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Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

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VÄSTRA GÖTALANDSREGIONEN
SAHLGRENSKA UNIVERSITETSSJUKHUSET

Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

[Automatiserad återkoppling baserad på digital uppföljning av patienter med unipolär depression som behandlas med läkemedel]

Hamlin M[1*], Aiff H[1], Ali L[1], Holmberg A[2], Sjögren P[3], Steingrimsson S[1], Svanberg T[2,3], Wesén L[4], Wartenberg C[3]

[1] Region Västra Götaland, Sahlgrenska University Hospital, Psykiatri Affektiva, Department of Psychiatry, Gothenburg, Sweden

[2] Region Västra Götaland, Sahlgrenska University Hospital, Medical Library, Gothenburg, Sweden

[3] Region Västra Götaland, HTA-centrum, Gothenburg, Sweden

[4] Region Västra Götaland, Department of digitalization, Gothenburg, Sweden

[*]Corresponding author

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1. Abstract

Background

Patients with unipolar depression are often treated pharmacologically. Continuous follow-up is recommended as treatment adjustments may be needed and, in case of remission, for tapering off the medication. Follow-up routines vary substantially between healthcare units in Sweden. In this context, digitalized follow-up – i.e. collecting patient data on, for instance, depressive symptoms, medication adherence et cetera, and transferring this information to the healthcare unit – is considered an opportunity, in particular if accompanied by an automated protocol to limit the need for clinical staff resources and to highlight information that needs the attention of staff.

Question at issue

In adults with unipolar depression receiving pharmacotherapy, does automated digitalized follow-up alone or in addition to treatment as usual compared with follow-up without such digitalized follow-up (treatment as usual or other comparator) result in improvement regarding depressive symptoms, health-related quality of life (HrQoL), reduced suicidal behaviour, complications, everyday functioning, duration of sick leave, patient reported experience, number of healthcare visits, adherence to medication, or system usability?

Methods

Database searches in Medline, Embase, the Cochrane Library and APA PsycINFO were performed on May 5th, 2023. Titles and abstracts, and subsequently full text articles, were independently screened by at least two authors, and final inclusion was decided in consensus amongst all authors. Included studies were critically appraised, and data were extracted. For outcomes and pre-specified subgroups (by severity of depression, age, intensity of follow-up) where comparative data were available, certainty of evidence was assessed using the GRADE approach.

Results

No studies were identified comparing automated digitalized follow-up with treatment as usual in patients receiving pharmacological treatment due to unipolar depression.

A single RCT with 120 patients, recently discharged after hospitalization due to a unipolar depressive episode, compared smartphone-based monitoring in addition to treatment as usual with treatment as usual alone. All patients in the study were included after discharge from hospitalization due to a unipolar depressive disorder and can be considered a sub-group regarding severity of depression. The study was considered to have major limitations regarding directness, as well as very serious study limitations and serious imprecision regarding the outcomes of interest in this report.

The outcomes depressive symptoms, HrQoL, number of healthcare visits (studied in terms of rehospitalization), adherence to medication, and everyday functioning were evaluated in the RCT. There were no statistically significant differences between the treatment groups for any of the studied outcomes. It is uncertain whether there is any difference regarding these outcomes between digitalized follow-up provided in addition to treatment as usual, compared with treatment as usual alone (GRADE ⊕◯◯◯). No data were reported on suicidal behaviour, complications, duration of sick leave, patient reported experience, and system usability (ease of use).

Costs and ethical aspects

The broad search in this project revealed that there can be a wide variety of systems for automated digital follow-up of the patient population. Up to now, there is no established plan

for what kind of system could be considered for use in Region Västra Götaland. Further, the scientific evidence identified in this HTA-project is very limited. Therefore, detailed analyses of costs and of ethical aspects were not considered feasible at this point. Development and use of systems in this area need to consider the vulnerability of the targeted population, and special attention needs to be paid to ensuring data integrity.

Conclusion

The use of automated digitalized follow-up instead of standard follow-up visits for these patients has not been studied.

Based on very low certainty of evidence from one RCT in patients receiving pharmacotherapy due to unipolar depression, it is uncertain whether adding automated digitalized follow-up to treatment as usual results in any difference regarding depressive symptoms, HrQoL, number of healthcare visits, adherence to medication, and everyday functioning. No data regarding suicidal behaviour, complications, duration of sick leave, patient reported experience, and system usability were reported.

2. Populärvetenskaplig sammanfattning – Plain language summary in Swedish

I denna rapport utvärderades om automatiserad, digital uppföljning av patienter som behandlas med läkemedel för unipolär depression medför förbättringar eller risker jämfört med sedvanlig uppföljning.

Slutsats

Ingen studie identifierades som jämförde *enbart* automatiserad digital uppföljning med sedvanliga uppföljningsbesök**.**
I en randomiserad, kontrollerad studie undersöktes effekten av automatiserad digital uppföljning som *tillägg* till sedvanlig uppföljning, efter utskrivning från sjukhusbehandling för unipolär depression. Baserat på studiens resultat är det osäkert huruvida automatiserad digital uppföljning som *tillägg* till sedvanlig uppföljning medför någon skillnad avseende depressiva symptom, hälsorelaterad livskvalitet, antal sjukvårdsbesök, följsamhet till läkemedelsordination, och vardaglig funktion. Det saknas vetenskapligt underlag avseende komplikationer, suicidalt beteende, tid av sjukskrivning, patientens upplevelse av behandlingen, samt användbarheten av systemet (användarvänlighet).

Bakgrund

Många vuxna patienter med unipolär depression behandlas med läkemedel. Enligt rekommendation ska den här patientgruppen ha kontinuerlig uppföljning för att justera medicineringen i förhållande till patientens aktuella mående. Uppföljningen sker på olika sätt vid olika mottagningar i Sverige. En digitaliserad uppföljning – tex genom att samla in information om patientens depressiva symptom eller följsamhet till läkemedelsbehandling, och att tillgängliggöra dessa data för sjukvården - ses i sammanhanget som en möjlighet. Speciellt system som även erbjuder en automatiserad bearbetning av dessa data och kan begränsa behov av personalresurser eller som kan lyfta fram information som kräver sjukvårdspersonalens uppmärksamhet skulle kunna vara av särskilt intresse.

Metod

Databassökningar gjordes den 5 maj 2023. Urval av artiklar gjordes av minst två författare och projektgruppen beslöt gemensamt vilka artiklar som var relevanta för frågeställningen och skulle inkluderas i rapporten. De ingående studiernas kvalitet granskades och data extraherades i tabeller. Resultatens tillförlitlighet bedömdes enligt GRADE för de utfall och

de i förväg definierade subgrupperna (enligt svårighetsgrad av depressionen, ålder, eller intensitet i den digitaliserade uppföljningen) där jämförande data fanns tillgängliga.

Resultat

Ingen studie identifierades som jämförde enbart automatiserad, digital uppföljning med sedvanliga uppföljningsbesök.
I utvärderingen identifierades enbart en randomiserad, kontrollerad studie som undersökte huruvida tillägg av automatiserad, digital uppföljning till sedvanlig vård medför förbättringar för patienter som behandlas med läkemedel p.g.a. unipolär depression. Studien gällde patienter i efterförloppet efter inneliggande vård, vilket är en delmängd av de patienter som frågeställningen i denna rapport gäller. Studien omfattade 120 individer och visade inga signifikanta skillnader mellan behandlingsgrupperna avseende depressiva symptom, hälsorelaterad livskvalitet, antal återinläggningar, följsamhet till läkemedelsbehandling eller funktion i vardagen. Inga resultat avseende suicidalt beteende, komplikationer, sjukskrivningsperiod, patientupplevelse, eller användbarhet av systemet rapporterades i studien. Studiens överförbarhet, studiekvalitét och precision bedömdes begränsa tillförlitligheten i det vetenskapliga underlaget.

Kostnader och etiska aspekter

I projektets kartläggning framkom att utformningen av ett automatiserat digitalt system kan variera. Eftersom det än så länge inte finns något utarbetat upplägg för en tilltänkt automatiserad digital uppföljning i Västra Götalandsregionen och då det vetenskapliga underlaget är mycket begränsat, har inga detaljerade analyser avseende kostnader genomförts och inga etiska överväganden återges.

Utveckling och användning av system inom detta område behöver ta särskild hänsyn till att det gäller en patientgrupp med särskild sårbarhet och att dataintegritet behöver säkerställas.

The above summaries were written by representatives from the HTA-centrum. The HTA report was approved by the regional board for quality assurance of activity-based HTA. The abstract is a concise summary of the results of the systematic review. The plain language summary in Swedish is intended for decision makers.

Ylva Carlsson, Associate professor, MD
Head of HTA-centrum of Region Västra Götaland, Sweden, 22 may 2024

Main parts of this HTA-report were developed in 2023 with Christina Bergh, Professor, MD, as head of HTA-centrum of Region Västra Götaland, Sweden

Quality control group	
Bergh, Christina	MD, Professor emeritus
Carlsson, Ylva	MD, Associate professor
Ekerstad, Niklas	Associate professor, adjunct university lecturer
Jivegård, Lennart	MD, Senior university lecturer
Khan, Jahangir	Health economist, Professor
Larsson, Anders	MD, PhD
Nelzén, Olle	MD, Associate professor
Petzold, Max	Statistician, Professor
Rylander, Christian	MD, Associate professor
Sjögren, Petteri	DDS, PhD
Skogby, Maria	RN, PhD
Svanberg, Therese	HTA librarian
Wallerstedt, Susanna	MD, Professor
Wartenberg, Constanze	Psychologist, PhD

DDS Doctor of Dental Surgery

MD Medical Doctor

PhD Doctor of Philosophy

RN Registered Nurse

3. Summary of findings

Outcomes	Study design Number of studies	Effect (absolute respectively relative effect as available in publication)	Certainty of evidence GRADE
Automated follow-up to replace treatment as usual (TAU) physical visits – no data			
Automated follow-up as add on to TAU vs TAU			
Depressive symptoms	1 RCT 120 patients	Between group difference [1] (automated digitalized follow-up add on to TAU – TAU): **HDRS-17:** Δ= 0.36, 95% CI: -2.07 to 2.78, p=0.77 **BDI 21:** Δ= -0.46, 95% CI: -4.43 to 3.52, p=0.82 **HAM-D6:** Δ= -0.39, 95% CI: -2.46 to 1.68, p=0.71	⊕◯◯◯ (very low) [2]
HrQoL	1 RCT 120 patients	Between group difference [1] (automated digitalized follow-up add on to TAU – TAU): **WHOQOL:** Δ= 1.30, 95% CI: -5.04; 7.64, p=0.68 **WHO-5:** Δ= 1.03, 95% CI: -1.56; 3.63, p=0.22	⊕◯◯◯ (very low) [2]
Number of healthcare visits	1 RCT 120 patients	Hazard Ratio for readmission (automated digitalized follow-up add on to TAU vs TAU): 0.95 (0.45 to 2.02) p=0.9	⊕◯◯◯ (very low) [2]
Adherence to medication	1 RCT 120 patients	Between group difference [1], (automated digitalized follow-up add on to TAU – TAU): **MARS:** Δ=0.46, 95% CI: -0.28 to 1.20, p=0.22	⊕◯◯◯ (very low) [2]
Everyday functioning	1 RCT 120 patients	Between group difference [1], (automated digitalized follow-up add on to TAU – TAU): **FAST:** Δ=-3.13, 95% CI: -8.13 to 1.86, p=0.22	⊕◯◯◯ (very low) [2]
Suicidal behaviour, complications, duration of sick leave, patient treatment experience, and system usability were not reported			

Footnotes: [1]Between group differences from mixed effects model adjusting for differences in baseline values of the outcome and the stratification variables (a) psychiatric center and (b) number of prior hospitalizations.

[2] Downgraded one step for serious limitations of directness (population limited to patients after hospitalization which is a subset of the population in PICO), two steps for very serious study limitations (substantial missing data at follow-up), and one step for serious limitations of precision (large confidence intervals, limited information available in the publication, one study only).

BDI-21: Beck's Depressive Inventory 21-item (higher scores indicate increased depressive symptoms), FAST: Functional Assessment Short Test (higher values indicate worse every day functioning), MARS; Medicine Adherence Rating Scale (higher values indicate better medical adherence), HAM-D6: Hamilton Depression Self-rating Scale 6-item (higher scores indicate increased depressive symptoms), HDRS 17: Hamilton Depression Rating Scale 17-items (higher scores indicate increased depressive symptoms), RCT: randomized controlled trial, TAU: Treatment as usual, WHOQOL: WHO Quality of Life-BREF (higher values indicate a better quality of life), , WHO-5: WHO (five) Wellbeing Index (higher values indicate a better quality of life).

Certainty of evidence

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

4. Abbreviations/Acronyms

BDI-21	Beck's Depressive Inventory 21-item
CI	Confidence Interval
DSM	Diagnostic and Statistical Manual of Mental Disorders
FAST	Functional Assessment Short Test
GAF	Global Assessment of Functioning
HAMD or HDRS	Hamilton Depression Rating Scale
HrQoL	Health-related quality of life
MARS	Medicine Adherence Rating Scale
RCT	Randomized Controlled Trial
SSRIs	Selective serotonin reuptake inhibitors
TAU	Treatment as usual
VGR	Västra Götalandsregionen
WHO	World Health Organization

5. Background

Depression is the most common mental disorder among adults and a leading cause of the disease burden worldwide (WHO, 2022), associated with an increased psychiatric and somatic comorbidity, elevated mortality, and high societal expenses (Lundberg, 2022). Depression is typically diagnosed and classified by fulfilling specific symptom criteria using the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) and International Statistical Classification of Diseases and Related Health Problems Tenth Revision (ICD-10). Mandatory symptoms include a persistent condition of depressed mood and significant loss of interest. Additional symptoms may be fatigue, psychomotor agitation, insomnia/hypersomnia, sense of guilt, suicidal thoughts, or ideation. The severity of disease can differ from mild with a low impact on everyday functioning, to severe impact, with risk for suicide and/or psychotic symptoms (Socialstyrelsen, 2021). Half of the 800,000 completed suicides globally in 2015 were reported as related to a depressive disorder (Bachmann, 2018).

Prevalence and incidence

The World Health Organization (WHO) estimated a global prevalence in 2019 of 280 million people living with a depressive disorder (including major depressive disorder and dysthymia) (WHO, 2022). In Sweden the incidence is about 5-8 per cent (Nationellt system för kunskapsstyrning hälso- och sjukvård, 2023), and the lifetime prevalence is 35% for women, and 25% for men. The disorder occurs at all ages, with a higher prevalence among elderly (Socialstyrelsen, 2021). According to the Swedish National Board of Health statistics, 36 019 men (0.6%) and 58 547 (1.1%) women got a diagnosis of depression in specialized psychiatric care in the year 2021.

Patients with mild or moderate depression are usually treated in primary care, while patients with severe depression often are referred to specialist psychiatry. For the year 2021, the total costs for patients with depression (ICD-10 F32 and F33) amounted to two billion Swedish kronor within primary care, including the costs for medical and technical resources used in the diagnosis and treatment of patients. During 2021, the total number of patients with ICD codes F32-33 reported in primary care of Region Västra Götaland amounted to 70 636, and nationally it is estimated that there are approximately 427 000 patients (Nationellt system för kunskapsstyrning hälso- och sjukvård, 2023).

In 2022, approximately 46 307 individuals in Sweden were on sick leave for depression (ICD-10 F32 and F33) at some point during the year, according to data from the Swedish Social Insurance Agency (Försäkringskassan, 2023).

Present treatment

The main goal when treating depression is for the affected person to fully recover and regain a good level of function. This includes not only symptom relief, but also a return to daily activities, social contexts, and regaining a good quality of life. The treatment approach is tailored based on the severity of illness, but when moderate to severe, it commonly involves a combination of psychotherapy, pharmacological antidepressants, and in some cases electric convulsive treatment (ECT). Initial treatment often involves pharmacological antidepressants with selective serotonin reuptake inhibitors (SSRIs) being the most common. The superior effect of antidepressants compared to placebo is well established (Cipriani, 2018). Even so, one-third of the patients do not adhere to newly prescribed antidepressants (defined as discontinuation of any cause within three months) (Cipriani, 2018), and comparable rates of premature discontinuation are observed when changing dosage, combining different antidepressants, or change of antidepressant (Sanglier, 2012). Furthermore, many patients do not reach optimal treatment dosage of antidepressants which can affect the treatment response (Lisinski, 2021).

Normal pathway through the healthcare system and current wait time for medical assessment/treatment

Most adult patients with depressive symptoms seek primary care as an initial step and >70% of them are thereafter diagnosed and treated within primary care. A first clinical assessment should be offered urgently, mainly to discover severe conditions and also because an early treatment start is associated with an improved outcome. However, somatic status, work capacity, need of rehabilitation, and the need for involvement of other actors such as social services should also be considered. Continuous evaluation in a structured manner is thereafter recommended when treatment is initiated, with a suggested first evaluation after two weeks. The evaluation should include one of the validated instruments MADRS-S or PHQ-9 as a complement to the clinical assessment. Potential dose adjustments should also be considered,

either increased dose if partial response is seen or a decrease if the patient experiences side-effects (Nationellt system för kunskapsstyrning hälso- och sjukvård, 2024). The risk of relapse is highest during the first six months after symptom relief, however, continuation of antidepressants one year after reduces the likelihood of relapse compared to placebo. Discontinuation of antidepressants may be considered six months after recovery primarily in milder first-time episodes, however, given the risk of relapse and discontinuation symptoms, it requires a personalized and thorough prior evaluation (Kato, 2021).

Specialized psychiatric care can be necessary in cases of severe depression or other complicating factors such as therapy resistance or suspected psychiatric comorbidity. Approximately 20% of patients with depression in primary care are referred to specialized psychiatric care. Patients can also initiate a self-referral to tertiary care. Acute psychiatric care and compulsory care can be necessary, otherwise, an assessment is suggested within 30 days (Nationellt system för kunskapsstyrning hälso- och sjukvård, 2024).

Challenges with the health care system of depression have been identified based on patients' and relatives' experiences. Key challenges are lack of accessibility, lack of information and involvement of patient, insufficient plan of treatment, and lack of continuity (Socialstyrelsen, 2021).

Number of patients per year who undergo current treatment regimen

According to data from the Swedish National Board of Health and Welfare, 1 160 361 (66.78/1000 citizens) prescriptions of antidepressant were prescribed. Differences in gender were seen with 43.44/1000 among the male citizens and with 90.44/1000 among female citizens. In Region Västra Götaland (VGR) there were 125 522 (71.94/1000 citizens) antidepressant prescriptions in 2022. Of note, antidepressants are not only prescribed for depression but also for anxiety disorder, eating disorders, obsessive compulsive disorder and other disorders. Furthermore, antipsychotics (e.g., quetiapine, lurasidone) are frequently prescribed for depression as well as mood stabilizers (e.g., lithium, lamotrigine).

Present recommendations from medical societies or health authorities

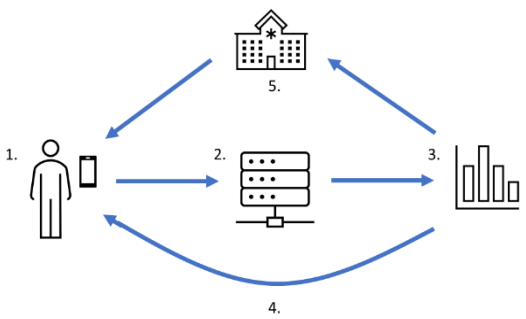
The Swedish national guidelines from the National Board of Health and Welfare (Socialstyrelsen, 2021) state that individualized treatment and health care is crucial as depression manifests in diverse ways, both in terms of severity and in the specific nature of symptoms. Furthermore, accessibility, continuity, and a good reception are key components in individualized treatment of depression (Nationellt system för kunskapsstyrning hälso- och sjukvård, 2024). Automated digitalized follow-up may be an opportunity to provide this treatment, yet it is not mentioned in the current guidelines.

6. Health technology at issue: automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

Digitization and digitalization are key concepts to be differentiated when describing innovative digital technologies.

Digitization implies that specific elements in a process are replaced by digital technology – e.g. asking patients to fill in electronic questionnaires instead of using paper and pencil. Digitalization on the other hand refers to a more profound change of an existing process (Gradillas, 2022), using eg automated processes based on the patients' data to provide feedback to the patient and to support healthcare personnel in focusing patients based on defined algorithms.

Figure 1 illustrates how an automated *digitalized* follow-up is intended to be delivered and managed at specific times of initiation, dose adjustment or combination of pharmacological antidepressants in patients with depression. The intervention is described for a specific population and situation, yet we envision it as an approach that may be customized and applied to other conditions and situations.



1. A patient uses e.g. a mobile application in their smartphone, to record his/her health and medical data. This may include active data - requiring the patient to enter information e,g, by answering standardized diagnostic questionnaires (for example information regarding mood, medication intake, side-effects, or sleep, etc). Passive data are recorded automatically by the device eg by sensors, this can e.g. be location tracking, app usage patterns, and communication patterns.
2. Data is received and stored but not processed.
3. A predefined algorithm analyzes the data in order to provide feedback to the patient and/or the healthcare professional.
4. An automated feedback loop enables a patient to self-monitor and receive automated feedback based on the data collected. (e.g. information regarding side effects of antidepressants and their expected time course. It can also be an urge to contact the treating physician or nurse when predefined cut-offs in validated instruments or other direct questions indicate deterioration in the depressive episode.)
5. An automated algorithm-based filter of data allows healthcare workers to focus their attention on patients in need of immediate care.

The intention with the intervention of automated follow-up for depression is to increase availability and continuity to health care, especially as healthcare workers at psychiatric outpatient clinics in VGR have experienced challenges with non-adherence to antidepressants. Non-adherence to antidepressant pharmacotherapy is recognized as a major contribution to ineffective treatment outcomes and as mentioned over one third of patients discontinue their treatment within three months rather than the medication being ineffectual (Cipriani, 2018). The short-term effect of non-adherence can be discontinuation symptoms, and in long-term the effect can be deterioration of psychiatric symptoms and increased utilization of acute psychiatric care. Given the incidence in Sweden of 5-8% among adults (approximately 350.000-600.000 individuals), non-adherence results in not only suffering at an individual level but also an increased social economic burden (Ho, 2016).

7. Focused question

In adults with unipolar depression receiving pharmacotherapy, does automated digitalized follow-up alone or in addition to treatment as usual compared with follow-up without digitalized follow-up (treatment as usual or other comparator) result in improvement regarding depressive symptoms, health-related quality of life (HrQoL), reduced suicidal behaviour, complications, everyday functioning, duration of sick leave, patient reported experience, number of healthcare visits, adherence to medication, or system usability?

PICO: P= Patients, I= Intervention, C= Comparison, O=Outcome

P	Adult patients receiving pharmacological treatment due to unipolar depression.
I	Digitalized follow-up of patient data transferred to healthcare with automated protocol for feedback to patient offered alone or in addition to treatment as usual
C	Follow-up without digitalized transfer of patient data to healthcare (treatment as usual or other comparison)
O	<u>Critical for decision making</u> • Depressive symptoms (assessed by validated instrument) • Suicide (risk) – e.g. rate of suicide attempts/self-harm or suicidality assessed with a validated instrument • Health related quality of life <u>Important for decision making</u> • Complications • Everyday functioning • Duration of sick leave • Patient treatment experience • Number of healthcare visits/contacts related to depression • Adherence to prescription of antidepressant medication <u>Less important for decision making</u> • System Usability (according to validated scale)
	Controlled studies including at least 10 patients per group, and qualitative studies regarding patient experience Note, for the initial overview, the limitation to controlled studies was not applied.
	Planned subgroup analyses: Regarding intervention - Digitalized follow-up in addition to treatment as usual - Digitalized follow-up replacing treatment as usual

	Regarding intervention - low intensity follow-up (data transfer only) - high intensity follow-up (system with additional features to support the patient other than data transfer) Regarding population - subgroups according to severity of depression - subgroups according to age

8. Methods

Systematic literature search (Appendix 1)

During May 2023 two authors (TS, AH) performed systematic searches in Medline, Embase, the Cochrane Library and APA PsycINFO. The websites of SBU and Folkehelseinstituttet were visited. Reference lists of relevant articles were also scrutinised for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are presented in Appendix 1. These authors conducted the literature searches, and independently of one another assessed the obtained abstracts and made a first selection. All abstracts were screened by at least two authors using the Rayyan tool. Any disagreements were resolved by consensus. The remaining abstracts were assessed by all the participants of the project group and a selection of full-text articles to screen for inclusion/exclusion was made. These articles were read by at least two authors independently of one another and it was finally decided in a consensus meeting which articles should be included in the assessment.

The HTA was registered in PROSPERO the November 14th, 2023 (registration code CRD42023473956) prior to data extraction.

Critical appraisal and certainty of evidence

Included studies have been critically appraised using an adjusted checklist from the Swedish Agency for Health Technology Assessment and Assessment of social Services (SBU) for assessment of randomised controlled trials. The results of each study have been summarised per outcome in Appendix 4. When possible, data were planned to be pooled for meta-analysis in RevMan 5.4 using a random effects model. Summary results per outcome and the associated certainty of evidence are presented in a Summary-of-findings table. Certainty of evidence for each outcome was assessed using the GRADE approach (Atkins et al., 2004; GRADE Work group).

Sub-group analyses according to type of intervention (monitoring with additional features), and according to population (subgroup according to severity of depression) were prespecified.

Ongoing research

A search in Clinicaltrials.gov (Dec 15th, 2023) using the search terms *depression OR "mental illness" OR depressive OR "mood disorder" OR "unipolar disorder" (Disorder) AND ((electronic OR digital OR automated OR automatic OR remote) AND (follow-up OR monitoring OR self-monitoring OR reminder OR notification)) OR telemonitoring OR "tele-monitoring" OR homemonitoring OR home-monitoring OR "digital medicine" OR mobile OR*

"app-based" OR smartphone OR "smart-phone" OR app OR apps OR sensor OR "smart pill" OR "digital pill" OR "electronic pill" OR "wireless pill" OR "ingestible sensor" OR "ingestible microsensor" OR "ingestible event" OR "medication event monitoring system" OR "ingestible electronic sensor" OR "cellularly enabled pill" OR wearable OR "digital phenotyp" (Intervention) identified 2793 trials.

9. Results

Search results and study selection (Appendix 1)

The literature search identified 3945 records after removal of duplicates. After reading the abstracts 3896 records were excluded. 49 reports were assessed for eligibility by at least two authors, and one report (RCT) was included in the final assessment (Appendix 2).

Reasons for exclusion

Of the 49 articles read in full text, one article Tønning et al. (2021) was included. All remaining articles were excluded in most cases due to

- Wrong population – with no antidepressant medication or unclarity about antidepressant medication, or a broader patient population with a majority of patients having other diagnoses than unipolar depression.
- Wrong intervention – As outlined above, the project team was interested in digitalization as intervention. The most common reasons for excluding for wrong intervention were that the investigated intervention was a mere digitisation of an existing process or that an intervention did not imply following a treatment course. Examples of interventions that led to exclusion of articles are:
    - Prediction of worsening of depression (ecological momentary assessment without follow-up of treatment)
    - Detecting suicidal thoughts (ecological momentary assessment without follow-up of treatment)
    - Interventions without transfer of information to a healthcare unit (e.g. mood monitoring as part of self-monitoring)
    - Patient education / information without interaction with healthcare
    - Motivational messages/information
    - Medication adherence monitoring
    - Follow-up with intensified individual healthcare interaction
    - Interventions without automatic follow-up.

Included studies

No study regarding the comparison of automated digitalized follow-up instead of treatment as usual (TAU) was identified.

One RCT, Tønning et al. (2021), conducted in Danmark was included. In this study 120 patients who were discharged from a psychiatric hospital after hospitalization due to a depressive episode, were randomised either to the intervention group - smartphone-based monitoring in addition to TAU - or a control group receiving TAU alone. The smartphone-based system used in the intervention group included both functions to monitor symptoms,

share data with a study nurse and receive feedback. Also, the smartphone-based system provided the patient with information based on cognitive-behavioral therapy (CBT). Patients in the control group also installed the smartphone-based system, but could only use it for monitoring their systems – without the functionality of interaction with clinical staff and no access to the CBT material. Patients were assessed by a blinded clinician, and provided self-assessments at baseline, as well as after 3 months and 6 months follow-up. The study was considered to have serious limitations regarding directness, as the study was restricted to patients at discharge from psychiatric hospital which is a subgroup of the intended population in the PICO. Further, recruitment problems were reported which presumably implies limitations in directness as many patients declined participation. Study limitations of this RCT due to risk of bias were considered very serious as there was substantial missing data for the outcomes of interest in this HTA (between 30% and 38% of patients did not complete questionnaires at different times for follow-up) and descriptive statistics as well as detailed information on the data available for analysis is missing. Also, given the nature of the intervention, patients and their nurse were not blinded. It was noted that two of the authors of this publication are co-founders of the company that developed the monitoring system used in this study. The study was considered to have serious problems regarding precision as confidence intervals for the outcomes considered in our PICO were wide. Also, the power calculation (based on the study's primary endpoint of readmission to hospital) was to include 100 patients per group, yet due to recruitment problems this sample size was not reached. For the endpoints relevant in our PICO the number of observations included in the analyses is not provided in the publication.

Results per outcome

Tønning et al. (2021) only report between group differences from linear mixed model analysis adjusting for differences in baseline values of the outcome and the stratification variables (a) psychiatric center and (b) number of prior hospitalizations. The publication does not provide descriptive statistics for results in each group. The article presents results from ITT analyses, for the outcomes relevant for this HTA the analysis. Imputation of missing outcomes data is performed assuming that data are missing at random.

Outcomes, critical for decision-making

Depressive symptoms assessed by validated instrument (Appendix 4.1)

Baseline mean score for HDRS-17 in the intervention group was 14.5 (SD 5.77) and 13.9 (6.26) in the control group. No other mean scores regarding depressive symptom assessments at baseline or follow-up were reported. There were no significant differences in depressive symptoms between the groups assessed by HDRS-17 (Δ=0.36, 95% CI: -2.07 to 2.78, p=0.77), HAM-D6 (Δ=-0.39, 95% CI: -2.46 to 1.68, p=0.71) or BDI 21 (Δ=-0.46, 95% CI: -4.43 to 3.52, p=0.82).

The validated scales used in the measure of depressive symptoms are presented in Table 1. The assessments were conducted at baseline, after 3 months and after 6 months. The minimal important differences (MID) estimates of depression outcome measures presented in Table 1 should be interpreted with caution (Hengartner, 2020). Yet this information indicates that the confidence intervals of depressive symptoms in the study can be considered wide in relation to the MID.

Table 1. Scales of depressive symptoms

Scale	Range	Direction indicating increased depressive symptoms	MID	Average treatment effect of antidepressant	Administratio
BDI 21	0-63	↑	3-6	2	Self-rated
HAM-D6	0-24	↑	3-6	1.5	Self-rated
HDRS-17	0-52	↑	3-5	2	Clinician-assessed

MID: Minimal important difference, BDI 21: Beck´s Depressive Inventory 21 item, HAM-D6: Hamilton Depression Self-rating Scale 6-item, HDRS-17: Hamilton Depression Rating Scale 17-items

Conclusion: It is uncertain whether there is any difference in symptoms of depression between automated digitalized follow-up of antidepressant medication as add on to TAU compared with TAU (very low certainty of evidence, GRADE ⊕◯◯◯).

Suicide (risk) – e.g. rate of suicide attempts/self-harm or suicidality assessed with a validated instrument

The outcome was not reported.

Health-related quality of life (HRQoL) (Appendix 4.2)

Health-related quality of life was assessed by World Health Organization Quality of Life-BREF (WHOQOL) and Wellbeing according to WHO (five) wellbeing Index (WHO-5). The range of WHOQOL is 0 to100 with higher scores indicating better quality of life. The range of WHO-5 is 0 to 25 with higher scores indicating better quality of life. No mean scores at baseline or follow-up were reported. There were no significant differences in Health-related Quality of Life between the groups assessed by WHOQOL (Δ=1.30, 95% CI: -5.04 to 7.64, p=0.68) or WHO-5 (Δ=1.03, 95% CI: -1.56 to 3.63, p=0.22).

Conclusion: It is uncertain whether there is any difference in HRQoL between automated digitalized follow-up of antidepressant medication as add on to TAU compared with TAU (very low certainty of evidence, GRADE ⊕◯◯◯).

<u>Outcomes, important for decision-making</u>

Number of healthcare visits/contacts related to depression (Appendix 4.3)

Number of healthcare visits/contacts related to depression were assessed in terms of rate and accumulated duration of psychiatric re-admissions (primary outcomes in Tønning et al., 2021). The probability of readmission within 6 months in the intervention group was 23% (95% CI: 11% to 33%) and 23% (95% CI: 12% to 33%) in the control group. There were no significant differences in readmission between groups (p=0.9).

The average length of readmission was 35.2 days (SD=32.6) in the intervention group and 51.6 days (SD=44) in the control group. The difference between the groups was not significant (Δ:-16.41, 95% CI: -47.32 to 25.5, p=0.3). A large variability within groups and outliers with occasional long-term readmissions was noted by the authors.

Conclusion: It is uncertain whether there is any difference in the number of healthcare visits in terms of readmissions between automated digitalized follow-up of antidepressant medication as add on to TAU compared with TAU (very low certainty of evidence, GRADE ⊕○○○).

Adherence to prescription of antidepressant medication (Appendix 4.4)
Adherence to prescription of antidepressant medication was assessed by Medicine Adherence Rating Scale (MARS). The range of MARS is 0 to10 with higher scores indicating better adherence. No mean scores at baseline or follow-up were reported. There were no significant differences in MARS between groups (Δ=0.46, 95% CI: -0.28 to 1.2, p=0.22).

Conclusion: It is uncertain whether there is any difference in the adherence to prescription of antidepressant medication between automated digitalized follow-up of antidepressant medication as add on to TAU compared with TAU (very low certainty of evidence, GRADE ⊕○○○).

Everyday functioning (Appendix 4.5)
Psychosocial functioning was assessed with the Functional Assessment Short Test (FAST). The range of FAST is 0 to 72 with higher scores indicating worse everyday functioning. No scores at baseline or follow-up were reported. There were no significant differences in FAST between groups (Δ=-3.13, 95% CI: -8.13 to 1.86, p=0.22).

Conclusion: It is uncertain whether there is any difference in everyday functioning between automated digitalized follow-up of antidepressant medication as add on to TAU compared with TAU (very low certainty of evidence, GRADE ⊕○○○).

The included RCT (Tønning et al., 2021) did not report any of the following outcomes: **complications, duration of sick leave,** and **patient treatment experience.**

<u>Outcomes, less important for decision-making</u>

System Usability (according to validated scale)
The outcome was not reported in the included study.

10. Organisational aspects

Considerations regarding the use of automated digitalized follow-up of patients with unipolar depression receiving pharmacotherapy are at an early stage, and scientific evidence on this intervention is as described above very low. Therefore, analyses of organisational aspects were not considered feasible at this point. Different scenarios of organizing the intervention at issue can be considered – e.g. the follow-up may be managed by the healthcare professionals currently involved in the standard of care at psychiatric units. Alternatively, a different professional group or separate unit may be involved in provision of this intervention.

11. Economic aspects

In line with chapter 10, analyses of economic aspects were not considered feasible at this point. However, as referenced in the background, the National Board of Health and Welfare reports that over 10% of the adult population in 2022 received a prescription of antidepressants (Socialstyrelsen, 2024). As described in the background section above, a large proportion of patients do not adhere to prescribed antidepressants and do not reach optimal treatment dosage of antidepressants which can affect the treatment response (Lisinski, 2021). This implies that if an intervention achieves an optimisation of the initiation, dosage and tapering of antidepressant, this could theoretically have a large impact on the health care system.

12. Ethical aspects

In line with above, detailed information on ethical aspects is considered premature. Yet the following aspects can be noted.

Individuals suffering from psychiatric disorders may be considered a vulnerable group (Declaration of Hawaii, 1978). Given that patients suffering from depression is a heterogenous group and with variation in the severity of mental illness, the vulnerability and autonomic capacities must be individually evaluated concerning risk-benefit. An individual assessment of an ethical and protected use of digitalized tools can to a higher extent be ensured when used in alliance with a health care provider and where data is protected. An uncontrolled industry of digitalized tools to mitigate mental illness without clinical evidence can potentially be harmful and exploit this group.

For the intervention at issue, ensuring data integrity is of utmost importance. This is a key aspect when using mobile applications in healthcare as highlighted in the comprehensive app evaluation model promoted by the American Psychiatric Association (2024) and in an overview by E-hälsomyndigheten (2022). Access to healthcare is a basic human right, therefore the increasing use of digitalized tools requires ethical considerations concerning digital literacy and the barriers to access it may entail. Digital literacy refers to the ability to critically use, navigate, and evaluate digital tools. However, as digitization and digitalization rapidly increase in all health care, it is becoming more difficult to separate it from the concept of adequate health literacy (Campanozzi, 2023).

13. Discussion

Summary of main results

This HTA aimed to assess whether digitalized follow-up of patient data transferred to healthcare with automated protocol for feedback - offered alone or in addition to TAU - is effective compared with follow-up without such digitalized follow-up (TAU alone), for adults with unipolar depression treated with pharmacotherapy. Based on one RCT, a rigorous clinical trial, that met the criteria for our PICO, there were no significant differences compared to TAU alone in two of three outcomes critical for decision making: depressive symptoms and health-related quality of life. The third outcome considered critical - suicidal behaviour - was not studied. Furthermore, there were no significant differences between intervention and control group in any of the other outcomes, considered important for decision making. The certainty of evidence was assessed as very low (GRADE ⊕◯◯◯), due to very serious study limitations, as well as limitations in directness, and precision, and as only one study met the predefined inclusion criteria.

Overall completeness and applicability of evidence

The PICO included a strict definition of the intervention to solely capture empirical clinical trials that have tested digitalized tools i.e. automated rather than mere digital tools that replace a physical visit by a real-time virtual one. This resulted in only one included study, which of course limits the completeness and applicability of evidence.

The included study had limitations concerning directness (only patients recently discharged from psychiatric hospital included), precision (wide confidence intervals) and study limitations (substantial missing data and limited presentation of information).

A consideration regarding the area of research is that standards for approval and preconditions of use for these kinds of systems are still emerging. Given the dynamics of irregulated changes and updates in mobile applications concerning mental health, The American Psychiatry Association (APA) have developed an app evaluation model to be used by physicians, to assess the suitability of a mobile application to an individual in a specific time and situation. It consists of a six-step model, prioritizing elements such as data safety and privacy, ownership of data, and consideration of patient benefit and risk (American Psychiatric Association, 2024). In Sweden, E-hälsomyndigheten (2022) has published an overview on key preconditions for use of mobile applications regarding health.

Agreements and disagreements with other studies and reviews

The literature search did not identify any systematic reviews that fulfilled the PICO criteria. Even so, it is worth mentioning a meta-analysis conducted by Linardon et al. (2024) with focus on smartphone-based mental health applications for symptoms of depression or anxiety. The analysis reported a modest yet significant impact on depression. However, of the 176 included trials 46% included CBT (Cognitive Behavioral Therapy), only 11% were compared with TAU, and only 14% of the trials offered human guidance.

In a clinical review as a consensus point for future of digital mental healthcare, Smith et al. (2023) highlighted the importance of digitalization as a complement rather than a replacement of face-to-face or virtual care, requiring sustained engagement with human interaction when needed. Furthermore, they suggest that hybrid approaches in a clinical setting can maximize efficiency by combining digital and traditional care.

Implications for research

This HTA illustrates the challenges in research design and implementation of digitalized technologies into real-world health care settings. Digitalized technologies in mental health care are rapidly developing and encompass a wide range of interventions, with varying features and functionalities. For example, in the included study, the smartphone-based system comprised multiple functions - features to follow-up symtoms, and features to provide patients with information based on cognitive-behavioral therapy (CBT). Any effects of the intervention may be due to one or a combination of these features which also may counteract each other. Given this development defining adequately specific PICO and evaluating the generalizability of results is a challenge. The current HTA-report highlights the need for rigorous studies regarding the issue at question. To ensure the relevance and sustainability of research findings, the perspective of various stakeholders should be considered.

14. Future perspectives

Scientific knowledge gaps

A number of questions need to be addressed in future studies:

Patient related

- Does an automated feedback loop based on active and/or passive data ensure efficacy and safety for patients?
- Does automated digitalized feedback optimize treatment with antidepressants in terms of dosage, additional medication, or withdrawal of medication?
- Are digitalized interventions effective on patient outcomes beyond symptom reduction, including quality of life, treatment adherence, and self-empowerment?

Health care

- Does a predefined algorithm analyzing various data points from the patient decrease the administrative burden for health care workers?
- Does a predefined algorithm analyzing various data points from the patient reduce unnecessary visits?

Societal impact

- Does automated digitalized follow-up enhance availability of psychiatric care?

Ongoing research

The search in the ClinicalTrials.gov database for ongoing studies identified 2793 records, two of which corresponded to the PICO in this HTA and were included. All other identified records were excluded as they did not correspond to the PICO. Both records that were included were registered as completed in the clinical trials database, yet no publication on these studies could be retrieved.

Table 2: Studies corresponding to the PICO of this report, that are completed but where no publications are registered according to ClinicalTrials.gov

Trial number Country	Study description	Primary outcome	Estimated enrollment	Expected completion date
NCT01882608 Canada	RCT comparing mental health telemetry (an evolution of Ecological Momentary Assessment) as add on to usual care with usual care of patients with major depression disorder, bipolar depression disorder or dysthymia	Rehospitalization at 6 months	33 patients	Completed 2016,
NCT02710344 USA	RCT comparing psychiatric telehealth program including remote monitoring as add on to usual care with usual care of patients with serious mental illness (schizophrenia, schizoaffective disorder, bipolar disorder, post-traumatic stress disorder, or major depression)	Cost of emergency room visits and hospital days 12 months prior to up to 12 months after baseline assessment	303 patients	Completed 2020,

15. Participants in the project

The question was nominated by

Steinn Steingrimsson, MD, reader (docent) and specialist in psychiatry, Department of Psychiatry, and R&D unit, Sahlgrenska University Hospital Östra, Region Västra Götaland.

Participating healthcare professionals

Harald Aiff, Psychiatrist PhD, Region Västra Götaland

Lilas Ali, Nurse, PhD, Region Västra Götaland

Matilda Hamlin, AT-physician and PhD-Student, R&D unit, Östra Sjukhuset, Region Västra Götaland.

Steinn Steingrimsson, PhD, consultant in psychiatry, Department of Psychiatry, Sahlgrenska University Hospital Östra, Region Västra Götaland.

Linda Wesén, regional developer/nurse, Utbildning, Department of digitalization, Region Västra Götaland

Participants from HTA-centrum

Jahangir Khan, health economist, professor, HTA-centrum, Region Västra Götaland

Petteri Sjögren, DDS, PhD, HTA-centrum, Region Västra Götaland

Constanze Wartenberg, psychologist, PhD, HTA-centrum, Region Västra Götaland

Participants from the Medical Library

Agnes Holmberg, Librarian, Medical Library, Sahlgrenska University Hospital, Region Västra Götaland

Therese Svanberg, Librarian, Medical library, Sahlgrenska University Hospital, Region Västra Götaland

External reviewers

Robert Sigström, MD, PhD, Specialist in Psychiatry, Department of Cognition and Old Age Psychiatry Sahlgrenska University Hospital, Region Västra Götaland

Ulla Wide, Psychologist, professor, Sahlgrenska Academy, University of Gothenburg, Sweden

Declaration of interests

None of the authors have any conflicts of interest to declare.

Project time

The HTA was accomplished during the period of 2023-04-20 – 2024-05-22.

Literature searches were made on 2023-05-23.

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

Appendix 1: PICO, study selection, search strategies, and references

Question at issue:
In adults with unipolar depression receiving pharmacotherapy does automated digitalized follow-up alone or in addition to treatment as usual compared with follow-up without such digitalized follow-up (treatment as usual or other comparator) result in improvement regarding depressive symptoms, health-related quality of life (HrQoL), reduced suicidal behaviour, complications, everyday functioning, duration of sick leave, patient reported experience, number of healthcare visits, adherence to medication, or system usability?

PICO: (*P=Patient I=Intervention C=Comparison O=Outcome*)

PICO	
P	Adult patients receiving pharmacological treatment due to unipolar depression
I	Digitalized follow-up of patient data transferred to healthcare with automated protocol for feedback to patient
C	Follow-up without digitalized transfer of patient data to healthcare (treatment as usual or other comparison)
O	<u>Critical for decision making</u> • Depressive symptoms (assessed by validated instrument) • Suicide (risk) – e.g. rate of suicide attempts/self-harm or suicidality assessed with a validated instrument • Health related quality of life <u>Important for decision making</u> • Complications • Everyday functioning • Duration of sick leave • Patient treatment experience • Number of healthcare visits/contacts related to depression • Adherence to prescription of antidepressant medication <u>Less important for decision making</u> • System Usability (according to validated scale)

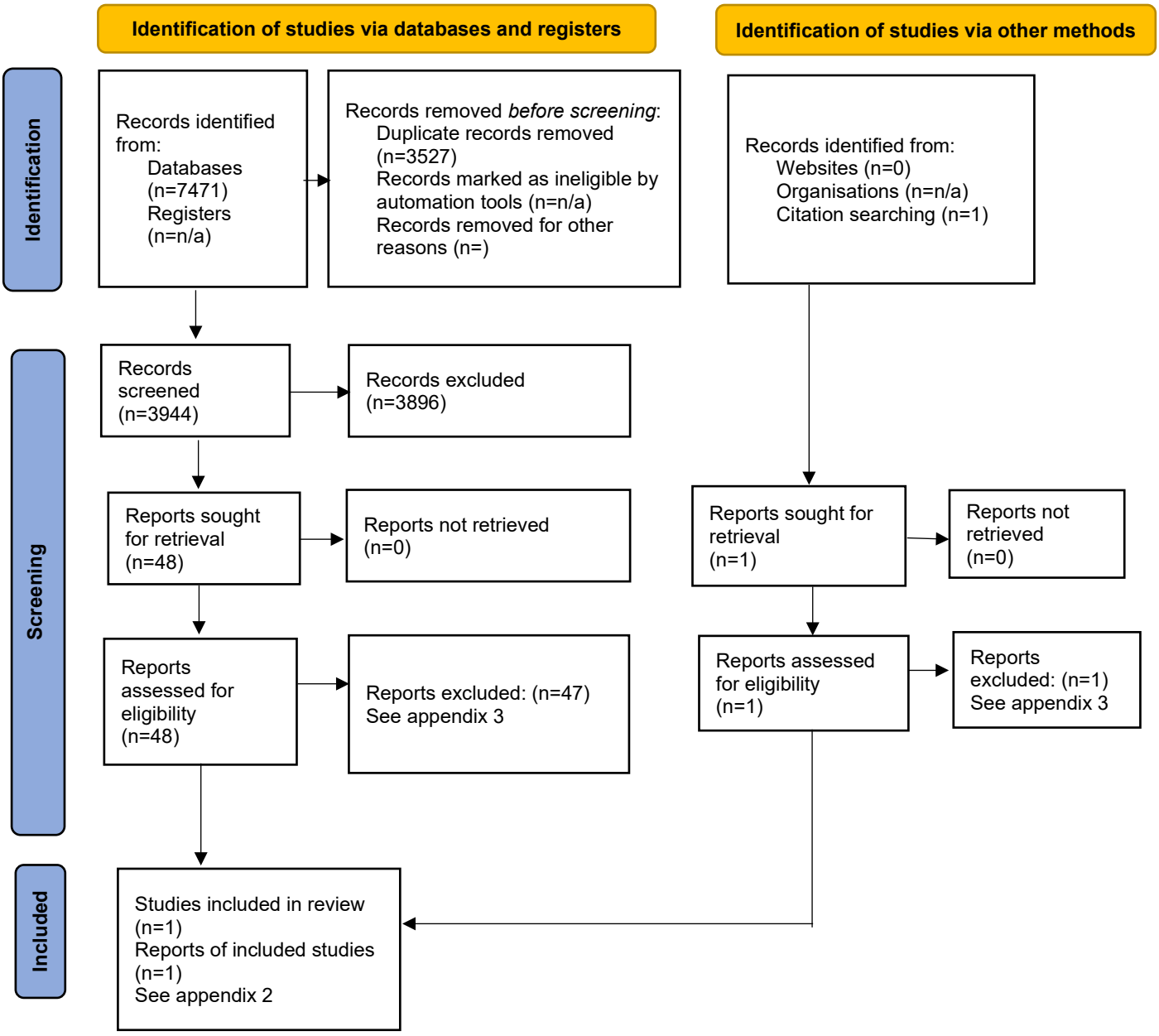
<u>Eligibility criteria</u>
Study design:
Controlled studies including at least 10 patients per group, and qualitative studies regarding patient experience.
Note, for the initial overview, the limitation to controlled studies is not applied.

Language:
English, Swedish, Norwegian, Danish

Publication date: 2010-

Selection process – flow diagram

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



From: Page MJ et al, 2021

Search strategies

Database: Ovid MEDLINE(R) ALL (OvidSP)
Date: 05 May 2023
No. of results: 2,692

#	Searches	Results
1	Depression/ or depressive disorder/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or Mood Disorders/	260600
2	(depress$ or mental illness or mood disorder or mood disorders or antidepress$ or mood or psychiatric or affective or anti-depress$ or unipolar disorder or unipolar disorders).ti.	314195
3	1 or 2	415810
4	Smartphone/ or Mobile Applications/ or Wearable Electronic Devices/ or Monitoring, Ambulatory/	32633
5	((electronic$ or digital$ or automat$ or remote) adj3 (follow-up or monitor$ or self-monitor$ or report$1 or self-report$1 or reminder$1 or notification$1)).ti,ab,kf.	20765
6	(telemedicine or tele-medicine or telehealth or tele-health or eHealth or e-health or mHealth or eMental or e-mental or telemental or tele-mental or digital mental or digital health).ti.	23423
7	(telemonitor$ or tele-monitor$ or homemonitor$ or home-monitor$ or digital medicine or mobile or app-based or smartphone$1 or smart-phone$1 or app or apps or smart pill$ or digital pill$ or electronic pill$ or wireless pill$ or ingestible sensor$1 or ingestible microsensor$1 or ingestible event or medication event monitoring system or ingestible electronic sensor$1 or cellularly enabled pill$ or wearable$1 or digital phenotyp$).ti,ab,kf.	202191
8	4 or 5 or 6 or 7	246571
9	3 and 8	3167
10	limit 9 to yr="2010 -Current"	2836
11	(comment or editorial or letter).pt.	2154532
12	10 not 11	2791
13	animals/ not (animals/ and humans/)	5083886
14	(animal or animals or rat or rats or mouse or mice or rodent or rodents or dog or dogs or cat or cats or hamster or hamsters or rabbit or rabbits or swine or murine or porcine or horses or horse).ti.	2094820
15	13 or 14	5490548
16	12 not 15	2743
17	**limit 16 to (danish or english or norwegian or swedish)**	**2692**

Database: Embase 1974 to 2023 May 03 (OvidSP)
Date: 05 May 2023
No. of results: 2,247

#	Searches	Results
1	*depression/ or *mood disorder/ or *chronic depression/ or *major depression/ or *treatment resistant depression/	230331
2	(depress$ or mental illness or mood disorder or mood disorders or antidepress$ or mood or psychiatric or affective or anti-depress$ or unipolar disorder or unipolar disorders).ti.	382937
3	1 or 2	436367
4	*smartphone/ or exp *mobile application/ or *wearable sensor/ or *ambulatory monitoring/ or *medication adherence monitoring system/ or *home monitoring/	27670

5	((electronic$ or digital$ or automat$ or remote) adj3 (follow-up or monitor$ or self-monitor$ or report$1 or self-report$1 or reminder$1 or notification$1)).ti,ab,kf.	31686
6	(telemedicine or tele-medicine or telehealth or tele-health or eHealth or e-health or mHealth or eMental or e-mental or telemental or tele-mental or digital mental or digital health).ti.	29533
7	(telemonitor$ or tele-monitor$ or homemonitor$ or home-monitor$ or digital medicine or mobile or app-based or smartphone$1 or smart-phone$1 or app or apps or smart pill$ or digital pill$ or electronic pill$ or wireless pill$ or ingestible sensor$1 or ingestible microsensor$1 or ingestible event or medication event monitoring system or ingestible electronic sensor$1 or cellularly enabled pill$ or wearable$1 or digital phenotyp$).ti,ab,kf.	268092
8	4 or 5 or 6 or 7	323026
9	3 and 8	3619
10	limit 9 to yr="2010 -Current"	3300
11	limit 10 to (embase or medline)	2424
12	limit 11 to (article or article in press or conference paper or note or "review")	2353
13	animal/ not (animal/ and human/)	1178236
14	(animal or animals or rat or rats or mouse or mice or rodent or rodents or dog or dogs or cat or cats or hamster or hamsters or rabbit or rabbits or swine or murine or porcine or horses or horse).ti.	2272080
15	13 or 14	3176517
16	12 not 15	2311
17	**limit 16 to (danish or english or norwegian or swedish)**	**2247**

Database: The Cochrane Library
Date: 05 May 2023
No of results: 938
Cochrane reviews: 13
Cochrane protocols: 0
Trials: 925
Editorials: 0
Special collections: 0
Clinical answers: 0

ID	Search	Hits
#1	MeSH descriptor: [Depression] this term only	18299
#2	MeSH descriptor: [Depressive Disorder] this term only	9123
#3	MeSH descriptor: [Depressive Disorder, Major] this term only	6441
#4	MeSH descriptor: [Depressive Disorder, Treatment-Resistant] this term only	628
#5	MeSH descriptor: [Mood Disorders] this term only	1015
#6	(depress* or "mental illness" or "mood disorder" or "mood disorders" or antidepress* or mood or psychiatric or affective or anti-depress* or "unipolar disorder" or "unipolar disorders"):ti (Word variations have been searched)	57041
#7	#1 or #2 or #3 or #4 or #5 or #6	66835
#8	MeSH descriptor: [Smartphone] this term only	1006
#9	MeSH descriptor: [Mobile Applications] this term only	1538
#10	MeSH descriptor: [Wearable Electronic Devices] this term only	228
#11	MeSH descriptor: [Monitoring, Ambulatory] this term only	626

#12	((electronic* or digital* or automat* or remote) NEAR/3 (follow-up or monitor* or self-monitor* or report or reports or self-report or self-reports or reminder or reminders or notification or notifications)):ti,ab,kw (Word variations have been searched)	5384
#13	(telemedicine or tele-medicine or telehealth or tele-health or eHealth or e-health or mHealth or eMental or e-mental or telemental or tele-mental or "digital mental" or "digital health"):ti (Word variations have been searched)	4109
#14	(telemonitor* or tele-monitor* or homemonitor* or home-monitor* or "digital medicine" or mobile or app-based or smartphone or smartphones or smart-phone or smart-phones or app or apps or (smart NEXT pill*) or (digital NEXT pill*) or (electronic NEXT pill*) or (wireless NEXT pill*) or "ingestible sensor" or "ingestible sensors" or "ingestible microsensor" or "ingestible microsensors" or "ingestible event" or "medication event monitoring system" or "ingestible electronic sensor" or "ingestible electronic sensors" or ("cellularly enabled" NEXT pill*) or wearable or wearables or (digital NEXT phenotyp*)):ti,ab,kw (Word variations have been searched)	49968
#15	#8 or #9 or #10 or #11 or #12 or #13 or #14	56903
#16	#7 and #15	1947
#17	(conference proceeding):pt	219918
#18	#16 not #17	1798
#19	(clinicaltrials OR trialsearch):so	458730
#20	#18 not #19	1080
Limit search to publication year 2010-2023		**938**

Database: PsycINFO (EBSCOhost)
Date: 05 May 2023
No. of results: 1,594

#	Query	Results
S11	**S3 AND S8 Narrow by Language: - english**	**1,594**
S10	S3 AND S8 Limiters - Published Date: 20100101-20231231	1,645
S9	S3 AND S8	1,937
S8	S4 OR S5 OR S6 OR S7	45,809
S7	TI (telemonitor* or tele-monitor* or homemonitor* or home-monitor* or "digital medicine" or mobile or app-based or smartphone or smartphones or smart-phone or smart-phones or app or apps or "smart pill*" or "digital pill*" or "electronic pill*" or "wireless pill*" or "ingestible sensor" or "ingestible sensors" or "ingestible microsensor" or "ingestible microsensors" or "ingestible event" or "medication event monitoring system" or "ingestible electronic sensor" or "ingestible electronic sensors" or "cellularly enabled pill*" or wearable or wearables or "digital phenotyp*") OR AB (telemonitor* or tele-monitor* or homemonitor* or home-monitor* or "digital medicine" or mobile or app-based or smartphone or smartphones or smart-phone or smart-phones or app or apps or "smart pill*" or "digital pill*" or "electronic pill*" or "wireless pill*" or "ingestible sensor" or "ingestible sensors" or "ingestible microsensor" or "ingestible microsensors" or "ingestible event" or "medication event monitoring system" or "ingestible electronic sensor" or "ingestible electronic sensors" or "cellularly enabled pill*" or wearable or wearables or "digital phenotyp*") OR KW (telemonitor* or tele-monitor* or homemonitor* or home-monitor* or "digital medicine" or mobile or app-based or smartphone or smartphones or smart-phone or smart-phones or app or apps or "smart pill*" or "digital pill*" or "electronic pill*" or "wireless pill*" or "ingestible sensor" or "ingestible sensors" or "ingestible microsensor" or "ingestible microsensors" or "ingestible event" or "medication event monitoring system" or "ingestible electronic sensor" or "ingestible electronic sensors" or "cellularly enabled pill*" or wearable or wearables or "digital phenotyp*")	36,295
S6	TI telemedicine or tele-medicine or telehealth or tele-health or eHealth or e-health or mHealth or eMental or e-mental or telemental or tele-mental or "digital mental" or "digital health"	4,382
S5	TI ((electronic* or digital* or automat* or remote) N3 (follow-up or monitor* or self-monitor* or report or reports or self-report or self-reports or reminder or reminders or notification or notifications)) OR AB ((electronic* or digital* or automat* or remote) N3 (follow-up or monitor* or self-monitor* or report or reports or self-report or self-reports or reminder or reminders or notification or notifications)) OR KW ((electronic* or digital* or automat* or remote) N3 (follow-	3,292

	up or monitor* or self-monitor* or report or reports or self-report or self-reports or reminder or reminders or notification or notifications))	
S4	DE "Smartphones" OR DE "Mobile Applications" OR DE "Wearable Devices" OR DE "Self-Monitoring"	9,171
S3	S1 OR S2	281,804
S2	TI depress* or "mental illness" or "mood disorder" or "mood disorders" or antidepress* or mood or psychiatric or affective or anti-depress* or "unipolar disorder" or "unipolar disorders"	240,235
S1	DE "Major Depression" OR DE "Treatment Resistant Depression" OR DE "Persistent Depressive Disorder"	149,979

The websites listed below were visited 29 Feb 2024.
Nothing relevant to the question at issue was found.

Sökkällor	Sökord/ Browsa	Antal träffar	Antal relevanta träffar
SBU www.sbu.se	Depression Antidepressiva Follow-up Uppföljning Digital Automatiserad	174 27 76 168 54 5	0 0 0 0 0 0
Folkehelseinstituttet (Norge) https://www.fhi.no/ku/metodevurdering/	Browsat kategori Metodevurdering - Rapporter		0
Behandlingsrådet (Danmark) https://behandlingsraadet.dk/	Browsat		0
Nationale Kliniske Anbefalinger og Retningslinjer (Danmark) https://www.sst.dk/da/Fagperson/Retningslinjer-og-procedurer/NKA-og-NKR/NKR-og-NKA-efter-omraade	Browsat kategori Psykisk sygdom og mental sundhet		0
CAMTÖ https://www.regionorebrolan.se/sv/forskning/kontakt-och-organisation/hta-enheten-camto/	Browsat		0
HTA Region Stockholm https://www.chis.regionstockholm.se/hta/rapporter/	Browsat		0
Regional samverkansgrupp HTA (tidigare Metodrådet) i Sydöstra sjukvårdsregionen https://sydostrasjukvardsregionen.se/samverkansgrupper/hta/genomforda-bedomningar/	Browsat		0
HTA Syd https://vardgivare.skane.se/kompetens-utveckling/sakkunniggrupper/hta-skane/#110365	Browsat		0
Medicinska rådet, Region Dalarna https://www.regiondalarna.se/plus/vard/ovrig-halso--och-sjukvard/medicinska-radet/	Browsat		0

Reference lists
A comprehensive review of reference lists brought 1 record.

Reference lists

Included reports:

Tønning ML, Faurholt-Jepsen M, Frost M, Martiny K, Tuxen N, Rosenberg N, et al. The effect of smartphone-based monitoring and treatment on the rate and duration of psychiatric readmission in patients with unipolar depressive disorder: The RADMIS randomized controlled trial. J Affect Disord. 2021;282:354-63. doi:https://dx.doi.org/10.1016/j.jad.2020.12.141

Excluded reports:

Anton MT, Greenberger HM, Andreopoulos E, Pande RL. Evaluation of a Commercial Mobile Health App for Depression and Anxiety (AbleTo Digital+): Retrospective Cohort Study. JMIR Formative Research. 2021;5(9):e27570. doi: https://dx.doi.org/10.2196/27570

Bauer AM, Iles-Shih M, Ghomi RH, Rue T, Grover T, Kincler N, et al. Acceptability of mHealth augmentation of Collaborative Care: A mixed methods pilot study. Gen Hosp Psychiatry. 2018;51:22-9. doi: https://dx.doi.org/10.1016/j.genhosppsych.2017.11.010

Ben-Zeev D, Brian RM, Jonathan G, Razzano L, Pashka N, Carpenter-Song E, et al. Mobile Health (mHealth) Versus Clinic-Based Group Intervention for People With Serious Mental Illness: A Randomized Controlled Trial. Psychiatr Serv. 2018;69(9):978-85. doi: https://dx.doi.org/10.1176/appi.ps.201800063

Ben-Zeev D, Buck B, Chu PV, Razzano L, Pashka N, Hallgren KA. Transdiagnostic Mobile Health: Smartphone Intervention Reduces Depressive Symptoms in People With Mood and Psychotic Disorders. JMIR Mental Health. 2019;6(4):e13202. doi: https://dx.doi.org/10.2196/13202

Ben-Zeev D, Chander A, Tauscher J, Buck B, Nepal S, Campbell A, et al. A Smartphone Intervention for People With Serious Mental Illness: Fully Remote Randomized Controlled Trial of CORE. J Med Internet Res. 2021;23(11):e29201. doi: https://dx.doi.org/10.2196/29201

Ben-Zeev D, Razzano LA, Pashka NJ, Levin CE. Cost of mHealth Versus Clinic-Based Care for Serious Mental Illness: Same Effects, Half the Price Tag. Psychiatr Serv. 2021;72(4):448-51. doi: https://dx.doi.org/10.1176/appi.ps.202000349

Bhat A, Goud BR, Pradeep JR, Jayaram G, Radhakrishnan R, Srinivasan K. Can Mobile Health Improve Depression Treatment Access and Adherence Among Rural Indian Women? A Qualitative Study. Cult Med Psychiatry. 2020;44(4):461-78. doi: https://dx.doi.org/10.1007/s11013-019-09664-3

Birney AJ, Gunn R, Russell JK, Ary DV. MoodHacker Mobile Web App With Email for Adults to Self-Manage Mild-to-Moderate Depression: Randomized Controlled Trial. JMIR MHealth and UHealth. 2016;4(1):e8. doi: https://dx.doi.org/10.2196/mhealth.4231

Bogner HR, de Vries HF, O'Donnell AJ, Morales KH. Measuring concurrent oral hypoglycemic and antidepressant adherence and clinical outcomes. Am J Manag Care. 2013;19(3):e85-92. doi:

Brandt LR, Hidalgo L, Diez-Canseco F, Araya R, Mohr DC, Menezes PR, et al. Addressing Depression Comorbid With Diabetes or Hypertension in Resource-Poor Settings: A Qualitative Study About User Perception of a Nurse-Supported Smartphone App in Peru. JMIR Mental Health. 2019;6(6):e11701. doi: https://dx.doi.org/10.2196/11701

Bruhns A, Baumeister A, Demeroutis G, Jahn H, Willenborg B, Shaffy A, et al. A mobile-based aftercare intervention to increase self-esteem in inpatients diagnosed with depression: A randomized

controlled trial. Psychotherapy Research. 2023:1-20. doi: https://dx.doi.org/10.1080/10503307.2022.2157226

Cho CH, Lee T, Lee JB, Seo JY, Jee HJ, Son S, et al. Effectiveness of a Smartphone App With a Wearable Activity Tracker in Preventing the Recurrence of Mood Disorders: Prospective Case-Control Study. JMIR Mental Health. 2020;7(8):e21283. doi: https://dx.doi.org/10.2196/21283

Cho Y, Lim K, Lee S, Kim Y, Kim M, Kim CO, et al. Developing a Multimodal Monitoring System for Geriatric Depression: A Feasibility Study. CIN: Computers, Informatics, Nursing. 2023;41(1):46-56. doi: https://dx.doi.org/10.1097/CIN.0000000000000925

Corden ME, Koucky EM, Brenner C, Palac HL, Soren A, Begale M, et al. MedLink: A mobile intervention to improve medication adherence and processes of care for treatment of depression in general medicine. Digital Health. 2016;2:2055207616663069. doi: https://dx.doi.org/10.1177/2055207616663069

de Angel V, Adeleye F, Zhang Y, Cummins N, Munir S, Lewis S, et al. The Feasibility of Implementing Remote Measurement Technologies in Psychological Treatment for Depression: Mixed Methods Study on Engagement. JMIR Mental Health. 2023;10:e42866. doi: https://dx.doi.org/10.2196/42866

Dinkel D, Harsh Caspari J, Fok L, Notice M, Johnson DJ, Watanabe-Galloway S, et al. A qualitative exploration of the feasibility of incorporating depression apps into integrated primary care clinics. Transl Behav Med. 2021;11(9):1708-16. doi: https://dx.doi.org/10.1093/tbm/ibab075

Dubad M, Elahi F, Marwaha S. The Clinical Impacts of Mobile Mood-Monitoring in Young People With Mental Health Problems: The MeMO Study. Frontiers in psychiatry Frontiers Research Foundation. 2021;12:687270. doi: https://dx.doi.org/10.3389/fpsyt.2021.687270

Forchuk C, Reiss J, Eichstedt J, Singh D, Collins K, Rudnick A, et al. The youth-mental health engagement network: An exploratory pilot study of a smartphone and computer-based personal health record for youth experiencing depressive symptoms. Int J Ment Health. 2016;45(3):205-22. doi: 10.1080/00207411.2016.1204823

Forchuk C, Rudnick A, Corring D, Lizotte D, Hoch JS, Booth R, et al. A Smart Technology Intervention in the Homes of People with Mental Illness and Physical Comorbidities. Sensors. 2022;23(1):30. doi: https://dx.doi.org/10.3390/s23010406

Frank E, Wallace ML, Matthews MJ, Kendrick J, Leach J, Moore T, et al. Personalized digital intervention for depression based on social rhythm principles adds significantly to outpatient treatment. Frontiers in Digital Health. 2022;4:870522. doi: https://dx.doi.org/10.3389/fdgth.2022.870522

Fru FM. Medication adherence in major depressive disorder: ProQuest Information & Learning; 2023.

Gonzales S, Okusaga OO, Reuteman-Fowler JC, Oakes MM, Brown JN, Moore S, et al. Digital Medicine System in Veterans With Severe Mental Illness: Feasibility and Acceptability Study. JMIR Formative Research. 2022;6(12):e34893. doi: https://dx.doi.org/10.2196/34893

Hantsoo L, Criniti S, Khan A, Moseley M, Kincler N, Faherty LJ, et al. A Mobile Application for Monitoring and Management of Depressed Mood in a Vulnerable Pregnant Population. Psychiatr Serv. 2018;69(1):104-7. doi: https://dx.doi.org/10.1176/appi.ps.201600582

Harrison P, Carr E, Goldsmith K, Young A, Ashworth M, Fennema D, et al. Antidepressant Advisor (ADeSS): a decision support system for antidepressant treatment for depression in UK primary care - a

feasibility study. BMJ Open. 2023;13(3):e060516. doi: https://dx.doi.org/10.1136/bmjopen-2021-060516

Hetrick SE, Goodall J, Yuen HP, Davey CG, Parker AG, Robinson J, et al. Comprehensive online self-monitoring to support clinicians manage risk of suicide in youth depression: A pilot study. Crisis: The Journal of Crisis Intervention and Suicide Prevention. 2017;38(3):147-57. doi: 10.1027/0227-5910/a000422

Incecik E, Taylor RW, Valentini B, Hatch SL, Geddes JR, Cleare AJ, et al. Online mood monitoring in treatment-resistant depression: qualitative study of patients' perspectives in the NHS. Bjpsych Bulletin. 2020;44(2):47-52. doi: https://dx.doi.org/10.1192/bjb.2019.92

Kelders SM, Bohlmeijer ET, Pots WTM, van Gemert-Pijnen JEWC. Comparing human and automated support for depression: Fractional factorial randomized controlled trial. Behav Res Ther. 2015;72:72-80. doi: 10.1016/j.brat.2015.06.014

Kramer I, Simons CJ, Hartmann JA, Menne-Lothmann C, Viechtbauer W, Peeters F, et al. A therapeutic application of the experience sampling method in the treatment of depression: a randomized controlled trial. World Psychiatry. 2014;13(1):68-77. doi: 10.1002/wps.20090

Kroenke K, Theobald D, Wu J, Norton K, Morrison G, Carpenter J, et al. Effect of telecare management on pain and depression in patients with cancer: a randomized trial. JAMA. 2010;304(2):163-71. doi: https://dx.doi.org/10.1001/jama.2010.944

Lauritsen L, Andersen L, Olsson E, Sondergaard SR, Norregaard LB, Loventoft PK, et al. Usability, Acceptability, and Adherence to an Electronic Self-Monitoring System in Patients With Major Depression Discharged From Inpatient Wards. J Med Internet Res. 2017;19(4):e123. doi: https://dx.doi.org/10.2196/jmir.6673

Maatoug R, Peiffer-Smadja N, Delval G, Brochu T, Pitrat B, Millet B. Ecological Momentary Assessment Using Smartphones in Patients With Depression: Feasibility Study. JMIR Formative Research. 2021;5(2):e14179. doi: https://dx.doi.org/10.2196/14179

Matcham F, Leightley D, Siddi S, Lamers F, White KM, Annas P, et al. Remote Assessment of Disease and Relapse in Major Depressive Disorder (RADAR-MDD): recruitment, retention, and data availability in a longitudinal remote measurement study. BMC Psychiatry. 2022;22(1):136. doi: https://dx.doi.org/10.1186/s12888-022-03753-1

McClintock HF, BeKampis AN, Hartmann E, Bogner HR. Adherence to Antidepressants in Underserved Communities: A Comparison of Electronic Monitoring and Self-report Measures. Community Ment Health J. 2020;56(4):727-34. doi: https://dx.doi.org/10.1007/s10597-019-00533-2

McCue M, Blair C, Fehnert B, King J, Cormack F, Sarkey S, et al. Mobile App to Enhance Patient Activation and Patient-Provider Communication in Major Depressive Disorder Management: Collaborative, Randomized Controlled Pilot Study. JMIR Formative Research. 2022;6(10):e34923. doi: https://dx.doi.org/10.2196/34923

Mohr DC, Stiles-Shields C, Brenner C, Palac H, Montague E, Kaiser SM, et al. MedLink: A Mobile Intervention to Address Failure Points in the Treatment of Depression in General Medicine. International Conference on Pervasive Computing Technologies for Healthcare. 2015;2015:100-7.

Okonkwo B. Increasing medication adherence among young male African Americans with depression using a mobile app intervention: ProQuest Information & Learning; 2022.

Ornée DA, Oldehinkel AJ, Bastiaansen JA. Comparison of two ecological momentary intervention modules for treatment of depression on momentary positive and negative affect. Collabra: Psychology. 2021;7(1). doi: 10.1525/collabra.18910

Pfeiffer PN, Bohnert KM, Zivin K, Yosef M, Valenstein M, Aikens JE, et al. Mobile health monitoring to characterize depression symptom trajectories in primary care. J Affect Disord. 2015;174:281-6. doi: https://dx.doi.org/10.1016/j.jad.2014.11.040

Piette JD, Sussman JB, Pfeiffer PN, Silveira MJ, Singh S, Lavieri MS. Maximizing the value of mobile health monitoring by avoiding redundant patient reports: prediction of depression-related symptoms and adherence problems in automated health assessment services. J Med Internet Res. 2013;15(7):e118. doi: https://dx.doi.org/10.2196/jmir.2582

Place S, Blanch-Hartigan D, Smith V, Erb J, Marci CD, Ahern DK. Effect of a Mobile Monitoring System vs Usual Care on Depression Symptoms and Psychological Health: A Randomized Clinical Trial. JAMA Network Open. 2020;3(1):e1919403. doi: https://dx.doi.org/10.1001/jamanetworkopen.2019.19403

Schaffer A, Kreindler D, Reis C, Levitt AJ. Use of mental health telemetry to enhance identification and predictive value of early changes during augmentation treatment of major depression. J Clin Psychopharmacol. 2013;33(6):775-81. doi: https://dx.doi.org/10.1097/JCP.0b013e31829e8359

Simons CJP, Hartmann JA, Kramer I, Menne-Lothmann C, Höhn P, van Bemmel AL, et al. Effects of momentary self-monitoring on empowerment in a randomized controlled trial in patients with depression. Eur Psychiatry. 2015;30(8):900-6. doi: 10.1016/j.eurpsy.2015.09.004

Straczkiewicz M, Wisniewski H, Carlson KW, Heidary Z, Knights J, Keshavan M, et al. Combining digital pill and smartphone data to quantify medication adherence in an observational psychiatric pilot study. Psychiatry Res. 2022;315:114707. doi: https://dx.doi.org/10.1016/j.psychres.2022.114707

Torous J, Staples P, Shanahan M, Lin C, Peck P, Keshavan M, et al. Utilizing a Personal Smartphone Custom App to Assess the Patient Health Questionnaire-9 (PHQ-9) Depressive Symptoms in Patients With Major Depressive Disorder. JMIR Mental Health. 2015;2(1):e8. doi: https://dx.doi.org/10.2196/mental.3889

van Os J, Delespaul P, Barge D, Bakker RP. Testing an mHealth momentary assessment Routine Outcome Monitoring application: a focus on restoration of daily life positive mood states. PLoS ONE [Electronic Resource]. 2014;9(12):e115254. doi: https://dx.doi.org/10.1371/journal.pone.0115254

Wahle F, Kowatsch T, Fleisch E, Rufer M, Weidt S. Mobile Sensing and Support for People With Depression: A Pilot Trial in the Wild. JMIR MHealth and UHealth. 2016;4(3):e111. doi: https://dx.doi.org/10.2196/mhealth.5960

White KM, Dawe-Lane E, Siddi S, Lamers F, Simblett S, Riquelme Alacid G, et al. Understanding the Subjective Experience of Long-term Remote Measurement Technology Use for Symptom Tracking in People With Depression: Multisite Longitudinal Qualitative Analysis. JMIR Human Factors. 2023;10:e39479. doi: https://dx.doi.org/10.2196/39479

Zimmerman N. Telemonitoring of medication adherence in patients with major mental illness: watching the patient as well as the pills. Stud Health Technol Inform. 2012;182:189-96.

Other references:

American Psychiatric Association. The App Evaluation Model [Internet]. Washington: American Psychiatric Association; 2024 [cited 2024 May 2]. Available from: https://www.psychiatry.org/psychiatrists/practice/mental-health-apps/the-app-evaluation-model

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004;328(7454):1490-4. doi: 10.1136/bmj.328.7454.1490.

Bachmann S. Epidemiology of Suicide and the Psychiatric Perspective. Int J Environ Res Public Health. 2018;15(7). doi: 10.3390/ijerph15071425

Campanozzi LL, Gibelli F, Bailo P, Nittari G, Sirignano A, Ricci G. The role of digital literacy in achieving health equity in the third millennium society: A literature review. Front Public Health. 2023;11:1109323. doi: 10.3389/fpubh.2023.1109323

[Checklist from SBU regarding randomized controlled trials]. (Modified) Version 2021]. [Internet]. [cited 2023 Oct 16]. Available from: https://mellanarkiv-offentlig.vgregion.se/alfresco/s/archive/stream/public/v1/source/available/sofia/su4372-1728378332-412/native

Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet. 2018;391(10128):1357-66. doi: 10.1016/s0140-6736(17)32802-7

Declaration of Hawaii. J Med Ethics. 1978;4(2):71-3. doi: 10.1136/jme.4.2.71

E-hälsomyndigheten. Hälsoappar – förutsättningar och användning [Internet]. Kalmar: E-hälsomyndigheten; 2022. Kartläggningar; 2022-04. [cited 2024 May 2]. Available from: https://www.ehalsomyndigheten.se/globalassets/ehm/3_om-oss/rapporter/halsoappar---forutsattningar-och-anvandning.pdf

Försäkringskassan. Utbetald sjukpenning för olika diagnoser [Internet]. Försäkringskassan; 2023. Korta analyser; 2023:7. [cited 2024 May 2]. Available from: https://www.forsakringskassan.se/download/18.68ee6a4218b7864af03131/1702374638400/utbetald-sjukpenning-for-olika-diagnoser-korta-analyser-2023-7.pdf

GRADE Working Group. [Internet]. [Place unknown]: GRADE Working Group, c2004-2021 [cited 2021 Feb 13]. Available from: http://www.gradeworkinggroup.org

Gradillas M, Thomas LDW. Distinguishing digitization and digitalization: A systematic review and conceptual framework. Journal of Product Innovation Management. 2023;1-32. doi: https://doi.org/10.1111/jpim.12690

Hengartner MP, Plöderl M. Estimates of the minimal important difference to evaluate the clinical significance of antidepressants in the acute treatment of moderate-to-severe depression. BMJ Evid Based Med. 2022;27(2):69-73. doi: 10.1136/bmjebm-2020-111600

Ho SC, Chong HY, Chaiyakunapruk N, Tangiisuran B, Jacob SA. Clinical and economic impact of non-adherence to antidepressants in major depressive disorder: A systematic review. J Affect Disord. 2016;193:1-10. doi: 10.1016/j.jad.2015.12.029

Kato M, Hori H, Inoue T, Iga J, Iwata M, Inagaki T, et al. Discontinuation of antidepressants after remission with antidepressant medication in major depressive disorder: a systematic review and meta-analysis. Mol Psychiatry. 2021;26(1):118-33. doi: 10.1038/s41380-020-0843-0

Linardon J, Torous J, Firth J, Cuijpers P, Messer M, Fuller-Tyszkiewicz M. Current evidence on the efficacy of mental health smartphone apps for symptoms of depression and anxiety. A meta-analysis of 176 randomized controlled trials. World Psychiatry. 2024;23(1):139-49. doi: 10.1002/wps.21183

Lisinski A, Hieronymus F, Eriksson E, Wallerstedt SM. Low SSRI dosing in clinical practice-a register-based longitudinal study. Acta Psychiatr Scand. 2021;143(5):434-43. doi: 10.1111/acps.13275

Lundberg J, Cars T, Lööv S, Söderling J, Tiihonen J, Leval A, et al. Clinical and societal burden of incident major depressive disorder: A population-wide cohort study in Stockholm. Acta Psychiatr Scand. 2022;146(1):51-63. doi: 10.1111/acps.13414

Nationellt system för kunskapsstyrning hälso- och sjukvård. Konsekvensbeskrivning för personcentrerat och sammanhållet vårdförlopp depression hos vuxna [Internet]. Nationellt system för kunskapsstyrning hälso- och sjukvård; 2023. [cited 2024 May 2]. Available from: https://kunskapsstyrningvard.se/download/18.565a1fb118a82e14f675c971/1695110477137/Konsekvensbeskrivning-vardforlopp-depression.pdf

Nationellt system för kunskapsstyrning hälso- och sjukvård. Vårdförlopp depression [Internet]. Nationellt system för kunskapsstyrning hälso- och sjukvård; 2024. [cited 2024 Feb 8]. Available from: https://kunskapsstyrningvard.se/kunskapsstyrningvard/kunskapsstod/publiceradekunskapsstod/psykiskhalsa/vardforloppdepression.75042.html

Sanglier T, Milea D, Saragoussi D, Toumi M. Increasing escitalopram dose is associated with fewer discontinuations than switch or combination approaches in patients initially on escitalopram 10 mg. Eur Psychiatry. 2012;27(4):250-7. doi: 10.1016/j.eurpsy.2010.08.009

Smith KA, Blease C, Faurholt-Jepsen M, Firth J, Van Daele T, Moreno C, et al. Digital mental health: challenges and next steps. BMJ Ment Health. 2023;26(1). doi: 10.1136/bmjment-2023-300670

Socialstyrelsen. Nationella riktlinjer för vård vid depression och ångestsyndrom : stöd för styrning och ledning [Internet]. Stockholm: Socialstyrelsen; 2021a. [cited 2024 Feb 19]. Available from: https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/nationella-riktlinjer/2021-4-7339.pdf

Socialstyrelsen. Diagnoser i sluten vård och specialiserad öppenvård [Internet]. Stockholm: Socialstyrelsen; 2024. [cited 2024 Feb 8]. Available from: https://www.socialstyrelsen.se/statistik-och-data/statistik/statistikdatabasen/

von Knorring AL, von Knorring L, Waern M. Depression från vaggan till graven. Läkartidningen. 2013;110(9-10):480-3.

World Health Organization. World mental health report: transforming mental health for all [Internet]. Geneva: World Health Organization; 2022. [cited 2024 Feb 19]. Available from: https://www.who.int/teams/mental-health-and-substance-use/world-mental-health-report

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

Appendix 2 – Characteristics of included studies

Author Year Country	Study Design	Length of Follow-Up	Study Groups; Intervention vs control	Patients (n)	Mean Age (years)	Men (%)	Outcome variables
Tønning et al 2021 Denmark	RCT	6 months	Active use of smartphone-based monitoring and treatment system + standard treatment vs Standard treatment alone	120	44	48%	• Depressiv symptoms • HrQoL • Number of readmissions • Adherence to medication • Everyday functioning

HrQoL: Health related quality of life

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy
Appendix 3.
Excluded articles

Author, year	Reason for exclusion
Anton et al 2021	Wrong intervention
Bauer et al 2018	Wrong population
Ben-Zeev et al 2018	Wrong population
Ben-Zeev et al 2019	Wrong population
Ben-Zeev et al 2021a	Wrong population
Ben-Zeev et al 2021b	Wrong population
Bhat et al 2020	Wrong intervention
Birney et al 2016	Wrong intervention
Bogner et al 2013	Wrong intervention
Brandt et al 2019	Wrong population
Bruhns et al 2023	Wrong intervention
Cho et al 2020	Wrong intervention and population
Cho et al 2023	Wrong intervention and population
Corden et al 2016	Wrong study design
De Angel et al 2023	Wrong intervention and population
Dinkel et al 2021	Wrong intervention and population
Dubad et al 2021	Wrong population
Forchuk et al 2016	Wrong population
Forchuk et al 2022	Wrong population
Frank et al 2022	Wrong intervention
Fru 2023	Wrong study design
Gonzales et al 2022	Wrong intervention and population
Hantsoo et al 2018	Wrong population
Harrison et al 2023	Wrong intervention
Hetrick et al 2017	Wrong intervention and population
Incecik et al 2020	Wrong intervention
Kelders et al 2015	Wrong population
Kramer et al 2014	Wrong intervention
Kroenke et al 2010	Wrong intervention and population
Lauritsen et al 2017	Wrong intervention
Maatoug et al 2021	Wrong intervention
Matcham et al 2022	Wrong intervention
McClintock et al 2020	Wrong study design
McCue et al 2022	Wrong intervention
Mohr et al 2015	Wrong study design

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Appendix 3.
Excluded articles

Author, year	Reason for exclusion
Okonkwo 2022	Wrong publication type
Ornée et al 2021	Wrong intervention and population
Pfeiffer et al 2015	Wrong study design
Piette et al 2013	Wrong study design
Place et al 2020	Wrong intervention
Schaffer et al 2013	Wrong study design
Simons et al 2015	Wrong intervention
Straczkiewicz et al 2022	Wrong study design
Torous et al 2015	Wrong study design
Van Os et al 2014	Wrong study design
Whale et al 2016	Wrong study design
White et al 2023	Wrong intervention
Zimmerman 2012	Wrong publication type

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

* + No or minor problems
? Some problems
- Major problems

Appendix 4.1
Outcome variable: Depressive symptoms

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention **Automated digitalized follow-up + treatment as usual**	**Control** **treatment as usual**				
Tønning 2020 Denmark	RCT	N=120 I=59 C=61	I= withdrawal 7 no show 11 C= no show 8-9	**HDRS-17** Baseline: 14.5 (SD 5.77)	**HDRS-17** Baseline: 13.9 (SD 6.26)	*Scales:* HDRS-17 scores (clinician-assessed) (range: 0 – 52) < 7 absence/remission of depression 7-17 mild depression 18-24 moderate depression ≥ 25 represent severe depression BDI 21 (self-rating) (range: 0-63) Higher scores indicate increased depressive symptoms HAM-D6 (self-rating) (range: 0-24) Higher scores indicate increased depressive symptoms *Sample-note:* Baseline score for HDRS-17 is mentioned. No other score at baseline or follow-up (3m, 6m) is mentioned. The number of completed questionnaires vary at each follow-up (3m, 6m) without further explanation on which questionnaires were completed (I=41-42, C=39-44)	?	?	-
				Between group difference[1], (automated digitalized follow up add on to TAU – TAU): **HDRS-17** Δ=0.36, 95% CI: -2.07 to 2.78, p=0.77 **BDI 21** Δ=-0.46, 95% CI: -4.43 to 3.52, p=0.82 **HAM-D6** Δ=-0.39, 95% CI: -2.46 to 1.68, p=0.71					

HDRS-17: Hamilton Depression Rating Scale 17-items, HAM-D6: Hamilton Depression Self-rating Scale 6-item, BDI 21: Beck's Depressive Inventory 21-item
[1] Between group differences from mixed effects model adjusting for differences in baseline values of the outcome and the stratification variables (a) psychiatric center and (b) number of prior hospitalizations.

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

* + No or minor problems
? Some problems
- Major problems

Appendix 4.2
Outcome variable: Health-related Quality of Life

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention Automated digitalized follow-up + treatment as usual	Control Treatment as usual				
Tønning 2020 Denmark	RCT	N=120 I=59 C=61	I= withdrawal 7 no show 11 C= no show 8-9	Between group difference [1], (automated digitalized follow up add on to TAU – TAU): **WHOQOL** Δ=1.30, 95% CI: -5.04; 7.64, p=0.68 **WHO-5** Δ=1.03, 95% CI: -1.56; 3.63, p=0.22		*Scale:* WHOQOL (self-reported) Range (0-100) Higher values indicate a better quality of life WHO-5 (self-reported) Range (0-25) Higher values indicate a better quality of life *Sample note:* No mean score at baseline or follow-up (3m, 6m) is provided. Completed questionnaires vary at each follow-up (3m, 6m) without further explanation which questionnaires were completed (I=41-42, C=39-44)	?	?	-

WHOQOL: WHO Quality of Life-BREF, WHO-5: WHO (five) Wellbeing Index
[1] Between group differences from mixed effects model adjusting for differences in baseline values of the outcome and the stratification variables (a) psychiatric center and (b) number of prior hospitalizations.

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

* + No or minor problems
? Some problems
- Major problems

Appendix 4.3
Outcome variable: Number of healthcare visits

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention **Automated digitalized follow-up + treatment as usual**	**Control** **Treatment as usual**				
Tønning 2020 Denmark	RCT	N=120 I=59 C=61	I= withdrawal 7 no show 11 C= no show 8-9	**Readmission** Probability of readmission <6 months: 23% (95% CI: 11%; 33%) **Accumulated duration of readmission** Average length of readmittance: 35.2 days (SD 32.6)	**Readmission** Probability of readmission <6 months: 23% (95% CI: 12%; 33%) Hazard Ratio for readmission 0.95 (0.45 to 2.02) p=0.9 **Accumulated duration of readmission** Average length of readmittance: 51.6 days (SD 44) Difference between groups: Δ=-16.41, 95% CI: -47.32 to 25.5, p=0.3	Note, the outcome of interest according to PICO was number of healthcare visits. Tønning reports on specific type of healthcare visits – readmission only.	?	?	-

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

* + No or minor problems
? Some problems
- Major problems

Appendix 4.4
Outcome variable: Adherence to medication

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention Automated digitalized follow-up + treatment as usual	Control Treatment as usual				
Tønning 2020 Denmark	RCT	N=120 I=59 C=61	I= withdrawal 7 no show 11 C= no show 8-9	Between group difference, [1] (automated digitalized follow up add on to TAU – TAU): **MARS** Δ=0.46, 95% CI: -0.28 to 1.2, p=0.22		*Scale:* MARS (self-reported) Range (0-10) Higher values indicate better medical adherence. *Sample-note:* No score at baseline or follow-up (3m, 6m) is mentioned. Completed questionnaires vary at each follow-up (3m, 6m) without further explanation (I=41-42, C=39-44)	?	?	-

MARS: Medicine Adherence Rating Scale
[1] Between group differences from mixed effects model adjusting for differences in baseline values of the outcome and the stratification variables (a) psychiatric center and (b) number of prior hospitalizations.

Project: Automated feedback based on digitalized follow-up of patients with unipolar depression receiving pharmacotherapy

* + No or minor problems
? Some problems
- Major problems

Appendix 4.5
Outcome variable: Everyday functioning

Author year country	Study design	Number of patients n=	Withdrawals - dropouts	Results		Comments	Directness *	Study limitations *	Precision *
				Intervention Automated digitalized follow-up + treatment as usual	Control Treatment as usual				
Tønning 2020 Denmark	RCT	N=120 I=59 C=61	I= withdrawal 7 no show 11 C= no show 8-9	Between group difference, [1] (automated digitalized follow up add on to TAU – TAU): **FAST** Δ=-3.13, 95% CI: -8.13 to1.86, p=0.22		FAST (clinician-assessed) Range (0-72) Higher values indicate worse every day functioning *Sample-note:* No score at baseline or follow-up (3m, 6m) is mentioned. Completed questionnaires vary at each follow-up (3m, 6m) without further explanation (I=41-42, C=39-44)	?	?	-

FAST: Functional Assessment Short Test
[1] Between group differences from mixed effects model adjusting for differences in baseline values of the outcome and the stratification variables (a) psychiatric center and (b) number of prior hospitalizations.

Innehållsdeklaration

Denna HTA-rapport är baserad på följande moment:

- [x] Metodbeskrivning
- [x] PICO
- [x] Uttömmande litteratursökning
- [x] Flödesschema
- [x] Urval relevans
- [x] Kvalitetsgranskning
- [x] Tabelldata
- [ ] Sammanvägning av resultat
- [ ] Metaanalys
- [x] Evidensgradering enligt GRADE
- [x] Sammanfattning
- [x] Ekonomi
- [x] Organisation
- [x] Etik
- [x] Pågående studier
- [x] Exkluderade artiklar
- [x] Expertgrupp deltar
- [x] Extern granskning
- [x] Kunskapsluckor identifierade
- [x] Jävsdeklaration inhämtad från projektdeltagarna