Virtual Care for the Longitudinal Management of Chronic Conditions: A Systematic Review

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program comprises three ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee composed of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.

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ACKNOWLEDGMENTS

This topic was developed in response to a nomination by Carolyn Turvey, Office of Rural Health, for the purpose of informing future research and to support adoption of effective virtual care service models. The scope was further developed with input from the topic nominators (*ie*, Operational Partners), the ESP Coordinating Center, the review team, and the Technical Expert Panel (TEP).

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend TEP participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

Carolyn Turvey, PhD
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Technical Expert Panel (TEP)

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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INTRODUCTION

The onset of the COVID-19 pandemic led to an unprecedented growth in synchronous virtual care via phone and video encounters as a means to mitigate the risk of viral transmission to both patients and clinicians. The impact of COVID-19 on ambulatory care was such that outpatient visits across the United States decreased by nearly 60% by the end of March 2020. In response, many health systems rapidly converted 70% or more of their outpatient visits to phone or video delivery. Even after the pandemic recedes, it is likely that synchronous virtual care will remain a larger part of usual ambulatory care and longitudinal chronic disease management than ever before.

As both the largest integrated health system and largest provider of virtual care in the country, the Veterans Health Administration (VHA) has a particular interest in understanding how best to implement and utilize virtual care or the management of chronic conditions. VHA has a robust and widespread virtual care infrastructure including services such as MyHealtheVet secure messaging, Home Telehealth, and the VA Video Connect (VVC) video platform for synchronous visits within both specialty and primary care among other digital innovations. Given the importance that virtual care will likely retain following the COVID-19 pandemic, understanding the strengths and limitations associated with synchronous virtual care for chronic conditions will be critical in shaping how VHA utilizes this approach going forward.

Particularly important within VHA is the chronic management of congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), and type 2 diabetes mellitus (T2DM), as these are among the most common and costly conditions, affecting nearly 5%, 10%, and 25% of all Veterans, respectively. Our systematic review examined the use of synchronous virtual care as a substitute for in-person care in the context of chronic management for CHF, COPD, and T2DM.

At the request of the VA Office of Rural Health (ORH) leadership, we conducted a systematic review to address the following key questions (KQ):

KQ 1a: Among adults, what is the effect of synchronous virtual care (*ie*, phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *congestive heart failure (CHF)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

KQ 1b: Does this effect differ by race/ethnicity, gender, age, and rural status?

KQ 2a: Among adults, what is the effect of synchronous virtual care (*ie*, phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *chronic obstructive pulmonary disease (COPD)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

KQ 2b: Does this effect differ by race/ethnicity, gender, age, and rural status?

KQ 3a: Among adults, what is the effect of synchronous virtual care (*ie,* phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *type 2 diabetes mellitus (T2DM)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

KQ 3b: Does this effect differ by race/ethnicity, gender, age, and rural status?

KQ 4: What are the adverse effects of synchronous virtual care for chronic management of CHF, COPD, and T2DM as compared to in-person care (or compared to phone if synchronous video care) on patients (*ie*, hypoglycemic events), clinical team members *(ie,* burnout*),* and clinics *(ie,* increase in resource costs*)*?

METHODS

We developed and followed a standard protocol for this review in collaboration with operational partners and a technical expert panel (PROSPERO registration number CRD42021239756).

Data Sources and Searches

We searched MEDLINE (via Ovid), Embase (via Elsevier), and Cochrane Central Register of Controlled Trials (via Ovid) from inception through February 7, 2021. We also examined the bibliographies of recent reviews for additional relevant studies.

Study Selection

In brief, the major eligibility criteria were randomized or quasi-experimental studies that evaluated the effect of synchronously delivered care (*ie*, virtual care) for relevant chronic conditions that occurred over ≥ 2 encounters and in which some or all in-person care is supplanted by care delivered virtually (*ie*, phone or video). The virtual care must have been delivered remotely by a clinician with a scope of practice that included independent prescribing, diagnosis, and/or chronic management (*ie*, physician, nurse practitioner, physician assistant, clinical pharmacist) for a patient who was not physically present in the same clinic (*ie*, teleconsultation, video conferencing) and which was administered within the context of longitudinal care provision (even if individual visits are for acute concerns). Interventions were not required to deliver all care virtually; rather, virtual visits could be combined with other asynchronous virtual care tools (*eg*, remote monitoring systems), virtual care manager support, or in-person visits with a prescribing clinician as long as there were virtual visits which replaced in-person visits. Remote monitoring that triggers synchronous care was eligible if remote monitoring occurred in both treatment and comparison arms and visits were with a prescribing clinician. We did not include studies that tested virtual care interventions in which the virtual care component was care provided in addition to regular in-person care rather than as a substitute. Using these prespecified inclusion/exclusion criteria, our team of investigators screened titles and abstracts to identify potentially eligible studies. Studies that met all eligibility criteria at full-text review were included for data abstraction.

Data Abstraction and Quality Assessment

Data elements included descriptors to assess applicability, quality elements, intervention details, and outcomes including adverse events. For included studies, study risk of bias (ROB) was assessed using the Cochrane Effective Practice and Organisation of Care (EPOC) ROB tool.

Data Synthesis and Analysis

We summarized the primary literature using relevant data abstracted from the eligible studies. Summary tables describe the key study characteristics of the primary studies: study design, patient demographics, and details of the intervention and comparator. We considered quantitative synthesis (meta-analysis) in cases where identified study interventions had sufficient conceptual homogeneity; otherwise, we described findings narratively, focusing on identifying patterns in efficacy and safety of the interventions across conditions and outcome categories.

Analysis of Subgroups or Subsets

We considered variations of effect by subgroup of interest as described in the KQs. Prespecified potential effect modifiers included study design characteristics (*eg*, allocation concealment), disease context (*ie*, CHF, COPD, T2DM), and intervention type (*eg*, virtual care modality). Regarding patient-level characteristics of interest (*ie*, race/ethnicity, gender, age, rural status), we looked for analyses conducted within the primary literature that sought to identify effect modification (*eg*, subgroup analyses, regression model explanatory variables). We narratively considered the representation of subgroups within identified studies in comparison to the VA population.

RESULTS

Results of Literature Search

The literature search identified 8,662 citations, of which 129 were reviewed at the full-text stage. Five articles relevant to KQs 1, 3, and 4 were retained for data abstraction, all of which were randomized trials. No articles were identified for KQ 2 (COPD). No quantitative syntheses were performed due to the conceptual heterogeneity of the identified interventions

Summary of Results for Key Questions

KQ 1: Synchronous virtual care for chronic management of congestive heart failure

Only 1 study met the inclusion criteria for synchronous virtual care for chronic management of CHF. This study by Hansen et al was conducted in Germany and enrolled 210 patients with CHF and a recent implantation of either an implanted cardioverter defibrillator (ICD) or cardiac resynchronization therapy-defibrillator (CRT-D) and randomized them to receive quarterly automated asynchronous web-based review and follow-up of telemetry data versus synchronous personal follow-up (in-person vs phone based) for 1 year. This study was found to have a high ROB due to low numbers of patients enrolled, an unclear randomization method, and poor description of both patient dropout and how primary outcomes were assessed.

KQ 1a: Among adults, what is the effect of synchronous virtual care (ie, phone and/or video) compared to in-person care (or compared to phone if synchronous video care)

for chronic management of congestive heart failure (CHF) on key disease-specific clinical outcomes and health care utilization (ie, hospital admission, hospital re-admission, ER visits)?

A 3-way comparison across study arms found no significant differences in a composite CHF score or other clinical outcomes such as mortality, CHF-related admissions, New York Heart Association (NYHA) class, and change in reported quality of life.

KQ 1b: Does this effect differ by race/ethnicity, gender, age, and rural status?

Hansen et al described the age (overall mean 63.8 years) and gender of their patient population (84.3% male); however, details regarding race/ethnicity and rural status were not reported. Furthermore, the authors did not perform any subgroup analyses examining the effect of age or gender on outcomes.

KQ 2: Synchronous virtual care for chronic management of chronic obstructive pulmonary disease

No studies met inclusion criteria for synchronous virtual care for chronic management of COPD.

KQ 3: Synchronous virtual care for chronic management of Type 2 diabetes mellitus

We identified 4 studies – all of which were randomized trials – that evaluated the provision of synchronous virtual care compared to in-person care for chronic management of T2DM. Two studies were conducted in the United States, 1 in South Korea, and 1 in Denmark. One study was conducted with military patients. Intervention duration varied across studies from less than 8 weeks to 52 weeks. Three studies included 60 or fewer patients and 1 study included 338 patients. Interventions also varied in the way that they incorporated virtual care into chronic T2DM management. Three studies used technology that facilitated synchronous bidirectional communication between the patient and clinician, and 1 study relied on telephone and email. Two studies included remote monitoring as an adjunct virtual care modality.

ROB for patient-reported outcomes was judged low for 1 study, unclear for 1 study, and high for 1 study; 1 study did not examine patient-reported outcomes. For objective outcomes (*eg*, hemoglobin A1c), ROB was judged low for 2 studies and high for 2 studies. Patterns that led to high ROB included (1) missing or unclear data on randomization methods, data collection, and analysis; (2) unblinded treatment arm; (3) no predetermined intervention assessment patterns in the protocol; (4) unclear primary outcomes; and (5) unclear or missing reporting of patient-reported outcomes.

KQ 3a: Among adults, what is the effect of synchronous virtual care (ie, phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of type 2 diabetes mellitus (T2DM) on key disease-specific clinical outcomes and health care utilization (ie, hospital admission, hospital re-admission, ER visits)?

For KQ 3a, we present the detailed results ordered by outcome: (1) A1c, (2) hospitalizations, (3) ER visits, and (4) number of contacts and utilization.

A1c

All 4 studies compared change in A1c from baseline to end of study between synchronous virtual care and in-person study arms. The 1 adequately powered, low ROB study by Jeong et al was a 24-week, 3-arm trial that enrolled 338 patients and compared usual care, telemonitoring (remote monitoring and automated clinical-decision support with in-person endocrine follow-up appointments), and telemedicine (remote monitoring and automated clinical-decision support with video-based endocrine follow-up appointments). No difference was seen at baseline for A1c across groups: usual care (8.39% SD 1.10), telemonitoring (8.21%, SD 0.93), and telemedicine (8.39%, SD 1.10). A statistically significant difference was seen for within-group decrease in A1c from baseline to 24 weeks for all groups ranging from -0.66 to -0.81 ($p < 0.001$). However, no statistically significant difference was noted for A1c reduction across groups. Among the smaller trials (all $n < 60$), 2 found greater A1c reductions between virtual care arms versus comparator; 1 trial only reported a significant within group difference.

Hospitalizations

Two studies examined hospitalizations. In the study by Jeong et al, only 1 patient in the telemonitoring arm experienced a diabetes complication-related hospitalization, and no patients in the control or telemedicine arms experienced diabetes-related hospitalizations at 24 weeks. In the second study, by Klingeman et al, 3 out of 30 patients in the experimental arm and 7 out of 30 patients in the control arm experienced a diabetes-related hospital admission.

ER Visits

Two studies examined emergency room (ER) visits. In the first study by Jeong et al, across the 3 study arms, no patients experienced diabetes-related visits to the ER out of the 338 patients enrolled in the study. In the second study, by Klingeman et al, no patients in the experimental arm and 1 patient in the control arm experienced a diabetes-related emergency-room visit.

Number of Contacts and Utilization

Three studies reported collecting data on number of contacts and utilization among patients receiving in-person or virtual care. The study by Klingeman et al designed the experimental arm for variable frequency of contact using a specialty clinic model. Pre-planned contacts (via email, phone call, or visit) were determined at baseline and amended over time; contact was tailored upon each patient's outcomes, adverse reactions, and changes in disease state; the control arm received usual endocrine care. Klingeman et al reported that when diabetes education visits were combined with clinician diabetes-related visits in the endocrinology clinic, the experimental group had fewer overall visits than the control group. Specifically, the experimental group had 1.5 (SD 0.7) visits versus 3.6 (SD 4.0) visits over 12 months ($p = 0.0001$). However, the experimental group had significantly more email contacts than in the control arm with 11.1 (SD 6.4) email interactions in the experimental group and 1.8 (SD 3.5) email interactions in the control group ($p < 0.0001$). (Note: email communication was a focus in the experimental arm.)

The study by Rasmussen et al, which compared standard care and video consultation for home treatment of T2DM, reported on (1) number of visits and missed visits, and (2) consultation time. The video consultation group had 4.1 visits on average with no missed visits; however, the usual-

care group had on average 3.8 visits with 13% missed visits. In regards to consultation time, the video consultation group averaged 18 minutes and the usual care group averaged 23 minutes.

The study by Whitlock et al did not report results on number of contacts and utilization despite describing collecting the number of clinic visits before and during the study in the methods.

KQ 3b: Does this effect differ by race/ethnicity, gender, age, and rural status?

Only 1 of the included studies reported on subgroup analysis by patient characteristics. Jeong et al analyzed 2 subgroups of interest: (1) gender and (2) age. No statistically significant difference was found between men and women or by age groups (< 55 years of age, ≥55 years of age).

KQ 4: What are the adverse effects of synchronous virtual care for chronic management of CHF, COPD, and T2DM as compared to in-person care (or compared to phone if synchronous video care) on patients (ie hypoglycemic events), clinical team members (ie, burnout), and clinics (ie, increase in resource costs)?

Two studies reported adverse events. The study by Jeong et al described 4 groups of adverse events: (1) general events, (2) diabetes-related events, (3) serious events, and (4) biochemical events. General adverse events were noted in the control (n = 33 or 29.2%, in-person appointments at 8, 16, 24 weeks), telemonitoring (n = 30 or 26.5%, in-person appointments at 8, 16, 24 weeks with remote monitoring of blood glucose data), and telemedicine (n = 23 or 20.5%, video visits at 8 and 16 weeks, in-person visit at 24 weeks) arms. Diabetes-related events were noted in the control (n = 7 or 6.2%), telemonitoring (n = 7 or 6.2%), and telemedicine (n = 3 or 2.7%) arms. Serious reported adverse events were noted in the control (n = 2 or 1.8%), telemonitoring (n = 2 or 1.8%), and telemedicine (n = 1 or 0.9%) arms, and included angina pectoris, rotator cuff syndrome, malignant hepatic neoplasm, skin ulcer, and hematuria. Biochemical parameters for serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and creatinine levels were measured and samples obtained at baseline and 24 weeks; each value was classified as normal or abnormal. Subgroup analyses indicated that ALT was the only biochemical parameter showing a significant difference between the telemonitoring (n = 0) and telemedicine (n = 7, 6.3%) arms (p = 0.014) and that 5 (4.4%) patients in the control arm had worsening ALT from a normal baseline. The study by Klingeman et al described 2 types of adverse events: (1) severe hypoglycemia and (2) foot ulcers. Severe hypoglycemia was noted in the experimental (n = 1 or 0.9%) arm but not in the control (n = 0) arm. Foot ulcers were noted in the experimental (n = 1 or 0.9%) and control (n = 3 or 2.6%) arms.

DISCUSSION

Key Findings

The COVID-19 pandemic precipitated a rapid massive shift from in-person to virtual health care delivery without an understanding about the impact of virtual care on important health outcomes. In this review, we evaluated the impact of real-time, virtual care in lieu of face-to-face care for the chronic management for CHF, COPD, and T2DM. Our review is notable in its use of a clear definition of virtual care, consideration of disease-specific clinical needs, focus on high-quality study designs, and rigorous analysis of studies that address synchronous virtual care. Overall, we found very few studies evaluating the effect of synchronous virtual care compared to in-person

care for chronic T2DM, COPD, and CHF management (only 4 in T2DM 1 in CHF, and none for COPD). Among the included studies, there was significant heterogeneity related to the structure, purpose, and delivery of virtual care visits. The findings from this small number of studies have limited generalizability as all included studies took place in specialty care clinics while much of the long-term management for chronic conditions such as T2DM, CHF, and COPD occurs within the context of primary care. Primary care teams provide care for multiple conditions simultaneously, which may not support the single-disease-focused care described in the included studies.

Prior Systematic Reviews

Previous systematic reviews have examined various ways of utilizing virtual care modalities in the context of chronic conditions, but none focused on *replacing* in-person care with virtual visits as has been the case during the COVID-19 pandemic. For example, a 2016 Agency for Healthcare Research and Quality (AHRQ) evidence map found 58 existing systematic reviews supporting the use of telehealth interventions for communication/counseling or remote monitoring for chronic conditions. Our review sought to extend the existing literature by addressing telehealth as a replacement for in-person care in chronic disease management. We found scant evidence examining chronic disease management delivered by synchronous virtual care compared to in-person delivery for T2DM, COPD, and CHF.

Horizon Scan

Given the limited existing literature addressing our key question, we sought to assess ongoing studies that might add relevant findings in the near future. We applied our previously developed search terms to the Cochrane Central Register of Controlled Trials and found 1,787 unique studies. However, we only found 3 potential studies that might meet our inclusion criteria based on disease of interest and virtual care intervention. All 3 are randomized controlled trials that were designed before the COVID-19 pandemic. Two of the studies focus on T2DM while the third concerns CHF. Thus, it appears that there is little trial-based research currently in the pipeline to inform our key questions in this review.

Applicability

While none of the included studies were conducted explicitly with Veterans, 1 study occurred in a military setting. Two studies were conducted in countries with nationalized health care (*ie*, South Korea, Denmark), which may increase relevance to VHA. Identified studies included primarily older participants, which is similar to the population of Veterans who have chronic disease.

Research Gaps/Future Research

Overall, there are 5 key areas in which future research on this topic could fill existing gaps and/or could improve the approach. First, and perhaps most critical, virtual care interventions should be thoroughly described in order to maximize reproducibility and generalizability in other clinical contexts. Guidance exists on mobile and web-based interventions, which may provide indirect suggestions about key characteristics for virtual care intervention description. Second, there is a need to evaluate how best to integrate virtual care as a replacement for in-person care, or as an adjunctive technology (*eg*, remote monitoring); further, there is a need to evaluate which

clinical settings are best suited to the virtual environment (*eg*, primary care vs specialty care settings). Approaches to integrating virtual care can be expected to vary across settings with different workflow patterns, clinical resources, and competing clinical demands, which emphasizes the need for solid evidence. Third, outcomes varied across included studies and some important outcomes were not addressed by any study (*eg*, impact on clinical workflow, patient satisfaction with virtual care experience, and subsequent utilization). Fourth, investigators should be encouraged to consider *a priori* subgroup evaluations or make individual patient-level data available, so that future reviews can identify patient-level characteristics associated with better outcomes with virtual care. Such information could guide clinics and health care systems to offer optimal patient-centered virtual care delivery and support efforts to ensure equitable benefit and access to virtual care. Finally, investigators should consider utilizing non-inferiority analytic approaches when hypotheses center on whether virtually delivered care is *equally effective to* in-person care.

Conclusions

Virtual modalities such as video or telephone have increasingly been used to replace in-person clinic visits for managing chronic conditions, particularly during the COVID-19 pandemic. However, currently there is scant evidence of the effect of virtual care as a replacement for in-person visits in the context of chronic management of T2DM or CHF, and no evidence for COPD. Health care systems need evidence-based guidance about the effect of well-described virtual care interventions in order to deliver high-quality care using the right modality for the right patients with the right clinical condition at the right time.

ABBREVIATIONS TABLE

A1c	Hemoglobin A1c
AHRQ	Agency for Healthcare Research and Quality
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
CHF	Congestive heart failure
COPD	Chronic obstructive pulmonary disease
CRT-D	Cardiac Resynchronization Therapy-Defibrillator
EPOC	Effective Practice and Organization of Care
ER	Emergency room
ESP	Evidence Synthesis Program
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICD	Implanted Cardioverter Defibrillator
KQ	Key question
NYHA	New York Heart Association
OECD	Organization for Economic Co-operation and Development
ORH	Office of Rural Health
PICOTS	Population, intervention, comparator, outcome, timing, setting
PRESS	Peer Review of Electronic Search Strategies
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta Analyses
PROSPERO	The International Prospective Register of Systematic Reviews
RFA	Request for applications
RM	Remote monitoring
ROB	Risk of Bias
T2DM	Type 2 diabetes mellitus
TEP	Technical Expert Panel
VHA	Veterans Health Administration
VVC	VA Video Connect

EVIDENCE REPORT

INTRODUCTION

As both the largest integrated health system and largest provider of telehealth in the country, the Veterans Health Administration (VHA) has a particular interest in understanding how best to implement and utilize virtual care. VHA has long embraced virtual care as part of its mission to "serve all who have served" regardless of their socioeconomic and geographic circumstances. Having begun conducting "virtual care" in the 1960s when doctors first communicated with patient's via TV screens,[1] VHA has since provided over 2.6 million episodes of care to more than 900,000 Veterans in 2019[2] and has distributed over 50,000 data- and video-enabled iPads for Veterans throughout the country.[3] Virtual care within VHA includes services such as MyHealtheVet secure messaging, the Home Telehealth program that combines case management principles with remote monitoring to improve access and coordinate care, and the VA Video Connect (VVC) video platform for synchronous visits within both specialty and primary care.[4] Increasing Veteran access to care via virtual care has been an integral part of VHA's strategy for improving chronic disease management for a population that is on average older and sicker than their civilian counterparts.[5,6] Given the importance that virtual care has for Veteran care even beyond the COVID-19 pandemic, understanding the strengths and limitations associated with synchronous virtual care will be critical in shaping how VHA utilizes virtual care going forward.

Virtual care can be defined as the use of technology to facilitate an interaction between a patient and their health care team across distance or time.[7] This broad definition includes a wide variety of technologies and interventions, such as text messages and email communications, asynchronous remote monitoring, and synchronous (*ie,* real-time) phone/video visits.[7] Given the large heterogeneity of care delivery that falls under the umbrella of virtual care, its impact is dependent upon the specific modality and application as well as the patient populations involved. For example, a systemic review and evidence map of virtual care literature in 2016 published by the Agency for Healthcare Research and Quality (AHRQ) which focused largely on virtual care when used in addition to in-person care found consistent evidence of benefit for virtual care with counseling and remote monitoring of chronic conditions but found unclear evidence supporting virtual care for clinical consultation or maternal and child health among other clinical circumstances.[7] Importantly, specific virtual care modalities can have different impacts depending on the clinical situation and patient population. For example, chronic conditions which depend on physical assessment to determine clinical status (*eg,* congestive heart failure [CHF] or chronic obstructive pulmonary disease [COPD]) or the presence of complications (*eg,* diabetes mellitus) may have different challenges compared to other conditions which can largely be managed without physical exam (*eg,* mental health). Understanding when virtual care is most effective will be particularly important as we try to right size the implementation of virtual modalities after the initial dramatic increase due the COVID-19 pandemic.

COVID-19 has had a profound impact on ambulatory care delivery. The onset of the COVID-19 pandemic in early 2020 led to an unprecedented growth in synchronous virtual care delivery via phone and video encounters as a means of mitigating the risk of viral transmission for both patients and clinicians. The impact of COVID-19 on ambulatory care was so profound that it is estimated that outpatient visits across the entire country decreased by nearly 60% by the end of

March.[8] In response, many health systems rapidly converted 70% or more of their outpatient visits to virtual care delivery via phone or video.[9-13] To support the US health care system during the crisis, the Centers for Medicare and Medicaid Services issued an emergency ruling aimed at decreasing regulatory requirements for virtual care and created payment parity between in-person care and virtual care delivered via phone or video.[14] Although in-person care visits have since increased, as more has become known about COVID-19 transmission and prevention practices, virtual care continues to have a much larger role in outpatient care than prior to the pandemic.[8,15] Even after the pandemic recedes, it is likely that synchronous virtual care will remain a large part of ambulatory care. Therefore, a close examination of this specific model of virtual care and its strengths and limitations is warranted.

Prior to the pandemic, virtual care was used to shift workload from clinicians to other clinical team members and to supplement rather than replace in-person care. For example, remote monitoring has been combined with phone calls from virtual care nurses or case managers to supplement care for patients with CHF and type 2 diabetes mellitus (T2DM).[16,17] In essence, many prior virtual care studies focused on augmentation of usual care, whereas now it is important to understand which patients and conditions can be managed by clinicians with only limited in-person evaluation. In this context, there are many unanswered questions. First, does synchronous virtual care result in similar clinical outcomes compared with in-person care? Second, in what context is virtual care appropriate as a substitute for in-person care? Furthermore, what are the risks for harm such as missed or delayed diagnoses, increased health care disparities, and worse clinical outcomes? Understanding the evidence for benefit and harm with this specific application of virtual care will help shape current practice and inform future research and investments in virtual care.

Particularly important within VHA is the chronic management of CHF, COPD, and T2DM, as these are among the most common and costly conditions affecting nearly 5%, 10%, and 25% of all Veterans, respectively.[18,19] In addition, these conditions typically require physical assessment to establish disease status and the presence and extent of exacerbations. Despite the reliance on physical assessment, during the COVID pandemic we experienced a near complete shift to managing care of such conditions virtually. Moving forward, we will need to match the best care modality by condition for specific patient populations. This is a priority within VHA.[20] Thus, our systematic review examined the use of virtual care as a substitute for in-person care in the context of chronic management for CHF, COPD, and T2DM.

METHODS

We followed a standard protocol for this review developed in collaboration with operational partners and a technical expert panel. The PROSPERO registration number is CRD42021239756. The protocol was developed prior to conducting the review, and there were no significant deviations after registration. Each step was pilot tested to train and calibrate study investigators. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines.[21]

TOPIC DEVELOPMENT

This topic was proposed by the leadership of the Office of Rural Health (ORH). Key questions as outlined below were driven in particular by the ORH's desire to better understand virtual care access and use by marginalized patient populations given inequities exposed by shifts in care during the COVID-19 pandemic and concerns about the potential worsening of existing or creation of new sources of health disparities. Findings will be used to inform the development of Request for Applications (RFAs) on virtual care implementation research and to support the adoption of effective virtual care service models.

Key Questions

The Key Questions (KQs) for this report were:

KQ 1a: Among adults, what is the effect of synchronous virtual care (*ie*, phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *congestive heart failure (CHF)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

KQ 1b: Does this effect differ by race/ethnicity, gender, age, and rural status?

KQ 2a: Among adults, what is the effect of synchronous virtual care (*ie*, phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *chronic obstructive pulmonary disease (COPD)* on key disease-specific clinical outcomes and health care utilization (*ie,* hospital admission, hospital re-admission, ER visits)?

KQ 2b: Does this effect differ by race/ethnicity, gender, age, and rural status?

KQ 3a: Among adults, what is the effect of synchronous virtual care (*ie*, phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *type 2 diabetes mellitus (T2DM)* on key disease-specific clinical outcomes and health care utilization (*ie,* hospital admission, hospital re-admission, ER visits)?

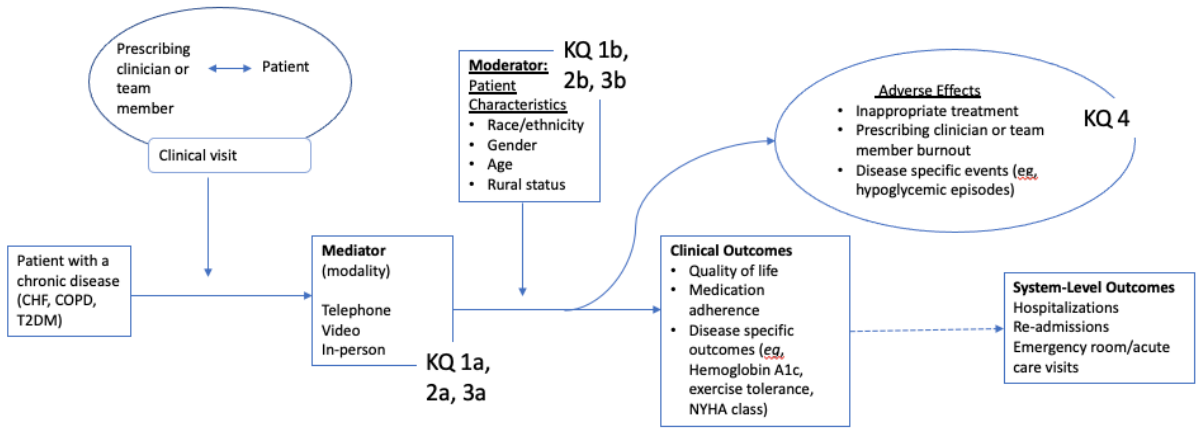
KQ 3b: Does this effect differ by race/ethnicity, gender, age, and rural status?

KQ 4: What are the adverse effects of synchronous virtual care for chronic management of CHF, COPD, and T2DM as compared to in-person care (or compared to phone if synchronous video care) on patients (*ie*, hypoglycemic events), clinical team members (*ie,* burnout), and clinics (*ie,* increase in resource costs)?

Conceptual Model

Figure 1 depicts our conceptual model. Our analysis of virtual care begins with the patient who has a chronic disease (*eg*, CHF, COPD, or T2DM), and the clinical visit (*eg*, purposeful interaction between the prescribing clinician and patient), which encompasses all activities between the prescribing clinician and patient. Following review of the literature and team discussions, we are considering the virtual care modality (*eg*, telephone, video, in-person) to mediate the relationship between the clinical visit and prespecified clinical- and system-level outcomes. Of note, we acknowledge that individual patient characteristics (*eg*, race/ethnicity, gender, age, rural status) may moderate the relationship between the modality in which the clinical visit occurs and any clinical- and system-level outcomes. Given the focus of our key questions, we also specified that the care delivered virtually should be for clinical activities provided by a prescribing clinician such as evaluation, diagnosis, or medication prescription and not for the provision of self-management education and/or other support provided adjunctively by a clinical team member other than the prescribing clinician (*eg*, nurse care manager) as such interventions have been previously evaluated.[7] The conceptual model outlines the population, outcomes, mediation effect of the modality, moderation effect of patient characteristics, and any adverse effects. The virtual care interventions map to our operationalized definition of virtual care and also include important contextual elements such as delivery mode (*eg*, telephone, video, in-person), dose (*eg*, duration and frequency of contact), and clinical context of care provision.

Figure 1. Virtual Care Conceptual Model



SEARCH STRATEGY

In collaboration with an expert medical librarian, we conducted a primary literature search from inception to February 7, 2021, of MEDLINE® (via Ovid®), Embase (via Elsevier). We used database-specific subject headings and keywords searched in the titles and abstracts (Appendix A). The search strategies were peer reviewed by another expert medical librarian prior to execution using the Peer Review of Electronic Search Strategies (PRESS) Checklist.[22] We hand-searched previous systematic reviews conducted on this or a related topic for potential inclusion.

STUDY SELECTION

Studies identified through our primary search were classified independently by 2 investigators for relevance to the KQs based on title and abstract from our *a priori* established eligibility criteria. All citations classified for inclusion by at least 1 investigator were reviewed at the full-text review level. The citations designated for exclusion by 1 investigator at the title and abstract level underwent screening by a second investigator. If both investigators agreed on exclusion, the study was excluded. All articles meeting eligibility criteria were included for data abstraction. All results were tracked in an electronic database (for referencing, EndNote®, Clarivate Analytics, Philadelphia, PA; for data abstraction, DistillerSR; Evidence Partners Inc., Manotick, ON, Canada).

Table 1 describes the study eligibility criteria organized by PICOTS elements (population, intervention, comparator, outcome, timing, setting) and other criteria such as study design, language, and publication type. Specifically, for the virtual care intervention we sought to identify studies that evaluated the effect of synchronously delivered care for relevant chronic conditions that occurred over ≥ 2 encounters and in which some or all in-person care is supplanted by virtual care (*ie*, phone or video). The virtual care must be delivered remotely by a clinician with a scope of practice that includes independent prescribing, diagnosis, and/or chronic management (*ie*, physician, nurse practitioner, physician assistant, clinical pharmacist) for a patient who is not physically present in the same clinic (*ie*, teleconsultation, video conferencing) and that is administered within the context of longitudinal care provision (even if individual visits are for acute concerns). Interventions are not required to be exclusively virtual care provided by a clinician as described above; rather, they may include the above with other asynchronous virtual care tools (*eg*, remote monitoring systems), virtual care manager support, or in-person visits with a prescribing clinician as well. Remote monitoring that triggers synchronous care would be eligible if remote monitoring occurs in both treatment and comparison arm and visits are with a prescribing clinician. We did not include studies that tested virtual care interventions in which the virtual care component was care provided *in addition* to regular in-person care rather than as a substitute.

Table 1. Study Eligibility

Study Characteristic	Inclusion Criteria	Exclusion Criteria

Population	• Adults (≥ 18 years of age) with the following chronic conditions:
	  ○ CHF
	  ○ COPD
	  ○ T2DM; at least 75% if a mix of type 1 and type 2
	• Clinicians/clinics conducting virtual care for chronic conditions if relevant to harms
		• Inpatient populations (*eg*, tele-ICU)
		• Patients receiving care in an ER or tele-urgent care setting
		• Intervention limited only to the management of complications of these chronic conditions such as stroke, retinopathy, neuropathy, and foot ulcers

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Intervention	• Synchronous care delivered over ≥ 2 encounters for the long-term management of relevant chronic conditions in which some or all in-person care is supplanted by virtual care (*ie*, phone or video) and which is delivered remotely by an independently licensed clinician • May include asynchronous virtual care tools (*eg*, remote monitoring systems), if in both arms.	• Supplemental nurse care management • Virtual care interventions that don't involve synchronous care delivered by a clinician to a patient (*eg*, one-way automated texts, reminder systems,) • Tele-cardiac or tele-pulmonary rehabilitation
Comparator	In-person care without any virtual care delivery, or care delivered by telephone if compared to video	No comparator
Outcome	• Key clinical outcomes (*eg*, medication adherence, quality of life, depression) and by condition: o CHF (*eg*, NYHA class/symptoms) o COPD (*eg*, exercise tolerance, dyspnea) o T2DM (*eg*, A1c) • Clinical utilization *(ie*, hospitalization, hospital re-admissions, emergency room visits/urgent care) • Adverse effects (*eg,* hypoglycemic episodes, inappropriate treatment, clinician burnout)	Any outcomes not listed
Timing	No limit	Not applicable
Setting	Any outpatient setting (*ie,* general medical or specialty care clinic)	Intervention delivered primarily in hospital inpatient setting (including emergency room)
Study design	• EPOC criteria studies that have prospective data collection: o Randomized trials o Non-randomized trials • Controlled before-after studies • Interrupted time-series studies or repeated measures studies	• Not a clinical study (*eg*, editorial, letter to an editor) • Uncontrolled clinical study • Qualitative studies • Prospective or retrospective observational studies • Clinical guidelines • Measurement or validation studies • Studies that look at mixed chronic conditions if results for specified conditions are not reported separately
Countries	OECD[a]	Non-OECD

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Publication types	Full publication in a peer-reviewed journal	Letters, editorials, reviews, dissertations, meeting abstracts, protocols without results

Abbreviations. A1c = hemoglobin A1c; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; EPOC = effective practice and organization of care; ER = emergency room; ICU = intensive care unit; NYHA = New York Heart Association; T2DM = type 2 diabetes mellitus.
[a]OECD = Organization for Economic Co-operation and Development includes Australia, Austria, Belgium, Canada, Chile, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Korea, Latvia, Luxembourg, Mexico, Netherlands, New Zealand, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom, and United States.

DATA ABSTRACTION

Data from published reports were abstracted into a customized DistillerSR database by 1 reviewer and over-read by a second reviewer. Disagreements were resolved by consensus or by obtaining a third reviewer's opinion. Data elements included descriptors to assess applicability, quality elements, intervention details, and outcomes including adverse events.

Key characteristics abstracted included participant descriptors (*eg,* race/ethnicity, gender, age, rural status), intervention characteristics (*eg*, clinician type, virtual care modality), comparator, and outcomes. We abstracted all outcomes used to evaluate virtual care but prioritized outcomes identified *a priori* in collaboration with our stakeholders for analysis. Multiple reports from a single study were treated as a single data point, prioritizing results based on the most complete and appropriately analyzed data. When critical data were missing or unclear in published reports, we requested supplemental data from the study authors. Key features relevant to applicability included the match between the sample and target populations (*eg*, age, Veteran status).

For details of study characteristics, see Appendix B. Appendix C presents details of the intervention characteristics. Appendix D lists all outcomes reported in the included studies, and Appendix E lists excluded studies and the reason for exclusion.

RISK OF BIAS (QUALITY) ASSESSMENT

Quality assessment was done by the investigator abstracting or evaluating the included article and was over-read by a second, highly experienced investigator. Disagreements were resolved by consensus between the 2 investigators or, when needed, by arbitration by a third investigator.

For randomized, non-randomized, and controlled before-after studies, we used criteria from the Cochrane EPOC ROB tool.[23] These criteria are adequacy of randomization and allocation concealment; comparability of groups at baseline; blinding; completeness of follow-up and differential loss to follow-up; whether incomplete data were addressed appropriately; validity of outcome measures; protection against contamination; selective outcomes reporting; and conflict of interest. We assigned a summary ROB score (low, unclear, high) to individual studies, defined as follows:

- Low ROB: Bias, if present, is unlikely to alter the results seriously.

- Unclear ROB: Information required to determine ROB was not clearly specified in the peer-reviewed paper or unable to be obtained to make a judgment.
- High ROB: Bias may alter the results seriously.

DATA SYNTHESIS

We summarized the primary literature using relevant data abstracted from the eligible studies. Summary tables describe the key study characteristics of the primary studies: study design, patient demographics, and details of the intervention and comparator. Because of the conceptual heterogeneity of the identified study interventions, we did not complete a quantitative synthesis (*ie*, meta-analysis) to estimate summary effects. Rather we describe the findings from included studies narratively focusing on documenting and identifying patterns in efficacy and safety of the interventions across conditions and outcome categories.

Continuous outcomes were summarized using the mean difference (follow-up minus baseline) when all studies reported the outcome using the same scale. For studies not directly reporting mean and standard deviation of patient differences, we used difference in means between follow-up and baseline. For 1 study,[24] we computed standard deviation of difference based on reported p-value for difference between the 2 arms, assuming the same correlation between follow-up and baseline in each arm. When studies reported only medians and ranges, we translated them to means and standard deviations[25] and if a study reported only baseline standard deviation, assumed the same standard deviation at follow-up. Finally, in absence of other information, we assumed 0.5 correlation between follow-up and baseline.

Analysis of Subgroups or Subsets

We sought to consider variations of effect by subgroup of interest, specifically age, rurality, gender, and race/ethnicity. Prespecified potential effect modifiers of interest included study design characteristics (*eg*, allocation concealment), disease context (*ie,* CHF, COPD, T2DM), and potentially intervention type (*eg*, virtual care modality). Regarding patient-level characteristics of interest (*ie*, race/ethnicity, gender, age, rural status), we looked for analyses conducted within the primary literature that sought to identify effect modification (*eg*, subgroup analyses, regression model explanatory variables). We narratively considered the representation of subgroups within identified studies in comparison to the VA population.

GRADING THE CERTAINTY OF EVIDENCE

The certainty of evidence for each key question was assessed using the approach described by Grading of Recommendations Assessment, Development and Evaluation (GRADE).[26] We limited GRADE ratings to those key questions which had at least 2 includes. In brief, this approach requires assessment of 4 domains: ROB, consistency, directness, and precision. Additional domains to be used when appropriate are coherence, dose-response association, impact of plausible residual confounders, strength of association (magnitude of effect), and publication bias. We considered these domains qualitatively and assigned a summary rating after discussion by a sub-team of 5 investigators (KG, CW, AL, AG, and BE) as high, moderate, or low strength of evidence. In some cases, high, moderate, or low ratings were impossible or imprudent to make. In these situations, a grade of insufficient was assigned.

PEER REVIEW

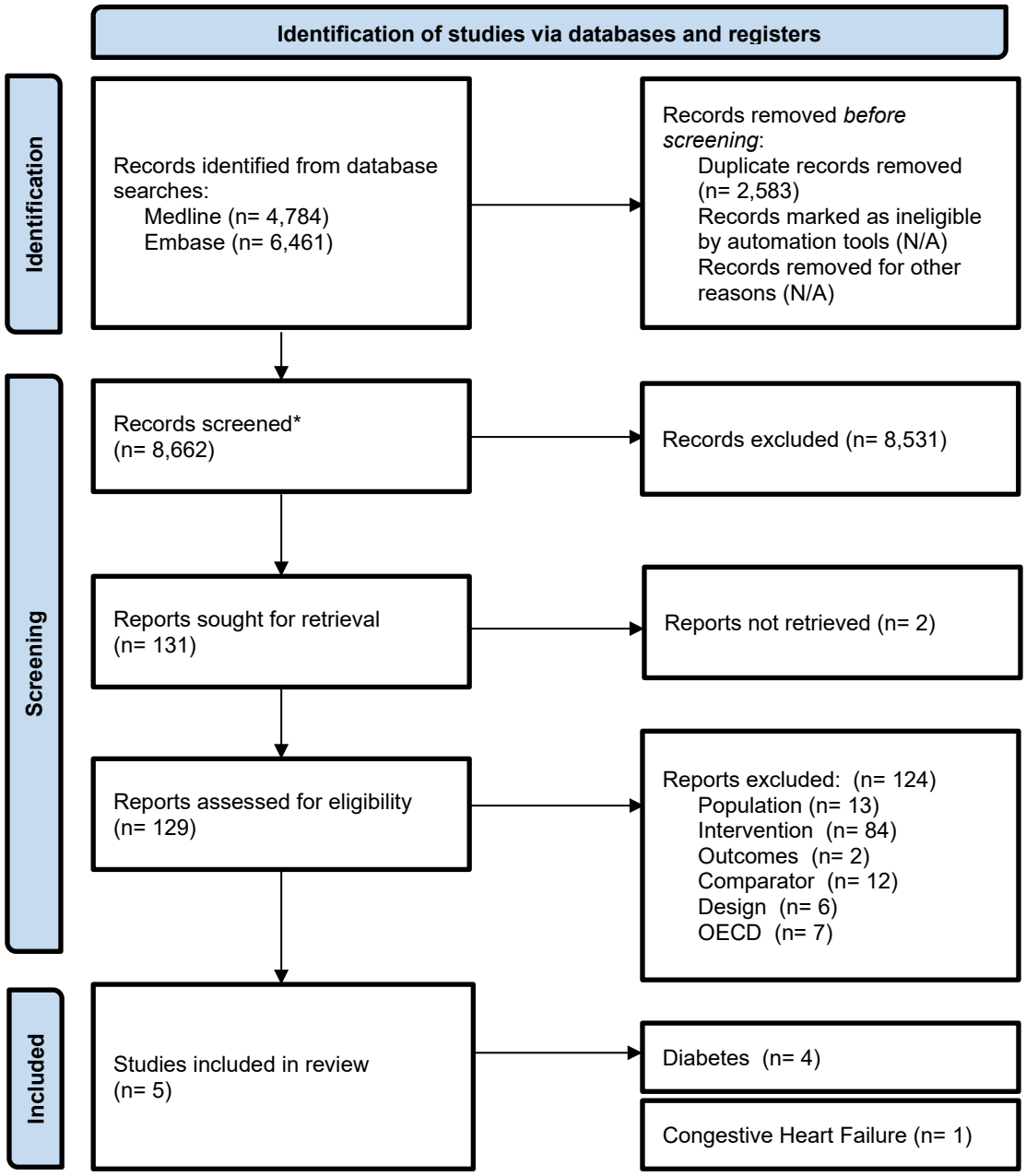
A draft version of this report was reviewed by technical experts and clinical leadership. A transcript of their comments and our responses is in Appendix F.

RESULTS

LITERATURE FLOW

We identified 11,245 studies through searches of MEDLINE® (via Ovid®) and EMBASE (Figure 2). After removing duplicates, there were 8,662 articles. After applying inclusion and exclusion criteria to titles and abstracts, 129 articles remained for full-text review. Of these, 5 unique studies were retained for data abstraction. Of the studies retained, 4 were related to diabetes and 1 was related to CHF. Table 2 summarizes the details of the included studies. Common reasons for excluding studies by intervention included virtual care that supplemented rather than replaced in-person care, virtual care interventions delivered by non-prescribing clinicians, and virtual care delivered asynchronously only.

Figure 2. Literature Flow Chart



* Search results from Medline (4,713) and Embase (3,949) were combined.

Table 2. Evidence Profile of Included Studies (n = 5)

Number of studies: 5 randomized studies
Number of participants: 676 participants[a]
Regions: USA (n = 2); Europe (n = 2); Asia (n = 1)
Disease focus: T2DM (n = 4); CHF (n = 1); COPD (n = 0)
Patient demographics: Median age = 58 years old; 25% Women; Race: 92% White (3 studies NR); 10% Black (4 studies NR); 2% Hispanic (4 studies NR); 2% Other (4 studies NR)
Intervention mode:[b] RM + video (n = 1); video (n = 2); RM + telephone (n = 1); telephone (n = 1);
Comparisons:[b] RM + in-person care (n = 2); Usual in-person care(n=3)
Outcomes reported: A1c (n = 4); NYHA class/symptoms (n = 1); hospitalization (n = 3); ED visit (n = 2)
Risk of bias:
Objective: High Risk (n = 2), Unclear Risk (n = 1), Low Risk (n = 2)
Patient reported: High Risk (n = 2), Unclear Risk (n = 1), Low Risk (n = 1), Not Applicable (n = 1).

Abbreviations. A1c= hemoglobin A1c; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; NR = not reported; NYHA= New York Heart Association; RM= remote monitoring; T2DM = type 2 diabetes mellitus.

[a] One study[27] reported half of the participants (n = 338)

[b] More than 1 category possible per study

KEY QUESTION 1

1A: Among adults, what is the effect of synchronous virtual care (*ie,* phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *congestive heart failure (CHF)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

1B: Does this effect differ by race/ethnicity, gender, age, and rural status?

Key Points

- Only 1 study met the inclusion criteria for synchronous virtual care for chronic management of CHF.
- The 1 included study enrolled 210 patients with CHF and a recent implantation of either an implanted cardio-defibrillator (ICD) or cardiac resynchronization therapy-defibrillator (CRT-D) and randomized them to receive quarterly automated asynchronous web-based review and follow-up of telemetry data versus synchronous personal follow-up (in-person vs phone-based) for 1 year. The comparison of the 2 types of synchronous follow-up met our inclusion criteria. A 3-way comparison across study arms found no significant differences in reported composite Packer scores or other clinical outcomes such as mortality, CHF-related admissions, NYHA class, and change in reported quality of life.
- Outcomes based on race/ethnicity, gender, age, and rural status were not reported.

Detailed Findings: KQ 1a

We identified only 1 study that met the inclusion criteria for synchronous virtual care for chronic CHF management[28] and found it to have a high ROB. Based in Germany, this study enrolled 210 patients with CHF with recent placement of an ICD or CRT-D who were then randomized to receive completely asynchronous web-based automated review and follow-up of telemetry data every 3 months (n = 102) or personal physician contact every 3 months in addition to remote monitoring. The personal contact group was further randomized to personal contact via telephone calls (n = 53) or personal contact via in-person visits (n = 55). The primary outcome was the proportion of patients with worse Packer Heart Failure Clinical Composite Response scores at 13 months compared to 1 month after device placement. The Packer composite response score gives a stepwise assessment and incorporates CHF death/hospitalization, change in NYHA class, and self-assessed health status. Secondary outcomes assessed were all-cause mortality, CHF-related hospitalizations, arrhythmias, and change in reported quality of life. There were no significant differences in Packer scores in a 3-way comparison between the telemetry arm compared to the personal contact subgroups (remote + phone vs remote + in-person visit) (p = 0.967). Similarly, there were no significant differences in secondary outcomes in mortality between subgroups (4.9% vs 7.5% vs 3.6%, p = 0.645), CHF-related hospitalization between subgroups (9.8% vs 11.3% vs 12.7%, p = 0.851), the detection of supraventricular

tachycardia between subgroups (17.6% vs 7.5% vs 12.7%, p = 0.216), detection of ventricular tachycardia (19.6% vs 15.1% vs 16.4%, p = 0.752), or reported change in quality of life (p = 0.724). Overall, the authors found that there were no significant differences between the subgroups in any outcome measured.

Quality of Evidence for KQ 1a

The single study that met our inclusion criteria[28] was found to have a high ROB due to low numbers of patients enrolled, an unclear method for patient randomization, and poor description of both patient dropout and how primary outcomes were assessed.

Detailed Findings: KQ 1b

The single study that met inclusion criteria[28] described the age (overall mean 63.8 years) and gender of their patient population (84.3% male); however, details regarding race/ethnicity and rural status were not reported. Furthermore, the authors did not perform any subgroup analyses examining the effect of age or gender on outcomes.

KEY QUESTION 2

2A: Among adults, what is the effect of synchronous virtual care (*ie,* phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *chronic obstructive pulmonary disease (COPD)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

2B: Does this effect differ by race/ethnicity, gender, age, and rural status?

No studies were identified that addressed KQ 2.

KEY QUESTION 3

3A: Among adults, what is the effect of synchronous virtual care (*ie,* phone and/or video) compared to in-person care (or compared to phone if synchronous video care) for chronic management of *Type 2 diabetes mellitus (T2DM)* on key disease-specific clinical outcomes and health care utilization (*ie*, hospital admission, hospital re-admission, ER visits)?

3B: Does this effect differ by race/ethnicity, gender, age, and rural status?

Key Points

- Four studies (n = 466) evaluated synchronous chronic care for patients with diabetes in comparison to in-person care. All were conducted in specialty endocrine clinics.
- No studies were conducted in VHA or reported enrolling Veterans.
- Interventions may decrease A1c, but the certainty of evidence is very low. In the 1 adequately powered study, there was no significant effect.
- Minimal data was provided on hospitalizations, ER visits, and utilization.
- Intervention approaches to the use of virtual care varied greatly, from remote monitoring of blood glucose combined with video versus in-person visits, a specialized endocrinology clinic that individually tailored the frequency of virtual visits, to a brief, 3-week intervention to stabilize uncontrolled diabetes remotely.

Characteristics of Included Studies

For KQ 3a, we present the detailed results ordered by outcome: (1) A1c, (2) hospitalizations, (3) ER visits, and (4) number of contacts and utilization.

We identified 4 studies – all of which were randomized trials[24,27,29,30] – that evaluated the provision of synchronous virtual care compared to in-person care for chronic management of T2DM. Two studies were conducted in the United States,[24,30] 1 in South Korea,[27] and 1 in Denmark.[29] One study was conducted with military patients.[30] Intervention duration varied across studies from fewer than 8 weeks to 52 weeks. Intervention approach varied across the 4 studies in duration and mode of incorporating virtual care into chronic diabetes management. Three studies included 60 or fewer patients[24,29,30] and 1 study included 338.[27] Three studies used technology that facilitated synchronous bidirectional communication between the patient and clinician[27,29,30] and 1 study relied on telephone and email.[24] Two studies included remote monitoring.[27,30] Additional details on study characteristics are in Appendix B, and intervention characteristics are in Appendix C.

Detailed Findings: KQ 3a

A1c

All 4 studies compared change in A1c reduction from baseline to end of study between synchronous virtual care and in-person study arms (Figure 3).[24,27,29,30]

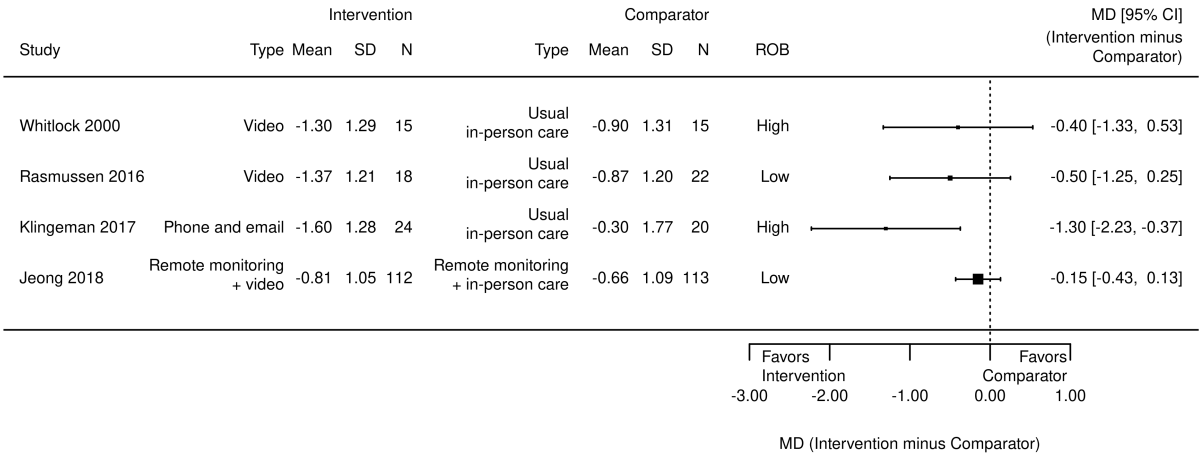
The first study[27] by Jeong et al was a 24-week 3-arm trial that compared usual care, telemonitoring (remote monitoring with automated clinical decision support with in-person endocrine follow-up appointments), and telemedicine (remote monitoring with automated clinical decision support with video-based endocrine follow-up appointments). They enrolled 338 patients with a baseline mean age of 53. No statistically significant difference was seen at baseline for A1c across groups: usual care (8.39% SD 1.10), telemonitoring (8.21, SD 0.93%), and telemedicine (8.39, SD 1.10). A statistically significant difference was seen for within-group decrease in A1c from baseline to 24 weeks for all groups ranging from -0.66 to -0.81 ($p < 0.001$). No statistically significant difference was noted for size of A1c reduction across groups: usual care versus telemonitoring groups ($p = 0.6127$), usual care versus telemedicine ($p = 0.162$), and telemonitoring versus telemedicine groups ($p = 0.343$).

The second study[24] led by Klingeman et al was a 52-week, 2-arm trial consisting of usual endocrine care versus an experimental group that enrolled 60 patients with T2DM. The setting for the study was an endocrinology clinic at an academic medical center where patient care was provided by endocrinologists. Patients not in the experimental arm received usual care provided by usual clinic endocrinologists. The specialty clinic model in the experimental group included an endocrinologist and nurse educator who focused on patients with advanced diabetes; contact with the patients in this arm was designed to be variable and patient-specific. Pre-planned contacts (via email, phone) were determined at baseline and amended over time, and ad hoc in person visits occurred if clinically required. Contact was individually tailored upon each patient's outcomes, adverse reactions, and changes in disease state. The control arm received usual endocrine care which included the ability for the patients to contact (via email and phone) clinicians as needed. Hemoglobin A1c levels were noted between groups at baseline usual care (8.9% SD 0.8%) versus specialty clinic model (9.5%, SD 0.9%). Additionally, a greater proportion of White patients were enrolled in the intervention arm (96.6%) compared to the usual care (76.8%) group. Analysis of data at 52 weeks found a greater decrease in A1c with the specialty clinic model of -1.7% (from 9.6 to 7.9%) as compared to the usual endocrine care at 0.3% (from 8.9 to 8.6%) with $p = 0.004$. Of note, a sensitivity analysis was conducted that dropped data from 1 outlier patient in the usual care group with worsened A1c values (8.3% to 13.5%), but this did not change the results.

The third study[29] by Rasmussen et al was a 2-arm trial comparing 3 weeks of brief standard in-person endocrine care versus telemedicine (video-based endocrine care) to stabilize patients with poorly controlled T2DM. They enrolled 40 patients with baseline A1c in standard care group of 8.1% (range 6.1 to 10.7) and 9.0% (7.6 to 12) in the telemedicine group. At 6 months the A1c ranged from 8.1% to 7.2% for the standard care group and 9.1% to 7.7% for the telemedicine group. The percent change in A1c was statistically significant with a decrease of 14.6% in telemedicine and 10.6% in standard care ($p = 0.016$) across groups. Of note, although this study framed its hypothesis as that "the treatment by telemedicine at home was similar to standard care", the analysis methods employed did not employ non-inferiority analytic approaches.

The fourth study by Whitlock et al, which tested usual care and telemonitoring visits with a case manager and physician,[30] enrolled 28 patients in a 36-week 2-arm trial consisting of a standard of care control versus experimental telemonitoring group. In this study, both groups were referred for multidisciplinary diabetic education classes, and the experimental group then received weekly telemonitoring with video by a case manager and then monthly telemonitoring by video with study physicians. Standard of care patients received routine in-person care with their primary care clinician. A statistically significant within-group difference ($p < 0.05$) was noted for the experimental telemonitoring arm from baseline A1c of 9.5 (8.1 to 12.6) to an end A1c of 8.2 (5.7 to 10.2). For the comparator, the mean baseline A1c was 9.5 (8.1 to 11.9) and end A1c was 8.6 (7.1 to 11.9).

Figure 3. Change in A1c Between Intervention and Comparator Arms Across KQ 3a Studies



Hospitalizations

Two studies examined hospitalizations.[24,27] In the study[27] by Jeong et al, only 1 patient in the telemonitoring arm experienced a diabetes complication-related hospitalization, and no patients in the control or telemedicine arms experienced diabetes-related hospitalizations. In the second study[24] by Klingeman et al, 3 patients out of 30 in the experimental arm and 7 patients out of 30 in the control arm experienced a diabetes-related hospital admission.

ER Visits

Two studies examined emergency room (ER) visits.[24,27] In the first study[27] by Jeong et al, across the 3 study arms, no patients experienced diabetes-related visits to the ER out of the 338 patients enrolled in the study. In the second study[24] by Klingeman et al, no patients in the experimental arm and 1 patient in the control arm experienced a T2DM-related ER visit.

Number of Contacts and Utilization

Three studies reported collecting data on number of contacts and utilization[24,29,30] among patients receiving in-person or virtual care.

The study[24] by Klingeman et al reported on (1) study completion, (2) diabetes education referrals, (3) diabetes-related visits, (4) utilization of modality, and (5) number of interactions and A1c. The study by Klingeman et al designed the experimental arm for variable frequency of contact using a specialty clinic model. Pre-planned contacts (via email, phone call, or visit) were determined at baseline and amended over time; contact was tailored upon each patient's outcomes, adverse reactions, and changes in disease state; the control arm received usual endocrine care. Klingeman et al reported that when diabetes education visits were combined with clinician diabetes-related visits in the endocrinology clinic, the experimental group had fewer overall visits than the control group. Specifically, the experimental group had 1.5 (SD 0.7) visits versus 3.6 (SD 4.0) visits over 12 months ($p = 0.0001$). However, the experimental group had significantly more email contacts than in the control arm, with 11.1 (SD 6.4) email interactions in the experimental group and 1.8 (SD 3.5) email interactions in the control group ($p < 0.0001$). (Note: email communication was a focus in the experimental arm.)

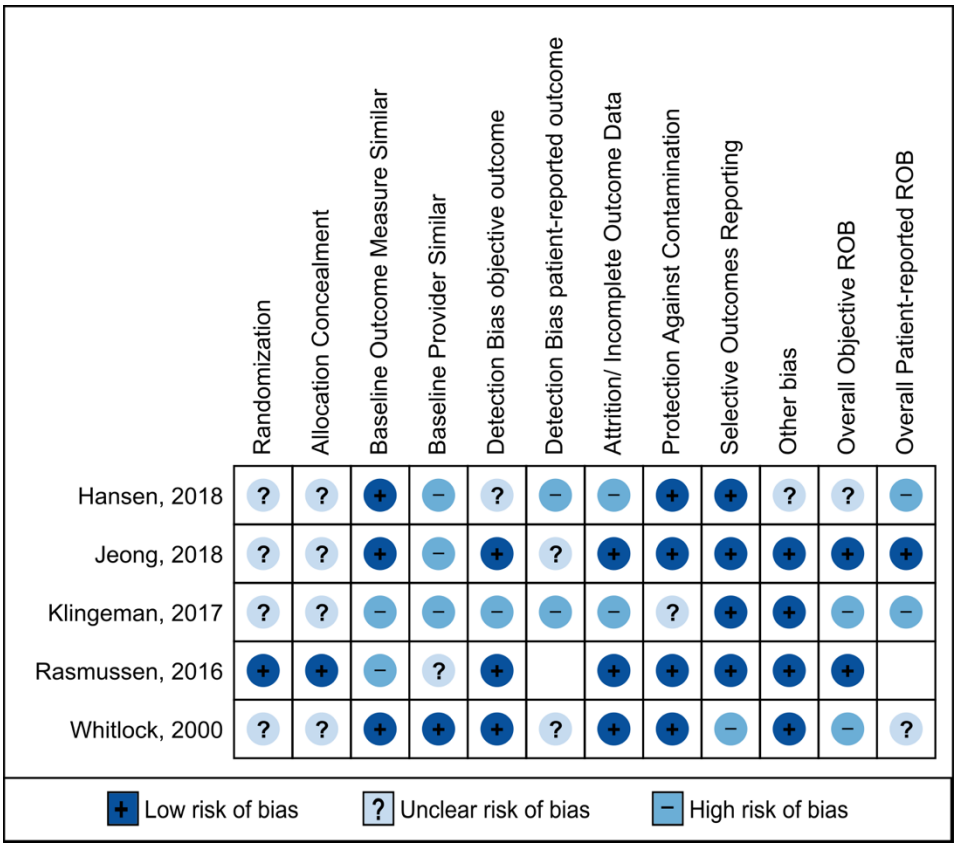
The study by Rasmussen et al, which tested standard care and video consultation for home treatment of T2DM,[29] reported on (1) study completion, (2) number of visits and missed visits, and (3) consultation time. Study completion did not differ significantly between telemedicine (n = 20) and standard care (n = 20) groups. The telemedicine group had 4.1 visits on average with no missed visits; however, the usual care group had on average 3.8 visits with 13% missed visits. In regards to consultation time, the telemedicine group averaged 18 minutes and the usual care group averaged 23 minutes.

The study by Whitlock et al,[30] reported no results on number of contacts and utilization despite describing collecting the number of clinic visits before and during the study in the methods.

Quality of Evidence for KQ 3a

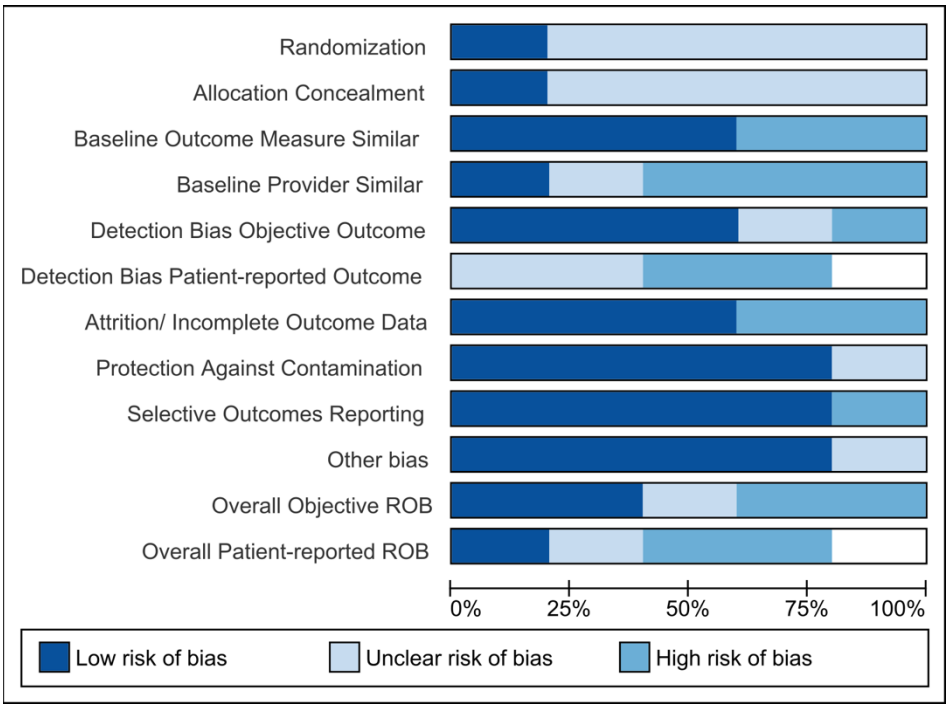
For the 4 randomized studies, the ROB (Figure 4) for patient-reported outcomes was judged low for 1 study, unclear for 1 study, and high for 1 study; 1 study did not report this type of outcome.[24,27,29,30] For objective outcomes, ROB was judged low for 2 studies[27,29] and high for 2 studies.[24,30] Patterns that led to judgements of low ROB (Figure 5) included (1) noting randomization of study participants; (2) collecting objective outcome data; and (3) general limited expected impact of bias from patient knowledge of treatment arm. Patterns that led to high ROB included (1) missing or unclear data on randomization methods, data collection, and analysis; (2) unblinded treatment arm; (3) no predetermined intervention assessment patterns in the protocol; (4) unclear primary outcomes; and (5) unclear or missing reporting of patient-reported outcomes.

Figure 4. Risk of Bias Assessment for Included Studies in KQ 3a



Abbreviations. ROB = risk of bias.

Figure 5. Risk of Bias Assessment Across Included Studies (n = 4) in KQ 3a



Abbreviations. ROB = risk of bias.

Detailed Findings: KQ 3b

Only 1 of the included studies reported on subgroup analysis[27] by patient characteristics. Jeong et al analyzed 2 subgroups of *a priori* interest: gender and age. No statistically significant difference in reduction of A1c was found for men (-0.76 ± 1.11 telemonitoring vs -0.89 ± 1.12 telemedicine; p = 0.88) or women (-0.46 ± 1.05 vs -0.63 ± 0.87; p = 0.16). Nor was a statistically significant difference in reduction of A1c seen by age < 55 years of age (-0.63 ± 1.26 telemonitoring vs -0.87 ± 1.15 telemedicine; p = 0.21) nor with age ≥ 55 years (-0.68 ± 0.88 telemonitoring vs -0.73 ± 0.93 telemedicine; p = 0.83). In addition, Jeong et al reported on additional subgroups of potential interest. High compliance users (defined as users with > 90% of number of records or data transmitted compared to recommended number of records) had no difference in reduction of A1c versus those with lower compliance levels across the study arms of interest (-0.93 ± 0.99 telemonitoring vs -1.08 ± 0.96; p = 0.47). Similarly, there was no significant difference in reduction of A1c between patients who had a high school education or less in the telemonitoring (-0.65 ± 0.93) and telemedicine (-0.94%, ±1.1) arms (p = 0.26).

KEY QUESTION 4: What are the adverse effects of synchronous virtual care for chronic management of CHF, COPD, and T2DM as compared to in-person care (or compared to phone if synchronous video care) on patients (*ie,* hypoglycemic events), clinical team members (*ie*, burnout), and clinics (*ie,* increase in resource costs)?

Detailed Findings: KQ 4

Two studies on T2DM reported adverse events.[24,27] The study[27] by Jeong et al described 4 groups of adverse events: (1) general events, (2) diabetes-related events, (3) serious events, and (4) biochemical events. Adverse events were noted in the control (n = 33 or 29.20%, in-person appointments at 8, 16, 24 weeks), telemonitoring (n = 30 or 26.55%, in-person appointments at 8, 16, 24 weeks with remote monitoring of blood glucose data), and telemedicine (n = 23 or 20.54%, video visits at 8 and 16 weeks, in-person visit at 24 weeks) arms. Diabetes-related events were noted in the control (n = 7 or 6.19%), telemonitoring (n = 7 or 6.19%), and telemedicine (n = 3 or 2.68%) arms. Serious reported adverse events were noted in the control (n = 2 or 1.7%), telemonitoring (n = 2 or 1.70%), and telemedicine (n = 1 or 0.90%) arms, and included angina pectoris, rotator cuff syndrome, malignant hepatic neoplasm, skin ulcer, and hematuria[27]. Biochemical parameters for serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and creatinine levels were measured and samples obtained at baseline and 24 weeks[27]; each value was classified as normal or abnormal. ALT was the only parameter that showed a significant worsening from a normal baseline across groups; specifically, 0 telemonitoring arm participants (0%) versus 7 telemedicine participants (6.7%) (p = 0.014) experienced a worsening of ALT values. Authors also noted that 5 patients (4.8%) in the control arm experienced a decline in ALT from a baseline normal value. The study by Klingeman et al described 2 types of adverse events: (1) severe hypoglycemia and (2) foot ulcers.[24] Severe hypoglycemia was noted in the experimental (n = 1 or 3.3%) arm but not in the control (n = 0 or 0%) arm. Foot ulcer was noted in the experimental (n = 1 or 3.3%) and control (n = 3 or 10%) arms.

SUMMARY AND DISCUSSION

SUMMARY OF EVIDENCE BY KEY QUESTION

KQ 1a: The 1 study that met inclusion criteria enrolled patients with CHF who had a recent implantation of either an ICD or a CRT-D and randomized them to receive quarterly automated web-based review and follow-up of telemetry data versus synchronous personal follow-up (in-person vs phone-based) for 1 year and found no significant differences in clinical outcomes between the 3 groups. The certainty of evidence was downgraded to very low certainty because of serious ROB, indirectness, and imprecision (Table 3).

KQ 1b: The included study did not report outcomes by race/ethnicity, gender, age, and rural status.

KQ 2a, KQ 2b: We found no studies on the effect of synchronous virtual compared to in-person care for chronic management of COPD.

KQ 3a: We identified 4 studies (n = 466 participants)[24,27,29,30] that evaluated the provision of synchronous virtual care compared to in-person care for chronic management of T2DM. The 1 adequately powered, low ROB study found no statistically significant reduction in A1c between synchronous virtual care compared to usual care and asynchronous virtual care. Overall, findings from this review indicate that the impact of virtual care as a substitute for in-person care on A1c remains unclear. Hospitalizations, ER visits, number of contacts, and utilization were not uniformly reported across studies. Number of contacts and utilization varied by study and were not consistently reported. The certainty of evidence was downgraded to very low certainty because of serious ROB, indirectness, and imprecision.

KQ 3b: The 1 adequately powered, low ROB study was the only to report subgroup analyses by patient characteristics of interest, specifically age and gender. They found no statistically significant difference in reduction of A1c by age (< 55 years of age, ≥ 55 years) or gender.

KQ 4: Two of the studies on diabetes reported adverse events. There were small event rates and no evidence of differences by study arms.

Table 3. Certainty of Evidence for KQ 1 and 3

Outcome	Number of Studies (N patients)	Range of Effects	Certainty of Evidence (Rationale)
Type 2 Diabetes Mellitus			
A1c	4 randomized trials (339 patients)	Range from -0.15 to -1.30 difference in mean difference between intervention and comparator A1c	**Very low certainty that virtual care has an effect on A1c** (rated down for serious risk of bias, indirectness, and imprecision)
Hospital admission	2 randomized trials (285 patients)	Range from 0 to 3 admissions in the intervention arm and 0 to 7 admissions in comparator arm	**Very low certainty that virtual care has an effect on hospital admissions** (rated down for serious risk of bias, indirectness, and imprecision)

Outcome	Number of Studies (N patients)	Range of Effects	Certainty of Evidence (Rationale)
Emergency department visits	2 randomized trials (285 patients)	0 emergency department visits in the intervention arms and range from 0 to 1 visit in comparator arm	**Very low certainty that virtual care has an effect on emergency department attendance** (rated down for serious risk of bias, indirectness, and imprecision)
Congestive Heart Failure			
NYHA class/ symptoms	1 randomized trial (219 patients)	Between-group difference p = 0.967	**Very low certainty that virtual care has an effect on NYHA class/symptoms** (rated down for serious risk of bias, inconsistency, indirectness, and imprecision)
Hospital admission	1 randomized trial 219 patients)	RM (9.8%) vs RM + phone (11.3%) vs in-person visit (12.7%), p = 0.851	**Very low certainty that virtual care has an effect on hospital admission** (rated down for serious risk of bias, inconsistency, indirectness, and imprecision)

Abbreviations. A1c = Hemoglobin A1c; NYHA = New York Heart Association; RM = Remote Monitoring

PRIOR SYSTEMATIC REVIEWS

A 2016 AHRQ evidence map found 58 existing systematic reviews supporting the use of telehealth interventions for communication/counseling or remote monitoring for chronic conditions.[31] Previous systematic reviews have examined various ways of utilizing virtual care modalities in the context of these conditions of interest, but none focused on *replacing* in-person care with virtual visits. Our review sought to extend the existing literature by addressing telehealth as a replacement for in-person care in chronic disease management. We found scant evidence examining chronic disease management delivered by synchronous virtual care compared to in-person delivery for T2DM, COPD, and CHF.

Based on prior reviews, there is evidence that virtual care as an *adjunctive* strategy to typical in-person care can be associated with a decrease in A1c in patients with both type 1 and type 2 diabetes. For example, 1 systematic review by Hu et al included studies using various strategies such as remote monitoring, smart device, software, or web-based applications for patients with type I and II diabetes which led to decreased hemoglobin A1c compared to control. Additionally, Lee et al found a 0.43% reduction in A1c in patients with T2DM at 6 months across 107 randomized control trials with implementation of telemedicine strategies such as tele-monitoring, tele-education, or tele-consultation delivered by a variety of disciplines in comparison to usual care.[32,33] This is also supported by an umbrella review of 95 systematic reviews for patients with type 1 and type 2 diabetes noting a reduction in A1c by 0.2-0.4% when using mHealth (messaging or mobile applications) and virtual care (synchronous electronic communication) specifically.[34] Polisena et al[35] completed a systematic review on home remote monitoring and telephone support for patients with diabetes. The home remote monitoring led to a decrease in A1c and a decrease in overall hospital utilization and mixed emergency department use. The telephone support group had mixed results related to A1c with a non-significant effect on hospital and emergency department utilization (based on a single study for each). Utilization was not specifically related to T2DM complications. Patient satisfaction was equal to or improved in both groups compared to usual care.

While we only found 1 study on virtual care for chronic management of heart failure as a substitution for in-person care, prior systematic reviews report on the impact of other types of

virtual care on heart failure outcomes. A systematic review by Yun et al[36] included 37 studies evaluating telemonitoring which found reductions in all-cause and heart failure-related mortality compared to usual care. The same study also observed a non-statistically significant trend towards decreased heart failure-related hospitalizations, but no differences in all-cause hospitalizations. The Yun et al review showed improvement in the quality of life, but not patient satisfaction for the intervention compared to usual care. Similarly, an umbrella review on telemonitoring for heart failure by Bashi et al[37] found reductions in hospitalizations and mortality with increased quality of life. However, a systematic review of mHealth interventions (mobile devices for monitoring or messaging) with heart failure patients found mixed results for all-cause and cardiovascular mortality, heart failure-related hospitalizations and NYHA classification score.[38]

Overall, there is a strong body of evidence that virtual care modalities can improve health outcomes through the supplementation of in-person management of certain chronic diseases, particularly with approaches such as remote monitoring and patient education. Our review sought to build on this existing body of literature by evaluating the effectiveness of virtual care-delivered visits as a substitute for in-person visits for chronic disease management. However, we found that the research in this field remains insufficient and methodologically inconsistent.

HORIZON SCAN

Given the limited amount of existing literature we identified that addressed our key question, we sought to assess the pool of ongoing studies in the pipeline that would add relevant findings in the near future. To conduct such a scan of the literature on the horizon, we applied our previously developed search terms to the Cochrane Central Register of Controlled Trials. This search identified 1,787 unique records (see Table 4). At least 1 reviewer screened these at title and abstract. Included records were verified by a second reviewer.

We found only 3 records[39-41] that referenced studies without published results in our horizon scan (see Table 4). Studies that may potentially meet the inclusion criteria of our systemic review. All 3 of these studies are randomized controlled trials that were designed before the COVID-19 pandemic. Two of the 3 studies focus on T2DM[39,40] while the other is on CHF.[41] One of the T2DM studies is a non-inferiority study[40]; however, it is being conducted in Brazil (a non-OECD country) and therefore the findings may not be applicable to the Veteran population. The other T2DM study[39] is specifically focused on reducing emergency diabetes care for older (> 50 years) African Americans. The CHF study by Komkov et al has very limited detail. Thus, it appears that there is little trial-based research currently in the pipeline to inform our key questions in this review.

Table 4. Ongoing Studies on Virtual Care for Chronic Conditions

First author, year	Recruitment target Study design	Disease state	Intervention/Comparator	Planned duration	Clinical trials #
Rovner, 2018[39]	African Americans, > 50 years, T1DM or T2DM, after DM-related emergency department visit	T2DM	Multi-component intervention including behavioral activation and the facilitation of telehealth visits with	12 months	NCT03466866

	Single blind, Randomized controlled trial		primary care and a DM nurse educator vs multi-component intervention without telehealth facilitation or behavioral activation		
Rodrigues, 2019[40]	Patients with T2DM, > 18 years, referred from primary care Pragmatic, open-label, phase 2, non-inferiority, randomized controlled trial	T2DM	Teleconsultation with endocrinologist by video vs face-to-face	unclear	WHO Clinical Trials Registry ID: RBR-8gpgyd
Komkov, date unknown[41]	Patients with CHF discharged from the hospital Randomized controlled trial	CHF	Short-term education + active telephone calls by physician vs usual care	12 months	unknown

Abbreviations. CHF = congestive heart failure; DM = diabetes mellitus; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus; WHO = World Health Organization.

CLINICAL AND POLICY IMPLICATIONS

We found limited literature evaluating the effect of synchronous virtual care compared to in-person care for chronic disease management of common conditions, namely T2DM, COPD, and CHF. Among the included studies, there was significant heterogeneity around the structure, purpose, and delivery of virtual care visits. While not statistically significant and with very low certainty of evidence, our analysis suggested a trend toward greater A1c reduction among virtual care interventions versus comparators. The clinical significance of this finding is unknown. In addition, the generalizability of these findings is limited as all included studies took place in specialty care clinics whereas much of the long-term management for chronic conditions such as T2DM, CHF, and COPD occurs within the context of primary care. Primary care teams provide care for multiple conditions simultaneously which may not support the single disease-focused care described in the included studies.

The COVID-19 pandemic led to an increase in the use of virtual care as a way of making health care more accessible to patients while reducing potential infection risk associated with in-person care.[42] Specifically, the pandemic necessitated *replacement* of in-person care with virtual care, rather than simply supplementing existing visits. The significant shift in patient care delivery from in-person to virtual care has impacted clinical workflows, workforce needs, and patient experience. However, there is currently a paucity of trial data to describe the outcomes associated with replacing in-person care with virtual care for chronic disease management or to recommend substituting video visits as the standard of care for managing CHF, COPD, or T2DM moving forward. In addition, none of the included studies evaluated patient satisfaction with this change in patient care delivery. Ultimately, it will be critical to clarify if the scientific question of interest is whether virtual care delivery for chronic conditions is *more effective* than in-person or if it is *as effective* as in-person care. The difference between these objectives will need to drive study design. A recent commentary by Hertzer and Pronovost[43] pointed out that a better understanding of virtual care with respect to patient safety, effectiveness, efficiency, and equity will be necessary in order for optimal incorporation into clinical practice.

LIMITATIONS

Our findings should be considered within the context of limitations of the included studies and of our methodologic approach.

Limitations of Identified Literature

Publication Bias

Given the small number of studies we identified, statistical methods to detect publication bias were not conducted. While it is possible that individual health systems or clinics have conducted quality improvement studies evaluating differences in experiences between synchronous and in-person care – especially during the COVID-19 pandemic – we suspect it is unlikely that studies meeting EPOC criteria on this intervention have not been published given the recent emphasis on the role of virtual care.

Study Quality

We identified few studies overall and most had fewer than 100 patients and were assessed as unclear or high ROB. Intervention core components, intervention fidelity, or the impact of intervention on clinical workflow were not reported by any study. In addition, the interactions between clinicians and patients during virtual care episodes were not adequately or explicitly described. These omissions limit the interpretation and replication of evaluated interventions. While all studies for T2DM reported change in A1c, this is likely inappropriate for shorter durations of follow-up. Taking the standard duration for measuring changes from diabetes chronic management into account, studies should be at least 6 months in length, while durations of 12 months would be preferable. The majority of our outcomes of interest were not consistently reported across the studies. For example, while several studies provided some information on utilization and adverse events, this information on outcomes was not consistently or thoroughly reported. Only 1 study by Jeong et al[27] had an optimal study design for our question regarding the effectiveness of synchronous virtual care compared to in-person care; the other included studies featured this comparison as a secondary focus or delivered the virtual care intervention with co-interventions such as remote monitoring and other clinical activities.

Heterogeneity

Heterogeneity was noted across the identified literature. First, included virtual care interventions used different virtual care modalities (*eg*, email, phone, video), with different hardware, delivered via different numbers of clinical interactions between patients and clinicians, and over a wide range of intervention durations. Second, studies occurred in different health care systems and countries, which likely have varied broadband access, existing virtual care infrastructure, clinical resources, and workflow processes. Finally, the identified interventions demonstrated marked variation around the clinical focus (*eg,* short-term stabilization of recently hospitalized poorly controlled diabetes, longer-term management of patients with diabetes not on insulin) and team structure of virtual care delivery (*eg,* clinicians alone vs nurses with clinician consultation).

Limitations of Our Methodologic Approach

Our review benefited from being protocol driven, leveraging input from an expert panel consisting of clinicians and virtual care researchers, identifying disease-specific clinical outcomes, using a conceptual model to guide understanding of virtual care modalities, and using a detailed approach to categorizing and defining virtual care components in chronic disease self-management. Despite these strengths, limitations exist to our approach. We only included studies that met EPOC criteria in this review; however, observational studies may have findings relevant to the provision of synchronous virtual care for chronic illness management. Only 6 studies were excluded due to study design. It is possible that additional observational studies conducted since the onset of the COVID-19 pandemic may provide useful information (*eg*, NCT02788903). In addition, we focused this review on 3 of the most prevalent chronic diseases, but there may be appropriately designed studies that targeted other conditions that we did not include. Finally, we only included studies conducted in OECD countries, and as a result we may have missed relevant studies not conducted in these countries.

Applicability of Findings to the VA Population

None of the included studies were conducted in VHA or reported specifically targeting Veterans. However, 1 study among patients with T2DM occurred in a military setting with an average age of 63 years. Two studies were conducted in countries with nationalized health care (*ie,* South Korea, Denmark), which may increase relevancy to VHA. Identified studies included primarily older participants, which is similar to the population of Veterans who have chronic disease.

RESEARCH GAPS

We identified several areas that are worthy of further exploration in order to strengthen future research in this area. To systematically identify these gaps in the current literature, we used an existing framework (Table 5) by Robinson and colleagues[44] which proposes to identify gaps categorically using the PICOTS framework (population, intervention, comparator, outcome, timing, and setting). In addition, they include standardized reasons that the current literature is insufficient to answer the question at hand (insufficient or imprecise information, biased information, inconsistency, and/or not the right information).

Overall, there are 5 key areas in which future research on this topic could fill existing gaps and/or could improve the approach. First, and perhaps most importantly, virtual care interventions should be thoroughly described in order to be replicated (*eg,* number of patient contacts, the type of training for clinician using virtual care) and to determine if findings are generalizable to specific clinical setting. Guidance exists on mobile and web-based interventions which may provide indirect suggestions about key characteristics for virtual care intervention description.[45] Further efforts to outline key characteristics of virtual care interventions could be valuable. Second, there is a need to evaluate how best to integrate virtual care as a substitute for in-person care (*eg,* replace all vs a portion), when to include other adjunctive virtual care technologies (*eg,* remote monitoring), and in which clinical settings (*eg,* primary care vs specialty care settings) as the challenges and effectiveness can be expected to vary across settings with different workflow patterns, clinical resources, and competing clinical demands. Third, outcomes varied across included studies and omitted some key outcomes relevant to interpreting the benefits and risks of this type of intervention including impact on clinical

workflow, patient satisfaction with virtual care experience, and subsequent utilization. Fourth, investigators should consider utilization of non-inferiority analytic approaches when, in fact, the question at hand is whether or not virtually delivered care is *as good as* in-person delivered care. Finally, investigators should be encouraged to consider *a priori* identified subgroup evaluations or make individual patient-level data available for future combined analyses that could identify which patient-level characteristics are associated with better outcomes with virtual care as a substitute for in-person care. The VA is well-positioned to conduct needed evaluations of synchronous virtual care given its well-established virtual care infrastructure, uptake of virtual visits, regular assessment of patient satisfaction, and available administrative data. Such information could guide clinics and health care systems to offer optimal patient-centered virtual care delivery.

A critical concern about the proliferation and acceleration of virtual modalities to deliver health care is the potential to introduce or increase existing health care access disparities. Individuals without camera-ready devices, adequate broad-band internet connections, or comfort with technology will have greater challenges in fully engaging in virtual health care offerings. This disparity may be more common amongst some patient populations (*eg,* rural dwelling, older age, racial/ethnic underrepresented groups) and may exacerbate historically inequitable treatment and institutional racism by the medical establishment. To adequately study such disparities in future systematic reviews, specific methodological approaches are needed. As noted above, primary research studies must include adequately powered *a priori* subgroup analysis of patient populations of interest and include enhanced recruitment and retention strategies to achieve enrollment targets. In addition, reporting outcomes by subpopulation could support hypothesis generation for future study even when not adequately powered for definitive analysis. Reporting findings by subpopulation and making patient-level data available for individual patient data meta-analysis could support the ability to generate meaningful evidence synthesis about effect variation by patient-level characteristics. New platforms and open access websites have developed to enable the sharing of deidentified datasets for such purposes. Such steps would allow future research to address concerns about equitable benefit and access to virtual care.

Table 5. Evidence Gaps and Areas for Future Research Consideration

Evidence Gap/Area for Future Exploration	Reason	Types of Studies to Consider
Population		
• Patients with poorly controlled chronic conditions • Patients with well-controlled chronic conditions • Patients with various social/digital determinants of health • Patients who are earlier in their course of chronic illness or at various stages of disease	Insufficient information/ Not the right information	Well-designed subgroup analyses or individual patient-data meta-analysis from randomized trials Qualitative and mixed methods studies
Interventions		
• Video-based and/or phone-based care to replace *some portion* of in-person all chronic	Insufficient or imprecise information	Randomized trials Non-randomized trials

disease management by specialists and/or primary care • Video-based and/or phone-based care to replace *all* chronic disease management by specialists and/or primary care • Different models of combining video-based and/or phone-based care with in-person care for chronic disease management • Interventions using currently available and widely used virtual care platforms (*eg,* Zoom, Apple Health *etc*)		Qualitative and mixed methods studies
Comparators		
• Routine in-person care • Telephone vs video-based care	Insufficient information	Randomized trials Non-randomized trials
Outcomes		
• Patient utilization (*eg,* downstream in-person care including hospitalization and urgent care visits) • Process variables (*eg,* time providing direct and indirect care, number of missed visits, consultation time) • Costs • Patient satisfaction • Clinician satisfaction • Impact on clinical workflow • Harms (delayed care, missed diagnoses, *etc*) • Fidelity to virtual care and in-person care (*eg,* topics covered, care delivered)	Insufficient information/ imprecise information; inconsistent information	Randomized trials Non-randomized trials Qualitative and mixed methods studies
Setting		
• Primary care • Variety of clinical settings (*eg*, large health care systems, smaller community-based practices)	Insufficient information	Randomized Trials Non-randomized Trials

CONCLUSIONS

Virtual modalities such as video or telephone have increasingly been used to replace in-person clinic visits with prescribing clinicians for the management of chronic conditions, particularly during the COVID-19 pandemic. However, currently there is scant evidence of the effect of virtual care as a replacement for in-person visits in the context of common chronic conditions such as T2DM or CHF, and no evidence for COPD. Health care systems need evidence-based guidance about the effect of well-described virtual care interventions in order to deliver high-quality care using the right modality for the right patients with the right clinical condition at the right time.

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APPENDIX A. SEARCH STRATEGIES

Database: MEDLINE (via Ovid MEDLINE(R) ALL 1946 to February 5, 2021)
Search Date: 2/7/2021

Search Set	Search Strategy	Results
#1 *Virtual Care terms*	exp Telemedicine/ or exp Remote Consultation/ or Videoconferencing/ or Telephone/ or exp Cell Phone/ or exp Computers, Handheld/ or (virtual or virtually or telehealth or tele-health or telemedicine or tele-medicine or telemedical or tele-medical or telecare or tele-care or teleconsult* or tele-consult* or telecommunicat* or tele-communicat* or telemanag* or tele-manag* or telehome or tele-home or telepharmac* or tele-pharmac* or telecardiol* or tele-cardiol* or tele-cardiac or teleintervention* or tele-intervention* or teleconferenc* or tele-conferenc* or telephon* or tele-phon* or cellphon* or cell-phon* or smartphon* or "mobile phone" or "mobile phones" or e-visit* or evisit* or e-care or ecare or e-consult* or econsult* or e-diagnos* or ediagnos* or e-medicine or emedicine or e-physician* or ephysician* or eclinician* or e-clinician* or e-pharm* or epharm* or "communication technology" or "communication technologies" or eHealth or e- health or "e health" or mHealth or m-health or "m health").ti,ab.	271,845
#2 *Virtual care terms, cont.*	((mobile or digital) adj health*).ti,ab.	6,153
#3 *Virtual care terms, cont*	((videoconferenc* or video-conferenc* or webconferenc* or web-conferenc* or webex or zoom or skype or ooVoo or FaceTime or Tango or GoToMeeting or "web based" or web-based or webbased) adj2 health*).ti,ab.	711
#4 *Virtual care terms, cont.*	(tele adj (care or diagnos* or health* or intervention* or manag* or therap* or treat* or medicine or medical or prescrib* or prescript*)).ti,ab.	404
#5 *Virtual care terms, cont.*	((remote* or video* or internet or web or online) adj2 (meet* or call* or chat* or conferenc* or consult* or care or counsel* or visit*)).ti,ab.	8,431
#6 *combining*	1 or 2 or 3 or 4 or 5	279,398
#7 *HF terms*	exp Heart Failure/ or (CHF or CCF or HFpEF or HFrEF or "systolic dysfunction" OR "diastolic dysfunction").ti,ab.	144,721
#8 *HF terms, cont.*	((heart or cardiac or cardiogenic) adj1 (failure or shock or arrest)).ti,ab.	226,892
#9 *HF terms, cont.*	((preserved or reduced) adj2 "ejection fraction").ti,ab.	9,110
#10	exp Diabetes Mellitus, Type 2/ or (DM or DM2 or DMii or T2D or T2DM or NIDDM or IDDM or MODY).ti,ab.	199,623

T2DM terms		
#11 *T2DM terms, cont.*	(diabet* adj2 ("type 2" or "type two" or II or "adult onset" or adult-onset or noninsulin or "non insulin" or non-insulin or maturity-onset or "maturity onset" or "slow onset" or slow-onset)).ti,ab.	165,479
#12 *COPD terms*	exp Pulmonary Disease, Chronic Obstructive/ or (COPD or COAD or emphysema*).ti,ab.	89,548
#13 *COPD terms, cont.*	(obstruct* adj2 (pulmonary or lung* or airflow* or airway* or bronch* or respirat*)).ti,ab.	87,246
#14 *COPD terms, cont.*	(chronic adj2 bronchit*).ti,ab.	11,051
#15 *combining*	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	653,893
#16 *combining*	6 and 15	7,731
#17 *Animal-only study exclusion*	16 not (exp animals/ not exp humans/)	7,532
#18 *Population exclusion*	17 not ((exp adolescent/ or exp child/ or exp infant/) not exp adult/)	7,345
#19 *Study designs*	exp Evaluation Studies as Topic/ or exp Cohort Studies/ or exp Longitudinal Studies/ or randomized controlled trial.pt. or controlled clinical trial.pt. or comparative study.pt. or clinical trial.pt. or evaluation study.pt. or (randomized or randomised or randomization or randomisation or placebo or randomly or trial or groups or "clinical trial" or "clinical trials" or "evaluation study" or "evaluation studies" or "intervention study" or "intervention studies" or cohort or longitudinal or longitudinally or prospective or prospectively or "follow up" or "comparative study" or "comparative studies" or nonrandom or "non-random" or nonrandomized or "non-randomized" or nonrandomised or "non-randomised" or quasi-experiment* or quasiexperiment* or quasirandom* or quasi-random* or quasi-control* or quasicontrol* or "pre-post" or posttest or "post-test" or pretest or "pre-test" or "repeated measure" or "repeated measures").ti,ab.	7,831,571
#20 *Study designs*	(before and after).ti,ab.	771,878
#21 *Study designs*	(before and during).ti,ab.	403,950
#22 *Study designs*	("time series" and interrupt*).ti,ab.	3,697
#23 *Study designs*	("time points" and (multiple or one or two or three or four or five or six or seven or eight or nine or ten or month or monthly or day or daily or week or weekly or hour or hourly)).ti,ab.	69,056
#24	19 or 20 or 21 or 22 or 23	8,265,282
#25	18 and 24	4,784

Database: EMBASE (via Elsevier)
Search date: 2/7/2021
Note: search from the Results page

Search Set	Search Strategy	Results
#1 *Virtual Care terms*	'telemedicine'/exp OR 'teleconsultation'/exp OR 'videoconferencing'/exp OR 'telephone'/exp OR 'mobile phone'/exp OR 'personal digital assistant'/exp OR (virtual OR virtually OR telehealth OR tele-health OR telemedicine OR tele-medicine OR telemedical OR tele-medical OR telecare OR tele-care OR teleconsult* OR tele-consult* OR telecommunicat* OR tele-communicat* OR telemanag* OR tele-manag* OR telehome OR tele-home OR telepharmac* OR tele-pharmac* OR telecardiol* OR tele-cardiol* OR tele-cardiac OR teleintervention* OR tele-intervention* OR teleconferenc* OR tele-conferenc* OR telephon* OR tele-phon* OR cellphon* OR cell-phon* OR smartphon* OR smart-phon* OR 'mobile phone' OR 'mobile phones' OR e-visit* OR evisit* OR e-care OR ecare OR e-consult* OR econsult* OR e-diagnos* OR ediagnos* OR e-medicine OR emedicine OR e-physician* OR ephysician* OR eclinician* OR e-clinician* OR e-pharm* OR epharm* OR 'communication technology' OR 'communication technologies' OR eHealth OR e- health OR 'e health' OR mHealth OR m-health OR 'm health'):ti,ab	324,073
#2 *Virtual care terms, cont.*	((mobile OR digital) NEAR/1 health*):ti,ab	6,902
#3 *Virtual care terms, cont*	((videoconferenc* OR video-conferenc* OR webconferenc* OR web-conferenc* OR webex OR zoom OR skype OR ooVoo OR FaceTime OR Tango OR GoToMeeting OR 'web based' OR web-based OR webbased) NEAR/2 health*):ti,ab	767
#4 *Virtual care terms, cont.*	(tele NEAR/1 (care OR diagnos* OR health* OR intervention* OR manag* OR therap* OR treat* OR medicine OR medical OR prescrib* OR prescript*)):ti,ab	896
#5 *Virtual care terms, cont.*	((remote* OR video* OR internet OR web OR online) NEAR/2 (meet* OR call* OR chat* OR conferenc* OR consult* OR care OR counsel* OR visit*)):ti,ab	11,958
#6 *combining*	#1 OR #2 OR #3 OR #4 OR #5	334,175
#7 *HF terms*	'heart failure'/exp OR (CHF OR CCF OR HFpEF OR HFrEF OR 'systolic dysfunction' OR 'diastolic dysfunction'):ti,ab	570,806
#8 *HF terms, cont.*	((heart OR cardiac OR cardiogenic) NEAR/1 (failure OR arrest OR shock)):ti,ab	383,299
#9	((preserved OR reduced) NEAR/2 'ejection fraction'):ti,ab	18,518

HF terms, cont.		
#10 *T2DM terms*	'non insulin dependent diabetes mellitus'/exp OR (DM OR DM2 OR DMii OR T2D OR T2DM OR NIDDM OR IDDM OR MODY):ti,ab	360,063
#11 *T2DM terms, cont.*	(diabet* NEAR/2 ('type 2' OR 'type two' OR II OR 'adult onset' OR adult-onset OR noninsulin OR 'non insulin' OR non-insulin OR maturity-onset OR 'maturity onset' OR 'slow onset' OR slow-onset)):ti,ab	249,817
#12 *COPD terms*	'chronic obstructive lung disease'/exp OR (COPD OR COAD OR emphysema*):ti,ab	196,655
#13 *COPD terms, cont.*	(obstruct* NEAR/2 (pulmonary OR lung* OR airflow* OR airway* OR bronch* OR respirat*)):ti,ab	130,569
#14 *COPD terms, cont.*	(chronic NEAR/2 bronchit*):ti,ab	17,776
#15 *combining*	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	1,242,111
#16 *combining*	#6 AND #15	17,245
#17 *Animal-only study exclusion*	#16 AND [humans]/lim	15,940
#18 *Population exclusion*	#17 NOT (([child]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim) NOT ([adult]/lim OR [middle aged]/lim OR [young adult]/lim))	15,600
#19 *Study designs*	'randomized controlled trial'/exp OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'single blind procedure'/exp OR randomization:ti,ab OR randomisation:ti,ab OR randomized:ti,ab OR randomised:ti,ab OR randomly:ti,ab OR crossover:ti,ab OR 'cross over':ti,ab OR placebo:ti,ab OR 'double blind':ti,ab OR 'double blinded':ti,ab OR 'single blind':ti,ab OR 'single blinded':ti,ab OR 'clinical study'/exp OR 'clinical trial':ti,ab OR 'clinical trials':ti,ab OR 'controlled study'/exp OR 'evaluation study'/exp OR 'evaluation study':ti,ab OR 'evaluation studies':ti,ab OR 'intervention study'/exp OR 'intervention study':ti,ab OR 'intervention studies':ti,ab OR 'case control study'/exp OR 'case control':ti,ab OR 'cohort analysis'/exp OR cohort:ti,ab OR cohorts:ti,ab OR longitudinal:ti,ab OR longitudinally:ti,ab OR prospective:ti,ab OR prospectively:ti,ab OR retrospective:ti,ab OR 'follow up'/exp OR 'follow up':ti,ab OR 'comparative effectiveness'/exp OR 'comparative study'/exp OR 'comparative study':ti,ab OR 'comparative studies':ti,ab	17,359,756
#20 *Study designs*	'pre post':ti,ab OR prepost:ti,ab OR 'post test':ti,ab OR posttest:ti,ab OR pretest:ti,ab OR 'pre test':ti,ab OR 'quasi experiment':ti,ab OR quasiexperiment:ti,ab OR 'quasi experimental':ti,ab OR quasiexperimental:ti,ab OR quasirandom:ti,ab OR 'quasi	132,600

	random':ti,ab OR 'quasi control':ti,ab OR quasicontrol:ti,ab OR 'repeated measure':ti,ab OR 'repeated measures':ti,ab	
#21 *Study designs*	('time series':ti,ab AND interrupt*:ti,ab) OR (before:ti,ab AND after:ti,ab) OR (before:ti,ab AND during:ti,ab)	1,360,078
#22 *Study designs*	'time points':ti,ab AND (multiple:ti,ab OR one:ti,ab OR two:ti,ab OR three:ti,ab OR four:ti,ab OR five:ti,ab OR six:ti,ab OR seven:ti,ab OR eight:ti,ab OR nine:ti,ab OR ten:ti,ab OR month:ti,ab OR monthly:ti,ab OR day:ti,ab OR days:ti,ab OR daily:ti,ab OR week:ti,ab OR weekly:ti,ab OR hour:ti,ab OR hourly:ti,ab)	115,754
#23 *combining*	#19 OR #20 OR #21 OR #22	17,784,738
#24 *combining*	#18 AND #23	11,324
#25 *exclusions*	#24 NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR [editorial]/lim OR 'letter'/exp OR [letter]/lim OR 'note'/exp OR [note]/lim OR [conference abstract]/lim OR 'conference abstract'/exp OR 'conference abstract'/it)	6,461

Database: Cochrane Central Register of Controlled Trials (via Ovid)
Search date: 6/29/2021
Note: through May 2021

Search Set	Search Strategy	Results
#1 *Virtual Care terms*	exp Telemedicine/ or exp Remote Consultation/ or Videoconferencing/ or Telephone/ or exp Cell Phone/ or exp Computers, Handheld/ or (virtual or virtually or telehealth or tele-health or telemedicine or tele-medicine or telemedical or tele-medical or telecare or tele-care or teleconsult* or tele-consult* or telecommunicat* or tele-communicat* or telemanag* or tele-manag* or telehome or tele-home or telepharmac* or tele-pharmac* or telecardiol* or tele-cardiol* or tele-cardiac or teleintervention* or tele-intervention* or teleconferenc* or tele-conferenc* or telephon* or tele-phon* or cellphon* or cell-phon* or smartphon* or "mobile phone" or "mobile phones" or e-visit* or evisit* or e-care or ecare or e-consult* or econsult* or e-diagnos* or ediagnos* or e-medicine or emedicine or e-physician* or ephysician* or eclinician* or e-clinician* or e-pharm* or epharm* or "communication technology" or "communication technologies" or eHealth or e- health or "e health" or mHealth or m-health or "m health").ti,ab.	44,030
#2 *Virtual care terms, cont.*	((mobile or digital) adj health*).ti,ab.	1,594
#3 *Virtual care terms, cont*	((videoconferenc* or video-conferenc* or webconferenc* or web-conferenc* or webex or zoom or skype or ooVoo or FaceTime or	277

	Tango or GoToMeeting or "web based" or web-based or webbased) adj2 health*).ti,ab.	
#4 *Virtual care terms, cont.*	(tele adj (care or diagnos* or health* or intervention* or manag* or therap* or treat* or medicine or medical or prescrib* or prescript*)).ti,ab.	182
#5 *Virtual care terms, cont.*	((remote* or video* or internet or web or online) adj2 (meet* or call* or chat* or conferenc* or consult* or care or counsel* or visit*)).ti,ab.	3,208
#6 *combining*	1 or 2 or 3 or 4 or 5	46,651
#7 *HF terms*	exp Heart Failure/ or (CHF or CCF or HFpEF or HFrEF or "systolic dysfunction" OR "diastolic dysfunction").ti,ab.	14,236
#8 *HF terms, cont.*	((heart or cardiac or cardiogenic) adj1 (failure or shock or arrest)).ti,ab.	33,892
#9 *HF terms, cont.*	((preserved or reduced) adj2 "ejection fraction").ti,ab.	2,416
#10 *T2DM terms*	exp Diabetes Mellitus, Type 2/ or (DM or DM2 or DMii or T2D or T2DM or NIDDM or IDDM or MODY).ti,ab.	30,890
#11 *T2DM terms, cont.*	(diabet* adj2 ("type 2" or "type two" or II or "adult onset" or adult-onset or noninsulin or "non insulin" or non-insulin or maturity-onset or "maturity onset" or "slow onset" or slow-onset)).ti,ab.	42,140
#12 *COPD terms*	exp Pulmonary Disease, Chronic Obstructive/ or (COPD or COAD or emphysema*).ti,ab.	19,378
#13 *COPD terms, cont.*	(obstruct* adj2 (pulmonary or lung* or airflow* or airway* or bronch* or respirat*)).ti,ab.	16,735
#14 *COPD terms, cont.*	(chronic adj2 bronchit*).ti,ab.	1,877
#15 *combining*	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	109878
#16 *combining*	6 and 15	4,022
#17 *Animal-only study exclusion*	16 not (exp animals/ not exp humans/)	4,022
#18 *Population exclusion*	17 not ((exp adolescent/ or exp child/ or exp infant/) not exp adult/)	4,008
#19 *Study designs*	exp Evaluation Studies as Topic/ or exp Cohort Studies/ or exp Longitudinal Studies/ or (randomized or randomised or randomization or randomisation or placebo or randomly or trial or groups or "clinical trial" or "clinical trials" or "evaluation study" or	1,390,806

	"evaluation studies" or "intervention study" or "intervention studies" or cohort or longitudinal or longitudinally or prospective or prospectively or "follow up" or "comparative study" or "comparative studies" or nonrandom or "non-random" or nonrandomized or "non-randomized" or nonrandomised or "non-randomised" or quasi-experiment* or quasiexperiment* or quasirandom* or quasi-random* or quasi-control* or quasicontrol* or "pre-post" or posttest or "post-test" or pretest or "pre-test" or "repeated measure" or "repeated measures").ti,ab.	
#20 *Study designs*	("time series" and interrupt*).ti,ab.	395
#21 *Study designs*	("time points" and (multiple or one or two or three or four or five or six or seven or eight or nine or ten or month or monthly or day or daily or week or weekly or hour or hourly)).ti,ab.	20,644
#22	19 or 20 or 21	1,391,931
#23	18 and 22	3,637

APPENDIX B. STUDY CHARACTERISTICS TABLE

Study Country # Enrolled # Arms Funding Source Companion Paper	Type of intervention Frequency Duration	Eligibility	Population Mean Age (SD) Female % Race % VA based	Outcomes Types	Risk of Bias for Objective and Patient-Reported Outcomes
Congestive heart failure					
Hansen, 2018[28] Germany 210 patients 3 arms Abbott	Remote monitoring +telephone; Remote monitoring + in-person; Remote monitoring + automated telemetry follow-up Quarterly 12 months	Inclusion criteria: (1) 18-80 years; (2) CHF w/ LVEF ≤ 35%, NYHA class I-III; (3) home infrastructure to support use of a home transmitter and status post ICD/CRT-D implantation (new, upgrade, or generator replacement). Exclusion criteria: (1) 2nd degree Mobitz type II AV block; (2) 3rd degree AV block; (3) severe renal insufficiency; (4) less than 1-year life expectancy; (5) pregnant; (6) already enrolled in a study; (7) MI/ cardiac catheter within 3 months prior to the study.	Mean age: 65.1 (10.1) Female: 14.8% Race: NR Not VA based	NYHA class/symptoms Hospitalization	Objective: Unclear Patient reported: High
Type 2 diabetes mellitus					
Jeong, 2018[27] South Korea 338 patients 3 arms	Remote Monitoring + video; In-person 3 times 24 weeks	Inclusion criteria: T2DM with A1c range 7-11%. Exclusion criteria: (1) using insulin (basal or premixed insulin) more than twice a day; (2) unable to use a personal	Mean age: 53 (9.10) Female: 33% Race: NR Not VA based	A1c ER visits Hospitalization	Objective: Low Patient reported: Low

Korea Ministry of Health & Welfare		computer to access the Internet at home; (3) acute illness, liver dysfunction, renal dysfunction, or chronic lung disease, or any other medical conditions that could affect glycemic level.			
Klingeman, 2017[24] USA 60 patients 2 arms University of Michigan	Telephone and email monitoring; In-person Variable number of contacts per patient 1 year	Inclusion criteria: (1) adults w/ T2DM w/ 3+ diabetes meds +/- insulin; (2) A1c >/= 8%, </= 11; (3) able and willing to use telephonic communication regularly between visits; and (4) new patients prior to first visit to the endocrinology clinic. Exclusion criteria: (1) non-English speakers; (2) patients already treated by an endocrinologist; (3) shortened life expectancy.	Mean age: 54.4 (9.6) Female: 47% Race: 87% White; 10% Black; 2% Hispanic; 2% Other Not VA based	A1c ER visits Hospitalization	Objective: High Patient reported: High
Rasmussen, 2016[29] Denmark 40 patients 2 arms Danish National Health Department	Video visits conducted via specialized equipment (TandBerg E20) 3 weeks	Inclusion criteria: (1) live at home; (2) able to communicate by video telephone; (3) no psychiatric disorders; (4) age 40-85 years; (5) able to administer medication themselves. Exclusion criteria: (1) type 1 diabetes mellitus; (2) speech disabilities; (3) non-Danish speakers; (4) severe chronic disease (renal failure, liver insufficiency, current cancer treatment).	Median age: 62.7 Female: 32% Race: 100% White Not VA based	A1c	Objective: Low Patient reported: NA
Whitlock, 2000[30] USA 28 patients	Video telemedicine was delivered via the Aviva tele-care equipment	Inclusion criteria: (1) adults with a A1c > 8%; (2) diagnosis of T2DM.	Mean age: 63 (NR) Female: 61% Race: NR Not VA based	A1c	Objective: High

2 arms Department of Defense	which included a blood pressure meter and an electronic stethoscope. Nurse case manager contact once a week and physician contact once a month 3 months	Exclusion criteria: (1) inability to use equipment; (2) pending surgery; (3) documented psychiatric history; (4) A1c < 8.0%.			Patient reported: Unclear

Abbreviations. A1c = Hemoglobin A1c; AV = atrioventricular; CHF = congestive heart failure; CRT -D = cardiac resynchronization therapy-defibrillator; ER = emergency room; ICD = implanted cardioverter defibrillator; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NR = not reported; NYHA= New York Heart Association; T2DM = type 2 diabetes mellitus.

APPENDIX C. INTERVENTION CHARACTERISTICS TABLE

Author, Year # Enrolled # Arms	Intervention description	Mode of intervention Platform Type of Clinician(s)	Frequency of contacts Duration of contact	Data available at the time of the virtual interaction	Comparator
Congestive heart failure					
Hansen 2018 [28] 210 patients 3 arms	Patients with CHF followed for 12 months between first and 13th month post-implantation of ICD/CRT-D – 1 arm with remote telemetry monitoring with automated quarterly follow-up and a second arm in which patients received personal, scheduled quarterly follow-up. Personal contact arm randomized to phone vs in-person contact for follow-up (comparison of interest).	Remote monitoring + telephone; Remote monitoring + in-person; Remote monitoring + automated follow-up Remote monitoring and automated follow-up were reported via Merlin.net and "Merlin@Home"™ transmitter Cardiologist	4 phone contacts; 4 face-to-face contacts 12 months	ICD/CRT-D telemetry data	Arm 1: Remote monitoring + in-person, previously scheduled visits; Arm 2: Remote monitoring + automated follow-up
Type 2 diabetes mellitus					
Jeong, 2018 [27] 338 patients 3 arms	Three arms (1 usual care, 2 active intervention); comparison of interest among 2 intervention arms Telemonitoring group: involves asynchronous transmission of home glucose values via "Smart Care Unit" and receives automated responses by algorithm and weekly general DM education with in-person follow-up on 8, 16, 24 weeks	Video; In-person Smart care unit: personal tablet with abilities to: (1) video conference and text message endocrinologist; (2) auto-transmit blood glucose data from patient's glucometer; (3) provide additional	8, 16, 24 weeks 24 weeks	Remote monitoring home glucose values; body composition analyzer	Arm 1: Conventional care; Arm 2: telemonitoring with all visits in-person

	Telemedicine group: involves telemonitoring as described but follow-up with endocrinology were by video at weeks 8 and 16 while 24-week follow-up was in person.	information to support diabetes self-care. Endocrinologist			
Klingeman, 2017 [24] 60 patients 2 arms	The intervention consisted of endocrinology clinic-initiated and pre-scheduled phone calls or emails; frequency of interaction was tailored to each patient. Interactions consisted of reviewing glucose readings and monitoring blood pressure. Ad hoc clinic visits could be added as indicated, and pre-scheduled contact intervals adjusted.	Telephone; In-person; email Endocrinologist	Variable "tailored" per patient 1 year	BP, glucose checks	Usual In-person care
Rasmussen, 2016[29] 40 patients 2 arms	Tested home treatment of T2DM by video consultation versus standard outpatient care. Patients who completed higher-level T2DM care with an endocrinologist for poor metabolic control were transferred back to their GP at the completion of this care (usually 3 weeks). The intervention consisted of video consultations alternating between the clinician or nurse and patient. The control group attended outpatient visits.	Video Videophone (model TandBerg E20) Endocrinologist; Nurses	NR 3 weeks	BP	Usual In-person care
Whitlock, 2000[30] 28 patients	Over a 3-month study period, the intervention group received weekly telemonitoring (voice and video interaction) visits by the case manager and once a	Video Video system: Aviva 20/20 and then 10/10	Nurse case manager contact once a week and physician contact once a month	Data from case manager: blood glucose readings, blood pressure, weight,	Usual In-person care

2 arms	month physician telemedicine (voice and video interaction) visits compared to the control group which received usual care. For intervention participants, the case manager, internist, and family practitioner emailed about the patient's status, progress, and medication.	Internist, family practitioner, case manager	3 months	hypoglycemic episodes	

Abbreviations. BP = blood pressure; CHF = congestive heart failure; CRT -D = cardiac resynchronization therapy-defibrillator; GP = general practitioner; ICD =implanted cardiac defibrillator; T2DM = type 2 diabetes mellitus

APPENDIX D. REPORTED OUTCOMES TABLE

Study	Outcomes reported
Type 2 diabetes mellitus	
Jeong, 2018[27]	- Change in A1c
Klingeman, 2017[24]	- Change in A1c
Rasmussen, 2016[29]	- Change in A1c
Whitlock, 2000[30]	- Change in A1c
Klingeman, 2017[24]	- Hospitalization
Klingeman, 2017[24]	- Hospitalization
Jeong, 2018[27]	- ED attendance
Klingeman, 2017[24]	- ED attendance
Congestive heart failure	
Hansen, 2018[28]	- NYHA class/symptoms
Hansen, 2018[28]	- Hospitalization
Harms	
Jeong, 2018[27]	- Adverse events - Death
Klingeman, 2017[24]	- Hypoglycemia
Other utilization outcomes	
Hansen, 2018[28]	- Unscheduled follow-ups - Proportion of all follow-ups that had disease-relevant findings
Klingeman, 2017[24]	- Additional diabetes education - Face-to-face visits - Phone calls - Emails
Rasmussen, 2016[29]	- Consultations
Other clinical outcomes	
Hansen, 2018 [28]	- Arrhythmias - Number of delivered/appropriate ICD Therapies - Changes in QoL - All-cause mortality
Jeong, 2018 [27]	- Frequency of hypoglycemia - Changes in fasting blood glucose - Lipid profiles

	- Body weight - BMI - Percent achieving goal A1c - Compliance with medications - Compliance with self-monitoring of blood glucose - Labs: AST, ALT, creatinine
Klingeman, 2017[24]	- Statin use - Insulin use - Foot ulcers - Blood pressure - BMI
Rasmussen, 2016[29]	- Mean glucose - Systolic blood pressure - Diastolic blood pressure - Cholesterol - LDL - Weight
Whitlock, 2000[30]	- Total body weight - Microalbumin - Creatinine - Triglycerides - LDL
Other outcomes	
Whitlock, 2000[30]	- DQOL survey and SF36 - Clinician survey (limited results reported in this paper)

Abbreviations. A1c = hemoglobin A1c; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; DQOL = Diabetes Quality of Life; ED = emergency department; ICD = implanted cardio-defibrillator; LDL = low density lipoprotein cholesterol; NYHA = New York Heart Association; QoL = quality of life; SF36 = Medical Outcome Study Health Survey

APPENDIX E. EXCLUDED STUDIES

	Exclusion Reason					
Study	**Not OECD**	**Not Population**	**Not Intervention**	**Not Outcomes**	**Not Comparator**	**Not Design**
Antonicelli, 2010[1]			X			
Basudev, 2016[2]			X			
Bekelman, 2015[3]			X			
Benatar, 2003[4]			X			
Bentley, 2014[5]			X			
Berkhof, 2015[6]			X			
Biermann, 2000[7]		X				
Blumenthal, 2014[8]			X			
Bowles, 2009[9]			X			
Brandon, 2009[10]			X			
Carral, 2015[11]		X				
Cartwright, 2013[12]			X			
Chen, 2019[13]	X					
Chen, 2011[14]	X					
Choe, 2005[15]			X			
Chwalow, 1989[16]			X			
Clifford, 2005[17]			X			
Cohen, 2020[18]					X	
Comin-Colet, 2016[19]			X			
Creason, 2001[20]			X			
Cui, 2013[21]			X			
Dadosky, 2018[22]			X			
Dale, 2007[23]						X
Dansky, 2008[24]			X			
Dansky, 2009[25]			X			
de la Porte, 2007[26]			X			

	Exclusion Reason					
Study	**Not OECD**	**Not Population**	**Not Intervention**	**Not Outcomes**	**Not Comparator**	**Not Design**
De Simone, 2015[27]			X			
de Vries, 2011[28]			X			
Dienstl, 2011[29]						X
Dixon, 2020[30]					X	
Doyle, 2017[31]			X			
Durso, 2003[32]			X			
Egede, 2018[33]			X			
Egede, 2017[34]			X			
Ell, 2012[35]		X				
Farrero, 2001[36]			X			
Farsaei, 2011[37]	X					
Gamez-Lopez, 2012[38]			X			
Gellis, 2012[39]			X			
González-Guerrero, 2018[40]			X			
Gorodeski, 2020[41]			X			
Hallberg, 2018[42]			X			
Hansen, 2017[43]			X			
Haynes, 2020[44]			X			
Herold, 2018[45]			X			
Holmen, 2016[46]			X			
Hsu, 2016[47]			X			
Huizinga, 2010[48]			X			
Inoriza, 2017[49]			X			
Jakobsen, 2015[50]		X				
Jakobsson, 2015[51]		X				
Jerant, 2003[52]			X			
Jimenez-Marrero, 2020[53]			X			
Kashem, 2008[54]			X			

	Exclusion Reason					
Study	**Not OECD**	**Not Population**	**Not Intervention**	**Not Outcomes**	**Not Comparator**	**Not Design**
Kashem, 2006[55]			X			
Kaur, 2015[56]	X					
Kessler, 2018[57]			X			
King, 2009[58]			X			
Kobb, 2003[59]		X				
Koehler, 2018[60]			X			
Koehler, 2011[61]			X			
Koehler, 2012[62]			X			
Krein, 2004[63]			X			
LaFramboise, 2003[64]			X			
Lam, 2011[65]					X	
Lauffenburger, 2019[66]					X	
Lauffenburger, 2019[67]					X	
Layman, 2020[68]			X			
Lehmann, 2006[69]			X			
Leichter, 2013[70]		X				
Lilholt, 2017[71]			X			
Liou, 2014[72]	X					
Litke, 2018[73]					X	
Lopez Cabezas, 2006[74]			X			
Lyons, 2016[75]		X				
Majithia, 2020[76]					X	
Martinez, 2013[77]				X		
Mayes, 2010[78]			X			
McElroy, 2016[79]		X				
Moayeri, 2019[80]			X			
Moore, 2017[81]		X				
Morguet, 2008[82]		X				

	Exclusion Reason					
Study	**Not OECD**	**Not Population**	**Not Intervention**	**Not Outcomes**	**Not Comparator**	**Not Design**
Mortara, 2009[83]			X			
Moyer-Knox, 2004[84]						X
Myers, 2020[85]					X	
Nakayama, 2020[86]			X			
Nguyen, 2008[87]			X			
Nield, 2012[88]			X			
Nouryan, 2019[89]			X			
Odegard, 2005[90]			X			
Odeh, 2015[91]			X			
Oh, 2003[92]			X			
Pare, 2006[93]			X			
Pedone, 2015[94]			X			
Perez-Rodriguez, 2015[95]			X			
Polonsky, 2020[96]					X	
Quinn, 2016[97]			X			
Ringbaek, 2015[98]			X			
Rodriguez-Idigoras, 2009[99]			X			
Rüter, 2014[100]			X			
Salvo, 2012[101]						X
Sarayani, 2018[102]	X					
Scalvini, 2005[103]						X
Scalvini, 2006[104]						X
Schmidt, 2019[105]					X	
Smith, 2008[106]				X		
Sorocco, 2013[107]		X				
Steventon, 2014[108]			X			
Stewart, 2015[109]			X			
Stone, 2010[110]					X	

	Exclusion Reason					
Study	**Not OECD**	**Not Population**	**Not Intervention**	**Not Outcomes**	**Not Comparator**	**Not Design**
Tabak, 2014[111]			X			
Taylor, 2009[112]			X			
Veenstra, 2015[113]					X	
Vidula, 2020[114]			X			
Vitacca, 2009[115]		X				
Wakefield, 2012[116]			X			
Wakefield, 2008[117]			X			
Whitten, 2007[118]			X			
Wild, 2016[119]			X			
Woodend, 2008[120]			X			
Wright, 2019[121]			X			
Wu, 2005[122]			X			
Yan, 2018[123]	X					
Yoo, 2009[124]			X			

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APPENDIX F. PEER REVIEW DISPOSITION

Question Text	Reviewer Number	Comment	Response
Are the objectives, scope, and methods for this review clearly described?	1	Yes	
	3	No - All of the KQs are written in this format: "Among adults, what is the effect of synchronous virtual care (*ie*, phone and/or video) compared to in-person care (or phone vs video)..." It is not clear from this wording what is the comparator. I am not sure what "phone vs. video" means in this context. I believe they are trying to say synchronous care compared to in-person care. KQ 4 is not really about patients. It should be reworded. This is really a systems question, not a patient question.	We appreciate the need for clarification in our KQs and have adjusted the wording to clarify that in-person care was an acceptable comparator, but that we would also accept phone if the synchronous care were delivered via video. KQ4 has been reworded to clarify that adverse effects of interest occurred at the patient, clinical team member, and clinic/facility levels.
	4	Yes	
	5	Yes	
	6	Yes	
	7	Yes	
Is there any indication of bias in our synthesis of the evidence?	1	No	
	3	No	
	4	No	
	5	No	
	6	No	
	7	No	
Are there any published or unpublished studies that we may have overlooked?	1	No	
	3	No	
	4	No	
	5	No	
	6	No	
	7	No	

Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.	1	The proposed project is of high significance and the research questions are appropriate. The project was very thorough and was well conducted. There seems to be a slight disconnect between paltry number of articles and the potential identified in the horizon scan. For the future, further consideration of increasing the inclusion criteria may be needed. Many of the comments below pertain to the inclusion/exclusion criterion	Noted
	1	For the future – the authors may want to include in addition to inter-individual differences (virtual versus in-person) intra-individual – examining differences within individuals who may be in-person and then for a period go to virtual. Covid as an event may make the intra-individual analyses complex, but it may also increase the potential studies available to inform the proposed questions.	We agree that looking at studies in which a given patient obtained care both virtually and in-person is important. Note that if the study design were appropriate, we would have included such a study but did not find any.
	1	It was surprising not to see hypertension as an area of focus which may be more amenable to virtual.	Note that we focused on studies related to diabetes, CHF, and COPD. They may be studies focusing specifically on synchronous virtual care for hypertension, but they would not have been included. Much work has been done in this area as an addition (vs replacement) to routine in-person care – see 2016 AHRQ review.[31]
	1	The 4 key areas to inform future research is highly significant. The proposal of formal review template for future authors to consider should be emphasized.	We appreciate the reviewer recognizing this point. We made edits to emphasize the importance of having virtual care interventions be thoroughly described in the peer-reviewed literature (see Page 44). Of note, members of this team will be working on a subsequent project further outline the types of key items important to report in future work.
	1	In addition, future discussion on fidelity of interventions, both in-person and virtual should be considered.	We have added this to Table 5 as an important aspect for future study.
	1	One wonders if there is a lot more data related to comparing the two modes of intervention administration, but these data are captured as quality improvement.	We agree and suspect this is the case and included this in the limitations of the existing literature. Future work could look at this literature though often QI does not end up in peer-review journals.

	1	Is it possible that virtual may not necessarily replace all vs. a portion, but also reinforce?	We agree that it is possible for virtual care to reinforce or boost in-person care – this has been the focus of much work previously. See AHRQ review for additional summary of this body of literature.[31]
	1	It would be important to describe how the proposed evidence synthesis differs from the one published in 2016 by AHRQ	We agree and have rewritten the introduction to the 'prior systematic reviews' section on page 40 to clarify the difference between our review and the 2016 AHRQ evidence map.
	1	Page 16. An additional unanswered question is in what context is virtual appropriate or should be used compared to in-person care.	We have added this question on page 18.
	1	Why was there a requirement that selected articles had to have >2 encounters? Did this significantly impacted the selection of articles?	We included this eligibility criteria to focus on literature describing the longitudinal care of a chronic condition compared to a one-time urgent care episode. Our center is working on a separate review of tele-urgent care.
	1	Related why was tele-cardiac and tele-pulmonary studies excluded?	We excluded tele-*rehab* studies because rehabilitation by nature is a discrete, time-limited course of care and so conceptually distinct from longitudinal care of chronic conditions. Of note, there are existing reviews of telecardiac.[46]
	1	Is it worth reporting proportion of disagreements given the low number of identified articles?	Our team had many discussions about eligibility criteria in order to align all team members prior to and during citation screening. All citations were reviewed by two team members at the full text level. Any disagreements were usually related to lack of clarity in description of intervention by a given citation. All disagreements were resolved by the two reviewers or sometimes by the larger study team as needed. Thus, we do not feel that the proportion of disagreements would lend valuable information. Non-specifically, we can share that common reasons for exclusion at full-text included the individual conducting the virtual care visit not being a prescribing

			clinician and the virtual care visit not replacing in-person care.
	1	Given the low number of articles identify, consider further explaining the transition from 129 to 5 included studies. It was not clear what was meant by population – something other than the three conditions?	Yes, articles that are studying a population other than what we have described in our PICOTS table for eligibility were excluded. For example, an otherwise eligible study about patients with thyroid disease or only among children would be excluded by "population".
	1	Worth further justifying/explaining why the focus of the project was on replacing versus adding intervention support.	This focus was chosen by our operations partner as the area of greatest interest. In addition, given the previous extensive work on telehealth as an adjunct to in-person care (see comments above) – it was determined that focusing on replacement of in-person care with virtual care would provide the greatest amount of new information to the large existing evidence base about telehealth.
	3	Beginning on page 13, line 21, it would be helpful if the authors included the citation for the studies that met the inclusion criteria.	Thank you, we do not usually add citations to the executive summary of the reports. The citations for included the included studies are listed in the results section of the main report.
	3	As there are so few studies that met the criteria, it would be helpful to readers for the authors to give some context for the studies that did meet the criteria (*eg,* US/non-US; Veteran population or not; etc.) within the KQs.	Reviewers are directed to the characteristics of included studies sections as well as Table 2 (evidence profile) and Appendix B (study characteristics table).
	3	In Table 2 (page 28), it is not clear why there is a footnote stating that one study had 225 participants. In fact, none of the studies seem to have that number of participants.	Thank you, we clarified the language and corrected the number of patients to 338 in Table 2.
	3	On page 33, line 49, the percentages for the post part of the study are reported in the opposite order of the pre- part of the study.	Thank you, we changed the order of the percentages for the intervention and the control arm at 6-months to match the order at baseline in the 4th paragraph of the Detailed Findings: KQ3a section.
	4	I applaud the study authors for their comprehensive review of the literature and adhering to rigorous methods of study evaluation and reporting. While the overall low number of studies that were able to be included was somewhat surprising (particular for COPD). This observation in and of itself highlights an important and unmet need.	Thank you.

	5	Overall, this Evidence-Synthesis is informative because it highlights the contrast between the paucity of data we have about the effectiveness of telehealth when it *replaces* in-person care, as compared with the large evidence base regarding telehealth when it *supplements* in-person care. The main take-home message of this review is that we still know very little about telehealth as a replacement for in-person care in terms of efficacy, equity, safety, and best practices. VHA, as the largest national program implementing telehealth, is in a unique position to explore these topics in the future.	Acknowledged.
	5	Unfortunately, as indicated above, the actual review of the literature was sparse. With no research in COPD, 1 study in heart failure, and 4 in diabetes- few definitive conclusions can be drawn from the research. This is in striking contrast to the broad expansion of telehealth in light of COVID-19. We really know very little as a field about this practice model. As the authors note, most likely this future evidence base will need to be explored in more pragmatic clinical trials that reflect the likely heterogeneity of what VHA clinics and virtual health clinics see in day-to-day practice. The investigators specifically added a focus on any differences by race/ethnicity, gender, age, and rural status. In light of the scant research and small sample sizes, it is not surprising there was no conclusive evidence for equity concerns. Nonetheless, it is important to start including this in reviews to highlight the need for such analyses in future (and ongoing) research.	Acknowledged. We agree and have added a sentence starting on page 42 to more clearly point to this need in future research.
	5	For this reviewer, one analytic question arose repeatedly throughout the review – what is the appropriate statistical analysis for comparing same-room care verses telehealth? This issue needs more discussion and the field needs more visible guidance. In this reviewer's opinion, the most appropriate framework would be comparative effectiveness research using non-inferiority statistical tests. In the report, it appears (but is not made entirely clear) that the predominant analysis was testing for group differences over time. Therefore, it is difficult to draw a conclusion when there are no group differences, as was predominantly the case. Generally, this would be a good sign, indicating telehealth could be a viable substitute for same-room care if confirmed in future research. If anything, the only indicator of a group difference was superiority for	This is an excellent point. Interestingly, one of our included studies noted a hypothesis which implied an equivalence objective though the study design and analysis did not use non-inferiority methods.[29] We have added discussion of the issue of appropriate statistical analysis to the discussion under "research gaps". And have noted the above point about Rasmussen in the results section. Finally, we also made note the analytical approaches as available in the horizon scan includes.

		telehealth. But again, what do we conclude from null findings in studies that do not appear to be using comparative effectiveness methods? The review authors cannot go back and redesign the studies reviewed but some discuss of the correct statistical analysis for future studies would be helpful.	
	5	In making recommendations for future research, telehealth offers some unique outcomes/process variables that are critical to VHA operations: number of visits, number of missed visits, and consultation time. The finding that veterans had fewer missed visits, but those visits were shorter (presumably more efficient) could make a huge difference IF virtual versus in-person care is non-inferior. This difference has been reported in the mental health telehealth literature. This gets at the question of value of telehealth and it is fairly easy data to collect. So it may be something you want to include in your recommendations for future research.	We appreciate this suggestion and have included this in our “research gaps” section (see page 44, Table 5).
	5	Page 8: The study selection specifications are thoughtful and well-operationalized. On line 59- it indicates that some telehealth interventions could include in-person visits. This needs a little more clarification and justification. Also, does this pertain to the one study reported where this model was used? If so, it could be mentioned that this was rare and the investigators had to make a decision about how to treat this one study. Nonetheless, in the future, it is possible and even likely that mixed telehealth/same room care models will proliferate so this specific inclusion criterion is informative for future work	The study selection specifications on page 9 apply to any screened study. This reviewer makes a good point. We would have included studies that had a mix of in-person and video (even if more than one in-person visit) as long as the video or phone visits replaced in-person visits. We did not find any additional such studies in our search. This is also mentioned in Table 5 as an evidence gap that could be addressed in future research.
	5	Page 11: Line 56-60. The description of the Klingemann study is confusing. Didn’t the protocol control for number of education visits? It is presented as an outcome. The same is true for use of email. Are these types of contact an outcome? The study treatment arms and main outcomes need to be specified more clearly.	In the identified section, we are describing the number of contacts and utilization of participants among those receiving virtual care visits vs usual in-person care. We have clarified the experimental and usual care arm in this paragraph.
	5	Page 12: The lack of differences in adverse events is promising but, of course, not conclusive. For some of the larger sample sizes, would it be helpful to provide N and then percentage? I defer to the authors on this judgement call, but it was hard for the reader to gage the burden of adverse events in the studies reported.	The reviewer makes a good point. We now include percentages to help the reader gauge the burden of adverse events in the studies reported.

	5	Page 13: The discussion of Future Research should include a separate paragraph discussing equity. As telehealth is critical to access to care both during and after pandemics, it is essential VA *does not* build in greater inequity which can only be assessed with research. The discussion of future research may also address the most effective design with a discussion of the relevance or not of comparative effectiveness methods. This reviewer does not require the recommendation of comparative effectiveness methods, but it needs to be discussed intelligently as it is an obvious application in this field of research.	We agree that this is an important point and have added a paragraph on page 45 as recommended.
	5	Page 16: Lines 20-25, one assumes the AHRQ synthesis was NOT addressing telehealth as a substitute for care. If that is the case, this should be made clear as the results discussed contradict what this report is stating. The distinction between “counseling” and “clinic consultation” is not clear. The final paragraph on this page is much more clear and does clarify -but this needs clarity is needed earlier also.	We have revised that line to make clear the AHRQ’s focus on virtual care in addition to in-person care.
	5	Page 17: Lines 33-40. I think this point deserves greater emphasis and placement earlier in the background justification. Chronic heart, lung, and metabolic disease are the bread and butter of VHA primary care and much of its specialty care. Nonetheless, we were thrown into a pandemic with broad telehealth expansion and very little knowledge of effectiveness of this modality. These disorders, in contrast with mental health, often call for physical touch to assess vitals and illness status, so the efficacy of telehealth is not self-evident and requires systematic exploration.	We have revised the sentence highlighted and added this point to the first paragraph of the introduction.
	5	Page 18: For topic development, I wish you would provide better context for the exploration of differences by age, gender, race/ethnicity, and rurality- even though the data was not available. This additional question was truly more than an afterthought to try and find some interesting publishable results. The authors could mention that the pandemic led to the topic choice of telehealth replacing in-person care. Then it is logical to elaborate that the pandemic also revealed the huge fault lines in our public health and health care system regarding race/ethnicity. Research going forward must determine the degree to which innovations are widening those gaps or overcoming them.	We have expanded the description of topic development to include these important points.
	5	Page 21: Given the paucity of studies that met criteria, this reviewer is curious how many studies were excluded because they were	While we do not collect specific details about why each study is excluded at full text review,

		uncontrolled, prospective or retrospective observational studies, or studies that looked at mixed chronic conditions. I am not arguing the inclusion/exclusion criteria but if these numbers are large, it is important to know there is preliminary work that could also guide future more tightly controlled studies. Similarly, on Page 24, it is indicated that 84 studies are excluded based on the intervention investigated. Can there be some narrative of what these were so we understand why this large number of studies were excluded?	some of this information is contained in Figure 2 and appendix E. Of note, there were only 6 studies excluded due to design. Common reasons for excluding studies by intervention included virtual care that supplemented rather than replaced in-person care and virtual care interventions delivered by non-prescribing clinicians. We have added detail to the limitations section (page 44) and to the description of the literature flow (page 27) to clarify this point.
	5	Page 26: Line 25-30: What do the authors mean by “quarterly automated telemetry”? What was this intervention? Did it involve any personal care? It is not clear to me what these intervention arms were.	We added additional text to clarify that that study arm received asynchronous web-based follow-up/review of telemetry data. However, our ability to describe the study further is limited by the somewhat unclear description from the primary paper by Hansen.
	5	Page 30 Lines 30-42: This description is confusing because the treatment arms are confusing. What does it mean that the differences are due to email exchange?	We amended the text to clarify the treatment arms and remote contact as much as able due to available description in the Klingemann article. In addition, we have moved detail about contact between arms to utilization finding section.
	5	Figures 3-5 are excellent.	Thank you.
	5	Page 34: The statistically significant difference by education needs better explanation. What was this actual finding? “Veterans with less than a high school degree.	We amended the text to clarify the results in regards to education.
	6	This is a very clearly written evidence synthesis, focused on how virtual care compares to in person care for people with CHF, COPD or DM.	Thank you.
	6	Page 13, paragraph 4, lines 35-56 – In this paragraph on “Research gaps/future research”, the four key areas outlined are excellent.	Thank you.
	6	Page 30, lines 24-26 and 44-46 – “usual endocrine care” (lines 24-26) and “endocrine care” (lines 44-46) are vague. Is this provided by an endocrinologist (*eg,* in Endocrine or Diabetes Clinic) or in primary care?	We amended the text to be more clear about the setting of the study.

	6	Page 30, lines 30-33 – In what I think is an RCT, the commentary talks about “statistically significant difference was seen at baseline”. In general, tests of significance are not appropriate for baseline data in an RCT. They look at the likelihood that observed differences could have happened by chance when baseline differences in an RCT are 100% likely to be by chance (since participants were randomized).	We agree with this reviewer’s point and have removed reference to statistically significant differences in baseline data but have left the notation that there were potentially clinically significant differences between treatment groups at baseline.
	6	Page 34, lines 12-16 – The report notes “There were statistically significant differences in reduction of A1c for all groups…” It is not clear what is being compared here. Is it high compliance vs. lower compliance?	Yes, the comparison in this study was among patients with high levels of compliance with monitoring blood glucose vs those with low compliance. We amended the text to clarify.
	6	Page 36, lines 27-30 – The sentence “Findings suggested that A1c may decrease…” seems overstated since “this finding was not statistically significant in the one adequately powered, low ROB study”.	We amended the text to clarify and reword the sentence to make it clear that there was suggestion of A1c decrease in only one adequately powered, low ROB study, but that overall conclusions cannot be drawn.
	6	Page 36, lines 35-36 – Change “low ROB studies” to “low ROB study”.	Thank you, this statement was adjusted to reflect the suggested change.
	6	Page 37 – The section “Prior Systematic Reviews” is really important, and a summary of this should make it into the Executive Summary.	We have added a summary of prior systematic reviews to the executive summary as suggested.
	6	Page 39, lines 11-17 – The last two sentences of the first paragraph is really important, pointing out that all of the covered studies took place in specialty clinics, while management of CHF, COPD and DM typically takes place in primary care.	Acknowledged.
	6	Page 40, lines 9-10 – The sentence “Given the standard deviation… would be preferable.” is grammatically incorrect and needs to be edited.	Thank you, this sentence was reworded.
	7	This is an extremely well-written and rigorous report with potential to inform future research in VA as well as short-term policy decisions regarding the use of virtual care (specifically synchronous virtual care as a substitute for in-person care) in specific contexts. It also underscores the critical need for additional research on this topic.	Thank you.

	7	Regarding the research gaps/future research section of the executive summary and the summary and discussion section at the end of the report, the first, third, and fourth noted (virtual care interventions should be thoroughly described, key outcomes were omitted from the reviewed studies, the a priori identification of subgroup evaluations) are less areas of future research focus and more suggestions for reporting and enhancing the quality and rigor of work in this area. The authors may want to consider rephrasing these points as such.	We have rephrased the identified areas for improvement to read “there are 5 key areas in which future research on this topic could fill existing gaps and/or could improve the approach” in both locations in the report.
	7	The distinction that the authors draw in the introduction between use of virtual care to augment usual care and the use of virtual care with only limited in-person evaluation is extremely important and clearly presented. This helps further sharpen the focus (use of synchronous virtual care as a substitute for in-person care in the management of select chronic conditions) of the review.	Thank you.
	7	Given the conceptual model that the authors present, key distinctions are being drawn between “providers” and other “care team members.” The authors appear to use these terms very intentionally throughout the report, but in a small number of instances, I questioned if the terms were being used more casually. The authors are encouraged review and confirm that these terms, along with other terms like “clinicians” are used as intended throughout the report. There are several minor typos across the document that should be corrected.	Thank you for this thoughtful comment. We agree that clarifying our terms is important in this review. We have amended the text to indicate “prescribing clinician” and “clinical team member” and removed instances of “provider/s” from the text. We have reviewed the text and resolved all noted typos.