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ORIGINAL ARTICLE

Determinants of adherence to recommendations for depressed elderly patients in primary care: A multi-methods study

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Abstract

Objective. It is logical that tailoring implementation strategies to address identified determinants of adherence to clinical practice guidelines should improve adherence. This study aimed to identify and prioritize determinants of adherence to six recommendations for elderly patients with depression. **Design and setting.** Group and individual interviews and a survey were conducted in Norway. **Method.** Individual and group interviews with healthcare professionals and patients, and a mailed survey of healthcare professionals. A generic checklist of determinants of practice was used to categorize suggested determinants. **Participants.** Physicians and nurses from primary and specialist care, psychologists, researchers, and patients. **Main outcome measures.** Determinants of adherence to recommendations for depressed elderly patients in primary care. **Results.** A total of 352 determinants were identified, of which 99 were prioritized. The most frequently identified factors had to do with dissemination of guidelines, general practitioners' time constraints, the low prioritization of elderly patients with depression, and the patients' or relatives' wish for medication. Approximately three-quarters of the determinants were from three of the seven domains in the generic checklist: individual healthcare professional factors, patient factors, and incentives and resources. The survey did not provide useful information due to a low response rate and a lack of responses to open-ended questions. **Implications.** The list of prioritized determinants can inform the design of interventions to implement recommendations for elderly patients with depression. The importance of the determinants that were identified may vary across communities, practices, and patients. Interventions that address important determinants are necessary to improve practice.

Key Words: Depression, determinants of practice, elderly patients, general practice, Norway, primary care, tailored implementation

Introduction

Many factors can affect adherence to guidelines and determine whether patients receive appropriate care [1,2]. These factors are referred to as barriers and facilitators, determinants of adherence, or determinants of practice [3]. Knowledge regarding determinants of practice can guide efforts to develop interventions that address identified determinants and thereby help to implement guidelines effectively.

The relative importance of determinants of practice may vary depending on the type of recommendation and the context of care. Investigating determinants of practice for specific recommendations is a prerequisite for tailoring implementation strategies.

Tailored Implementation for Chronic Diseases (TICD) is an international project that aims to develop valid and efficient methods of tailoring implementation interventions to address determinants of practice for chronic conditions [3,4]. Five participating countries are developing and testing tailored interventions to implement guidelines for five different chronic conditions [5–9].

TICD has developed a checklist of determinants of practice with 57 specific items in seven domains (guideline factors; individual healthcare professional factors; patient factors; professional interaction; incentives and resources; capacity for organizational change; and social, political, and legal factors) [10]. This checklist is accompanied by tools to guide the

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- Multiple factors might impede or facilitate general practitioners' (GPs') adherence to guidelines for the care of depressed elderly patients. Interviews and a survey were conducted to identify and prioritize such determinants of adherence.
- Factors related to dissemination of guidelines, GPs' time constraints, and the lack of priority given to elderly patients with depression were the most frequently suggested barriers to adherence.
- Other determinants were individual healthcare professional factors (e.g. their knowledge and skills), patient factors (e.g. their beliefs and preferences), incentives, and the availability of necessary resources.

process of identifying determinants of practice and developing interventions.

In Norway, we are studying tailored implementation of guidelines for elderly patients with depression. In this paper, "we" refers to the three authors. We are physicians and health service researchers. EA is a psychiatrist and a senior consultant in geriatric psychiatry. SF and AO have worked as general practitioners (GPs). AO and SF have previously conducted studies to assess the effectiveness of tailored interventions to implement guidelines in primary care and conducted systematic reviews of implementation strategies.

We identified 39 recommendations relevant to primary care from the Norwegian national guidelines for the management of adults with depression in primary and secondary care [11].

We performed a systematic review of guidelines for adults with depression [12]. The review was used as a basis to revise the Norwegian recommendations and to inform decisions concerning which recommendations to prioritize. We assessed the quality of the guidelines and compared the recommendations in the Norwegian guidelines with recommendations in the other international guidelines. We then prioritized the recommendations following a standardized procedure for the project [10]. For each recommendation we asked:

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?

We used a five-point scale (1 = no to 5 = yes) to answer each question. Based on our assessments for

each recommendation, we asked whether implementing the recommendation should be a priority using the same five-point scale. We gave 10 recommendations a score of 4 or 5 and discussed these with a reference group (see acknowledgements). According to the common protocol for TICD, each country selected between three and eight recommendations. The reference group for our project prioritized six recommendations (Table I).

The objective of this study was to identify determinants of practice for the six prioritised recommendations for the management of depressed elderly patients. We used the TICD checklist to help identify and categorize determinants, prior to tailoring interventions to implement the recommendations in primary care in Norway [8,10].

Material and methods

According to the common protocol for the TICD project [13], we used four methods to identify determinants of practice: a combination of open (unstructured) and structured group interviews, individual interviews, and a survey.

We describe the selection, recruitment, and characteristics of the participants in Supplementary Appendix A (available online at <http://informahealthcare.com/doi/abs/10.3109/02813432.2014.984961>). We stratified healthcare professionals for the group and individual interviews to ensure that we included a purposeful selection in each activity. We pre-randomized them to either group or individual interviews, using Zelen randomization [14]. EA and SF conducted two group interviews. One group had seven and the other nine healthcare professionals. EA conducted individual interviews with nine healthcare professionals and four patients.

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

In the group and individual interviews, EA first presented the six recommendations. For the groups we prepared a poster for each recommendation. The group and individual interviews started with individual brainstorming. In the groups we asked the participants to write their suggestions on post-its and to stick them to the relevant poster. After working individually, participants collectively discussed and prioritized determinants for each of the six recommendations. After the first open part of the interviews, we selected probes based on the TICD checklist to focus discussion on determinants that had not yet been considered. We conducted a survey

Table I. Six prioritized recommendations for managing depression in the elderly in primary care.

Prioritized recommendations	Full recommendation to be discussed in the groups and interviews
1. Social contact	Primary care physicians and other healthcare 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 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 ¹ 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 healthcare professionals should offer advice to elderly patients with depression regarding: • Self-assisted programmes, 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. Antidepressants in severe depression, recurrent and chronic 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 psychotherapy, patients should be referred to trained healthcare professionals

Note: ¹Municipalities are the atomic unit of local government in Norway and are responsible for outpatient healthcare services, senior citizen services, and other social services. There are 429 municipalities.

targeted at healthcare professionals in primary and specialist care, partly based on questions that were common to all TICD partners. We describe details of the survey in Supplementary Appendix B available online at <http://informahealthcare.com/doi/abs/10.3109/02813432.2014.984961>.

Analysis

We applied the five-step framework described by Glenton and colleagues [15] 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 [10].
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 categorized as "general".

4. *Charting*: EA put all identified determinants in separate cells in a spreadsheet using a separate column 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 standardized procedure for the TICD project to rank determinants according to the following criteria:

Table II. Probes for discussion in structured part of group sessions and interviews.

TICD checklist domains	Probes and their reference to the relevant item in the checklist ¹
1. Guideline factors	1. Accessibility to guidelines (accessibility of the recommendation, TICD check list No. 5) (10) 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
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. Patient's 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 organizations 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 organizational change	26. Priority – psychotherapy for depressed elderly (priority of necessary change No. 52) 27. Other
7. Social, political, and legal factors	No probes used

Note: ¹The TICD check list numbers refer to 64 items, due to one “other” option for each of the seven domains within the checklist.

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 five-point scale (plausibility: 1 = very low to 5 = very high; feasibility: 1 = very difficult to 5 = very easily).

We report illustrative quotes from participants in the interviews for each recommendation.

Results

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 (Supplementary Appendix B available online at <http://informahealthcare.com/doi/abs/10.3109/02813432.2014.984961>).

The respondents in the interviews and survey suggested a total of 352 determinants, of which 247 were for specific recommendations. We list all of the suggested determinants in Supplementary Appendix C available online at <http://informahealthcare.com/doi/abs/10.3109/02813432.2014.984961>.

Participants identified determinants in all seven domains of the checklist, but three-quarters of the total were in three of the seven domains on 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. In Table III, we present the groups of determinants with the largest number of suggestions (five or more).

Recommendation 1: Social contact

Of 247 suggestions that were specific for one of the six recommendations, 48 determinants were for this recommendation. These determinants were predominantly patient factors and individual healthcare professional factors (Table IV).

Social withdrawal may be a consequence of depression, and patient motivation was considered a barrier to implementing the recommendation:

If you suffer from what I think is depression, then you wouldn't have the energy to engage in social activities. (Nurse 1)

Table III. Related groups of determinants.¹

Group	Number of specific suggestions	Example of suggested determinants	Checklist item [10]				Recommendation or general	Method used to identify	Barrier/Enabler
			Domain	Factor	Sub-factor				
Dissemination of guidelines	16	Guidelines published in paper will not be read If presented properly it will work	Guideline factors Patient factors	Recommendation	Accessibility of the recommendation Patient behaviour		General	Structured group interview	B
Lack of time	11	Lack of time for GPs Talking is more time-consuming	Incentives and resources Incentives and resources		Non-financial incentives and disincentives Financial incentives and disincentives		Mild depression	Brainstorming	B
Lack of priority of the patient group	9	Depressed elderly are not prioritized Depressed elderly compete with other patient groups	Capacity for organizational change Capacity for organizational change		Priority of necessary change		Mild depression	HCP Interview	B
Patients' wish for medication in mild depression	7	Patients/relatives not satisfied if the GP doesn't prescribe "a pill"	Patient factors		Patient preferences		Collaborative care plan	Brainstorming	B
Existing or non-existing social network	6	I get calmer if my GP prescribes something Use already established social network	Patient factors		Patient preferences		General	HCP Interview	B
Changing the behaviour	6	I'm always finding excuses to avoid social contact	Patient factors		Patient motivation		Mild depression	Structured group interview	B
Limited knowledge of the condition	6	Lack of knowledge regarding algorithms for management	Individual healthcare professional factors	Cognition (including attitudes)	Self-efficacy		Social contact	Patient interview	B
Supervising HCPs	6	Community psychiatric nurses may supervise carers Elderly may be shy	Incentives and resources Patient factors		Availability of necessary resources Patient behaviour		Collaborative care plan	HCP interview	B
Frailty, low self-esteem	5	Labelling the patient's condition as depression without investigating The wish "to do something", prescribing antidepressants is easy	Individual healthcare professional factors	Knowledge and skills Cognition (including attitudes)	Domain knowledge Intention and motivation		Counselling	HCP interview	E
Limited focus on the patient group	5	Increased knowledge among patients and their relatives will reduce the wish for medication	Patient factors		Patient beliefs and knowledge		Depression care manager, counselling, severe depression	Brainstorming	B
Prescribing drugs is easy	5						Collaborative care plan	HCP interview	B
Information regarding ADs ² lack of effect in mild depression	5						Mild depression	Brainstorming	B
							Mild depression	HCP Interview	E

Notes: ¹Of the 352 determinants, 256 were related or somewhat similar to other suggestions. This table presents the 87 determinants that were most commonly related to other suggestions; i.e. for which there were five or more related suggestions. ²ADs = antidepressants.

Table IV. Suggested determinants categorized by recommendation and by domain in the TICD checklist.¹

	Guideline factors	Individual healthcare professional factors	Patient factors	Professional interaction	Incentives & resources	Capacity for change	Social, political and legal factors	Total
Social contact	0	12	20	4	8	3	1	48
Collaborative care	2	18	3	5	6	8	0	42
Care manager	2	9	8	3	9	4	3	38
Counselling	3	8	20	1	10	3	0	45
Mild depression	5	13	11	3	5	2	0	39
Severe depression	4	9	10	3	6	3	0	35
Total	16	69	72	19	44	23	4	247

Note: ¹Of the 352 suggested determinants, 247 could be linked to a specific recommendation and only those are included in this table. Many of the suggested determinants were related or somewhat similar to other suggested determinants (see Table III) so the numbers in this table do not represent unique determinants.

Frailty and difficulties in changing routines in old age may also be barriers to social contact. On the other hand, previous social networks may facilitate social activities and increase patients' self-esteem.

Recruiting volunteers to support social contact for depressed elderly patients might be challenging for several reasons. The service is limited in many municipalities. There may not be an identifiable person responsible for organizing the service, and there may be a lack of connection between the patient, the volunteer, and healthcare professionals. Volunteers may be reluctant to commit the time needed and they may lack training in communication with depressed patients.

GPs' or nurses' lack of knowledge concerning voluntary services in the community could also be a barrier:

GPs and other healthcare professionals are not aware of or do not know how to utilize voluntary services. (Group 1)

On the other hand:

Knowledge regarding the community's voluntary services makes the implementation of the recommendation easier. (Group 2)

The modest cost of using volunteers to support patients to be socially active was also considered a facilitator.

Recommendation 2: Collaborative care plan

Participants identified 42 determinants for this recommendation, predominantly individual healthcare professional factors.

Participants were concerned that a collaborative care plan, if there was one, might not be implemented:

Who has the responsibility? There is a risk that responsibility is fragmented, unless the implementation is subject to good leadership. (Psychiatrist 1)

Lack of involvement of key professionals in developing a plan and vague content might make it hard to implement:

Actionable plans with shared ownership increase the plan's feasibility. (Group 2)

Recommendation 3: Depression care manager

Participants identified 38 determinants for the use of a care manager. These were predominantly individual healthcare professional factors, incentives and resources, and patient factors.

Depression care managers might experience professional isolation. Participants perceived the quality of the relationship between the patient and the care manager as critical. It might either facilitate or impede implementation of this recommendation. Several of the participants criticized the recommendation for not emphasizing the professional qualifications of the care manager, and the discussion in the interviews tended to focus on limited availability of psychiatric nurses in the community. Participants thought it would be helpful if GPs had access to a system or manual for referral to and contact with care managers.

Recommendation 4: Counselling

Participants identified 45 determinants for this recommendation. These were predominantly patient factors, incentives, and resources, and healthcare professional factors.

One issue raised in all the interviews was the busy nature of general practice. Adhering to this recommendation would be time consuming:

Even if this service would have been good for me, I don't think that my GP would have time to offer it. (Patient 1)

Depressed elderly patients might lack motivation to engage in counselling in general, and computer skills to use web-based resources in particular. Patients who are not helped by counselling might lose motivation to adhere to treatment.

Lack of trained counsellors and variability in GPs' abilities was considered a barrier to providing counselling to depressed elderly patients:

You have to reduce the variability among GPs in order to change practice with regard to counselling. Perhaps psychiatry courses should be mandatory in order to get a license to practise as a GP. (GP1)

Recommendation 5: Antidepressants in mild depression

Participants identified 39 determinants of adherence to this recommendation. These were predominantly individual healthcare professional and patient factors. Some respondents were convinced that patients and their relatives might disagree with this recommendation:

In some ways, I feel calmer when my GP prescribes me a medication. (Patient 1)

One group noted:

Some patients with mild depression, or their relatives, might wish to receive a prescription despite knowing that the medication's efficacy is uncertain. (Group 1)

The busy nature of family practice may be a reason why it might be difficult to adhere to this recommendation:

GPs wish to do something and prescribing an antidepressant is easy. (Group 1)

Participants considered information to patients and the public about adverse effects and the limited effectiveness of antidepressants in patients with mild depression an important facilitator.

Participants highlighted that there is a lack of services in the community (such as volunteers, easy access to organized physical activity, and professionals who can provide counselling) that could support adherence to non-pharmacological interventions.

GPs' concerns that patients might worsen without antidepressants were also mentioned. In addition, one group suggested that GPs are accused of prescribing antidepressants too seldom, and that it is difficult to reverse a trend towards prescribing antidepressants.

Recommendation 6: Severe depression, recurrent and chronic depression, dysthymia

Participants identified 35 determinants for this recommendation. These were predominantly patient and individual healthcare professional factors.

Few GPs and psychiatric nurses provide cognitive therapy. Respondents in both groups and interviews claimed that depressed elderly patients were not prioritized for psychotherapy in primary or specialist care.

General determinants

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:

Guidelines published by the Directorate of Health or the Association of General Practitioners have more impact than guidelines from specialist healthcare groups. (GP1)

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 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 prioritized all determinants with a score of 4 or higher on both scales (plausibility = high or very high, or feasibility = easily or very easily addressed). This yielded 99 determinants that we attempted to address in designing an implementation strategy for the six recommendations. We list the 99 prioritized determinants in Supplementary Appendix D available online at <http://informahealthcare.com/doi/abs/10.3109/02813432.2014.984961>.

Survey findings

The results of the survey (Supplementary Appendix B available online at <http://informahealthcare.com/doi/abs/10.3109/02813432.2014.984961>) 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.

Discussion*Principal findings*

Through group and individual interviews, we identified a large number of determinants of practice for six recommendations for managing depressed elderly patients in primary care. We have categorized these according to a generic checklist [10]. Approximately three-quarters of the total were from three of the seven domains in the checklist.

Strengths and weaknesses

Strengths of this study include the use of multiple methods, participants, and investigators to identify determinants. There are few if any previous studies comparing different methods to identify determinants of practice. For this reason, across the five TICD partners, we used a common protocol and chose to use both qualitative methods and a quantitative survey, and all the interviews contained both an open brainstorming part and a more structured part. This helps to ensure that we have identified a comprehensive list of determinants, as well as contributing to the comparison of different methods [13].

Different types of knowledge and perspectives can be necessary to identify determinants of practice including health service researchers' experience and insight into mechanisms and knowledge regarding how and why a determinant influences practice, and healthcare professionals' experience and clinical knowledge. Patients' experiences, perceptions, and knowledge of their condition and circumstances may also be necessary. We included participants with all of these different perspectives. However, we interviewed only four patients, so our findings may not fully reflect the perspectives of depressed elderly patients. Elderly patients with present or past depression found the interview questions difficult. Thus we terminated recruitment of patients earlier than planned. An alternative might have been to recruit relatives of depressed elderly patients.

Another weakness of our study is that we did not collect information on participants' perceptions of the relative importance of the determinants that they identified. Our findings suggest that there is likely to be wide variation across communities, practices, healthcare professionals, and patients. Our prioritization 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 informed these assessments only to a limited extent. We will assess the degree to which we have identified the most important determinants by conducting a process evaluation alongside a cluster randomized trial of a tailored intervention that addresses the determinants that we prioritized [8,16].

Findings in relation to other studies

Other studies have explored barriers to detecting depression in the elderly [17,18]. McCabe and colleagues primarily focused on staff who worked with elderly patients in residential care. They found that staff resources, a lack of continuity of care, multiple comorbidities, reluctance of older people to discuss depression, and negative attitudes among carers, as well as a lack of skills, all contributed to a failure to detect and treat depression.

Gask and colleagues [19] identified three major barriers to the effectiveness of a complex educational intervention designed to provide GPs with training in the assessment and management of depression in adults. These were the lack of the GPs' belief that they could have an impact on the outcome of depression, the appropriateness of the training, and the organizational context in which doctors had to implement what they had learned.

Nutting and colleagues [20] 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 [10].

Implications for clinicians and policy-makers

The large number of determinants that we identified indicates the need for a systematic approach to prioritize 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 depressed elderly patients.

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Ethical approval

This project was approved by the Norwegian South-Eastern Health Authority's Regional Ethical Committee, registration n° 2011/2512-1.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Supplementary material available online

Supplementary Appendix A–D.