Tailored implementation for chronic diseases
Depression in the elderly

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To Hilde

Knowing is not enough; we must apply.

Willing is not enough; we must do.

Johann Wolfgang von Goethe

Content

Acknowledgments

For a number of years I had been looking for an appropriate research project, not necessarily to acquire a research degree, but to acquire the skills of research, statistics and methodology. In my opinion knowledge of research processes is an advantage for clinicians when dealing with complex problems in practice and this knowledge helps me as a clinician to better appraise the continuous flow of research information and to better plan my strategies to provide better healthcare for my patients.

The opportunity to engage in the international project, Tailored Implementation for Chronic Diseases (TICD), was a rare gift to me. It has given me invaluable experience and insight into a crucial and complex field in the intersection between clinical practice and evidence-based medicine.

Research projects are rarely the result of solo work, this project being no exception. To complete a collaborative research project this size, a joint effort by numerous researchers, healthcare professionals, colleagues and technical staff is required, to whom I'm very grateful.

First of all I would like to thank my primary supervisor, Signe Flottorp. Taking the task to guide an old-timer from clinical practice to research within the field of implementation science must have been quite a challenge! Her efforts to guide me through the art of evidence-based medicine and tailored implementation have been patient, instructive, modelling, inspiring, and lots of fun. Signe has clearly demonstrated how it is possible to integrate expertise within research with clinical practice, never forgetting the focus on patient care.

My secondary supervisor, Andrew D Oxman, was involved throughout the whole project. Andy is involved in numerous international projects, but still was closely involved in the TICD project and always at hand. His vast knowledge in research and his logical thinking proved invaluable to our discussions and the progression in our project.

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The Old Age Psychiatry Department in Innlandet Hospital Trust is one rare species! In spite of being one of the smallest departments within the mental health services, the department is housing the most proliferative research centre in the Hospital Trust. I'm truly proud of being a part of it. Head of the department, Susan Juell is to a large degree responsible for this; her pioneering approval of clinical research as a core feature of clinical practice in specialist healthcare is a true virtue. In collaboration with research

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To engage in a large research project that runs for several years is, of course, my own responsibility, but in order to reach a decision, support from my family was crucial. I'm infinitely grateful for the support and patience my wife, Hilde, has shown throughout the project. You are one of a kind! I also want to thank my children, Eskild for continuously reminding me of the importance of music, Hanne for introducing me to the larger questions in life and Lars for never accepting the easy answers.

Funding

Abstract

Background

Healthcare professionals are in general slow to adhere to clinical practice guidelines recommendations. The management of depression in elderly patients is no exception. Both general practitioners and nurses in primary care are less prepared to diagnose depression in elderly patients, and to initiate adequate treatment. Determinants of practice are factors that may facilitate or impede adherence to guideline recommendations. Knowing about determinants of practice, and planning interventions to address them prior to the implementation of clinical practice is a logical strategy to improve adherence rates. The aim of this project was to test the effectiveness of tailoring interventions to previously identified determinants of practice in a cluster-randomised trial in Norwegian primary care. The study was part of a larger EU-supported collaborative research effort called "Tailored Implementation for Chronic Diseases" (TICD) including research groups from Germany, the Netherlands, Norway, Poland, and the United Kingdom.

Methods

We conducted a systematic review of national and international clinical practice guidelines for the management of depression in adults and we prioritised six recommendations for managing depression in elderly patients in collaboration with a reference group consisting of a purposeful sample of stakeholders. We conducted a multi-methods study that included sequential steps from the identification of determinants of practice for these recommendations, using a generic checklist for identification of determinants of practice developed by the international research group, planning interventions that addressed the determinants using qualitative research methods, and finally, implemented these interventions in a pragmatic cluster-randomised trial to assess adherence to six recommendations for the management of elderly patients with depression. The primary outcome measure was general practitioners' adherence to the recommendations across patients and depression subtypes.

Results

In the first part of our study we identified approximately 350 determinants of practice for six recommendations for managing depression in primary care using group and individual interviews. We categorised these according to the checklist developed by the researchers in the TICD project. Approximately 3/4 of the total were from three of the seven domains in the checklist: individual healthcare professional factors, patient factors, and incentives and resources.

In the second part, based on our prioritised determinants of practice, we conducted group interviews with several stakeholders to inform our decisions about how to tailor implementation interventions to improve adherence to clinical practice guidelines for elderly patients with depression. Prior to the group interviews, the research group developed a draft plan consisting of 55 interventions that addressed determinants of practice for the six recommendations, organised in six domains: resources for the development of a collaborative care plan, resources for GPs and other healthcare professionals, resources for patients and their relatives, outreach visits to GPs, educational resources for GPs and web-based services. The draft plan covered many of the interventions that the groups suggested. However, the groups added many new ideas, and they modified approximately half of the interventions suggested in the draft plan. We finally developed a multi-faceted implementation plan that included 52 interventions.

In the third part of our study, we conducted a cluster-randomised trial and implemented the interventions in 40 Norwegian municipalities, whereas 40 municipalities served as a control group. We were not able to recruit the required number of GPs for the data collection, and our study did not have sufficient statistical power to detect potential effects of the interventions. Mean adherence to the recommendations among general practitioners was 58% in the intervention group and 53% in the control group. The estimated difference from univariate mixed model was 1.6% (CI – 6 to + 9), indicating that the effect size on the primary outcome was moderate, at best.

Discussion

Our study was inconclusive due to the low inclusion rate of study participants in the data collection in the final randomised trial. In the process of identifying determinants and plan interventions, we found the combination of a brainstorming group session and a probe-led focus group with the same participants in the same session both feasible and productive. However, we identified a large number of determinants related to the six recommendations, and an even higher number of suggested interventions to address these determinants, making prioritisation of all the suggestions a key feature when planning the interventions. Using the checklist was practical and helped us to organise suggested determinants in a systematic way.

Implications for research and practice

There is still need for more knowledge on how to improve adherence to guideline recommendation. Based on this study we cannot draw definite conclusions in terms of effectiveness, which was at best moderate. Using the checklist as a tool to identify determinants when planning a guideline implementation may be an option for healthcare planners and administrators. Conducting research projects in primary care is challenging, and better strategies, such as fee for participation and automatic data collection from the electronic medical records should be considered. In order to perform

real life implementation research in a large scale, randomised controlled trials may not always be suitable, because it may not be possible to test interventions with commonly used dissemination resources for healthcare professionals, such as popular online services. Thus, other research designs, such as interrupted time series, might be more appropriate.

Sammendrag

Bakgrunn

Helsepersonell bruker vanligvis lang tid på å ta i bruk anbefalinger fra kliniske retningslinjer. Håndtering av eldre pasienter med depresjon er ikke noe unntak. Både fastleger og sykepleiere i primærhelsetjenesten er i mindre grad forberedt på å diagnostisere depresjon hos eldre og til å starte adekvat behandling. Praksisdeterminanter er faktorer som kan bidra til at etterlevelse av anbefalinger styrkes eller svekkes. Å kjenne til determinanter og å planlegge intervensjoner som tar hensyn til dem kan være en logisk strategi for å bedre etterlevelse av anbefalinger. Målsettingen med dette prosjektet var å teste ut effektiviteten av å skreddersy intervensjoner til praksisdeterminanter som var identifisert på forhånd i en klynge-randomisert studie i norsk primærhelsetjeneste. Studien var del av et større EU-støttet forskningsprosjekt mellom fem europeiske land kalt «Tailored Implementation for Chronic Diseases» (TICD). Prosjektet involverte forskningsgrupper fra England, Nederland, Norge, Polen og Tyskland.

Metode

Vi gjennomførte en systematisk oversikt av nasjonale og internasjonale kliniske retningslinjer for identifikasjon og behandling av depresjon hos voksne. I samarbeid med en bredt sammensatt referansegruppe prioriterte vi seks anbefalinger for behandling av eldre med depresjon. Steg for steg, ved hjelp av flere kvalitative og kvantitative metoder, samt en generisk sjekkliste som var utviklet i TICD prosjektet (TICD-sjekklisten), identifiserte vi praksisdeterminanter for de seks prioriterte anbefalingene, planla intervensjoner som tok hensyn til determinantene og, til slutt, implementerte vi disse intervensjonene i en pragmatisk klynge-randomisert studie. Det primære effektmålet var fastlegenes etterlevelse av de seks anbefalingene på tvers av pasientene og depresjons-subtyper.

Resultater

I den første delen av studien identifiserte vi ca. 350 determinanter for de seks prioriterte anbefalingene ved hjelp av individuelle intervjuer og gruppeintervjuer. Vi kategoriserte disse i henhold til TICD-sjekklisten. Omtrent 3/4 av determinantene kom fra tre av de syv domenene i sjekklisten; «individuelle faktorer ved helsepersonell», «pasientfaktorer», samt «insentiver og ressurser».

Basert på de prioriterte determinantene fra første delstudie, gjennomførte vi i den andre delen av studien gruppeintervjuer med flere interessegrupper som kunne assistere oss i å skreddersy intervensjoner i den hensikt å bedre etterlevelse av anbefalingene. Før gruppeintervjuene utviklet forskningsgruppen et utkast bestående av 55 intervensjoner, delt i seks domener, som møtte de prioriterte determinantene. De seks domenene var: Ressurser for utvikling av en plan for samhandling om eldre pasienter med depresjon, ressurser for fastleger og annet helsepersonell, ressurser for pasienter og deres

pårørende, praksisbesøk til fastleger, ressurser for opplæring av fastleger samt internett-baserte ressurser. Selv om utkastet dekket mange av intervensjonene som gruppene foreslo, foreslo gruppene en del nye intervensjoner og modifiserte omtrent halvparten av de foreslåtte intervensjonene. Til slutt utviklet vi en sammensatt implementeringsplan som besto av 52 intervensjoner.

I vår tredje delstudie, gjennomførte vi en klynge-randomisert studie og implementerte intervensjonene i 40 norske kommuner, mens 40 kommuner var i en kontrollgruppe. Vi klarte ikke å rekruttere det tilstrekkelige antall fastleger til datainnsamling, og vår studie har derfor ikke tilstrekkelig statistisk styrke til å avsløre potensielle effekter av intervensjonen. Gjennomsnittlig etterlevelse av anbefalingene var 58 % i intervensjonsgruppen og 53 % i kontrollgruppen. Den estimerte forskjellen fra den univariate «mixed model» beregningen var 1.6 % (konfidensintervall – 6 til + 9), hvilket gir en indikasjon på at effektstørrelsen for primært effektmål var i beste fall moderat.

Diskusjon

Vår studie var ikke konklusiv på grunn av den lave inklusjonsraten for datainnsamling i den randomiserte studien. I den første delstudien fant vi at det var både praktisk og produktivt å gjennomføre gruppeintervjuer med de samme deltakerne i en kombinasjon av en «brainstorming»-del og en strukturert del basert på innspill fra gruppelederne. Imidlertid identifiserte vi et høyt antall determinanter relatert til de seks anbefalingene og et enda høyere antall foreslåtte intervensjoner som tok hensyn til determinantene. Dette innebærer at prioritering av alle forslagene er en nøkkel-aktivitet når intervensjoner skal planlegges. Den generiske sjekklisten var både praktisk i bruk og hjalp oss til å organisere de foreslåtte determinantene på en systematisk måte.

Implikasjoner for forskning og praksis

Mer kunnskap om hvordan etterlevelse av anbefalinger i kliniske retningslinjer kan bedres er fortsatt nødvendig. Vi kan ikke trekke sikre konklusjoner vedrørende effekt av denne studien, men i beste fall var den moderat. Å bruke en sjekkliste som et verktøy for identifikasjon av praksisdeterminanter når det planlegges implementering av retningslinjer er en mulighet for helsetjenesteplanleggers og administratorer. Å gjennomføre forskningsprosjekter i primærhelsetjenesten er utfordrende, og bedre strategier, som f.eks. honorar for deltakelse eller automatisert data innsamling fra elektronisk pasientjournal bør vurderes. Randomisert forskningsdesign er kanskje ikke det mest passende designet når implementeringsstudier gjennomføres i stor skala fordi det ikke er mulig å bruke ressurser som allerede er populære hos helsepersonell, som f.eks. bestemte internett-tjenester. Derfor kan andre forskningsdesign, som avbrutte tidsserier, være bedre egnet.

List of papers

I   **Aakhus E, Oxman AD, Flottorp SA.** Determinants of adherence to recommendations for depressed elderly patients in primary care: A multi-methods study. *Scandinavian Journal of primary health care* 2014, 32:4. doi:10.3109/02813432.2014.984961

II   **Aakhus E, Granlund I, Oxman AD, Flottorp SA.** Tailoring interventions to implement recommendations for the treatment of elderly patients with depression: a qualitative study. *International Journal of Mental health Systems* 2015, 9:36 doi:10.1186/s13033-015-0027-5

III **Aakhus E, Granlund I, Odgaard-Jensen J, Wensing M, Oxman AD, Flottorp SA.** Tailored interventions to implement recommendations for elderly patients with depression in primary care: a study protocol for a pragmatic cluster randomised controlled trial. *Trials* 2014, 15:16 doi:10.1186/1745-6215-15-16

IV   **Aakhus E, Granlund I, Odgaard-Jensen J, Oxman AD, Flottorp SA.** A tailored intervention to implement guideline recommendations for elderly patients with depression in primary care: a pragmatic cluster randomised controlled trial. *Implementation Science* 2016, 11:32 doi: 10.1186/s13012-016-0397-3

1. Background

1.1. Introduction

It might be easy to change clinical practice when a new technique or strategy is filling an obvious gap in patient care. Introducing a treatment for a disease for which no treatment previously exists or where the health benefits are large as compared with previous treatment strategies are examples where the journey from research evidence to new practice may be particularly short. After the British dentist James Robinson had demonstrated tooth extraction in ether anaesthesia and William Morton had induced anaesthesia before removal of a neck tumour in 1846, the new technique spread rapidly across the world [1, 2]. The prospect of operating on a sleeping rather than a screaming patient must have appeared so attractive; surgeons all over the world quickly adopted the new technique and never looked back. The Italian psychiatrist Ugo Cerletti and his colleague and engineer Lucio Bini introduced electroconvulsive therapy (ECT) for schizophrenia in 1937. Within a few years the technique was applied all over Europe and USA, although clinicians soon realised that ECT was more effective in treating patients with severe depression than patients with schizophrenia [3].

On the other hand, one can argue that clinical practice is in general slow to adopt new practices, even when the health benefits are obvious and the costs are low. For instance Dr Benjamin Spock's fatal recommendations regarding infants' sleeping position could have been challenged even when the book was published, whereas it took more than 40 years before the health care system changed their guidelines for preferred sleeping position from prone to supine in infants, resulting in a rapid decrease in the prevalence of sudden infant death syndrome [4, 5]. Alexander Fleming discovered the antibiotic properties of *Penicillium Rubens* in 1928, and Cecil Paine successfully treated a gonococcal infection in an infant in 1930, but it took another 12 years before the medication was available on a large scale [6]. Lack of enthusiasm among pharmaceutical companies and lack of robust methods for mass-production may have contributed to this latency [6].

The performance gap from robust evidence to change in practice has been described by Green and colleagues as the "17-year odyssey" [7] (figure 1). They describe how the production and transfer of knowledge from research to practice and policy usually enters a pipeline in which evidence is entered, then appraised, and disseminated to policymakers and healthcare professionals. Consequently, there is a profound leakage of research evidence in the pipeline due to narrowing, filtering and vetting of evidence. One example is the introduction of thrombolysis in acute coronary infarction. The first evidence that thrombolysis in myocardial infarction disease reduced mortality emerged at the end of the 1960's. An increasing body of evidence in favour of thrombolysis reducing mortality appeared during the 1970's, and a cumulative meta-analysis revealed that from mid-seventies there has been no doubt about the evidence for thrombolysis [8]. Still, it took almost 15 years before this treatment was established as routine practice. The need for large, randomised trials and safety assessments may have delayed

the implementation. Robust evidence from meta-analyses that supported decisions appeared first in the eighties. Furthermore, the cumulative meta-analysis was conducted some 20 years after the first robust evidence appeared. Thus, healthcare professionals and planners may not have been aware of the growing body of literature.

Figure 1. The 17-year odyssey [7, 9] (used with permission)
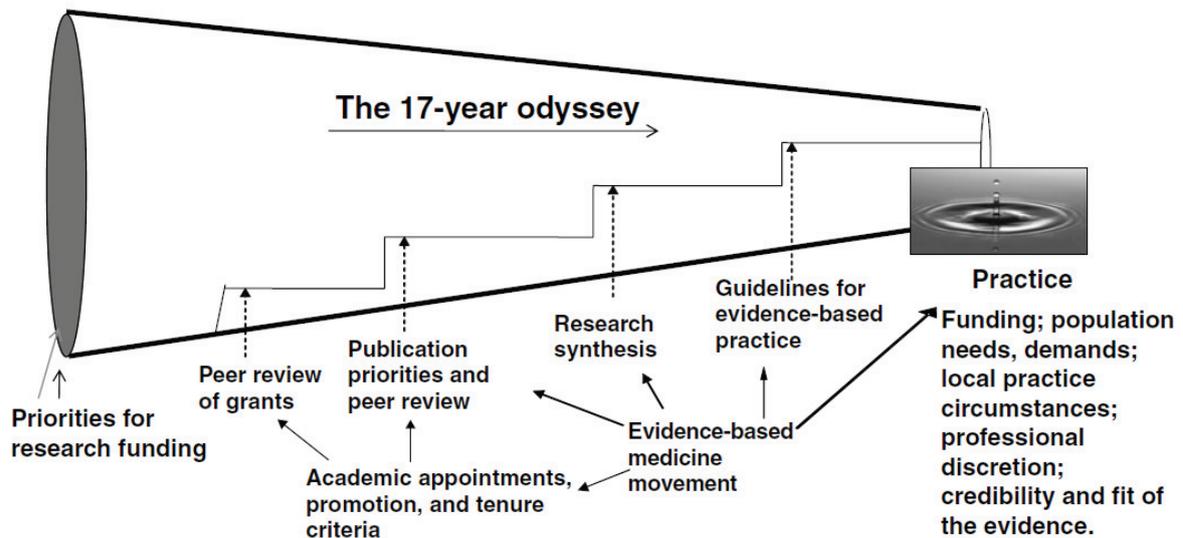
1.2. Clinical practice guidelines

Clinical practice guidelines have been developed for more than a century, but the rate of production of guidelines increased after the second World War II, and even more during the last 25 years [10]. It has been claimed that an Institute of Medicine report in 1992 introduced the modern era of guideline development [11]. Clinical practice guidelines are statements that include recommendations intended to optimise patient care [12]. Current understanding of the concept state that they are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative options [12]. Methods to develop clinical practice guidelines have improved, and guideline developers and users have several tools to develop guidelines, to adapt guidelines across healthcare systems and cultures and to critically appraise guidelines [13-15]. Guideline development has moved from being written on the basis of expert's opinions (illustrated by the phrase GOBSAT – "good old boys sat around a table" [16]) towards a more stringent and transparent methodology that provides a more systematic and transparent link between the body of evidence and the recommendations. Currently, the triad of scientific evidence, clinical experience and patients' values and preferences that

represent the concept of evidence-based medicine represent the core features that the development of many guidelines are based upon [17] and the model is constantly evolving [11, 18]. However, the quality of clinical practice guidelines is still variable [12]. Very often, recommendations presented in clinical practice guidelines are based on low quality evidence or clinical practice [12]. For instance, almost 60% of the 47 recommendations presented in the Norwegian Directorate of Health's clinical practice guideline for the management of depression in the adult population were given level 4/grade C strength (expert opinion) or they were labelled as a "good practice point". Only six recommendations (13%) received level 1 evidence and grade A strength, indicating that the recommendation was supported by "at least two randomised controlled studies or a meta-analysis of randomised controlled studies" [19]. This finding is consistent with the characteristics of clinical practice guidelines in other fields of healthcare, where few recommendations are based on systematic reviews, and the certainty of the evidence is predominantly low or very low [20-22].

Healthcare authorities and professional organisations develop clinical practice guidelines for a number of reasons. Aims may be grouped in two [23]:

1. Guidelines as professional aid; the guidelines should assist clinicians in their daily work; they should provide assistance to patients in their decision making; and they should provide assistance for healthcare planners to develop services for particular patient groups.

2. Guidelines as means to external control; key recommendations can be translated to performance indicators; they could be used in policy making and coverage decisions [23]. For instance they could provide recommendations that could change practice in a desirable direction if practice is diverse or questionable. In addition, clinical practice guidelines may be developed to provide services that are economically sound for the healthcare system, the patients and society [24]. Others claim that clinical practice guidelines may be developed to maintain or protect collective professional autonomy [10].

Clinician's appraisal and awareness of clinical practice guidelines may vary. Treweek and colleagues [25] showed that Norwegian general practitioners used clinical practice guidelines to a limited degree only, and that they preferred guidelines developed by professional organisations over guidelines developed by health authorities, a finding that has also been supported by others [26]. However, if a practitioner prefers to use a guideline developed by professional organisations, he/she also may select a guideline that has lower quality as compared with governmentally developed clinical practice guidelines as measured with the Appraisal of Guidelines, Research and Evaluation tool (AGREE) [27].

In spite of improved quality of guideline development and improved access due to online services, clinicians only adhere to clinical practice guidelines to a limited degree. Many factors may contribute to this. These are referred to as barriers and facilitators, or

determinants of practice. Knowledge about determinants of practice may help guideline developers to implement clinical practice guidelines more effectively.

1.1. Determinants of practice

We know that clinicians follow clinical practice guidelines for depressive disorder to a limited extent [28, 29]. Whether an implementation process is successful or not may depend on several factors; the innovation itself, the targeted group of professionals, the patients, the economic, administrative and organisational context, and the methods for dissemination and implementation [30].

Russel E. Glasgow proposed an intriguing scenario for the implementation of a diabetes prevention program [31]: Based on our knowledge that only a proportion of clinicians will adhere to the recommendations in a healthcare program, the desired practice will only reach a tiny fraction of the targeted patient group, due to a series of factors that affect the translation of the efficacious program into practice.

This applies to elderly patients with a depression. Take for example, a recommendation that all elderly patients with severe depression should be offered a combination of psychotherapy and an antidepressant. There is evidence that the combination of psychotherapy and antidepressants is more effective than each treatment strategy alone [32, 33]. Unpublished work from our project indicates that healthcare professionals in Norway have positive attitudes towards this recommendation. Of 127 healthcare professionals who responded to a survey, 73% partly or fully agreed with a recommendation for the combination of psychotherapy and antidepressants in severe depression in elderly patients. However, according to Glasgow [31] there is a number of filtering processes that apply to the implementation of such a recommendation. Firstly, only a proportion of general practitioners intend to adhere to the recommendation. Secondly, only a proportion of the clinicians that agree to adhere will actually do so by referring the patient to specialists or offer the patient psychotherapy in their own practice. Thirdly, only a proportion of elderly patients with severe depression will wish to be referred to a psychotherapist even if they could potentially benefit from the treatment. Fourthly, only a proportion of the elderly patients with depression who agree to be referred to psychotherapy will be offered the service, due to limited availability of psychotherapy in most parts of Norway and a prioritisation process that determines whether a patient is offered psychotherapy or not. Elderly patients with depression may not be prioritised when competing with younger patients. In our survey, only 33% of the healthcare professionals partly or fully agreed to the statement "Specialist health care services will provide elderly patients with such depression psychotherapy/psychological treatment to the same degree as younger adults". Finally, of those who are referred to psychotherapy and are offered the service, a proportion of patients will not attend the consultation. This occurs for several reasons, including lack of motivation, low self-esteem, cognitive difficulties and attitudes towards the service or the disorder itself.

Another example is social activities for depressed elderly patients. A recommendation to engage elderly patients in social activities to improve depression is uncontroversial and supported by fairly robust evidence [34-36]. We know that loneliness often leads to reduced physical activity, thus further increasing the risk for developing or worsening a depression [37, 38]. The patient may acknowledge that she has become less socially active in later years, and even more after acquiring a depression. Her family may realise that improving social activity may be good for her. The community psychiatric nurse could utilise resources in the community to improve social interactions for the patient, such as day care centres. Her general practitioner may realise that the patient has indicated a sense of loneliness, and may even be aware of the chance that her depression can improve if she becomes more socially active. Yet, the risk that the patient's social situation will remain unaltered is high for numerous reasons. For instance, we know that general practitioners may be less prepared to diagnose depression in their elderly patients as compared with their younger patients [39]. Characteristics of the general practitioners' practice may impede his ability to explore the patient's situation or solutions to her problems, such as a very busy practice, or lack of routines to diagnose depression. The community psychiatric nurse may not offer day care to the patient because the nurse senses that the patient is reluctant, there are no available places in the centre, or admission to the day care centre being restricted to patients with dementia. The patient may be passive due to her depression, and may dismiss family members' suggested activities to improve social contact. Negative thoughts due to the depression may lead the patient to believe that others, for instance family members and friends, have negative feelings towards her. The patient's family members may themselves suffer from a depression, given that being a family member of a depressed elderly patient is associated with an increased risk of developing depressive symptoms [40, 41].

There may be several other reasons for lack of adherence to this recommendation. Healthcare professionals may not be aware of new guidelines. They may experience difficulties in keeping track of updates or they may experience the load of current clinical practice guidelines as overwhelming [42]. They may feel that the patient's clinical presentation is too complex to fit with any particular clinical practice guideline or be sceptical of clinical practice guidelines in general [43]. They may feel that a recommendation is impractical in a clinical setting, due to limited resources or lack of skills. Additionally, local leaders may be reluctant to initiate a process to improve adherence to the recommendation, particularly if adherence implies a redistribution of already restrained resources or if the collaborative infrastructure necessary to implement the recommendation in the community is lacking.

Thus there are many factors that may facilitate or impede the probability of a recommendation being followed. These are referred to as barriers and enablers, barriers and facilitators, problems and incentives, determinants of change or determinants of practice [44].

The sheer number of potential determinants makes some categorisation necessary.

Flottorp and Oxman [45] used a checklist to guide their qualitative interviews when tailoring implementation interventions to improve management of sore throat and urinary tract infections. The items that were used in the qualitative group interviews were grouped in two domains:

1. Practice environment, including financial disincentives, organisational constraints, perception of liability, patient expectations, prevailing opinion, standards of practice, opinion leaders, medical training and advocacy

2. Knowledge and attitudes, including clinical uncertainty, sense of competence, compulsion to act, information overload

For the first systematic review of the effectiveness of tailored implementation in 2005, the Effective Practice and organisation of Care group (EPOC) classified barriers in seven domains: 1. information management or clinical uncertainty, 2. sense of competence, 3. perceptions of liability, 4. patient expectations, 5. standards of practice, 6. financial disincentives, 7. administrative constraints, and 8. others [46].

Cabana and colleagues [47] categorised barriers to physician adherence to guidelines in three domains:

1. knowledge, including lack of familiarity and lack of awareness,

2. attitudes, including lack of agreement, outcome expectancy, self-efficacy and motivation, and

3. Behaviour, including external barriers, such as patient factors, guideline factors (such as guideline characteristics) and environmental factors (such as lack of time or resources).

Michie and colleagues [48] used psychological theory to provide a theoretical framework for improving implementation of evidence-based guidelines. Following a rigorous six-step process to develop a consensus, they described 12 domains to explain behaviour change: 1. knowledge, 2. skills, 3. social/professional role and identity, 4. beliefs about capabilities, 5. beliefs about consequences, 6. motivation and goals, 7. memory, attention and decision processes, 8. environmental context and resources, 9. social influences, 10. emotion regulation, 11. behavioural regulation, and 12. nature of the behaviour

Rainbird and colleagues [49] described six levels at which barriers operate: 1. at the level of the innovation itself, 2. individual professional level, 3. patient level, 4. social context level, 5. organisational context level and 6. economic and political level.

Gurses and colleagues [50] proposed in their "Barrier Identification and Mitigation" (BIM) tool three domains in which barriers in healthcare could be identified and targeted:

1. Provider characteristics, including lack of knowledge or awareness about a guideline, disagreement with guideline content and reluctance to change practice,

2. Guideline characteristics, including guidelines not directly targeting the population, lack of evidence for the recommendations and lack of clarity in how tasks and roles are described, and

3. System characteristics, including problems related to the necessary tools, technologies and the performed tasks, physical environment and organisational structure and culture

Wensing and colleagues [51] categorised determinants of change in five domains:

1. Individual health professional factors, including knowledge and skills, cognition (including attitudes), and professional routines and characteristics,

2. Patient factors,

3. Professional interactions, including team processes, communication and influence, capacity for organisational change, organisational structure and capable leadership and organisational culture,

4. Incentives and resources, including availability of necessary resources, financial incentives and disincentives,

5. Social, political and legal factors, including legislation and health professions.

Flottorp and colleagues conducted a systematic review and included 12 frameworks for identifying determinants of practice [52]. In this review, they included any kind of study or paper that described a generic checklist of determinants for changing healthcare professional practice, organisational change, or changes in health system arrangements. To be included, the frameworks had to be used or been suitable for use in identifying determinants of practice prior to intervening to make improvements. They found that of the 12 included frameworks, all included determinants related to individual professionals, half of the included checklists included determinants related to the intervention, innovation or guidelines to be implemented. Five included determinants related to patients and four addressed professional interactions explicitly. Determinants of practice that were related to incentives and resources, capacity for change and social, political and legal factors were partly addressed in several, but not fully addressed in any of the frameworks. In terms of comprehensiveness, the authors found that none of the included frameworks were comprehensive when compared to the aggregated list of determinants and domains [52].

Based on this review the authors developed a 57-item checklist, based on nine attributes that a checklist for identifying determinants of practice should have: comprehensiveness, relevance, applicability, simplicity, logic, clarity, usability, and suitability [52]. The 57 items were organised in seven domains: 1. guideline factors, 2.

individual health professional factors, 3. patient factors, 4. professional interactions, 5. incentives and resources, 6. capacity for organisational change and, 7. social, political and legal factors. The full checklist is presented in table 1.

Table 1.The 57-item TICD checklist for identification of determinants of practice [52]

Domain	Section	Determinant*
Guideline factors	Recommendation	Quality of evidence supporting the recommendation
		Strength of recommendation
		Clarity
		Cultural appropriateness
		Accessibility of the recommendation
		Source of the recommendation
		Consistency with other guidelines
	Recommended clinical intervention	Feasibility
		Accessibility of the intervention
	Recommended behaviour	Compatibility
		Effort
		Trialability
		Observability
Individual health professional factors	Knowledge and skills	Domain knowledge
		Awareness and familiarity with the recommendation
		Knowledge about own practice
		Skills needed to adhere
	Cognition (including attitudes)	Agreement with the recommendation
		Attitudes towards guidelines in general
		Expected outcome
		Intention and motivation
		Self-efficacy
		Learning style
		Emotions
	Professional behaviour	Nature of the behaviour
		Capacity to plan change
		Self-monitoring and feedback
Patient factors		Patient needs
		Patient beliefs and knowledge
		Patient preferences
		Patient motivation
		Patient behaviour
Professional interactions		Communication and influence
		Team processes
		Referral processes

Incentives and resources	Availability of necessary resources
	Financial incentives and disincentives
	Nonfinancial incentives and disincentives
	Information system
	Quality assurance and patient safety systems
	Continuing education system
	Assistance for clinicians
Capacity for organisational change	Mandate, authority, accountability
	Capable leadership
	Relative strength of supporters and opponents
	Regulations, rules, policies
	Priority of necessary change
	Monitoring and feedback
	Assistance for organisational changes
Social, political and legal factors	Economic constraint on the health care budget
	Contracts
	Legislation
	Payer or funder policies
	Malpractice liability
	Influential people
	Corruption
	Political stability

*For each domain in the checklist, an additional "other"-option was included, to capture potential determinants other than those that are listed.

Although much effort has been invested in constructing theoretical frameworks for determinants of practice, there are very few evaluations that have tested these frameworks in large scale implementation trials.

1.2. Identification of determinants of practice

Having recognised the importance of determinants of practice, the next logical step is to find effective methods to identify the determinants for implementing a specific recommendation in a specific context [53]. A variety of methods is available, which can be grouped in two categories [54]:

1. *Exploratory methods:* In an Australian guide to identify barriers to evidence uptake, the authors listed nine techniques to investigate barriers. these are 1. brainstorming, 2. case studies, 3. key informants, 4. interviews, 5. focus groups, 6. direct observations, 7. surveys, 8. nominal group technique, and 9. Delphi technique [49]. The authors stated that most of the techniques are suitable across a range of practice settings, and a combination of techniques may be useful. Still, decisions about the most appropriate methods depend on a variety of factors,

such as available time, funding, desired rigorousness, and availability of expertise.

2. *Theory oriented models:* A range of theoretical and psychological approaches may be suitable for the identification of determinants of practice, such as the theory of planned behaviour [55] or the team climate inventory [56].

Currently there is no consensus on which methods are most appropriate for identifying determinants of practice in healthcare. Consequently, the selection of the appropriate method(s) will be guided by a number of factors, such as availability of evidence, preferences, skills to apply a specific method, financial issues and resources. In this project we compared several "exploratory" methods, including brainstorming, interviews, focus groups and a survey.

1.3. Diffusion, dissemination, implementation, and tailored implementation

Diffusion, dissemination, and implementation are related but distinct terms that describe different aspects of moving from evidence to change in practice [7]. The concepts of diffusion, dissemination, and implementation could be distinguished as progressively more active steps in the process of going from research evidence to clinical practice [57]. Many other terms are used to describe various aspects of using research to inform clinical practice, such as adoption, maintenance, and sustainability. For a comprehensive overview of terminology I recommend Rabin and Brownson's chapter in "Dissemination and Implementation Research in Health" [58].

1.3.1. Diffusion

Diffusion is the process by which information spreads uncontrolled and naturally in a passive way [59]. Davis and colleagues defined diffusion as "distribution of information and the practitioners' natural, unaided adoption of policies and practices" [60]. Lomas stated that the process of diffusion only works well when the "potential recipients are highly motivated, rewards of finding the information are high" [57]. Diffusion processes are related to communication within social systems, and are characterised by "early adopters" and "late adopters" over time [61, 62].

If sufficiently many people think that a new service is a good idea and it does not require a lot of resources, such as staff allocation and training, and a reward is expected (such as health benefit or personal satisfaction), then the service is likely to spread without much effort. One particularly striking example is the development of care farms for people with care needs in the Netherlands. Without much evidence for the benefits of the service, apart from positive experiences and word of mouth, this service spread rapidly across the Netherlands in a ten-year period at the beginning of the millennium. The number of care farms increased from 75 in 1998 to more than 800 in 2008 [63, 64]. Still, in 2014 evidence of the health benefits is lacking [65]. Greenhalgh and colleagues described the diffusion literature as the "letting it happen" literature [59]; when research literature is published the researchers leave it to others to utilise the results.

1.3.2. Dissemination

Dissemination may be defined as

> "the active and planned efforts to persuade target groups to adopt an innovation" [59],

whereas Davis and colleagues [60] defined dissemination as

> "communication of information to clinicians to improve their knowledge or skills; more active than diffusion, dissemination targets a specific clinical audience".

Thus, dissemination is the conscious efforts to spread new knowledge to target groups, such as policy makers, health care professionals, patients or the public, and has been described as the "helping it happen" strategy [7].

The U.S. National Institutes of Health defines dissemination as follows:

> "Dissemination is the targeted distribution of information and intervention materials to a specific public health or clinical practice audience. The intent is to spread ("scale up") and sustain knowledge and the associated evidence-based interventions" [66].

1.3.3. Implementation

Several attempts to define the term "Implementation" have been made:

Wensing and colleagues defined implementation as:

> "a planned process and systematic introduction of innovations and/or changes of proven value; the aim being that these are given a structural place in professional practice, in the functioning of organisations or in the health care structure" [67],

whereas Davis defined the term as:

> "Putting a guideline in place; more active than dissemination, involves effective communication strategies and identifies and overcomes barriers to change by using administrative and educational techniques that are effective in the practice setting" [60].

The U.S. National Institutes of Health defined implementation as follows:

> "Implementation is the use of strategies to adopt and integrate evidence-based health interventions and change practice patterns within specific settings" [66].

Fixsen and colleagues defined implementation as:

> "a specified set of activities designed to put into practice an activity or program of known dimensions" [68].

None of these definitions are conflicting, although they emphasize slightly different aspects of the process of implementation. For instance, in Davis' definition, the aspects of barriers to change are introduced, implying that implementation also may contain an evaluation of determinants of practice. In this sense, a process of tailoring implementation interventions may be included in the implementation process, and not be specified as a separate methodological approach as such. In both the National Institutes of Health's and Fixsen's definitions there is a focus on the practice setting ("change practice" and "put into practice", respectively). Following these definitions, implementation processes focus on healthcare practice. Hence, these definitions do not necessarily include implementation strategies that target healthcare authorities, local leaders or patients. In Wensing and colleagues' definition different levels of healthcare are noted ("in professional practice, in the functioning of organisations or in the health care structure") [67]. If we acknowledge that barriers to evidence-based healthcare practice can occur at different levels of the healthcare system, it is also logical that implementation includes all these levels and not professional practice alone.

1.3.3.1. Tailored implementation

Tailored implementation interventions are strategies that are designed to achieve desired changes in healthcare practice based on an assessment of determinants of healthcare practice [53]. The field of tailored implementation is still primarily a research field and will be further elaborated in section 1.5 Tailored implementation research.

1.4. Implementation research

Implementation science is the investigation of strategies to implement research evidence in clinical practice [69]. Typically, implementation strategies have been chosen a priori and been standardised across professions and targeted healthcare settings.

Implementation science is not a new research field [70]. The field of implementation science emerged from agricultural sciences, anthropology and sociology early in the 20th century [70]. However, implementation science in healthcare has grown more out of evidence-based medicine than out of those areas of research.

Eccles and colleagues [71] defined implementation research as follows: 'Implementation research is the scientific study of methods to promote the systematic uptake of clinical research findings and other evidence-based practices into routine practice, and hence to improve the quality (effectiveness, reliability, safety, appropriateness, equity, efficiency) of health care. It includes the study of influences on healthcare professional and organisational behaviour.'

The field of implementation research arose from the recognition that even if information and knowledge reach the targeted audience and they intend to adhere to recommended practice, practice may deviate from the intended practice. Thus, implementation science is characterised by targeting various audiences with various implementation interventions [72].

The term "dissemination and implementation" research is related to implementation science, but encompasses a broader understanding of the concept, including dissemination strategies [73]. The term knowledge translation is also closely related to implementation science. It has been defined by the Canadian Institutes of Health Research as "a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically sound application of knowledge to improve health, provide more effective health services and products, and strengthen the health care system" [74].

One of the challenges of this field of research is the lack of consensus on terminology [75, 76]. Fixsen and colleagues found reviewing the implementation research literature challenging due to lack of well-defined terms [68]. The terminology of implementation science/knowledge translation may be confusing and there is little consensus. One study that used semi-structured interviews with representatives from 33 funding agencies from the US, UK, France, the Netherlands, Scandinavia and Australia identified 29 synonyms for knowledge translation [77]. McKibbon and colleagues analysed all published articles that addressed the field of knowledge translation in 12 selected journals, and found that a total of 54 different terms were used to describe knowledge translation in one year [78]. They concluded that the plethora of terms and phrases that attempts to describe knowledge translation makes information retrieval and sharing of ideas and content difficult. "Quality improvement" (QI) is closely related to, if not synonymous with the term "implementation" [75]. Walshe described the phenomenon of creating new terminology as a process of "pseudoinnovation", which has led to a "waste of effort and resources, and a failure to achieve in all healthcare organizations the benefits that sustained and consistent investment in QI could have brought" [79].

The research field of implementation science may be regarded as young. Several parallel disciplines within the broad concept of implementation science have developed across the world:

The RE-AIM program [80], based in Virginia, USA, is a large implementation program that has been running since 1999 [81]. Originally emerging from diabetes care in 1999, RE-AIM provides a framework for improvement programs within a wide area of educational and healthcare systems. It provides a model to guide the development of "adequate multistage (reach, effectiveness, adoption, implementation, maintenance) and multilevel (individual, setting) indicators when evaluating D&I (dissemination and implementation) efforts" [58]. From the first description of the framework, RE-AIM has evolved to a large collaborative research consortium. In a systematic review that reports on the extent to which and how the RE_AIM framework was used, 71 articles that described the evaluation or empirical use of the framework were included [82]. The authors found that although a majority of the included articles (62%) reported on all five dimensions, none addressed all 34 criteria across the five dimensions. The most common problem appeared to be related to terminology; the most prevalent confusion was related to the definitions of "reach" and "adoption", and not reporting on a denominator for these dimensions [82].

The Promoting Action on Research Implementation in Health Services framework, or PARiHS, is another conceptual framework that posits key, interacting elements that influence successful implementation of evidence based practices [83]. This framework was based on the assumption that successful implementation is a relation between the nature of the evidence, the context in which the proposed change is to be implemented, and the mechanisms by which the change is facilitated [84]. Following this assumption, the authors introduced an equation SI=f(E, C, F), where SI is Successful implementation, f is "function of", E is Evidence, C is context and F is Facilitation. The E, C, and F domains each include three sub-elements that can be scored along an axis from low to high: "evidence" (research, clinical experience, patient preferences), "context" (culture, leadership, measurement) and "facilitation" (characteristics, role, style). A critical synthesis of literature in 2010 found that of 24 publications that reported on the use of the PARiHS framework in implementation projects and research, 18 were considered empirical, ranging from case reports to quantitative studies [85]. The authors found that the single greatest need for evaluating the validity of the framework was projects that studied the prospective use of the framework in implementation.

1.5. Tailored implementation research

Tailored implementation interventions are strategies that are designed to achieve desired changes in healthcare practice based on an assessment of determinants of healthcare practice [53]. Baker and colleagues defined tailored interventions as "strategies to improve professional practice that are planned, taking account of prospectively identified determinants of practice" [86]. The term may have been introduced first by Flottorp and colleagues [45], but the principles of tailoring were used in planning interventions from the 1990s and the oldest study to be included in Baker and colleagues' review was published in 1983 [87]. The first systematic review that summarised the effectiveness of tailored interventions, was published in 2005 [46]. Fifteen trials were included in this review. Of the 15 studies that were included in the meta-analysis, approximately half were published during 2001-2002, indicating the growing interest in the research field at the turn of the millennium.

Whereas commonly used implementation strategies do not explicitly identify determinants or select interventions to address identified determinants, tailored implementation requires identifying important determinants of practice and planning interventions that address these determinants when implementing the guidelines, in collaboration with a purposeful samples of stakeholders [53, 44].

Although most implementation interventions involve tailoring to some degree [53], systematic tailoring follows a step-wise procedure, as illustrated in figure 2.
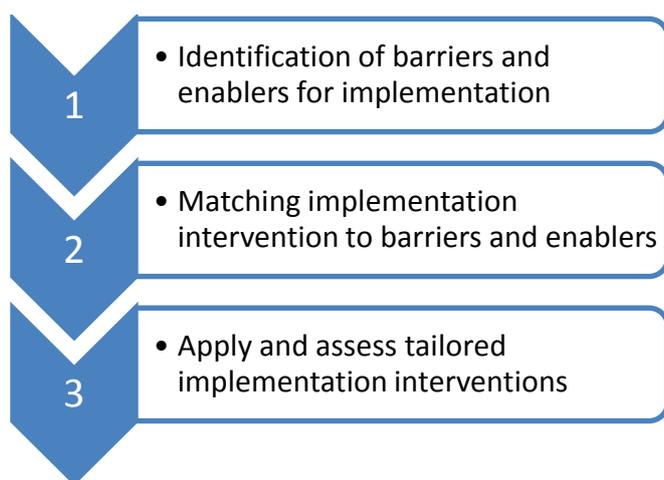
Figure 2: The step-wise procedure in tailoring [54]

Each of the three steps requires clear methods, in order to effectively implement guidelines. However, at present there is no consensus on which methods are effective [88]. A systematic review that assessed methods to identify barriers for change found that mostly qualitative methods were used for this purpose [89]. Thus, research projects that test the validity of a range of methods to tailor implementation interventions are needed.

There is a growing body of literature that tests various strategies to tailor implementation interventions. Baker and colleagues [86] reviewed 32 studies to assess the effectiveness of tailored implementation interventions. The review was an update of two previous reviews, from 2005 and 2010 respectively [46, 90]. Fifteen studies were included in a meta-regression analysis, of which two addressed adherence to guidelines for depression in primary care. The meta-regression analysis demonstrated a small to moderate effect on adherence (Odds ratio 1.56, CI 1.27-1.93). Data were insufficient to draw conclusions about healthcare outcomes, adverse effects and costs. The 17 additional studies in the review that were not eligible for the meta-regression analysis supported the findings from the meta-regression analysis. The two studies that addressed depression management in primary care supported the general finding of the meta-regression analysis [91, 92]. The included studies showed variability in methods to identify and target the determinants. These strategies were often poorly described. The authors called for further research, including trials comparing tailored interventions to no intervention or other interventions. They also recommended undertaking process evaluations or investigation of programme theory [93] alongside trials, taking into consideration the lack of clarity in terms of identifying determinants and planning the interventions.

1.5.1. Tailored Implementation for Chronic Diseases (TICD)

The international, EU FP7 Health programme funded research project Tailored Implementation for Chronic Diseases was a collaborative effort that included research teams from The Netherlands (Radboud University), Germany (University of Heidelberg),

Poland (University of Lodz), United Kingdom (University of Leicester) and Norway (Norwegian Knowledge Centre for the Health Services). The project ran from 2011 to 2015.

The background for the project was described in the application for the funding of the project:

> "Some approaches to tailoring are largely explorative, while other approaches are based on specific theoretical perspectives. Some approaches to tailoring use a systematic procedure that seeks generalizability while other approaches are empirical with limited or no generalization. The level of aggregation for tailoring differs. Tailoring may be applied at the level health professionals, patient care teams, healthcare organisations, or implementation projects. A range of specific methods and models are available for the different steps in tailoring, as will be outlined in the following sections. It is unclear which ones are most appropriate. Likewise, it is unknown whether the explicit use of theory on change of behaviour and organizations increases the effectiveness of tailoring of implementation interventions. And if so, what theory is most helpful in different situations. A wide range of theories is available and personal preference rather than research evidence seems to guide the choice of theory [94]. So, little is known about the validity and effectiveness of different methods and models of tailoring. It is exactly this area of controversy that is addressed by the TICD project. [54]

Four key objectives were defined: 1. To review research evidence regarding approaches to tailoring knowledge implementation in healthcare practice. 2. To test different approaches for identifying determinants of healthcare practice in chronic illness care. 3. To test different approaches for matching implementation interventions to identified determinants of healthcare practice in chronic illness care. 4. To assess the effectiveness of tailored implementation interventions in chronic illness care and the role of hypothesised determinants of healthcare practice in cluster-randomised trials. In addition a fifth work package included dissemination activities and planning a conference on experiences from the project. The first step, reviewing the evidence, was a joint effort with representatives from all research groups involved. This work resulted in a systematic review of taxonomies and frameworks for determinants that prevent or enable improvement in healthcare practice [52]. This work also produced a series of worksheets to guide people in the process of prioritising recommendations, identifying and prioritising determinants of practice the prioritised recommendations, and identifying and prioritising implementation interventions that address the identified determinants.

Thus, the TICD project aimed to apply the specific steps in figure 2 and to test this method in cluster-randomised trials.

1.6. Healthcare in chronic diseases

Chronic diseases are of long duration and generally slow progression [95]. According to WHO, the four main types of chronic diseases are cardiovascular diseases, cancer, chronic respiratory diseases an diabetes. Chronic diseases are the leading cause of death in the world, representing 63% of all annual deaths, most occur in low- and middle-income countries [96]. Healthcare programs to improve chronic care are numerous, although limited in their effectiveness [97]. Chronic disease care is often non-adherent to clinical practice guidelines [98, 99]. Co-morbidity in chronic diseases is frequent. Although the number of patients with multi-morbidity is higher among those younger than 65 years, the proportion of patients suffering from multi-morbidity as patients get older [100, 101]. In 1999, 65% of Medicare beneficiaries had two or more chronic conditions and accounted for 95% of Medicare expenditures [102]. Depression is a common co-morbidity in chronic diseases and contributes to an incrementally worsening of health in chronic disease [103].

The TICD project targeted five diagnostic groups within chronic diseases: cardiovascular disease (the Netherlands), chronic obstructive pulmonary disease (Poland), obesity (United Kingdom), multi-morbidity (Germany), and mental health (Norway).

1.7. Depression in the elderly

In the TICD project we were free to select a mental health disorder that represented chronic diseases. We chose depression in elderly patients, both because I, as a geriatric psychiatrist, pay special interest in this patient group, and because the risk of suffering from chronicity is high in this patient group.

Depression is one of the most common and disabling diseases of our time, and burden is increasing [104]. Lifetime prevalence has been estimated to be 10-17% [105, 106]. The World Health Organization (WHO) claims that more than 350 million people of all ages suffer from depression globally, and that it is the leading cause of disability worldwide [107]. Unipolar depression was in 2002 ranked as the fourth-most important global disease to affect disability adjusted life years (DALY), and is projected to be the second most important disease by 2030 [108]. The burden of depression, together with anxiety disorders, in the adult population in Norway is ranked as the second most important disease measured in Years lived with disability (YLD) [109]

A diagnosis of depression is made using clinical evaluation and/or diagnostic criteria. In Norway, in specialist health care, we use diagnostic criteria according to the International Classification of Diseases (ICD), published by WHO. The tenth revised version, ICD10, is currently in use [110].

Textbox 1. ICD10 Diagnostic criteria for depression [110]

A. Depressive episode
- mild (F32.0): at least two typical symptoms, plus at least two other common symptoms; none of symptoms intense
- moderate (F32.1): at least two typical symptoms, plus at least three other common symptoms; some symptoms marked
- severe (F32.2): all three typical symptoms, plus at least four other common symptoms; some symptoms severe with intensity
- severe with psychotic symptoms (F32.3): as described in F32.2 but with the presence of delusions, psychomotor retardation or stupor so severe that ordinary social activities are impossible

B. Recurrent depressive disorder (F33): at least two episodes that should have lasted a minimum of two weeks and should be separated by several months without significant mood disturbance.
- Current episode mild (F33.0), as described in F32 criteria for mild depressive episode
- Moderate (F33.1)
- Severe (F33.2)
- Severe with psychotic symptoms (F33.3)

C. Persistent mood disorders (F34.1): dysthymia. Feeling of depression and tiredness most of the time (often for months at a time) but do not currently fulfil the criteria for recurrent depression, with periods of days or weeks when they describe themselves as well.

Abridged criteria of depressive episode: minimum duration of episode: about 2 weeks

Typical symptoms (core symptoms):
1. depressed mood, 2. loss of interest and enjoyment, 3. reduced energy, increased fatigability

Other common symptoms:
1. reduced concentration and attention, 2. reduced self-esteem and self-confidence, 3. ideas of guilt and unworthiness, 4. agitation or retardation, 5. ideas or acts of self-harm or suicide, 6. disturbed sleep, 7. diminished appetite

The World Organisation of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians (WONCA) has developed a similar, but somewhat simplified diagnostic system, International Classification of Primary Care (ICPC), for primary care. The second revised version, ICPC2, is currently used by Norwegian general practitioners [111]. To diagnose subtypes of depression (depressive episode, recurrent depression, dysthymia) and severity of depression (mild, moderate and severe depression) according to criteria, using ICD10 or similar classification systems (e.g. Diagnostic and Statistical Manual of Mental Disorders, DSM) [112] is required. Currently a new revised version, DSM-5, has been released [113], but the research literature is predominantly based on previous versions (DSM-III and DSM-IV) .

In the following, any mention of this diagnostic system will refer to DSM IV, unless stated otherwise.

Elderly people are susceptible to developing depression. Risk factors such as loneliness, intractable pain, somatic co-morbidity and recent personal losses all contribute to the risk of developing depression [114]. A Norwegian study concluded that factors such as older age, male gender, perception of own health as poor, and impaired abilities all contributed to the risk of having depression, regardless of whether the patient was hospitalised in a general hospital or living at home [115]. The prevalence of depression in elderly patients is high [116]. The prevalence of depressive *symptoms* is higher than the prevalence of depression *disorder* (using depression rating scales yields higher prevalence rates than using diagnostic criteria) [117]. The incidence of depression increases with increasing age [118, 119] and varies in different populations within the group of elderly people [120]. Home-dwelling elderly patients are less susceptible to develop depression compared with elderly patients in nursing homes. Solhaug and colleagues [121] followed elderly patients over an 11-year course, and found that the risk of developing depression increased among elderly as they grew older. Although initial response rate to treatment is comparable to middle-age depressed patients, elderly patients with depression have an adverse longitudinal trajectory [122]. The risk that elderly patients with depression develop a chronic course is reported to be approximately 30% [123, 124]. Furthermore the risk for recurrences increases for each subsequent episode of depressive illness, and shortens recovery duration [125]. Once suffering from recurrent depression, the prognosis for remission is worse [126]. Cole and colleagues [127] found in a systematic review that after 24 months follow-up, one third of community-based elderly patients with depression still exhibited depressive symptoms, whereas 24% had deceased. Of those still alive, almost half of the patients exhibited depressive symptoms, "probably reflecting the chronic and relapsing course of the disorder" [127].

The disease mechanism in geriatric depression is complex and may be different from younger adults. Neurobiological, neurodegenerative and vascular factors may play important roles [128]. A vascular pathogenesis may be prominent, and vascular depression, characterised by psychomotor retardation, executive dysfunction and white matter lesions are more prevalent among elderly patients and often runs a more chronic, less responsive course [129]. Executive dysfunction in geriatric depression may be a prognostic factor for subsequent development of dementia [128]. Some claim that geriatric depression itself may be a prodromal stage of dementia [130]. Undoubtedly, patients suffering from depression in old age have an increased risk of developing dementia [131, 132]. Furthermore, elderly patients suffer from more complex, co-morbid conditions. They use more medications and are more susceptible to neuropsychiatric side effects such as depression, anxiety and cognitive decline both from their co-morbidities and their medications.

In Norway, general practitioners diagnose and treat most elderly patients with depression. Although awareness of recommendations in clinical practice guidelines may be high, adherence is in general considerably lower, in particular for elderly patients with depression [133, 134].

2. Objectives

For all the research projects in TICD, the overarching scope of the project was to develop valid and efficient methods of tailoring implementation interventions to address determinants of practice in chronic illness care [44]. For our project, the objectives were to identify and prioritise determinants of practice for selected recommendations for managing elderly patients with depression in primary care, to plan interventions that addressed these determinants, and finally to test the model in a cluster-randomised trial in Norwegian primary care.

I will present the objectives for each paper in the sequential order that illustrates the principles of tailored implementation. In paper 1 and 2 we describe how we identified and prioritised determinants of practice for recommendations and then planned interventions that addressed these determinants. Paper 3 is the protocol for the trial, and paper 4 is the results from the cluster-randomised trial.

Paper 1

The objective of this paper was to identify determinants of practice for six prioritised recommendations for the management of depressed elderly patients.

Paper 2

The objective of this paper was to describe how we developed implementation interventions based on the prioritised determinants of practice.

Paper 3

The objective of this paper was to describe the planned cluster-randomised study that evaluates the effectiveness of tailored interventions to implement six recommendations for the management of elderly patients with depression in primary care.

Paper 4

The objective of this paper was to evaluate the effectiveness of tailored interventions to implement six recommendations for the management of elderly patients with depression in primary care.

3. Methods

In this thesis, I will describe the work we did in the identification of determinants (Paper 1), the planning of interventions (Paper 2), and the cluster randomised trial to evaluate the effectiveness of the interventions (Papers 3 and 4). Initially I will present the work that preceded the research presented in these papers; how we organised the research project and how we prioritised the recommendations that we intended to implement.

3.1. Tailored implementation for elderly patients with depression

3.1.1. Organising the research project in Norway

Andy Oxman and Signe Flottorp at the Norwegian Knowledge Centre for the Health Services were responsible for the Norwegian arm of the TICD project. Eivind Aakhus was included in the research group as a primary researcher and PhD candidate. The group started its planning during summer 2010, and quickly organised a steering committee, including Per Vandvik and Knut Engedal.

Andy Oxman and Signe Flottorp are health care services researchers and have worked as general practitioners. Eivind Aakhus is a senior consultant in geriatric psychiatry. Per Vandvik is a researcher and works as an internist. Knut Engedal is a researcher and a geriatrician and psychiatrist.

TICD was funded from March 2011 to March 2015. In the autumn 2011, we invited a representative group of stakeholders in Norway to participate in the project in a reference group. These were the Norwegian Directorate of Health; Mental Health; Norwegian Nurses Organisation; Norwegian Psychiatric Association; Norwegian Association for Local and Regional Authorities; Norwegian Psychological Association; Ageing and Health – Norwegian Centre for Research, Education and Service Development; Norwegian Retirees Association; Department of General Practice and Community Medicine – University of Oslo; Norwegian Association of General Practitioners in the Norwegian Medical Association. Each of these organisations assigned one representative to participate in the reference group. For two organisations, representatives left the group for various reasons, and they were substituted with other representatives if possible. The reference group had two meetings early in the project, January 2012 and January 2013. During these meetings, the stakeholders contributed to the prioritisation of recommendations and the planning of the intervention.

In 2012 Ingeborg Granlund, a social educator, was included in the research group.

The international research group met annually to coordinate the project, starting in Arnhem, the Netherlands in April 2011, following in Heidelberg, Germany in April 2012, Leicester, UK February 2013, Warsaw, Poland October 2014 and Bergen, Norway February 2015. A couple of additional day-meetings in Frankfurt, Germany that included primarily the primary researchers from the national research groups were arranged.

In the description of our methods, I refer to particular persons in the project, using initials. EA is Eivind Aakhus, IG is Ingeborg Granlund, SF is Signe Flottorp, and AO is Andy Oxman.

3.1.2. From 13 guidelines to six recommendations

We selected six recommendations to be implemented in the project. To do this, we conducted a systematic review that included 13 clinical practice guidelines on management of depression in adults. We published the protocol of this work in the International Prospective Register of Systematic reviews (PROSPERO) [135]. Because the four papers included in this thesis do not sufficiently describe the process from the systematic review to the prioritisation of the recommendations, we present this work here. We searched the following sources for guidelines: International resources for guidelines, including Trip Database, Guidelines International Network (G-I-N), US National Guideline Clearinghouse, Best Practice and UpToDate. Electronic databases: Ovid MEDLINE, limited to Publication type: Guideline. Ovid PsycINFO and Embase, combined with search term Guideline. Web-sites for National Health Authorities and relevant professional health care associations. The Norwegian Electronic Medical Handbook (www.legehandboka.no)

We used the following search terms: depression, major depressive disorder, depressive disorder, major affective disorder, affective symptoms and mood disorder.

We included guidelines for the diagnosis and treatment of depression in adults (> 18 years) in primary health care, published by health authorities or professional health care associations in 2005 or later and written in English or Scandinavian (Norwegian, Swedish or Danish) languages.

We excluded guidelines

- for bipolar disorder
- where later updates had been published
- on specific tasks only within the management of depressive disorder (for instance screening, pharmacological treatment or specific patient populations other than the elderly)
- developed primarily for the specialist health care services
- with a low score (less than 50%) on the three items in "scope and purpose" from Appraisal of Guidelines for Research and Evaluation II (AGREE II) [15]
- published before 2005.

From 3617 screened records, we excluded 3598 hits, assessed 19 guidelines for eligibility and finally included 13 guidelines in our review (table 2).

Table 2. Guidelines included in the systematic review

Abbreviations, year of publishing	Country	Guideline group	Website	References
CA: CCSMH 2006	Canada	Coalition of Seniors' Mental Health	www.ccsmh.ca	[136]
DK: HMA 2007	Denmark	The Danish Health and Medicines Authority	www.sundhedsstyrelsen.dk	[137]
INT: WFSBP 2007	International	World Federation of Societies of Biological Psychiatry	www.wfsbp.org	[138]
NO: NDH 2009	Norway	The Norwegian Directorate of Health	www.helsedirektoratet.no	[139]
NO: NEL 2011	Norway	The Norwegian Electronic Medical Handbook	www.legehandboka.no	[140, 141]
NZ: NZGG 2008	New Zealand	New Zealand Guidelines Group	www.health.govt.nz/about-ministry/ministry-health-websites/new-zealand-guidelines-group	[142]
SE: NBHW 2010	Sweden	The Swedish National Board of Health and Welfare	www.socialstyrelsen.se	[143]
UK: BAP 2008	United Kingdom	British Association of Psychopharmacologists	www.bap.org.uk	[144]
UK: NICE 2009	United Kingdom	National Institute of Health and Clinical Excellence	www.nice.org.uk	[145, 146]

USA: ICSI 2010	USA	Institute for Clinical Systems Improvement	www.icsi.org	[147]
USA: KP 2010	USA	Kaiser Permanente	www.healthy.kaiserpermanente.org/html/kaiser/index.shtml	[148]
USA: UpToDate 2011	USA	UpToDate Inc	www.uptodate.com/contents/search	[149, 150]
USA: VA/DoD 2008	USA	Veterans Affairs/Department of Defence	www.va.gov	[151]

Two of the authors independently assessed each guideline.

We used AGREE II to assess the quality of the guidelines [15]. AGREE II is an internationally developed tool for assessing the methodological rigour and transparency of clinical guidelines. AGREE II consists of 23 items grouped in six domains:

1. Scope and purpose (item 1-3)
2. Stakeholder involvement (item 4-6)
3. Rigour of development (item 7-14)
4. Clarity of presentation (item 15-17)
5. Applicability (item 18-21)
6. Editorial independence (item 22-23)

Each item is scored on a 7-point Likert scale, from 1 (strongly disagree) to 7 (strongly agree). At least two people independently scored each guideline. In a number of cases we were uncertain whether a phrasing in the guideline was a recommendation or not. In such cases, we resolved disagreements by discussion. We calculated domain scores by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. Weighted Kappa-scores (w-κ) for each domain were calculated in order to assess inter-rater consistency.

Table 3 shows the results of the quality assessment.

Table 3. Quality of 13 guidelines, as assessed with AGREE II

	Scope and purpose	Stakeholder involvement	Rigour of develop-ment	Clarity of presentation	Applicability	Editorial independence	Mean for all six domains*
CA: CCSMH 2006	92	89	79	94	35	83	79
DK: HMA 2007	94	61	69	78	31	29	60
INT: WFSBP 2007	94	42	60	28	6	42	45
NO: NDH 2009	92	78	51	75	31	71	66
NO: NEL 2011	53	25	14	81	6	21	33
NZ: NZGG 2008	97	86	55	89	46	96	78
SE: NBHW 2010	78	75	70	81	52	38	66
UK: BAP 2008	69	47	43	67	8	4	40
UK: NICE 2009	94	86	68	67	37	67	70
USA: ICSI 2010	100	56	73	61	21	92	67
USA: KP 2010	69	42	78	86	10	29	53
USA: UpToDate	75	19	55	97	13	67	54

2011					
USA: VA/DoD 2008	92	61	74	89	25	58
Mean for domain*	_85_	_59_	_61_	_73_	_25_	_50_
w-κ	0.38	0.28	0.49	0.43	0.44	0.70

Guideline abbreviations: See Table 2. AGREE II score in %: [(Obtained score ÷ lowest score)/(highest score ÷ lowest score)]×100.

* 'Mean for all six domains' and 'Mean for domain' were calculated for illustrative purposes only, and is not described in the AGREE II manual.

The average score across the domains for all 13 guidelines was 59%. All but one guideline scored less than 50% on applicability (median 25%, range 6 to 52%). This part of AGREE II pertains to the likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guideline. Seven of the 13 guidelines scored less than 50% on editorial independence (median 42%, range 4 to 96%). The majority of guidelines scored above 50% on the rest of the AGREE II domains (median scores for scope and purpose 94%, stakeholder involvement 61%, methodological rigour 68%, clarity of presentation 81%). None of the 13 guidelines that were assessed eligible for inclusion scored lower than 50% on the item "Scope and purpose", thus all were included in the review. Agreement among the researchers using weighted kappa (w-k) varied from fair to good [152].

We extracted data from each included guideline using a data extraction form. We focused on recommendations regarding the following four clinical areas relevant to the management of depression:

1.   Screening for depression.
2.   Treatment recommendations.
3.   Tools for diagnosis and evaluation of treatment effect
4.   Collaboration/care management

We created 14 clinical questions within these areas. The data extraction form and its clinical questions are available in the protocol for the systematic review [135].

We considered the applicability of recommendations in each of the four areas for mild, moderate and severe depression, and for recurrent or treatment-resistant depression.

I present additional results in tables showing the guidelines' characteristics and findings relevant to our selection of recommendations in appendices 1-7.

We used the Norwegian guideline as a comparator; we identified all recommendations in the Norwegian guideline and we compared these with the recommendations in the other guidelines that were included in the review. In case of conflicting recommendations, we used the following criteria to determine the reasons for conflicting recommendations and, if possible, determined which recommendation was most appropriate in the Norwegian context [153]:

1.   Judgements about evidence that can lead to conflicting recommendations
    a.   Were the clinical questions different?
    b.   Were different studies considered?
    c.   Were the results combined and analysed differently?
    d.   Was the quality of the evidence assessed differently?
2.   Judgements about consequences that can lead to conflicting recommendations
    a.   Did estimates of effect for important outcomes differ?
    b.   Did judgment about the quality of the evidence differ?
    c.   Were health consequences weighted differently?

d.   Were economic consequences considered differently?

We identified 47 recommendations in the Norwegian clinical practice guideline for managing depression in adults. We assessed 40 of these to be relevant for the project, excluding recommendations for sub-groups not relevant to elderly patients with depression, such as pregnancy and post-partum depression, or addressing healthcare not relevant to primary care, such as electroconvulsive therapy. We compared these recommendations with the results from our review, and we prioritised the recommendations using a TICD-worksheet that was specifically designed for this purpose (Worksheet 3: Prioritisation of determinants) [52]. For each recommendation, the research group (EA, SF, AO) asked the following questions:

1.   Are the consequences of non-adherence serious?
2.   Is there a large amount of non-adherence or inequitable adherence?
3.   Is the recommended practice feasible in the targeted settings?
4.   Is implementing the recommendation a priority?

We scored questions 1-3 independently for each recommendation on a 5-point scale (1. No, 2. Probably not, 3. Uncertain, 4. Probably, 5. Yes), discussed our results and resolved disagreements. We made a common score for question 4 after this discussion. Each recommendation that was given a score of 4 or 5 on question 4 was assessed as eligible for prioritisation. Following this procedure, we prioritised 10 recommendations.

The common protocol for TICD stated that for each condition the research groups should identify the national guidelines or key recommendations applicable in each of the participant countries [44]. Furthermore, it stated that we should select a maximum of eight recommendations [52]. Our research group decided that we should prioritise six recommendations for further study. We assessed each of the ten recommendations in terms of clarity and attempted to re-phrase them if they lacked clarity. We then discussed these recommendations with the reference group.

For each of the recommendations we presented the underlying evidence, and we asked the participants to discuss and prioritise six of the recommendations for the project. The six prioritised recommendations are presented in table 4.

Table 4: Six prioritised recommendations for the management of depression in elderly patients.

Prioritised recommendations	Full recommendation to be discussed in the groups and interviews
1. Social contact	Primary care physicians and other health care professionals should discuss social contact with elderly patients with depression, and recommend actions (e.g. group activities) for those who have limited social contact. When needed, regular social contact should be provided with

	trained volunteers, recruited from Centres for Voluntary Organisations, the Red Cross, Mental Health or community day care centres. When possible, the patient's relatives should be involved in the plan to improve social contact.
2. Collaborative care plan	All municipalities should develop a plan for collaborative care for patients with moderate to severe depression. The plan should describe the responsibilities and communication between professionals who have contact with the patient, within primary care and between primary and specialist care. In addition, the plan should appoint depression care managers who have a responsibility for following the patient. The plan should describe routines for referral to specialist care.
3. Depression care manager	Primary care physicians should offer patients with moderate to severe depression regular contact with a depression care manager
4. Counselling	Primary care physicians or qualified health care professionals should offer advice to elderly patients with depression regarding: • Self-assisted programs, such as literature or web-based programs based on cognitive behavioural therapy principles • Structured physical activity programmes, individually or group-based • Healthy sleeping habits • Anxiety coping strategies • Problem solving therapy
5. Antidepressants in mild depression	Primary care physicians should usually not prescribe antidepressants to patients with mild depression. Primary care physicians may consider prescribing antidepressant medication to patients who suffer from a mild episode of depression and have previously responded to antidepressant medication when moderately or severely depressed.
6. Severe depression, recurrent depression and dysthymia	Primary care physicians should offer these patients a combination of antidepressant medication and psychotherapy. If the physician is not trained to provide the patient with psychotherapy, patients should be referred to trained health care professionals.

This research project addressed a limited amount of clinically relevant recommendations. However, although the reference group and the research group

agreed that these six recommendations were highly important, they did not represent a comprehensive clinical practice guideline. They do not target all core features in geriatric depression management; some recommendations for moderate depression and recommendations for managing suicidal ideation, co-morbidity and dementia are missing.

We found conflicting recommendations [153] regarding prescribing antidepressants in mild depression, and for screening for depression in the adult population. The European and the North American (US and Canadian) guidelines differed substantially regarding recommendations on pharmacological treatment and psychotherapy in mild depression. This may partly be due to the different diagnostic classification manuals that were used (answering "yes" on question 1a: "Were the clinical questions different?" in [153]). More criteria must be met for a diagnosis of mild depression in DSMIV than in ICD10. Thus mild depression in DSMIV is a more severe condition than mild depression in ICD10 [138]. Still, the NICE guideline, which is based on DSMIV, recommended low-intensity programs for mild depression. The evidence for the effect of antidepressants in mild depression is weaker than for more severe depression, the placebo effect may be larger, and the drop-out rate is reportedly higher (answering "yes" on question 2c: "Were health consequences weighted differently?"). Thus, treating patients with mild depression with antidepressants represents a trade-off between desired and undesired effects [154].

The recommendation for screening was not included in the six prioritised recommendations, and consequently, we did not analyse the reason for the conflict.

3.2. Inventory of current practice for the six recommendations

We lack routine data on quality of care and adherence to guidelines in primary care in Norway. We based the following description of usual care regarding depression management in the elderly in Norway on our experience as clinicians and researchers, governmental reports and scientific publications. We also included international data, if data specific for Norwegian practice were lacking.

Social contact

Isolation and loneliness are major risk factors for developing depression [155]. Although Norway has a scattered population, 44% live in one of the six largest city areas [156]. The proportion of elderly is higher in rural areas. The recommendation requires efforts from primary healthcare providers (physicians, nurses, occupational therapists) and voluntary organisations. Some municipalities have included voluntary organisations and volunteers in their healthcare planning, whereas others have no such collaboration. To some extent, volunteers are involved in the follow-up of psychiatric patients of all ages. We believe that the primary care practitioners in general have no routines for involving volunteers in the management of elderly patients with depression.

Collaborative care plan

Although some municipalities and city districts have developed a general plan for managing patients with mental health related disorders, we assumed that this was not the rule for most. A specific plan for depression care management is, at best, a part of such a general plan. Legal requirements from the national health authorities in Norway oblige municipalities and their health enterprises (constituting both somatic and psychiatric specialist healthcare) to assign mutual agreement for collaboration. These statements are merely advisory, and do not dictate healthcare providers' behaviour.

Depression care manager

A Norwegian register based study found that approximately 1/3 of the patients did not refill their prescription of antidepressants [157]. This may indicate that a more thorough follow-up, by a depression care manager, might improve the patients' adherence to the treatment plan. The evidence for this service as part of a collaborative care plan is substantial [158-160] but has, to our knowledge, not been evaluated systematically in Norway. The depression care manager is intended to be a service added to the care and follow-up offered by the general practitioners. Municipalities in Norway have developed community psychiatric nurse services to a large degree. This service is not developed to serve all patients who need such care, and, when resources are limited, we believe that elderly patients with depression are not prioritised in the community.

Counselling

This recommendation addresses several aspects of depression care management. The recommendation is primarily relevant to general practitioners, but also to specially trained nurses. In addition, some sort of coordination with voluntary organisations or enterprises that offer physical training or activity programmes may be needed. We believe that healthcare professionals frequently offer services described in this recommendation, albeit not in a systematic or coordinated way. Evidence-based tools for providing advice on self-help, sleep-problems, anxiety coping and problem solving therapy are available in English [161] and, to some extent, in Norwegian [162-165]. Training of health care professionals is needed for some of the actions, particularly problem solving therapy and coping strategies [161]. According to Bente Aschim, a general practitioner and experienced trainer of general practitioners in the techniques of cognitive behavioural therapy, approximately 10% of general practitioners have some formal training in cognitive behavioural therapy (Bente Aschim, personal communication).

Antidepressants in mild depression

We assumed that general practitioners often prescribe antidepressants as soon as they give a patient a diagnosis of depression, regardless of depression severity.

Severe depression, recurrent depression, and dysthymia

Elderly patients with chronic or recurrent depression may be referred to and, to some extent, followed up by specialists, primarily in out-patient clinics of geriatric psychiatry and to a smaller extent in community psychiatric centres [166]. Psychologists and psychiatrists in private practice offer to a very limited degree therapy to elderly patients with these forms of depressive disorders. Most of these patients receive pharmacotherapy. Although some general practitioners have received formal training in cognitive behavioural therapy, few elderly patients are offered adequate psychotherapy from their practitioners

3.3. Paper 1: Identifying determinants of practice

According to the common protocol for the TICD project [167, 44], we used five methods to identify determinants of practice: brainstorming sessions in groups, structured group interviews, individual interviews with professionals, individual interviews with patients and a survey.

We made a list of eligible healthcare professionals (general practitioners, primary care nurses, nurses and psychiatrists from specialist care, healthcare administrators and researchers) for the various interviews. We identified eligible interview candidates based on available lists of general practitioners published by national health authorities, recommendations from colleagues, leaders in primary and specialist care or personal knowledge. Patients were selected and asked to participate by their general practitioner. All participants gave informed consent.

3.3.1. Brainstorming/focus groups and individual interviews with professionals and patients

One group comprised healthcare professionals that practiced in an urban area (Oslo city) and one group that practiced in a rural area (Hedmark and Oppland counties). Individual interviews also included healthcare professionals from both urban and rural areas, whereas we selected patients from practices located in the town of Gjøvik.

We independently prepared a list of probes from the TICD checklist [52] and, by consensus, created a common list of probes for 21 determinants that we considered important for the six recommendations (Table 5).

Table 5. Probes for discussion in structured part of interviews

TICD check list domains	Probes (and the according item in the checklist)*
1. Guideline factors	1. Accessibility to guidelines (accessibility of the recommendation, No 5) 2. Source of guidelines (source of the recommendation, No 6) 3. Access to psychotherapy (accessibility of the intervention, No 9) 4. Problem not to give antidepressants (recommended clinical intervention – feasibility No 8 and recommended behaviour – effort No 11) 5. Difference between guidelines and practice (Recommended behaviour – compatibility No 10) 6. Other

TICD check list domains	Probes (and the according item in the checklist)*
2. Individual healthcare professional factors	7. Diagnosis of depression (Domain knowledge No 15) 8. Skills to provide counselling (skills needed to adhere No 18) 9. Disagreement with guidelines (Agreement with the recommendation No 19) 10. Agree that guidelines would improve practice (Expected outcome No 21) 11. Motivated to implement guidelines (Intention and motivation No 22) 12. Preferred learning style if training needed (Learning style No 24) 13. How do you feel it is to work with depressed elderly (Emotions No 25) 14. Feedback/monitoring of practice – would it help? (Self-monitoring and feedback No 28) 15. Other
3. Patient factors	16. Patients agreement with recommendations (Patient needs No 30, beliefs and knowledge No 31 and preferences No 32) 17. Motivation (Motivation No 33) 18. Other
4. Professional interactions	19. Influential organisations or people (Communication and influence No 36) 20. Sufficient types of health workers + communication (team processes No 37) 21. Referral to depression coordinator (referral processes No 38) 22. Other
5. Incentives and resources	23. Fee for counselling (Financial incentives and disincentives No 41) 24. What type of assistance (tools) (Assistance for clinicians No 46) 25. Other
6. Capacity for organisational change	26. Priority – psychotherapy for depressed elderly (priority of necessary change No 52) 27. Other
7. Social, political and legal factors	No probes used

* The TICD checklist numbers refer to 64 items, due to one "other" option for each of the seven domains within the checklist.

3.3.2. Survey

The international TICD research group developed five statements to be used for each recommendation by all participating research teams in the survey:

- I feel that this recommendation is feasible and practical to undertake in my setting
- I feel this recommendation fits with my current practice
- I/general practitioners have the knowledge required to implement this recommendation

- The benefits of implementing this recommendation outweigh the effort of implementing it
- I/general practitioners intend to implement this recommendation

The five common statements, originally written in English, were translated independently to Norwegian by three Norwegian researchers following the method described by Wild and colleagues [168]. The three translations were aggregated by a fourth researcher into the final Norwegian version. A British-born colleague, fluent in English and Norwegian, translated the final Norwegian version back into English. This version was presented to the UK authors who gave their approval.

In addition, we created from zero to five statements that were specific for each of the six recommendations to be implemented in our project. We created these statements after conducting the group and individual interviews. Our final questionnaire contained 59 items including one free-text option for each recommendation. A 5-point scale was used for each statement (1: Fully disagree, 2: Partly disagree, 3: Neither disagree nor agree, 4: Partly agree, 5: Fully agree).

3.3.3. Analysis of qualitative data

We applied a five-step framework described by Glenton and colleagues [169] for our analysis:

1. Familiarisation: All sessions were audio-recorded and transcribed in full. EA and SF independently reviewed transcriptions from one group and two individual interviews, and then compared and discussed the results. EA identified determinants from the remaining group and individual interviews

2. Identifying a thematic framework: We used the TICD checklist as a thematic framework [52].

3. Indexing: EA put all quotes that contained suggested determinants in tables and linked the identified determinants to the TICD checklist. Determinants that we considered to be important, but that we could not link to a specific recommendation, were categorised as "general".

4. Charting: EA put all identified determinants in separate cells in a spreadsheet using separate columns for each session. EA and SF independently analysed these data, assessing whether the suggested determinants were related to others, grouping related determinants, and labelling each group of related determinants. We then discussed our assessments and revised the final list of determinants for each recommendation based on a consensus among the three authors.

5. Mapping and interpretation: Finally, EA and SF reviewed all suggested determinants and grouped them across recommendations and checklist items. We used a

standardised procedure for the TICD project to rank determinants according to the following criteria:

> 1. How important is the determinant in influencing current practice (plausibility)?

> 2. To what extent can the determinant be addressed (feasibility)?

We scored these on a 5 point scale (plausibility: 1 = very low to 5 = very high; feasibility: 1 = very difficult to 5 = very easily). All determinants scoring 4 or 5 on both, were selected for further study.

3.4. Paper 2: Tailoring interventions to determinants of practice

Following identification and prioritisation of determinants of practice for the six recommendations, a logical next step was to discuss and plan interventions that addressed these determinants.

We selected 22 of the 99 prioritised determinants of practice in accordance with the internal protocol for this part of the TICD project [52]. We used the tools provided by Flottorp and colleagues (TICD Worksheet 4: Development of an implementation strategy). We independently assessed each of the 99 determinants by evaluating its likely impact (3 = major impact, 2 = moderate impact, 1 = minor impact) and the effect of the likely impact on adherence using a 7 point scale (-3=major reduction in adherence, 0=no effect in adherence and +3=major increase in adherence). This process yielded a product of the likely impact of the determinant and the likely effect on adherence (range -9 to +9). We then discussed potential implementation strategies, the likely impact of the implementation strategy, the feasibility of the implementation strategy and whether the strategy should be targeted (only implemented for selected general practitioners, practices or communities where the determinant could be identified) or adjusted to local circumstances. In addition, we assessed each determinant in light of what we could accomplish within the resources and timeframe of this project. We also assessed what might be realistic based on our knowledge of the Norwegian primary healthcare system. Thus, the prioritised determinants were not a result of the scoring process alone. We resolved disagreement by discussion.

We developed a draft of a plan with 55 interventions that addressed all the 22 prioritised determinants and the six recommendations. We grouped the 55 interventions in the plan in six different categories (Table 6).

Table 6. An overview of interventions in six domains

Domain
1. Support for a collaborative care plan for elderly patients with moderate or severe depression
a. Development of the plan (offer templates and reminders that were essential for the plan, and that could be tailored to each municipality)
b. Content of the plan (suggested content, including recommendations, that

	describes the management of depression in the elderly that the municipality could include in the plan)
2.	Resources for general practitioners and other health care personnel (leaflets, templates, manuals)
3.	Resources for patients and their relatives (leaflets, manuals)
4.	Outreach visits* for general practitioners (presentation of recommendations, the evidence for the recommendations, determinants of practice for the recommendation [9] and any local circumstances that may impede or facilitate adherence that would imply an adjustment of the strategy to local determinants)
5.	Educational courses for general practitioners, other health care professionals, patients and their relatives, including CME courses for general practitioners and courses approved for nurses and other healthcare professionals
6.	Online services (a web-site with all the resources, including e-learning courses)
	*Outreach visits (or educational outreach visits, academic detailing) are defined as personal visits by a trained person to health workers in their own settings, to provide information with the aim of changing practice **[170]**

We presented the selected 22 determinants to the groups. We did not present our draft plan to the participants, to avoid influencing their thinking.

3.4.1. Setting and sample

We conducted six group interviews, one for each of the following stakeholder groups: general practitioners, primary health care nurses, implementation researchers, quality improvement officers, professional and voluntary organisations, and relatives of elderly patients with a present or past history of depression.

3.4.2. Group interviews

The group interviews followed a standardised procedure according to the common TICD protocol. The interviews lasted 120 minutes and consisted of a brainstorming session followed by a structured interview phase. EA facilitated the groups. SF or IG were co-leaders, recorded all items, made field notes and asked questions as prompts when needed. First, EA introduced the project, the recommendations and information on the performance gap between clinical practice and the recommendations. Then each participant received a sheet with the six recommendations and the prioritised determinants. The participants brainstormed individually for 10 minutes and wrote down ideas for interventions to address each determinant for each recommendation. The group members then presented their suggested interventions to the group. EA recorded the suggestions for each determinant on a whiteboard. Following the principles of brainstorming we tried to avoid criticism, while we encouraged combining and extending previously suggested items [171]. There was no limit to the number or type of the items. After a short break, EA briefly presented current knowledge regarding effectiveness of strategies to implement depression guidelines. We then conducted the structured part of the focus group. EA instructed the participants to discuss the interventions that they had suggested through the brainstorming session, to add others, and to prioritise the suggested interventions.

We based the prioritisation process on the following considerations:
1. Perceived importance of the targeted determinant
2. Perceived impact of the implementation intervention
3. Research evidence underlying the effect of the intervention
4. Feasibility and cost of the intervention
5. Other considerations

3.4.3. Analysis

We applied the five-step framework described by Glenton and colleagues [169] for our analysis in both paper 1 and paper 2:

1. Familiarisation: We audio taped all group sessions, photographed the results from the whiteboard, and made short notes from the discussions. We used the whiteboard results as the primary source of information for the analysis. We used the audio-recordings and the notes to include additional material that we had not recorded on the board. EA put all quotes containing suggested interventions in tables, one column for each group and one table for each recommendation. SF and EA reviewed these tables.

2. Identifying a thematic framework: We used the drafted plan for an intervention package as a comparator.

3. Indexing: SF and EA independently analysed these data, assessing whether the interventions that we identified during each session were similar or different from each other or the intervention plan drafted by the research team. We categorised the interventions using the format of the drafted plan.

4. Charting: We discussed our assessments and revised the final list of interventions for each determinant based on a consensus. EA linked the suggested interventions to the drafted plan, either as extensions to interventions already described or as novel suggestions.

5: Mapping and interpretation: We all reviewed the revised intervention plan and grouped the interventions across recommendations and the TICD checklist items in order to identify any topics of related suggestions in the data-set. We used a standardised procedure to rank the interventions according to the following criteria:

1. Is it feasible? (Score 1=Yes, 2=Maybe, 3=No)
2. Will it help? (Score 1=Yes, 2=Maybe, 3=No)

3.5. Paper 3: Protocol

We developed a protocol for the planned intervention in accordance with the common plan for the TICD project.

3.5.1. Trial design

We described the conduction of a pragmatic cluster randomised trial comparing implementation of the six recommendations using tailored interventions with no intervention.

We randomised 80 municipalities into one of two groups: an intervention group, to which we delivered tailored interventions to implement the six recommendations, and a control group, to which we did not deliver any intervention. We randomised municipalities rather than patients, individual clinicians or practices because we wanted to deliver the intervention for the first three recommendations at the municipal level, and we wanted to minimise the risk of contamination across practices for the other three recommendations.

3.5.2. Participants and settings

We included 80 municipalities. We selected municipalities from these counties: Aust-Agder, Vest-Agder, Akershus, Oslo, Hedmark, Oppland and Troms (see Appendix C for details regarding each municipality).

At the healthcare professional level, we included general practitioners in the data collection. Although the resources provided applied to and were aimed at all health care professionals in the municipalities, we targeted our interventions mainly at general practitioners because their practice is a core service for most elderly patients, and we measured our primary outcome at the general practice level.

At the patient level, we included home dwelling elderly patients, 65 years or older, with a diagnosis of mild, moderate, severe or recurrent depression and who had consulted their practitioner within the last six months before the intervention.

3.5.3. Eligibility criteria

All practising GPs in the included municipalities were eligible. Eligible patients were identified by extracting information from the general practitioners' electronic medical records, using an algorithm based on ICPC 2 diagnostic codes, ICPC-2 diagnostic text, free text, prescription of antidepressants and billing codes. We used several criteria in order to identify depressed elderly patients, even if they did not have a recorded diagnosis of depression, because many practitioners will use other diagnostic codes. We assigned each patient with a number and, if the list contained more than six patients with a score of six, we selected patients randomly. A definite diagnosis and assessment of the severity of the patient's depression were based on the International Statistical Classification of Disease and Related Health Problems (ICD-10) [110] in order to distinguish each case with regard to depression severity (mild, moderate or severe) and depression type (single episode, recurrent depression or dysthymia).

Patients were excluded if they had a diagnosis of dementia, bipolar disorder, resided in nursing homes, or were assessed by their practitioner to have low life expectancy.

3.5.4. The logic model

We developed a logic model that explained the connection between the recommendation, the determinant, the planned intervention and the desired outcome (practice, patient outcome), see figure 3 [172].

Figure 3 The logic model, general structure
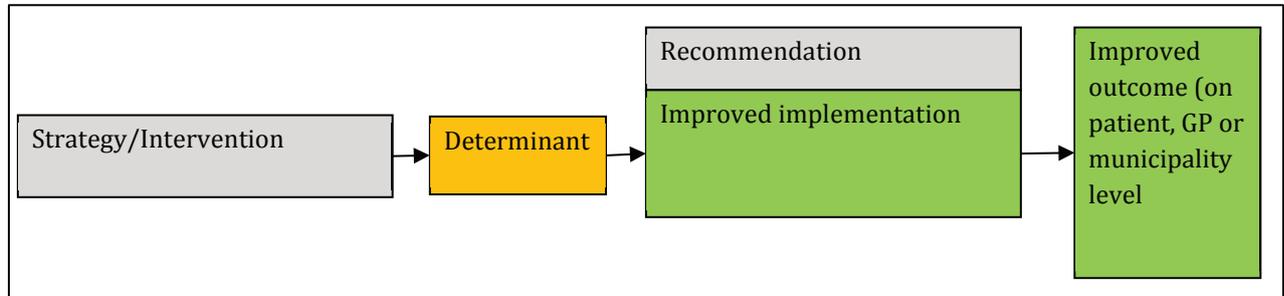
The tailored implementation interventions consisted of a package of strategies selected to address key determinants that we identified, which we assumed to affect the potential to improve the care of elderly patients with depression in primary care. A total of 52 strategies, addressing one or several determinants were to be implemented.

3.5.5. Outcome/measures

3.5.5.1. Primary outcome

The primary outcome was the proportion of recommendations that were implemented by the general practitioners. We developed a questionnaire to the general practitioner, and provided questions according to the depression severity and type. These questions were developed to assess adherence to the prioritised recommendations.

Mild depression (seven questions)

1.   Did the general practitioner offer the patient a self-help programme (web-based, book or course)?
2.   Was the patient offered antidepressants? If yes, did the patient previously respond to antidepressants when moderately or severely depressed?

For questions 3-7: Did the general practitioner discuss each of the following topics with the patient, and if the patient experienced the problem, was s/he offered advice about how to address the problem?

3.   Lack of social contact
4.   Sleep problems
5.   Lack of physical exercise
6.   Anxiety
7.   Difficulties problem solving

Moderate depression (seven questions)

1.   Did the general practitioner offer the patient a self-help programme (web-based, book or course)?
2.   Was the patient referred to a care manager?

For questions 3-7: Did the general practitioner discuss each of the following topics with the patient, and if the patient experienced the problem, was s/he offered advice about how to address the problem?*

3.   Lack of social contact
4.   Sleep problems
5.   Lack of physical exercise
6.   Anxiety
7.   Difficulties problem solving

Severe depression (two questions)

1.   Was the patient referred to a care manager?
2.   Were antidepressants prescribed AND was the patient offered psychotherapy?

3.5.5.2.   Secondary outcomes

We planned to measure the following patient outcomes from up to six patients for each general practitioner. Most of these outcomes were to be assessed by the patients themselves in response to a questionnaire.

1. Improvement in depression as assessed by general practitioner: Global improvement assessed by GP using the Clinical Global Impression Scale – Improvement (CGI-i) [173].
2. Improvement in depression as assessed by the patient or a family member:
   - Patient Global Impression – Improvement (PGI) [174, 175]. CGI-i and PGI are identical measures, using a 7-point Likert scale, where 1=very much improved, and 7 is very much deteriorated.
   - The presence of current symptoms of depression and/or anxiety using Hospital Anxiety and Depression Scale (HADS) [176]. HADS is a 14 item questionnaire, of which seven items measure depressive symptoms and seven items measure anxiety.
3. Loneliness – using a single item question regarding loneliness [177, 178].

- Do you sometimes experience loneliness? (0 = often, 1 = sometimes, 2 = seldom 3 = never)
4. Social contact
   - Did you lack social contact when you first discussed being depressed with your general practitioner? (yes/no)
   - If yes, did you subsequently establish social contact with the help of a voluntary organisation or by other means (0 = no, 1 = once only, 2 = more than once)
5. Physical activity
   - Were you physically inactive when you first discussed being depressed with your general practitioner? (yes/no)
   - If yes, have you subsequently become more physically active? (yes/no)
6. Sleep problems
   - Did you have a problem sleeping when you first discussed being depressed with your general practitioner? (yes/no)
   - If yes, has the sleeping problems improved?
7. Anxiety
   - Did you have a problem with anxiety when you first discussed being depressed with your general practitioner? (yes/no)
   - If yes, has your ability to cope with your anxiety improved?
8. Problem solving
   - Did you have difficulties with problem solving when you first discussed being depressed with your general practitioner?
   - If yes, has your ability to solve problems improved?
9. Use of a self-help programme or reading self-help literature
   - Have you used a self-help programme or read self-help literature? (yes/no)
10. Adherence with antidepressants
    - Self-Reported Measure of Medication Adherence [179, 180].
       - Do you ever forget to take your medication?
       - Are you careless at times about taking your medicine?
       - When you feel better, do you sometimes stop taking your medicine?
       - Sometimes when you feel worse, do you stop taking your medicine?
    - Each "yes" scores 1, a score of 0 suggests no problem with medicine taking and hence good compliance, whereas the maximum of 4 indicates major difficulties and suggests poor compliance.

We planned to assess whether the following items were present at the municipal level:

1. A collaborative care plan including a plan for elderly with depression (document).
2. An identifiable care manager.
3. Agreed referral processes.
4. Agreed communication processes within primary health care services.

5. Agreed communication processes between primary health care and specialist health care services.
6. A list of voluntary organisations.
7. Awareness of the collaborative care plan (proportion of general practitioners who are aware of the plan).
8. Knowledge about the collaborative care plan (proportion of general practitioners who can answer a factual question about the content of the plan).

We planned to collect data for the first six items above by questionnaires sent to municipality representatives and to collect data for the last two items during outreach visits at the end of the study.

3.5.6. Sample size

We planned to include 80 municipalities. We estimated that there was an average of 3.68 practices per municipality and 2.97 general practitioners per practice (10.93 general practitioners per municipality), based on data from the Norwegian Statistics and The Norwegian Medical Association. We conducted power calculations related to the primary outcome (adherence to recommendations defined as the proportion of recommendations that are implemented by the general practitioners) in samples with 60, 70 or 80 municipalities. We assumed an alpha (risk of type I error) of 0.05, the ability to detect a minimum difference of 0.05 between the control group and the intervention group regarding general practitioners' adherence to the recommendations (the primary outcome), a standard deviation of 0.17, an ICC of 0.02, and a 40, 50 and 60% of general practitioners consenting to data collection. Based on a previous study in which we randomised municipalities, we estimated that the intra-cluster correlation (ICC) would be less than 0.03 [181]. Based on the assumption that most general practitioners currently adhere on average to 4 or less of the 7 or 8 recommendations per patient, and a pilot survey among 11 general practitioners, we estimated that the standard deviation most likely was less than 0.2.

Based on these assumptions, our calculations indicated that the power to detect a minimum difference in adherence to the recommendations among general practitioners of 0.05 (scale 0-1) in a sample of 80 municipalities is 0.80 provided the standard deviation was 0.17, the ICC 0.02 and 50% of the general practitioners consented to data collection. With 80 municipalities, 437 general practitioners should be included in the study and would provide data for a maximum of 2622 patients.

3.5.7. Recruitment

All 80 selected municipalities were to be included in the study. We wanted to seek consent from all general practitioners in the 80 municipalities, prior to data collection, after the intervention was delivered. Participation in the intervention was optional; e.g. general practitioners could choose to participate in an outreach visit or not. After the intervention, general practitioners in both the intervention and control groups were to be invited to participate in the study as part of a free continuing medical education

module-based course on "Depression in the elderly", but for general practitioners in the control group this activity would start with data collection after the intervention. For this activity, they would get credits for obtaining or renewing their speciality in general practice. This course included data collection as part of an individual audit and feedback session. We wanted to offer general practitioners who did not want to participate in the course the option of audit and feedback with data collection alone. Patients should receive information about the study and a questionnaire and consent to participate by replying to the questionnaire.

3.5.8. Randomisation

A statistical consultant randomised the municipalities. Computer generated random numbers were assigned to all 80 municipalities at one time, without modifications in the group to which a municipality was randomly allocated. The municipalities were divided into four strata based on information retrieved from Statistics Norway:

1. Municipalities with city status or large population (>25000 inhabitants) vs.
2. Municipalities with smaller populations (<25000 inhabitants), and
3. Municipalities with a high proportion (>5%) vs.
4. A low proportion (<5%) of inhabitants 80 years or older.

We set the cut-off for small and large municipalities based on data from Statistics Norway. From a representative selection of 80 municipalities from Southern, Eastern and Northern Norway, we identified 19 municipalities with city status and/or population larger than 25000, 61 municipalities with a population less than 25000, 46 municipalities with more than 5% older than 80 years, and 34 municipalities with less than 5% over 80 years.

3.5.9. Blinding

Blinding of the participants and the researchers regarding the intervention was not possible. We analysed and interpreted the results without knowledge about the allocation. The interventions were to be implemented before we contacted the general practitioners and asked them to collect data for the study.

3.5.10.   Data Collection

At the start of the study, we planned to collect the following baseline data for each municipality:

- Number of inhabitants, number of elderly patients (65+), the proportion of inhabitants older than 80 years and number of general practitioners (from Statistics Norway and the municipalities).
- Whether the municipality had a collaborative care plan for elderly patients with depression, for adult patients with depression, or for adults with mental health problems including plans for elderly with depression (collected by questionnaire with telephone follow-up if needed). If so, we would obtain a copy for further analysis.

- Whether the municipality was part of the "Centre for Development of Institutional and Home Care Services" network [182].
- Did the primary care based psychiatric nurse team(s) provide regular services to the elderly population (65+)?

We planned to collect outcome data beginning three months after the delivery of the intervention. In both groups we would collect data for all eligible patients using general practitioners' medical records, structured interviews with general practitioners, brief questionnaires mailed to patients, and questionnaires mailed to each municipality (with telephone follow-up, if needed). We anticipated that treatment strategies provided to patients with depression might take up to three months to prove beneficial.

Prior to contact with general practitioners, we sent them a computer program that would extract and identify eligible patients from their electronic medical records. We planned to contact each general practitioners practice that has consented to participate by telephone calls. The general practitioners identified eligible patients in their electronic medical records using an algorithm and collected the following information using structured telephone interviews:

- Depression severity according to ICD10 for six patients identified with depression.
- Questions regarding general practitioner's adherence to recommendations (primary outcome measure)
- The general practitioner's assessment of the patient's improvement, as measured with Clinical Global Impression – Improvement (CGI-I) (secondary outcome measure)
- The general practitioner's awareness and knowledge of a collaborative care plan in the municipality

If the general practitioner faced any technical problems using the electronic device, we provided support to solve the problem and if needed we visited him/her to collect data.

Based on previous studies [183, 184] we anticipated that approximately 50% of GPs would consent to data collection.

All GPs that consented to participate were to be asked to mail a questionnaire to each of the six patients that was identified. Patients were asked to complete and return the questionnaire by mail. If a patient consented to participate in the study, but did not wish to complete the questionnaire, we offered the patient to appoint a family member to answer on behalf of the patient if possible. Alternatively, the patient could consent to being contacted and interviewed by telephone.

Each patient, general practitioners and municipality included in the study received a unique study ID-number that was available to the research group. A list at each general practitioner's practice coupled the patient's study ID-number and the patient's national

ID-number. We used patient ID-numbers that were generated by the general practitioners' electronic medical records systems. It was possible for the general practitioners to identify patients by these numbers, but the investigators did not have access to information identifying the patients, unless they first returned the questionnaire or a mailed consent form for a telephone interview. All communication (e.g. letters) with patients were otherwise through the patients' general practitioner.

We collected the following descriptive data:

General practitioner: Age, gender, years of clinical experience for GPs, whether the general practitioner was a specialist in primary care medicine, competency regarding Cognitive Behavioural Therapy (collected during the structured interviews) and the number of elderly patients (65+) on the patient list.

3.5.11.   Statistical methods

The primary outcome of interest for our analysis was the mean adherence rate per GP (based on six patients). We assessed the number of recommendations that were adhered to with regard to the severity of depression, and we calculated an over-all mean for adherence across disease severity for each general practitioner. The analysis was performed as an intention to treat analysis; we counted all general practitioners in the group to which they were assigned, regardless of whether they received the intervention or not.

All analyses were performed in SPSS v21 with random effects for municipality and practice to account for the clustered nature of the data. Continuous data were analysed assuming that the data followed a normal distribution (linear regression) and dichotomous data were analysed using the binomial distribution (logistic regression).

In the initial analyses only the allocation to intervention or control were included as an independent variable (Intervention = YES/NO) in the analysis.

The following factors/variables were assumed to be potential effect modifiers: If the municipality already had a collaborative plan (might improve adherence). If the access to cognitive behavioural therapy was poor (might reduce adherence). If municipalities were part of the "Centre for Development of Institutional and Home Care Services" network (might improve adherence). If the general practitioner had many elderly patients on the list (might improve adherence).

Each of the pre-specified effect-modifiers would then, one by one, separately, be included as independent variables (alongside allocation to intervention or control) in the model. All the effect-modifiers yielding a p-value less than 0.3 in the previous step were included as independent variables in a final multivariate model.

3.5.12.   Ethical considerations

The intervention was a package of strategies targeted at municipal officials and healthcare professionals with the aim of improving the delivery of recommended care to

elderly patients with depression, and ultimately patient outcomes. Municipalities and GPs in the intervention group were free to choose whether to use any of the intervention material that we sent to them, and general practitioners were free to choose whether to participate in outreach visits or courses. Consequently, no consent was required prior to the intervention. We sought informed consent from general practitioners prior to data collection, which should take place after the intervention.

General practitioners were given identification numbers and all data collected from them were stored, analysed and reported anonymously. The investigators would not collect information that enabled them to identify individual patients unless a patient first gave written informed consent to a telephone interview or returned the questionnaire. All patient information was stored, analysed and reported anonymously. The participants might withdraw their consent at any time after the data collection. This project was approved by the Regional Ethical Committee of the South-Eastern region of Norway (file n° 2013/572b)

3.6. Paper 4: Developing and conducting a multi-faceted intervention plan

The methods used in the planning and conducting of the cluster-randomised trial adhered for most parts with the protocol (paper 3), although with a few exceptions:

Outcome measures

Although not described in methods in the protocol, the outcome measures for severe depression applied to recurrent depression and dysthymia as well, and these were included in the analysis.

For data collected at the municipality level, we did not collect a list of voluntary organisations, nor did we obtain systematically copies of municipalities' psychiatry plans. On the level of general practitioners, we asked if they knew about a plan for collaborative care in their municipality, but we did not check their factual knowledge about the plan.

Data collection

Feedback from general practitioners during our outreach visits informed us that the planned two hours interview session was too time consuming. We reduced the number of patients to four, and instead performed diagnostic interviews for two additional patients if possible, enabling us to send questionnaires to up to six patients, although we obtained detailed management data for a maximum of four.

We did not collect the exact number of elderly patients on the general practitioner's list. Rather, we asked them to state whether they had many elderly patients on their list as compared with colleagues.

Due to the low response rate, we created a questionnaire that we sent to all general practitioners that had not responded to our invitation to participate in the interview. In this questionnaire we asked the general practitioners to indicate symptoms of depression in accordance to the ICD 10 diagnostic criteria for one elderly patient from their practice, and then to answer questions regarding their management of this patient.

4. Results

4.1. Paper 1. Identifying determinants of practice

Twenty-six healthcare professionals and four patients participated in group or individual interviews. Of 740 healthcare professionals, 131 (17%) responded to the survey after two reminders and 129 were included in the analysis.

The respondents in the interviews and survey suggested a total of 352 determinants, of which 247 targeted specific recommendations. Participants identified determinants in all seven domains of the checklist, but ¾ of the total were in three of the seven domains in the checklist: individual healthcare professional factors, patient factors, and incentives and resources. Ninety-four determinants were specific; that is, we could not identify any other related suggestions. The remaining 256 were related to other suggested determinants.

Of 247 suggestions that were specific for one of the six recommendations, 48 determinants were for the recommendation for improving social contact (predominantly patient factors and individual healthcare professional factors) , 42 for collaborative care plan (predominantly individual healthcare professional factors), 38 for a depression care manager (predominantly individual healthcare professional factors, incentives and resources, and patient factors), 45 for counselling (patient factors, incentives and resources, and healthcare professional factors), 39 for mild depression (individual healthcare professional and patient factors), and, finally, 35 for severe depression (predominantly patient and individual healthcare professional factors).

General determinants (not for specific recommendations)

Sixty-four suggested determinants of practice were not for a specific recommendation. These were generated by the probes used in the structured group discussions and individual interviews. One theme that recurred was how guidelines are disseminated. It is difficult for healthcare professionals to use guidelines disseminated as paper versions only. Participants preferred guidelines published in the *Norwegian Electronic Medical Handbook* or in other electronic systems, such as municipalities' websites and nurses' medical record systems. Participants suggested that the use of media campaigns to inform patients and their relatives would be helpful. They considered the source of the guideline to be important.

They suggested that disease-specific guidelines usually do not reflect the complexity of patients in clinical practice. They identified the need for learning new skills and a lack of continuing medical education credits for the necessary training of general practitioners as other barriers.

Ranking the determinants

We rated each of the 352 suggested determinants for plausibility (the importance of the determinant) and feasibility (the extent to which the determinant could be addressed). We prioritised all determinants with a score of four or higher on both scales (plausibility = high or very high, or feasibility = easily or very easily addressed). This yielded 99 prioritised determinants. Following the same procedure several times, we were able to reduce the number of prioritised determinants to the required number that were described in the common protocol for the TICD project, for which we attempted to address in designing an implementation strategy for the six recommendations.

Survey findings

The results of the survey generally supported the findings of the interviews. However, due to the poor response rate, it was not possible to know how representative the responses were.

4.2. Paper 2. Developing implementation interventions

Twenty-nine people participated in the various group sessions (five general practitioners, four implementation researches, six primary care nurses, six representatives from professional and voluntary organisations, five quality improvement officers and three relatives of elderly patients).

The six groups yielded approximately 450 suggested interventions, of which many were related to each other and to suggested interventions in the plan drafted by the research team. We found that approximately 70 suggestions contained statements or attitudes rather than interventions (such as "Lack of available services is more important than GPs' time constraints."). This left 379 suggestions of interventions for further analysis. In the first four group interviews, we presented the recommendations in the following order: social contact, collaborative care plan, depression care manager, counselling, mild depression and severe depression. There were 127 suggestions for interventions to improve adherence to the recommendation on social contact, 68 for collaborative care plan, 54 for depression care manager, 40 for counselling, 47 for mild depression, and 43 for severe depression. The groups with representatives of professional and voluntary organisations and quality improvement officers generated most suggestions, (106 and 96 respectively). The group with nurses generated 67 suggestions and the implementation researchers 36. The groups with general practitioners and relatives focused mainly on three selected recommendations. They generated 41 and 33 suggestions respectively.

We reduced the number of interventions from 379 to 65 based on our assessments of their likely effectiveness and feasibility. Of these, 28 were added or modified after the group sessions (18 extensions and 10 new interventions). We determined that 18 of the interventions should be adapted to municipalities or practices.

4.3. Paper 3: Protocol

There are no results to be presented from the protocol

4.4. Paper 4: Results from the cluster-randomised study

Of the 900 general practitioners, 141 consented to participate in the data collection (90 general practitioners consented to participate in telephone interview and 51 responded to a questionnaire). Of the general practitioners who consented to participate in telephone interviews, 13 were lost to follow up (not responding on the appointed time for interview, withdrawing consent due to time constraints or disagreement with our objectives), leaving 77 who completed the interview. They answered for the treatment of 268 patients (mean 2.2 patients per general practitioner) and diagnostic assessments for 339 patients (mean 2.7 patients per general practitioner). Of the 51 general practitioners who responded to the questionnaire, four were excluded (because the patients did not have depression according to the inclusion criteria), leaving 47 general practitioners who completed the questionnaire for one patient each (these patients did not receive a questionnaire). Thus, we collected data on the general practitioners' management for 319 patients. We excluded 14 patients who did not meet our inclusion criteria, leaving treatment data from 305 patients for the analysis. In total, 124 of 900 general practitioners (response rate 14%) participated in the data collection, 51 in the intervention group and 73 in the control group. Of 339 eligible patients, 134 responded to the questionnaire (response rate 40%), 68 in the control and 66 in the intervention group. A significantly higher proportion of the participating general practitioners in the intervention group worked in rural practices. They also had an older patient group and fewer female elderly patients.

Representatives from 51 (64%) of the 80 municipalities responded to the questionnaire. Forty-three municipalities (84%) had developed a plan for psychiatry, but only four had included a care plan for elderly patients with depression. Five of the plans described collaboration between healthcare professionals within the municipality and between primary and specialist care for elderly patients with depression. Six municipalities provided specific referral forms for elderly patients with depression. However, most of the respondents commented that although the municipality did not possess a specific referral form for elderly patients with depression, they provided referral forms that applied to the whole population. Only three plans described collaboration between the healthcare system and voluntary organisations. Very few general practitioners were aware of a collaborative care plan in the municipality (three general practitioners in the intervention and six general practitioners in the control group).

Among the 385 patients, 221 patients (58%) suffered from recurrent depression according to ICD-10 criteria. Of the remaining 164 patients with a first depressive episode, almost 40% suffered from a severe episode.

Primary outcomes

The mean adherence to the recommendations was 58% (SD 20%) in the intervention group and 53% (SD 18%) in the control group. The estimated difference in the mean adherence from the univariate mixed model was 1.6% (CI -6% to +9%, p=0.67). Multivariate linear regression analysis did not indicate that any of the potential effect modifiers could explain variations in effects.

Secondary outcomes

There was little difference between the intervention and control groups for any of the secondary outcomes. The confidence intervals for all of these outcomes were wide.

Post-hoc analyses

We investigated the general practitioners' adherence to the recommendations separately for mild, moderate, severe, and recurrent depression. We also investigated adherence to the individual recommendations. The difference in adherence varied from 15% reduced adherence (for mild depression) to 7% improved adherence (for moderate depression) in the intervention group compared with the control group. The confidence intervals for all of these estimates were wide. Adherence for the recommendation regarding improving social contact was high in both groups (75% in the intervention group and 92% in the control group), and this difference was statistically significant in favour of the control group in the univariate analysis but not in the multivariate analysis.

5. Discussion

5.1. Summary

In the first part of our study, we identified approximately 350 determinants of practice for six recommendations for managing depressed elderly patients in primary care using group and individual interviews. We categorised these according to a generic checklist developed by the researchers in the TICD project [52]. Approximately 3/4 of the total was from three of the seven domains in the checklist: individual healthcare professional factors, patient factors, and incentives and resources. In addition we tested several methods to identify determinants of practice [167]. Based on our experiences we decided to use a combination of structured and brainstorming-like group interviews in the second part of our study.

In the second part, based on our prioritised determinants of practice, the research group drafted an intervention plan. We then conducted group interviews with several stakeholders to inform our decisions about how to tailor implementation interventions

to improve adherence to clinical practice guidelines for elderly patients with depression. The draft plan covered many of the interventions that the groups suggested. However, the groups added many new ideas, and they modified approximately half of the interventions suggested in the draft plan. We were finally able to develop a multi-faceted implementation plan that included 52 interventions, small and large.

Finally, we conducted a cluster-randomised trial and implemented the interventions in 40 Norwegian municipalities, with 40 municipalities serving as a control group. We were not able to recruit the required number of general practitioners for the data collection, and our study did not have sufficient statistical power to detect potential effects of the interventions. The mean adherence to the recommendations among general practitioners was 58% in the intervention group and 53% in the control group. The estimated difference from univariate mixed model was 1.6% (CI – 6 to + 9), indicating that the effect size on the primary outcome was moderate, at best.

5.2. Strengths and limitations

The strengths of this study include the use of multiple methods and participants to identify determinants, a systematic approach to developing and prioritising interventions to be implemented, and the use of a cluster-randomised trial to evaluate our intervention. Across the five TICD partners, we used a common protocol for the two first studies (paper 1 and 2) and chose to use both qualitative and quantitative methods for our research. In the first part of our study we tested several methods to identify determinants of practice [167]. We then evaluated both productivity and feasibility of each method, and based on consensus, we selected the method to be used when planning the interventions. Thus, all interviews (individual or group) contained both an open brainstorming part and a more structured part. This helped us to ensure that we identified a comprehensive list of determinants, as well as contributing to the comparison of different methods and to use the same methodology when planning the interventions [167].

A weakness of our first study was that we did not collect information on the participants' perceptions of the relative importance of the determinants that they identified. Our findings suggested that there is likely to be wide variation across communities, practices, healthcare professionals and patients. Our prioritisation of determinants was based on our assessment of the importance of each determinant and the extent to which each determinant could be addressed. The findings of the interviews only informed these assessments to a limited extent.

The recommendations that we prioritised addressed several levels of the healthcare system, from the patients and their relatives to the healthcare professionals and the healthcare administration in the municipalities. The use of the TICD checklist to prioritise determinants and interventions made it possible to analyse the results in a systematic way. Nonetheless, the results from this part of the analysis were assessments

based on our considerations and judgments. An alternative strategy would be for representatives from the stakeholder groups to do this assessment. The wide range and the large number of interventions that the groups discussed within a limited time may have compromised more detailed and structured discussions, and may have resulted in superficial assessments for some determinants or interventions.

For the second part of our study, we included several stakeholder groups, to achieve a purposeful sample of healthcare professionals, relatives of elderly patients with depression, implementation researchers and others that might be able to suggest effective interventions to address the identified determinants of practice. This approach to tailoring an intervention to prioritised determinants was standardised across the five countries and disease groups in the TICD project [185, 186]. We are not aware of any other project that has addressed tailoring of implementation interventions in this comprehensive manner, using a framework or checklist systematically to identify and prioritise determinants of practice and to identify interventions that could address them. However, due to the complexity of our recommendations, the large number of prioritised determinants and the limited time available for the interviews, it was not feasible for us to address each of the suggested interventions in the systematic way stated in the common TICD protocol.

The number of suggested interventions for each determinant and recommendation varied. Recommendations presented early in the session appeared to yield the most suggestions (recommendations regarding social contact, collaborative care, and the depression care manager). These recommendations targeted mainly the community and municipalities, while the last recommendations targeted clinicians (counselling, antidepressants in mild depression, and combining psychotherapy and antidepressants in severe depression, recurrent depression and dysthymia). It is possible that the nature of the first recommendations generated more suggestions. It is also possible that there were fewer suggestions for the recommendations presented later in the interview because of exhaustion in the groups. One solution to this could have been to present the recommendations in a different order for each of the groups.

The large number of suggested interventions addressed only six recommendations, whereas clinical practice guidelines frequently contain many more recommendations. There is a risk that guideline developers will experience information overload, if they try to use this approach for a full guideline.

We excluded suggested interventions that could not be evaluated in our planned cluster randomised controlled trial. Thus, we omitted potentially useful dissemination channels such as media and web-based resources that are popular among healthcare professionals (The Norwegian electronic health library, the Norwegian Directorate of Health's web site and the Norwegian Electronic Medical Handbook). We received suggestions to use all of these during the design phase of our project. Not putting the resources on a website that general practitioners frequently use may have limited the

extent to which general practitioners used them. Another possible explanation for the modest use of the web-resources is that new cases of elderly patients with depression are rare in clinical practice. Thus, general practitioners' recall of this website or the perceived need to become familiar with it might have been low.

The major limitation of the cluster-randomised trial in our study is that we were not able to recruit a sufficient number of general practitioners to participate in the data collection within the time and resource limits that applied to our project. Thus, the study is underpowered and the results are inconclusive. Additionally, the low response rate resulted in samples that were not representative and might have biased the results, since it is possible that there were differences in general practitioners who participated in the data collection between the intervention and control groups. An alternative approach, seeking informed consent from the general practitioners prior to the intervention, might have resulted in a larger proportion of general practitioners participating in the data collection, but would have made the study less pragmatic and limited the extent to which the results could confidently be applied to general practitioners who elected not to participate in the study. Whether we would have reached the necessary power is also questionable.

Furthermore, we used two different methods, interviews and questionnaires, to obtain data from general practitioners regarding diagnosis and management of elderly patients with depression from their patient list. It is not possible to determine whether the two methods gave comparable results, due to the small sample size.

We did not collect baseline data due to the short period of the TICD project that we had planned for the intervention; collecting baseline data would have delayed the intervention substantially. Furthermore, we did not have the resources to collect such data.

5.3. Comparison with existing literature

Determinants of practice related to depression guidelines are numerous and apply to all levels of the healthcare system [187, 188].

Other studies have explored determinants to detecting depression in the elderly. McCabe and colleagues [189] primarily focused on staff who worked with elderly patients in residential care. They found that staff resources, a lack of continuity of care, multiple co-morbidities, reluctance of older people to discuss depression, negative attitudes among carers, as well as a lack of skills all contributed to a failure to detect and treat depression.

Gask and colleagues[190] identified three major barriers to the effectiveness of a complex educational intervention designed to provide general practitioners with training in the assessment and management of depression in adults. The general

practitioners did not believe that they could have an impact on the outcome of depression, the training was not appropriate (patients not fitting in), and the organisational context in which doctors had to implement what they had learned (for the most part time constraints).

Nutting and colleagues [191] highlighted the importance of the relationship between the care manager and the clinician, which we also identified as a determinant in our study. We identified more determinants than previous studies. This might be due to the use of multiple methods, multiple informants and a comprehensive checklist [52].

Relatively few studies on improving the care of patients with depression have described the development of a systematically planned intervention tailored to address identified determinants. Shirazi and colleagues [192] demonstrated that tailoring an educational intervention, based on general practitioners' readiness-to-change (high-low), improved their performances in hypothetical (role-playing) consultations as compared with controls. Verhaak and colleagues [193] found that disability (particularly disability that affects participation, self-care and social activities) had a major impact on depression in the elderly. One might argue that the interventions that we planned considered this aspect to a limited degree only. Nevertheless, we addressed social withdrawal and frailty in our planned interventions. Furthermore, their findings indicated that the effect of disability on depression was largest among the younger elderly (those between 60 and 70 years). We included patients 65 years or older in our study.

In a randomised controlled trial based on a psychological theoretical framework, Baker and colleagues [91] identified obstacles to adherence among 34 general practitioners, and tailored their intervention to each practitioner. They found that this strategy improved assessment of suicide risk and depression, assessed with Beck's Depression Inventory. They found little or no differences for anti-depressant therapy or utilisation of psychotherapeutic services. Addressing clinicians individually to identify determinants of practice is an attractive approach, but rarely realistic in large-scale efforts to implement clinical practice guidelines. We deemed this approach unfeasible in our project.

Sinnema and colleagues [194] conducted a pragmatic cluster randomised controlled trial testing the effectiveness of a tailored implementation programme to improve recognition, diagnosis and treatment of anxiety and depression in primary care in the Netherlands. The intervention package was developed on the basis of interviews with all participating general practitioners in the intervention group, identifying a list of 84 barriers [195]. Various tailored interventions were implemented in two different formats; "peer group supervision" and "personalised telephone consultation". They found that the intervention yielded a higher proportion of recognition of depression and anxiety and a higher number of consultations with the general practitioner.

Callahan and colleagues [92] found that tailoring information for the management of elderly patients with depression yielded a higher proportion of patients receiving a depression diagnosis and an antidepressant.

In a joint analysis of the studies to tailor interventions in the TICD project, Huntink and colleagues [196] found no relationship between the total number of suggested interventions and the number of unique suggestions (interventions only suggested by one group).

We have identified few studies that measure adherence to depression guidelines. A review of quantitative studies of adherence to mental health clinical practice guidelines found that general practitioners' adherence to mental health clinical practice guidelines was low [197]. Fernandez and colleagues [198] found in a large epidemiological study based on interviews with 21 425 home-dwelling persons in six European countries, that "treatment adequacy" for depression as defined by the research group was particularly low (23%) in the patient group that received management in "general medical care" (which included general practitioners and specialists other than psychiatrists and psychologists). Duhoux and colleagues [28] found that elderly patients (65+) received less guideline concordant management as compared with younger adults, regardless of which definition of concordance they selected. Smolders and colleagues [29] combined information from a patient questionnaire that measured depression and anxiety symptoms with general practitioners' performance as recorded in the electronic medical patient records. They found that only 42% of the depressed patients received evidence-based management of depression as defined by an expert panel. In our study adherence to the recommendations tended to be higher than in previous studies that have reported adherence to depression guidelines, 58% and 52% in intervention and control groups respectively. The weak recruitment of general practitioners to participate in the data collection might indicate that we were only able to collect data from general practitioners that were particularly interested in this patient group, both in the intervention and in the control group. For our primary outcome, we collected data from general practitioners who reported on their own practice. There is evidence that self-reporting on adherence to practice guidelines may be biased [199]. Both factors might explain the relatively high adherence rates in our sample.

We are not aware of any systematic reviews or trials that address the implementation of clinical practice guidelines for elderly patients with depression.

Richter-Sundberg and colleagues conducted a post-RCT qualitative study to identify barriers to the implementation of a clinical practice guideline for depression in Sweden [200]. In spite of fees for performance and consent to participate collected prior to the implementation process, the project was not able to recruit the required number of patients to reach sufficient statistical power (after 18 months only 30 patients were included). Based on the framework described by Grol and Wensing [201], the authors identified and sorted numerous barriers that hindered participation in the study. The

excessive workload associated with the research design was one major barrier. Introducing new psychological therapies that challenged established professional role identity was another [200].

5.4. Implications for practice and research

The large number of determinants that we identified indicates the need for a systematic approach to prioritise which determinants to target in an implementation strategy. Healthcare professionals might want to consider these determinants in their own practices and could address many of the identified determinants on their own. However, a collective effort is necessary to improve adherence to these recommendations and improve the care of and outcomes for depressed elderly patients. Organisations and institutions responsible for quality of care might also get useful information based on the identified determinants, and the suggested interventions. The web-site www.depresjonhoseldre.no has been available to healthcare professionals and patients and their relatives after the intervention, and is planned to be moved to a more accessible electronic platform (www.aldringoghelse.no) (Birger Lillesveen, personal communication).

The approach that we used to develop a package of tailored implementation interventions was both feasible and efficient. Those interested in tailoring interventions to implement guidelines can use the TICD checklist and the interview methods that we used in this study.

Our findings, which were inconclusive, may not have direct implications for practice. We believe that many of the resources that we developed would be helpful in daily practice, and make it easier for general practitioners and other health care professionals in the municipalities to provide evidence-based care to elderly with depression.

The challenges we encountered collecting data from general practitioners, which is the reason for our inconclusive findings, has implications for researchers. Although randomising general practitioners without their consent makes trials of implementation strategies more pragmatic, this creates problems if the data collection requires participation of the general practitioners. This might not be a problem if routinely collected data that is easily accessible can be used to measure outcomes. However, general practitioners do not routinely grade the severity of depression or the type of depression using diagnostic codes. Thus, collecting data on adherence to recommendations that apply to disease severity or subtypes of diagnoses, not automatically registered in clinical practice, requires an interview, completion of a questionnaire or conducting an observational study.

It is generally challenging to conduct both clinical and implementation research projects in primary care. A research network, with better infrastructure and incentives for general practitioners to participate, might facilitate recruitment of participants and data collection [202]. Alternatively, a fee for participating, either as part of national health authorities' support of research in primary care or as part of the research project

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funding might improve recruitment of participants for data collection [203], although the effectiveness of reimbursement may be debated [204].

Cluster randomised trials are considered a robust design for evaluating the effects of implementation strategies [205]. However, this study design prevented us from using the most common electronic dissemination resources as part of our intervention. A randomised design might not be appropriate if it places potentially important limitations on the implementation intervention as it did in this study. Interrupted time series analysis might be a better design in these circumstances [206].

We have conducted a process evaluation to investigate reasons for the observed effects of our tailored implementation strategies, including the extent to which we were able to identify and address the most important determinants of practice, as described in the logic models that we created [172]. We will report the results from the process evaluation in a separate paper.

6. Conclusions

If we assume that determinants of practice contribute to the probability that guideline recommendations are adhered to, it is reasonable to think that knowing these determinants and targeting interventions to address them is a logical strategy to improve guideline adherence.

A key message from this study for implementation researchers is that access to outcome data is essential. This trial included all general practitioners in 80 municipalities representing 20% of the Norwegian population with close to 1000 general practitioners. Randomising jurisdictions or large numbers of practices without consent, is a highly pragmatic approach to answering real world questions about how to improve the quality of care, provided access to outcome data is ensured, for example via routinely collected data. However, this approach proved to be challenging in this trial, because collecting outcome data required active participation of general practitioners.

Furthermore, identification of determinants of practice to guideline recommendations and the subsequent planning of interventions by using a purposeful sample of stakeholders must be expected to yield a vast amount of suggestions, making the prioritisation process crucial.

Randomised trial design may not be the best study design for answering a pragmatic question about how to improve practice when random allocation is not feasible. A major limitation of this trial was that we were not able to include what might have been important, effective components of our tailored implementation strategy, such as integrating our resources in widely used electronic information sources, because we could not randomly allocate these.

Future research evaluating methods for tailoring implementation strategies should directly compare tailored implementation strategies that use different methods to tailor

the interventions, as we did across the five national TICD studies. We still need more knowledge about how best to identify important determinants of practice, and how to select interventions to address them. The TICD project conducted new research comparing different methods for identifying determinants of practice and for linking interventions to those determinants. However, our trials were limited to comparisons of tailored strategies to no intervention. This research and the process evaluations linked to our trial can shed some light on why our tailored implementation strategy appeared to have, at best, modest effects.

A key message for general practitioners and policymakers is that to answer important questions about how to improve practice, general practitioners need to have time, resources and structures, such as research networks and fees for participating in prioritised research [207]. In the longer run, developing a "learning healthcare systems" as described by Olsen and colleagues [208] designed to "generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care" may provide a gold standard for future linkage between research and healthcare practice.

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Appendices

The work presented is the results from an unpublished systematic review on recommendations for the management of depression in elderly patients with depression in 13 clinical practice guidelines, conducted by:

Aakhus E, Vandvik PO, Brandt L, Oxman A, and Flottorp SA

The protocol for the systematic review is available [135]

Appendix 1. Guidelines characteristics, part 1

	Format accessed	Number of guidelines reviewed	Targeted population	Diagnostic classification system	Working group	Method for grading the evidence	Is the quality of the evidence graded?	Is the strength of the recommendations graded?	Is there a clear link between the underlying evidence and the recommendation?
CA: CCSMH 2006	PDF	1	Elderly patients in primary and specialist care	DSMIV/ ICD10	Inter-disciplinary, user representatives	Shekelle 1999	Yes	Yes	Yes
DK: HMA 2007	PDF	1	Adults in primary and specialist care	ICD10	Inter-disciplinary	Eccles 1998	Yes	Yes	Yes
INT: WFSBP 2007	Journal	1	Adults in primary care	DSMIV/ ICD10	Experts in the field	Own system	Partly	No	Partly
NO: NDH 2009	PDF, printed copy	1	Adults in primary and specialist care	ICD10	Inter-disciplinary	Eccles & Mason 2001, modified	Yes	Yes	No
NO: NEL 2011	Web-based	2*	Adults in primary care	ICD10	Experts in the field	Expert's opinion	No	No	No
NZ: NZGG 2008	PDF	1	Adults in primary and specialist care	DSMIV/ ICD10	Inter-disciplinary, user representatives	Own system	Yes	Yes	Yes
SE: NBHW 2010	Web-based,	1	Adults in primary and specialist care	ICD10	Inter-disciplinary	Own system	Yes	Yes	Yes

	excel-file								
UK: BAP 2008	Journal	1	Adults in primary and specialist care	DSMIV	psychiatrists, user representatives and staff from pharmaceutical companies	Shekelle 1999, modified	Yes	Yes	Yes
UK: NICE 2009	PDF, web-based	2*	Adults in primary and specialist care	DSMIV	Inter-disciplinary, user representatives	GRADE	No	No	Yes
USA: ICSI 2010	PDF	1	Adults in primary and specialist care	DSMIV	Health care professionals and administrators	Own system	Yes	No	Partly
USA: KP 2010	PDF	1	Adults in primary and specialist care	DSMIV	Physicians from primary and specialist care, other professionals where appropriate	Own system	Yes	Yes	Yes
USA: UpToDate 2011	Web-based	3*	Adults in primary and specialist care	DSMIV	Experts in the field	GRADE (adults), experts' opinion (elderly)	Partly	Partly	Yes
USA: VA/DoD 2008	PDF	1	Adults in primary and specialist care	DSMIV	Experts in the field	Own system (adapted from USPSTF 2001)	Yes	Yes	Partly

Guideline abbreviations see table 2

Appendix 2: Guideline characteristics, part 2

	Recommendations easily identified	No of pages	No of references	No of recommendations	No of specific recommendations for the elderly	How is elderly with depression addressed?	Other guidelines used as source for recommendations
CA: CCSMH 2006	Yes	66	213	73	73	Solely on elderly.	No
DK: HMA 2007	Yes	139	336	100	1	Section on elderly and integrated.	Yes (NICE, 2004, SBU* 2004)
INT: WFSBP 2007	Yes	38	389	23	1	Limited.	No
NO: NDH 2009	Yes	111	320	47	0	Section on elderly.	Yes (NICE 2004)
NO: NEL 2011	No	n/a	172	102** (of which 37 from NDH)	24	Chapter on elderly.	Yes (NDH)
NZ: NZGG 2008	Yes	216	580	89	14	Chapter on elderly.	No
SE: NBHW 2010	Yes	n/a	n/a	123**†	13	Chapter on elderly.	No
UK: BAP 2008	Yes	55	567	89	1	Integrated.	No
UK: NICE 2009	Yes	64+54	n/a	108+78	2 (1+1)	Integrated.	No
USA: ICSI 2010	No	99	310	65	0-1	Section on elderly and integrated.	No
USA: KP 2010	Yes	321	223	34	0	Limited.	No
USA: UpToDate 2011	Yes	n/a	371	38	16	Chapter on elderly.	No
USA: VA/DoD 2008	Yes	203	254	199	7	Integrated.	No

Guideline abbreviations: See Table 2. DSM IV: Diagnostic and Statistical Manual of Mental Disorders 4th Revision, ICD 10: International Statistical Classification of Diseases and Related Health Problems 10th Revision. *SBU: The Swedish Council of Health Technology Assessment, ** The counted number is approximate †From a comprehensive guideline for depression, bipolar disorder, anxiety and

obsessive-compulsive disorders in children, adolescents and adults, only recommendations regarding depression in adults were counted.. n/a: not applicable

Appendix 3: Recommendations for recurrent or chronic depression and for treatment resistant depression

	Recurrent or chronic depression	Treatment resistance
CA: CCSMH 2006	Monitor for re-occurrence for the first 2 years after treatment. PT in combination with AD should be available	Switch AD or add lithium or PT
DK: HMA 2007	Continue AD for 2 years to prevent relapse, consider longer treatment for patients with several previous episodes.	Dose adjustment, moderate depression: switch from SSRI to another class, consider adding lithium or T3. Severe depression: Combine SNRI or TCA with lithium
INT: WFSBP 2007	Continue AD that was effective during acute and continuation phase. Switch to AD from different class or switch to lithium or combine lithium and AD. Combine two ADs or combine lithium and carbamazepine or switch to carbamazepine	Reassess diagnosis, switch AD or combine ADs
NO: NDH 2009	PT in combination with AD if recurrence on AD. If 2 or more episodes; AD in at least 2 years.	Reassess treatment plan and diagnosis. Combine AD and PT. Combine ADs from different classes or add lithium to AD.
NO: NEL 2011	(From NDH) PT in combination with AD if recurrence on AD. If 2 or more episodes; AD in at least 2 years.	Combine AD and PT. Increase dose if no improvement. Switch AD.
NZ: NZGG 2008	None	Review treatment plan, consider increasing dose, change AD or change/add PT. Refer.
SE: NBHW 2010	Continue PT or AD to prevent relapse	Change from AD to PT or from PT to AD. Switch AD. Combine AD with lithium, mianserin, or mirtazapine
UK: BAP 2008	In higher risk patients (>5 lifetime episodes or 2 episodes in last few years, at least 2 years AD treatment	Assess risk and efficacy. Check dose and adherence. Switch between SSRIs. Switch from SSRI to venlafaxine. Combine TCA and lithium or T3, SSRI and antipsychotic or mirtazapine
UK: NICE 2009	Continue pharmacological treatment for at least 2 years if 2 or more episodes recently or other risk factors. CBT or mindfulness-based CT	Review adherence, reassess treatment plan. Switch from SSRI to SSRI or to new AD or combine AD and PT. Combine AD and lithium or anti-psychotic or another AD
USA: ICSI 2010	Lifelong treatment when ≥3 episodes, or ≥2 episodes and risk factors (rapid relapse, age >60, familial history, dysthymia	Reassess diagnosis. Switch from SSRI to SSRI. Switch from SSRI to another AD or combine Lithium or T3.
USA: KP 2010	Continue ADs for at least 15-28 months	Combine AD and PT or switch. Increase dose or switch to AD of same or different class. Combine SSRI with TCA, bupropion, buspirone,

		mirtazepine, lithium or T3
USA: UpToDate 2011	(Elderly) Continue pharmacological treatment for 2-3 years.	Combine AD and PT, switch from SSRI to SSRI, combine two ADs
USA: VA/DoD 2008	Continue AD in patients at high risk for recurrence	None

Guideline abbreviations: See Table 2. AD: Antidepressant, BT: Behavioural therapy, BT/AS: Behavioural therapy/activity scheduling, CBT: Cognitive behavioural therapy, DT: Dynamic therapy, IPT: Interpersonal therapy, NRI: Norepinephrine reuptake inhibitors, PST: Problem Solving therapy, PT: Psychotherapy, RT: Reminiscence therapy, SNRI: Serotonin/Norepinephrine reuptake inhibitors, SSRI: Selective serotonin reuptake inhibitors, TCA: Tricyclic antidepressant, T3: Liothyronine

Appendix 4. Recommendations for psychological and pharmacological treatment, self-help programmes, exercise etc

	Psychological treatment	Pharmacological treatment	Self-help programs, exercise etc
CA: CCSMH 2006	BT, CBT, PST, DPT, IPT, RT.	SSRI (not fluoxetine), SNRI, mirtazapine, bupropion	Not indicated
DK: HMA 2007	CBT, IPT or PST	SSRI. SNRI or TCA	Physical exercise in mild to moderate depression
INT: WFSBP 2007	CBT, IPT, PST	None preferred. SSRI, SNRI, mirtazapine and reboxetine are better tolerated	None
NO: NDH 2009	CBT, IPT, DT, Couple's therapy	Many ADs are effective	In mild depression, self-help programmes, encourage physical exercise
NO: NEL 2011	CBT, IPT, DT, Couple's therapy	None specified	Physical exercise is useful in mild-to-moderate depression
NZ: NZGG 2008	CBT or PST	SSRI	Active support, advise on exercise, psychosocial helping agencies
SE: NBHW 2010	Computerised CBT, CBT, IPT or DPT	TCA, SSRI, SNRI and others	Physical exercise in mild depression
UK: BAP 2008	CBT, BT/AS, IPT	SSRI together with other newer ADs	Computerised CBT, guided bibliotherapy and high intensity exercise as an adjunct to AD
UK: NICE 2009	Computerised CBT or CBT, IPT, couples therapy	SSRI	Computerised CBT, guided self-help based on CBT, structured group physical activity
USA: ICSI 2010	CBT, IPT, PST	SSRI, SNRI, NRI, bupropion	Patient self-management, physical exercise
USA: KP 2010	CBT, IPT, PST	Any class of AD, based on prior response, preferences, potential side effects and cost	Exercise, internet-based resources, bibliotherapy, befriending is an adjunct
USA: UpToDate 2011	CBT, IPT or PST	First line: SSRI. Second line: SNRI	None
USA: VA/DoD 2008	CBT, IPT or PST	SSRI, SNRI, bupropion or mirtazapine.	Physical exercise should be prescribed

Guideline abbreviations: See Table 2. BT: Behavioural therapy, BT/AS: Behavioural therapy/activity scheduling, CBT: Cognitive behavioural therapy, DPT: Dynamic psychotherapy, IPT: Interpersonal therapy, NRI: Norepinephrine reuptake inhibitors, PST: Problemsolving therapy, RT: Reminiscence therapy, SNRI: Serotonin/Norepinephrine reuptake inhibitors, SSRI: Selective serotonin reuptake inhibitors, TCA: Tricyclic antidepressant

Appendix 5. Recommendations for elderly patients with depression and patients with dementia and depression

	Treatment recommendations for elderly patients. Antidepressants (AD) and psychotherapy (PT)	Elderly with depression and dementia
CA: CCSMH 2006	First choice newer ADs. Caution TCA. PT: RT.	Psychosocial services, ADs should be offered in spite of lack of evidence
DK: HMA 2007	Caution some ADs	None
INT: WFSBP 2007	Start on lower oral dose	None
NO: NDH 2009	None	None
NO: NEL 2011	SSRI or bupropion. Caution when increasing AD, caution dosage adjustments due to age. PT: RT.	None
NZ: NZGG 2008	Caution when increasing AD, caution dosage adjustments due to age	Psychosocial services, ADs should be offered in spite of lack of evidence
SE: NBHW 2010	PT: Reminiscence therapy	AD (SSRI) should be offered in spite of lack of evidence
UK: BAP 2008	Caution when increasing AD, caution some ADs	No
UK: NICE 2009	Caution some ADs, caution dosage adjustments due to age	None
USA: ICSI 2010	Consider starting at the lowest possible dose and increase slowly: Tertiary amines should be avoided	None
USA: KP 2010	None	None
USA: UpToDate 2011	First choice SSRIs, caution dosage adjustments due to age, caution some ADs	AD (SSRI) should be offered
USA: VA/DoD 2008	Caution dosage adjustments due to age, caution some ADs. PT to patients with dysthymia or chronic depression	None

Guideline abbreviations: See Table 2. PT: Psychotherapy, RT: Reminiscence therapy, SSRI: Selective serotonin reuptake inhibitors, TCA: Tricyclic antidepressant.

Appendix 6. Collaboration and care management

	Collaboration with specialist care	Care management after the time of diagnosis	Referral to specialist care
Canada: CCSMH 2006	None specified	An inter-disciplinary model that promotes continuity of care. When starting medication patients should be seen weekly for several weeks.	Should: Psychotic depression, bipolar disorder, suicidal ideation or intent. May: with co-morbid substance abuse, severe depressive episode, with co-morbid dementia
Denmark: HMA 2007	"Shared care" or "collaborative care" is discussed.	None specified	None given
International: WFSBP 2007	"Stepped Care"	After 2-4 weeks of AD treatment response should be evaluated	Stepped Care
New Zealand: NZGG 2008	Stepped care model. If another health practitioner delivers psychotherapy (...) the primary care team should be in regular communication.	If risk of suicide or <30 years follow-up at 1 week and monitored 1-2 weekly, if not suicidal risk follow up at 1-2 weeks and monitored at least 2 weekly until clear improvement	Immediate: Serious suicidal intent, psychotic symptoms or severe and persistent self-neglect.
Norway: NDH 2009	Continuous and active	None specified	Regular referral: Insufficient response, relapse within one year, suicidal risk, self-neglect or patient's wish for referral Urgent referral: Suicidal intent, psychosis, severe depression with agitation, severe self-neglect
Norway: NEL 2011	May improve outcome,, Discuss with psychiatrist when MADRS>40 or earlier if severe single symptoms.	Initially frequent contact (every second week)	As in NDH, in addition bipolar disorder or severe depression (MADRS >35)
Sweden: NBHW 2010	"Collaborative care" model weak recommendation	None specified	None given
UK: BAP 2008	When GP feels insufficiently experienced or if two or more attempts to treat have failed	Case management. Scheduled follow-up and a strategy to enhance adherence to medication. Initially review patients every one to two weeks	Significant perceived risk of suicide, of harm to other or severe self-neglect, psychotic symptoms or history of, or likelihood of bipolar disorder
UK: NICE 2009	Stepped-care model, the least intrusive, most effective intervention is provided first	None specified	If patient are at significant risk of self-harm, have psychotic symptoms, require multi-professional care, or an

			expert opinion is needed
US: ICSI 2010	Shared care/ collaborative care in the primary care setting. When patient request for psychotherapy, severe symptoms and impairment, high suicide risk, other psychiatric condition, substance abuse, clinician's discomfort, patient's request for more specialised treatment	Collaborative care. Initially weekly follow-up, intervals may be extended if response, dependent on disease severity	Hospitalisation may be indicated in patients who have failed outpatient management, particularly if safety issues are a concern
US: KP 2010	When patient with Major depression expresses suicidal intent or plan, or for such a patient before prescribing TCAs or venlafaxine	Minimum follow-up frequency is one contact within the first month, at least one additional contact 4-8 weeks after the first contact.	Patients who endorse suicidal intent or plan.
US: UpToDate 2011	None	Patient should be contacted or seen within first 2 weeks and then within 2-4 weeks	Refer to psychiatrist if non-response after two anti-depressants have been tried
US: VA/DoD 2008	Collaborative care, refer if risk for medication discontinuation or treatment with psychotherapy	Monthly "Care management"	Unclear diagnosis, psychotic features, past-mania or hypomania, unable to treat in primary care, need for psychosocial interventions, patient preference

Guideline abbreviations: See Table 2. AD: Antidepressant, GP: General practitioner, MADRS: Montgomery and Asberg Depression Rating Scale, TCA: Tricyclic antidepressant

Appendix 7. Primary treatment recommendations according to disease severity

	Mild depression	Moderate depression	Severe depression
Canada: CCSMH 2006	PT or AD *or* PT and AD	PT or AD *or* PT and AD	PT and AD
Denmark: HMA 2007	Low intensity, consider PT in mild-to-moderate	PT or AD *or* PT and AD	AD
International: WFSBP 2007	PT, AD under special circumstances	PT and AD	PT and AD
New Zealand: NZGG 2008	Low intensity	PT or AD	PT and AD
Norway: NDH 2009	Low intensity. AD under special circumstances.	PT or AD	PT and AD
Norway: NEL 2011	Low intensity. AD under special circumstances	PT or AD, *or* PT and AD	PT and AD
Sweden: NBHW 2010	May offer PT. AD under special circumstances	PT and AD	AD
UK: BAP 2008	PT or AD, AD under special circumstances	PT or AD AD 1st choice in moderate-to-severe	AD or in combination with PT
UK: NICE 2009	Low intensity. AD or PT under special circumstances	PT or AD, PT and AD in moderate to severe	PT and AD
US: ICSI 2010	Mild to moderate: PT or AD *or* PT and AD	PT or AD.	Moderate to severe: PT or AD *or* PT and AD. Severe: PT and AD
US: KP 2010	PT or AD	PT or AD	PT and AD
US: UpToDate 2011	Mild to moderate: PT or AD	AD or in combination with PT	AD or in combination with PT
US: VA/DoD 2008	PT or AD	PT and AD	PT and AD

Guideline abbreviations: See Table 2. AD: Antidepressant. PT: Psychotherapy.

Errata

p. 59 The parenthesis "(see Appendix C for details regarding each municipality)" should be removed.