Nicolucci et al. 2015		X		
Rodriguez-Idigoras et al. 2009		X		
Schillinger et al. 2009		X		
Steventon et al. 2014		X		

Stone et al. 2010		X		
Wakefield et al. 2011		X		
Wild et al. 2016			X	
Total RCTs	0	7	3	1

Appendix Table 3.4 Description of included RCTs

Carter et al. 2011

Methods	Randomized controlled trial
Participants	**Description**: N=74 African American adults (mean age 51), HbA1C 8.9%, average blood pressure 147/88. BMI 35.8, 64% female. Comorbidities not reported. **Inclusion criteria:** Type 2 diabetes, 18 years or older, residing in the target area, having a primary care physician willing to participate in the project or being willing to be assigned to a participating primary care physician in their community, being African American, and having the ability to read at an eighth grade level or higher. **Exclusion criteria:** Visually or hearing impaired; non-English-speaking; dialysis requiring (because their disease is too far advanced for them to benefit from the proposed diabetes self-management program); and reliance on psycho-tropic medication (because their mental illness could lead to behavioral issues relative to treatment adherence that are beyond the scope of the proposed diabetes self-management program). **Context**: An urban primary care practice in USA.
Intervention	*Provider-assisted telehealth self-management*, 9 months.
Comparison	Usual care: contact with providers.
Outcomes	HbA1c, BMI, systolic blood pressure, diastolic blood pressure

Dario et al. 2017

Methods	Randomized controlled trial
Participants	N=299 adults (mean age 73). Comorbidities: 4.7% stroke, 6.3% COPD, 3.7% connective tissue disease, 8.3% renal disease. **Inclusion criteria:** Diabetes type II, HbA1c > 7% **Exclusion criteria:** Severe comorbidities with life expectancy <12 months, pregnancy, being cognitively unable to participate, and impossibility or inability to use the devices provided or to complete questionnaires in the native language **Context**: Local Health Authority in the Veneto Region of northern Italy.
Intervention	*Telemonitoring*, 12 months.
Comparison	Usual care: contact with providers, measured HbA1c using paper logbooks and shared these logs with providers during visits (unspecified frequency). Telehealth device operators routinely called patients for an overall health check.
Outcomes	Quality of life (SF-12/36), primary care physical visits with procedures, HbA1c, bed days for hospitalized patients (all-cause), bed days for hospitalized patients (diabetes-related), emergency department visit, outpatient visit with diabetologist, outpatient visit with procedures with diabetologist, HADS anxiety scale, HADS depression scale

Egede et al. 2017

Methods	Randomized controlled trial
Participants	N=113 adults (mean age 54). Average duration of diabetes type 2: 12.2 years. BMI 35.6, 28.6% male. Comorbidities: not reported. **Inclusion criteria:** type 2 diabetes and HbA1c ≥8%, 18 years of age or older, receiving care within a participating health center. **Exclusion criteria:** showed mental confusion on interview suggesting significant dementia, participating in other diabetes clinical trials, alcohol or drug abuse/dependency, active psychosis or acute mental disorder, life expectancy <6 months, pregnant and/or lactating females. **Context**: rural United States, recruited from health centers for low-income people.
Intervention	*Telehealth system monitoring*, 6 months
Comparison	Usual care: contact with providers. Specifically, providers determined treatment parameters, changed treatment regimens, or scheduled follow-up visits, in addition to three scheduled visits for data collection. Patients initiated contact between scheduled visits. Nurses followed up patients with abnormal results.
Outcomes	HbA1c

Magid et al. 2011

Methods	Randomized controlled trial
Participants	N=338 adults (mean age 66). 65% white, 65% male. Comorbidities: 46.4% diabetes or chronic renal disease. **Inclusion criteria:** patients with hypertension who were taking ≤ 4 antihypertensive medications and who had elevations in 2 of the 3 most recent electronic blood pressure measurements (>140 mm Hg for systolic or >90 mm Hg for diastolic; for patients with diabetes mellitus or chronic kidney disease, >130 mm Hg for systolic or >80 mm Hg for diastolic). **Exclusion criteria:** none reported. **Context**: three healthcare systems in Denver, USA, including a large health maintenance organization, a Veterans Affairs medical center, and a county hospital.
Intervention	*Home measurement reporting*, 6 months
Comparison	Usual care: patients received an educational pamphlet about hypertension and instructions to follow up with their provider.
Outcomes	systolic blood pressure, diastolic blood pressure, blood pressure normalization

Nicolucci et al. 2015

Methods	Randomized controlled trial
Participants	N=302 adults (mean age 58), diabetes type 2 for an average of 8.5 years. BMI 28.9. 62% male. Comorbidities: 75.9% hypertension; 43.8% dyslipidemia; 6.8% coronary heart disease; 3.6% congestive heart failure; 2.4% stroke/TIA; 5.6% myocardial infarction.

	Inclusion criteria: Type 2 diabetes; HbA1c between 7.5% and 10%; age >45 years; in treatment with sulfonylureas, alone or in association with other oral hypoglycemic agents, or treated with basal insulin, alone or in association with oral hypoglycemic agents; able to perform blood glucose self-monitoring; blood pressure >130/80mm Hg regardless of the presence of antihypertensive treatment. **Exclusion criteria:** Diabetes mellitus treated only with lifestyle intervention, or with monotherapy with metformin, glitazones, dipeptidyl peptidase-4 inhibitors, or glucagon-like peptide-1 analogs; multiple injections of insulin; mental conditions, depression, or high anxiety such as to render the subject incapable of understanding the nature, purpose, and possible consequences of the study; inability to use the telemedicine system; pregnancy; major cardiovascular event in the last 6 months (heart attack, stroke, intervention of coronary, carotid, or peripheral vascular reperfusion/revascularization); any serious health condition that substantially reduces life expectancy; any disease or condition, including abuse of drugs or alcohol, that in the opinion of the investigator could interfere with the completion of the study; non-adherence to the protocol (e.g., unreliability, inability to attend follow-up visits, and unlikely to complete the study procedures). **Context**: Two health districts in Italy.
Intervention	*Home telehealth*, 12 months
Comparison	Usual care: follow-up by provider.
Outcomes	HbA1c, achieved target HbA1c, Systolic blood pressure, diastolic blood pressure, quality of life (SF-12/36), cholesterol, participants with specialist visits, participants with hospitalizations or emergency room visits, participants with home visits, triglycerides

Rodriquez-Idigoras et al. 2009

Methods	Randomized controlled trial
Participants	N=328 adults (mean age 64 years), diabetes type for an average of 10.7 years. 78.4% obese, 48% female. Comorbidities: 69.2% hypertension; 39.0% dyslipidemia. **Inclusion criteria:** Type 2 diabetes, >30 years, on a self-monitoring plan for at least 6 months before the beginning of the study. **Exclusion criteria:** Patients with difficulties in using the system because of the number and severity of their complications and comorbidities of diabetes, as well as those who required a caregiver. **Context**: one province in Spain.
Intervention	*Teleassistance* and *telemedicine*, 12 months
Comparison	Usual care: not described. Usual contact with provider is implied.
Outcomes	HbA1c

Schillinger et al. 2009

Methods	Randomized controlled trial

Participants	N=226 adults (mean age 56) with diabetes type 2 for an average of 9.8 years. 57% female. Comorbidities: not reported. **Inclusion criteria:** Type 2 diabetes; HbA1c ≥8.0%; >17 years; speaks English, Spanish, or Cantonese; at least 1 primary care visit in the preceding 12 months. **Exclusion criteria:** Moderate to severe dementia, psychotic illness, end-stage renal disease, were not expected to live through the year, anticipated travel of >3 months in upcoming year, too ill or unable to travel to a group medical visit, no phone access, self-reported hearing impairment, visual acuity of >20/100, or inability to follow instructions on a telephone keypad. **Context**: four safety net clinics in San Francisco, USA.
Intervention	*Self-Management Support* and usual care, 9 months (outcome data collected there months after completion)
Comparison	Usual care: encouragement to visit providers.
Outcomes	Systolic blood pressure, diastolic blood pressure, HbA1c, BMI, cost-effectiveness

Steventon et al. 2014

Methods	Cluster randomized controlled trial
Participants	N=513 adults (mean age 65). BMI 31.1; 42% female. Comorbidities: Comorbidity: 14.2% COPD; 10.9% ischemic heart disease; 12.9% heart failure. **Inclusion criteria:** age 18 years or over, received pharmacological treatment for at least one year, diagnosis of diabetes type 2 as index condition. (This study analyzed a subset of a larger study that included patients with either diabetes type 1 or 2, heart failure, or chronic obstructive pulmonary disease). **Exclusion criteria:** not understanding the instructions for the equipment provided in English, or living in a home unsuitable for telehealth (for example, with inadequate telephone line connection). Patients with additional co-morbidities were not excluded. **Context**: three sites in England considered representative of the range of local health and social care systems (Cornwall, Kent, Newham in East London).
Intervention	*Telehealth* and usual care, 12 months.
Comparison	Usual care: contact with providers. May have included self-monitoring of HbA1c for some patients, but without the telehealth system.
Outcomes	HbA1c, achieved target HbA1c

Stone et al. 2010

Methods	Randomized controlled trial
Participants	N=150 adults (median age 59). 52% white, 99% male. Comorbidities: 35.7% coronary artery disease; 16.1% congestive heart failure, 7.3% COPD.

	Inclusion criteria: Diabetes type 2 for >12 months; HbA1c ≥7.5%; had at least one outpatient visit in a primary care clinic between 1 June 2004 and 31 December 2005, were aged <80 years, received pharmacological treatment for diabetes for ≥12 months, had no referrals to the local diabetes clinic in the preceding 18 months. **Exclusion criteria:** life expectancy of <6 months, participating in another study, resided in an institutional setting, or did not have a land-based, analog home telephone line as required for the home telemonitoring device used. **Context**: Veterans Administration primary care clinics around Pittsburgh, USA.
Intervention	*Home telemonitoring*, 6 months
Comparison	Monthly telephone contact with a diabetes nurse educator: patients kept logs of daily measurements (no further details) and discussed measurements and compliance with nurses.
Outcomes	HbA1c, systolic blood pressure, diastolic blood pressure, cholesterol, triglycerides

Wakefield et al. 2011

Methods	Randomized controlled trial
Participants	N=302 patients (mean age 68). BMI 33.5, 98% male and 96% white. Comorbidities: not reported. **Inclusion criteria:** coexisting diabetes II and hypertension, HbA1c >7%, a landline telephone in the home, receipt of primary care from the veterans administration in the previous 12 months, and anticipation of receiving primary care for the duration of study enrollment. **Exclusion criteria:** legally blind, residing in a long-term care facility, diagnoses indicating dementia or psychosis. **Context**: Veterans Administration medical center in Iowa City, USA, which provides care for 36,000 veterans.
Intervention	*Home telehealth* and *remote monitoring*, 6 months
Comparison	Usual care: scheduled follow-up appointments with the primary care clinic in the usual manner, and had access to the study nurse.
Outcomes	Systolic blood pressure, HbA1c

Wild et al. 2016

Methods	Randomized controlled trial
Participants	N=321 adults (mean age 61) with type 2 diabetes for an average of 7.2 years. BMI 32.9, 33% female. Comorbidities: not reported. **Inclusion criteria:** type 2 diabetes managed in family practice, >17 years, availability of a mobile telephone signal at home, and poor glycemic control, defined as HbA1c >58 mmol/mol (>7.5%). **Exclusion criteria:** blood pressure >210/135 mmHg, hypertension or renal disease managed in secondary care, treatment for a cardiac event or other life-threatening illness within the previous 6 months, major surgery within the last 3 months, atrial fibrillation unless successfully treated or cardioverted, inability to use self-monitoring equipment, pregnancy. **Context**: Recruited from family practices in United Kingdom.

Intervention	*Supported telemonitoring*, 9 months
Comparison	Usual care: Usual diabetes care in family practice is financially incentivized in the UK with targets set on a sliding scale of rewards for glycemic and blood pressure control. Well-controlled patients are reviewed at least once a year, but more frequent reviews are performed for people who have poor glycemic or blood pressure control.
Outcomes	HbA1c, systolic blood pressure, cholesterol, total HADS score, EQ-5D, general practitioner attendance count, practice nurse attendance count, emergency department visits, all-cause hospitalization, daytime ambulatory blood pressure, diabetes knowledge

Appendix 4. Assessing quality of documentation by GRADE

Appendix Table 4.5

Certainty assessment								№ of patients	
Outcome	№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	RPM	Usual care
HbA1c	10	randomised trials	not serious	not serious	serious [a]	not serious	none	1138	1054
Systolic blood pressure	7	randomised trials	not serious	not serious	serious [a]	not serious	none	689	718
Diastolic blood pressure	6	randomised trials	not serious	not serious	serious [b]	serious [c]	none	592	615
Cholesterol	3	randomised trials	not serious	serious [c]	not serious	serious [d]	none	323	341
Participants with hospitalizations or ER visits (all-cause)	1	randomised trials	serious [e]	serious [f]	not serious	not serious	none	11/114 (9.6%)	14/135 (10.4%)
Quality of life (SF-12/SF-36) mental health component	3	randomised trials	serious [h]	not serious	not serious	serious [i]	none	381	317
Quality of life (SF-12/SF-36) physical health component	3	randomised trials	serious [g]	not serious	not serious	serious [d]	none	381	317
Total HADS score	1	randomised trials	not serious	serious [g]	not serious	serious [j]	none	130	127

Explanations

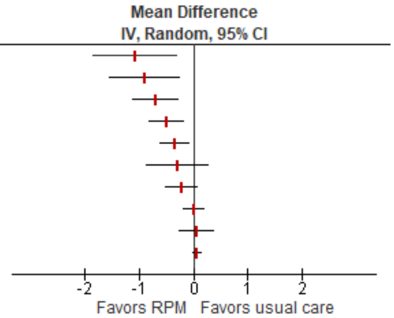
a. In four RCTs, patients differed significantly from the Norwegian patient population (e.g. American war veterans, urban poor, only men)
b. In two RCTs, patients differed significantly from the Norwegian patient population (e.g. American war veterans, urban poor, only men)
c. Effect estimates favor both RPM and usual care.
d. Wide confidence intervals, with studies showing both a moderately negative effect and a moderately positive effect
e. Likely bias related to study funding
f. One study
g. Performance bias, detection bias, attrition bias, and other bias.
h. Wide confidence interval and small number of participants.

Appendix 5. Further results

Forest plots displaying raw data values.

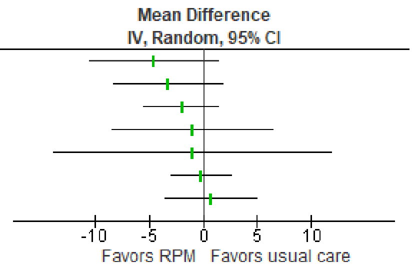
Appendix Figure 1 Forest plot of HbA1c [%]

Study or Subgroup	Mean Difference	SE	RPM Total	Usual care Total	Mean Difference IV, Random, 95% CI
Carter 2011	-1.08	0.3878	26	21	-1.08 [-1.84, -0.32]
Egede 2017	-0.9	0.3265	59	54	-0.90 [-1.54, -0.26]
Stone 2010	-0.7	0.2137	64	73	-0.70 [-1.12, -0.28]
Wild 2016	-0.5	0.1599	146	139	-0.50 [-0.81, -0.19]
Nicolucci 2015	-0.34	0.1332	114	135	-0.34 [-0.60, -0.08]
Schillinger 2009	-0.3	0.2876	101	103	-0.30 [-0.86, 0.26]
Steventon 2014	-0.23	0.1475	266	191	-0.23 [-0.52, 0.06]
Dario 2017	0	0.0918	168	78	0.00 [-0.18, 0.18]
Rodriguez Idigoras 2009	0.05	0.1574	146	151	0.05 [-0.26, 0.36]
Wakefield 2011	0.06	0.0411	93	107	0.06 [-0.02, 0.14]



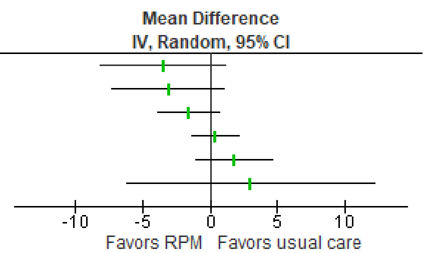
Appendix Figure 2 Forest plot of systolic blood pressure [mmHg]

Study or Subgroup	RPM Mean	RPM SD	RPM Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
Schillinger 2009	136.9	20.4	107	141.5	23.9	108	-4.60 [-10.54, 1.34]
Wakefield 2011	133.08	19.4	97	136.34	17	103	-3.26 [-8.33, 1.81]
Wild 2016	134.2	14.3	143	136.2	14.7	133	-2.00 [-5.43, 1.43]
Stone 2010	132	24.3	64	133	19	73	-1.00 [-8.38, 6.38]
Carter 2011	139	20.4	26	140	23.9	21	-1.00 [-13.88, 11.88]
Nicolucci 2015	135.7	9.6	114	135.9	12.4	135	-0.20 [-2.94, 2.54]
Magid 2011	137.4	19.4	138	136.7	17	145	0.70 [-3.56, 4.96]



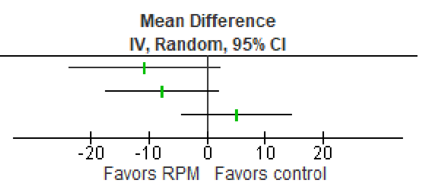
Appendix Figure 3 Forest plot of diastolic blood pressure [mmHg]

Study or Subgroup	RPM Mean	RPM SD	RPM Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
Stone 2010	72.4	14.6	64	75.9	13.2	73	-3.50 [-8.19, 1.19]
Schillinger 2009	75.4	12.3	107	78.5	18.5	108	-3.10 [-7.30, 1.10]
Wild 2016	79	9.6	143	80.6	10.2	133	-1.60 [-3.94, 0.74]
Nicolucci 2015	79.6	7.2	114	79.2	7	135	0.40 [-1.37, 2.17]
Magid 2011	82.9	12.9	138	81.1	11.7	145	1.80 [-1.07, 4.67]
Carter 2011	75	12.3	26	72	18.5	21	3.00 [-6.22, 12.22]



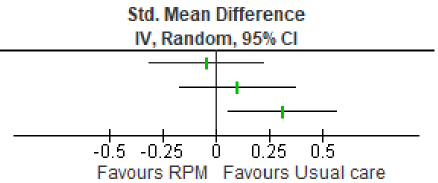
Appendix Figure 4 Forest plot of cholesterol [mg/dl]

Study or Subgroup	RPM Mean	RPM SD	RPM Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
Stone 2010	148.2	40.2	64	159.1	37.2	73	-10.90 [-23.93, 2.13]
Wild 2016	158.55	34.8	145	166.28	46.4	133	-7.73 [-17.44, 1.98]
Nicolucci 2015	184	40	114	179	35	135	5.00 [-4.42, 14.42]



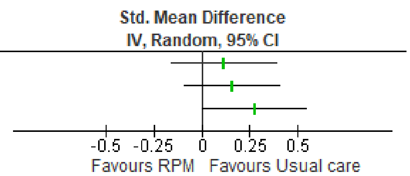
Appendix Figure 5 Forest plot of health-related quality of life (SF-12/36, mental component summary)

	RPM			Usual care			Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Dario 2017	47.76	3.07	166	47.9	3.49	77	-0.04 [-0.31, 0.23]
Schillinger 2009	67	25.8	101	64.2	27.2	105	0.11 [-0.17, 0.38]
Nicolucci 2015	50	10.8	114	46.7	10.2	135	0.31 [0.06, 0.56]



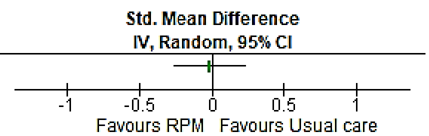
Appendix Figure 6 Forest plot of health-related quality of life (SF-12/36, physical component summary)

	RPM			Usual care			Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Schillinger 2009	60.2	29.1	101	56.7	31.3	105	0.12 [-0.16, 0.39]
Nicolucci 2015	46.9	8.8	114	45.4	10.2	135	0.16 [-0.09, 0.41]
Dario 2017	45	5.41	166	43.44	6.08	77	0.28 [0.00, 0.55]



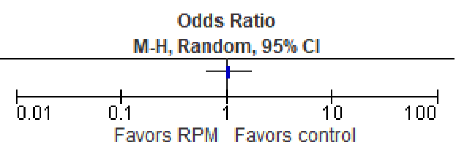
Appendix Figure 7 Forest plot of mental health symptoms (HADS)

	RPM			Usual care			Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Wild 2016	9.5	7.8	130	9.6	7.6	127	-0.01 [-0.26, 0.23]



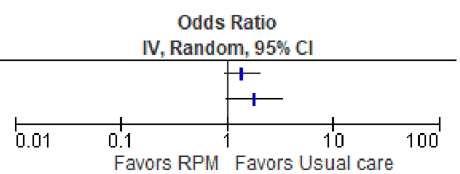
Appendix Figure 8 Forest plot of normal blood pressure achievement

	RPM		Usual care		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI
Magid 2011	50	138	51	145	1.05 [0.64, 1.70]



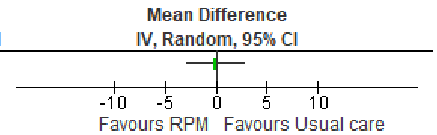
Appendix Figure 9 Forest plot of HbA1c target achievement

	RPM		Usual care		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	IV, Random, 95% CI
Steventon 2014	114	300	65	213	1.40 [0.96, 2.03]
Nicolucci 2015	32	114	24	135	1.80 [0.99, 3.29]



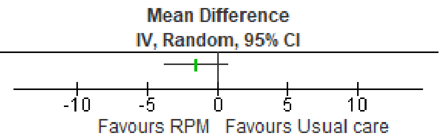
Appendix Figure 10 Forest plot of daytime ambulatory systolic blood pressure

	RPM			Usual care			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Wild 2016	133.7	11.3	121	133.8	10.5	108	-0.10 [-2.92, 2.72]



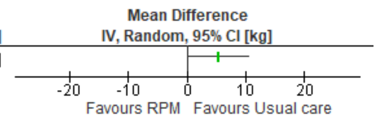
Appendix Figure 11 Forest plot of daytime ambulatory diastolic blood pressure

	RPM			Usual care			Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Wild 2016	76.2	8.8	121	77.7	8.5	108	-1.50 [-3.74, 0.74]



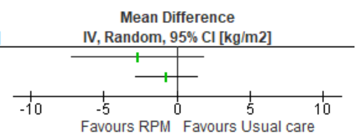
Appendix Figure 12 Forest plot of weight

	RPM			Usual care				Mean Difference
Study or Subgroup	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total	Weight	IV, Random, 95% CI [kg]
Wild 2016	96.9	22	145	91.5	20.5	135		5.40 [0.42, 10.38]



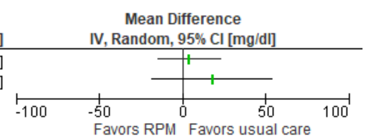
Appendix Figure 13 Forest plot of body mass index

	RPM			Usual care			Mean Difference
Study or Subgroup	Mean [kg/m2]	SD [kg/m2]	Total	Mean [kg/m2]	SD [kg/m2]	Total	IV, Random, 95% CI [kg/m2]
Carter 2011	23.8	6.9	26	26.5	8.5	21	-2.70 [-7.20, 1.80]
Schillinger 2009	30.7	6.9	104	31.4	8.5	105	-0.70 [-2.80, 1.40]



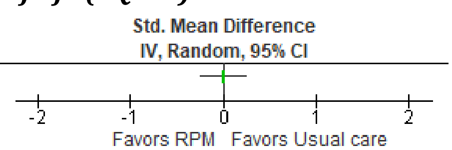
Appendix Figure 14 Forest plot of triglyceride levels

	RPM			Usual care			Mean Difference
Study or Subgroup	Mean [mg/dl]	SD [mg/dl]	Total	Mean [mg/dl]	SD [mg/dl]	Total	IV, Random, 95% CI [mg/dl]
Nicolucci 2015	149	73	114	145	79	135	4.00 [-14.90, 22.90]
Stone 2010	170	115.9	73	152	99.7	64	18.00 [-18.10, 54.10]



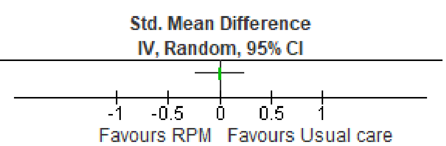
Appendix Figure 15 Forest plot of health-related quality of life (EQ-5D)

	RPM			Usual care			Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Wild 2016	0.8	0.3	136	0.8	0.3	130	0.00 [-0.24, 0.24]



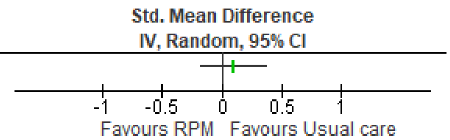
Appendix Figure 16 Forest plot of diabetes knowledge

	RPM			Usual care			Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI
Wild 2016	9	2.5	138	9	2.3	131	0.00 [-0.24, 0.24]



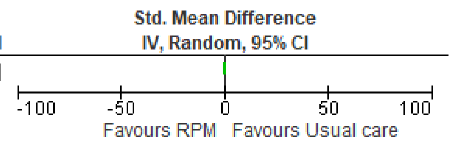
Appendix Figure 17 Forest plot of mental health symptoms (HADS-anxiety)

Study or Subgroup	RPM Mean	RPM SD	RPM Total	Usual care Mean	Usual care SD	Usual care Total	Std. Mean Difference IV, Random, 95% CI
Dario 2017	4.23	3.01	166	3.95	2.68	77	0.10 [-0.17, 0.37]



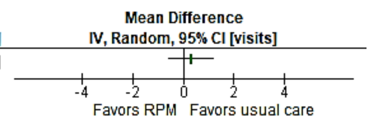
Appendix Figure 18 Forest plot of mental health symptoms (HADS-depression)

Study or Subgroup	RPM Mean	RPM SD	RPM Total	Usual care Mean	Usual care SD	Usual care Total	Std. Mean Difference IV, Random, 95% CI
Dario 2017	3.63	3.14	166	3.82	4.04	77	-0.05 [-0.33, 0.22]



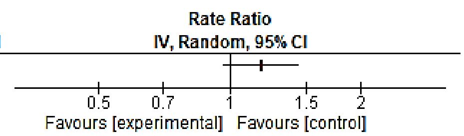
Appendix Figure 19 Forest plot of general practitioner visits

Study or Subgroup	RPM Mean [visits]	RPM SD [visits]	RPM Total	Usual care Mean [visits]	Usual care SD [visits]	Usual care Total	Mean Difference IV, Random, 95% CI [visits]
Wild 2016	5	4.3	156	4.7	3.7	151	0.30 [-0.60, 1.20]



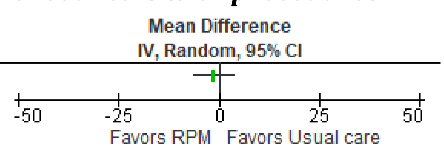
Appendix Figure 20 Forest plot of practice nurse visits

Study or Subgroup	log[Rate Ratio]	SE	RPM Total	Usual care Total	Rate Ratio IV, Random, 95% CI
Wild 2016	0.1655	0.1	156	151	1.18 [0.97, 1.44]



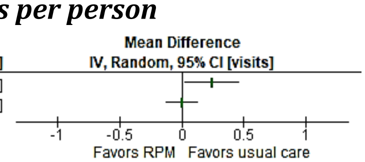
Appendix Figure 21 Forest plot of primary care physician encounters with procedures

Study or Subgroup	RPM Mean	RPM SD	RPM Total	Usual care Mean	Usual care SD	Usual care Total	Mean Difference IV, Random, 95% CI
Dario 2017	30.52	18.31	172	31.89	19.62	79	-1.37 [-6.49, 3.75]



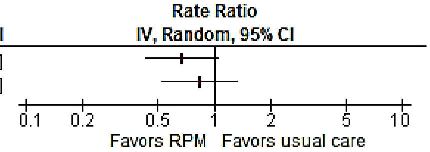
Appendix Figure 22 Forest plot of emergency department visits per person

Study or Subgroup	RPM Mean [visits]	RPM SD [visits]	RPM Total	Usual care Mean [visits]	Usual care SD [visits]	Usual care Total	Mean Difference IV, Random, 95% CI [visits]
Dario 2017	0.53	1.06	172	0.29	0.68	79	0.24 [0.02, 0.46]
Wild 2016	0.2	0.6	156	0.2	0.5	151	0.00 [-0.12, 0.12]



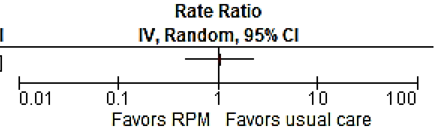
Appendix Figure 23 Forest plot of all-cause hospitalization/hospital attendance

Study or Subgroup	log[Rate Ratio]	SE	Experimental Total	Control Total	Rate Ratio IV, Random, 95% CI
Dario 2017	-0.4005	0.2263	172	79	0.67 [0.43, 1.04]
Wild 2016	-0.1744	0.235	156	151	0.84 [0.53, 1.33]



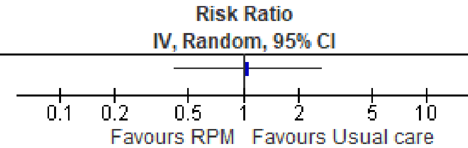
Appendix Figure 24 Forest plot of all-cause emergency hospitalizations

Study or Subgroup	log[Rate Ratio]	SE	RPM Total	Usual care Total	Rate Ratio IV, Random, 95% CI
Dario 2017	0.0296	0.3927	172	79	1.03 [0.48, 2.22]



Appendix Figure 25 Forest plot of patients with home visits

Study or Subgroup	RPM Events	RPM Total	Usual care Events	Usual care Total	Risk Ratio IV, Random, 95% CI
Nicolucci 2015	8	114	9	135	1.05 [0.42, 2.64]



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