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Effectiveness of clinical decision support systems and telemedicine on outcomes of depression: a cluster randomized trial in general practice

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Abstract

Background: Computerized Clinical Decision Support Systems (CCDSS) are information technology tools, designed to improve clinical decision-making. Telemedicine is a health care service delivery using videoconferencing, telephone or messaging technologies.
Objectives: Our project aimed at testing the effectiveness of a composite CCDSS and telemedicine approach designed to treat depression in primary care.
Methods: This cluster randomized trial involved four GP clinics located in Northern Italy. Two clinics were assigned to the experimental protocol, and two served as controls. The study compared the telemedicine group (TG), in which GPs had access to a CCDSS platform, with the control group (CG) in which GPs provided treatment as usual (TAU). Patients scoring ≥11 on Patient Heath Questionnaire and ≥26 on the Inventory of Depressive Symptomatology-Self-Report were eligible for participation. Patients were also administered the World Health Organization Quality of Life-BREF to assess quality of life and Medical Interview Satisfaction Scale 21 to assess satisfaction with the medical interview.
Results: Overall, 2810 patients were screened and 66 in the experimental group and 32 in the CG passed the screening stages and met inclusion criteria. The percentage of remitters at 6 months was significantly higher in the TG than in the CG group (24.1% versus 3.1%, $\chi^2 = 6.6$, $P = 0.01$). This difference remained significant after adjusting for baseline confounders. Physical and psychological quality of life improved significantly from baseline in both groups. Patients reported, on average, good satisfaction with the medical interview.
Conclusions: Our study showed that a combined CCDSS and telemedicine approach may be more effective than the TAU offered by GPs to patients with depression.
Trial registration: The trial was registered on https://clinicaltrials.gov/ on 5 October 2012 with identifier: NCT01701791. The first participant was enrolled on 5 May 2014 and the study was completed on May 2016.

Key words: Computerized Clinical Decision Support Systems, depression, patient–doctor relationship, primary care, quality of life, telemedicine.

Key Messages
- Diagnostic algorithms may support GPs for treatment decisions.
- Information technology tools may be superior to usual care in treating depression.
- These tools may be useful for remote monitoring of drug treatment.

Introduction

Treatment algorithms, guideline-based procedures and collaborative care systems based on electronic technology have been proposed and tested for optimizing the delivery of treatment for depression in primary care (1,2). However, the availability of the new technologies for the treatment of depression does not, *per se*, ensure good outcomes. The effectiveness of the procedures adopted in fact depends not only on how the treatment itself (technology) is delivered but also on the quality of the intervention content (adequacy and complexity).

Telemedicine is the simplest application of information technology for the treatment of medical diseases. It can be defined as a professional health care service delivery using information and communication technologies. It can support GPs in retrieving and exchanging valid information about diagnosis, treatment and prevention of different diseases and health problems. One possibility for telemedicine is offered by text messaging (SMS). Simon *et al.* compared antidepressant treatment in primary care with antidepressant treatment supported by SMS (3). They found that patients contacted with messages showed higher rates of antidepressant adherence, lower depression scores and greater satisfaction with treatment. Recently, Senanayake *et al.* reviewed nine telemedicine-based trials comparing text messaging interventions to a comparator group and found only marginal evidence supporting text messaging interventions as an effective treatment modality for depression (4).

A more complex intervention is that offered by Computerized Clinical Decision Support Systems (CCDSS). CCDSS are information systems designed to improve clinical decision-making. Characteristics of individual patients are recorded into a knowledge base, and software algorithms generate patient-specific recommendations. Treatment algorithms are explicit treatment protocols that, based on recorded data, suggest specific therapeutic pathways; they are also decision-making tools assisting physicians in critical decision points throughout a given treatment course (1). The CCDSS have been used for a variety of clinical conditions, but these systems were rarely applied in the management of mental health problems in primary care (5).

Our project aimed to test the effectiveness of a treatment algorithm designed to treat depression symptoms in GP versus treatment as usual (TAU). Our experimental procedure included some components of CCDSS and others of telemedicine (SMS). The CCDSS platform included an algorithm devised to guide the GPs' choice about the best clinical approach, both in terms of antidepressant drugs and psychotherapeutic interventions, or referral for a specialist consultation. The telemedicine component consisted of an SMS-based system aimed at reminding patients of medical prescriptions, scheduled appointments and regular exercise.

Methods

Study design

This cluster randomized trial involved four GP clinics located in two areas of Northern Italy (Brescia and Udine), for a total of 13 GPs. In each area, one clinic was randomly assigned to the experimental protocol, the other served as control. Patients were recruited in 1 year and were followed up for 6 months.

In the two clinics randomized to the telemedicine group (TG), GPs had access to the experimental platform and were allowed to use all its features. However, GPs were not obliged to follow the guidance of such tool: indeed, the algorithm did not force them in any way—which would have been impractical and inappropriate on medical law grounds. In the two clinics randomized to the control group (CG), GPs provided TAU, which included all treatment options considered as appropriate by the GP.

Experimental platform for the TG group

The algorithm used in this project was an adapted version of the algorithm developed within the Texas Medication Algorithm Project (TMAP) (6), which was subsequently implemented with a computerized version (CCDSS), called CompTMAP (7). Our algorithm was a computerized treatment system developed via expert consensus and used to treat depression (Fig. 1). It provided all prompts necessary to guide the GPs in the choice of the antidepressant and/or psychotherapeutic intervention and provided guidance about the need of a referral to a specialist service. The computer program also electronically recorded all patient information, medication information, drug dosages, scheduled visits and progress notes, making them easily accessible thereby. The reminder program was driven by an automatic messaging system in which GPs recorded patient names, telephone numbers and next appointment days. The system sent automatically a text message or a recorded voice mail to patients' mobile phone twice a week to remind patients to comply with drug treatment and any other prescriptions. It also sent automatically two reminders, one on each of the two previous days before each scheduled GP appointment. A Patient Form specifically developed for this project was used to survey patients' socio-demographic, clinical- and treatment-related data and care pathway information. The Patient Form and the instruments listed below were used to assess all enrolled patients at baseline.

The CCDSS/telemedicine system had the following functions:

(i) provide information to the GPs regarding patients' severity of depression;
(ii) support the GPs in the choice of the best treatment option;
(iii) increase patients' treatment adherence by means of SMS;
(iv) track GPs' clinical decisions about patients' depression;
(v) provide suggestions about the management of possible side effects.

At the follow-up visits, the GP could evaluate the results of his/her clinical decisions. In particular, it was possible to check patient's adherence to treatment and the side effects of the pharmacological treatment, if any.

The platform also included a section with additional materials of potential help to the GP: how to prevent relapses, possible psychotherapeutic options and a table summarizing the properties of the most important antidepressant medications, including official dosage recommendations.

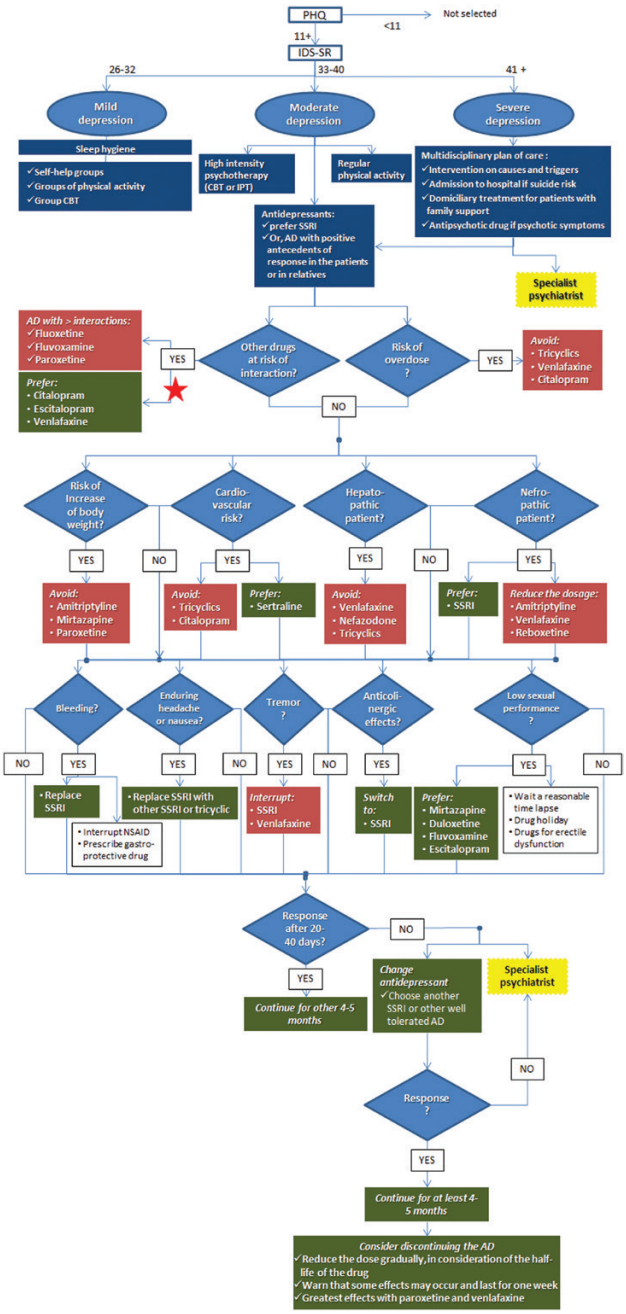

Figure 1. Treatment algorithm. The red star refers to a further level of deepening.

Inclusion and exclusion criteria

Inclusion criteria were age between 18 and 65 and moderate depressive symptomatology, defined by a score ≥11 on the Patient Health Questionnaire (PHQ)-9 and ≥26 on the Inventory of Depressive Symptoms Self-Report (IDS-SR).

Patients who met any of the following diagnostic criteria at baseline were excluded: any antidepressant treatment prescription in the previous 3 months, current alcohol or substance dependence, history of bipolar disorder, pregnancy, being in treatment with antipsychotic medications or any clinical condition requiring inpatient or day-hospital treatment.

Enrolment and monitoring procedures

A two-stage screening procedure was adopted to recruit study participants. All consecutive patients visiting the four GP clinics on index days were administered the PHQ-9 (8,9). This instrument assesses the presence and the frequency of the nine symptom criteria for Diagnostic and Statistical Manual-IV (DSM-IV) major depression over the previous 2 weeks. It was specifically designed for use in GP to establish the possible presence of DSM-IV major depression.

Patients scoring ≥11 on the PHQ-9 were administered the 30-item IDS-SR (10,11). This tool was used in several inpatient and outpatient psychiatric clinics and GP settings. Compared with the PHQ-9, it is more focused on physical symptoms that are the most common presentation of depression in GP. Overall scores on this inventory range from 0 to 84 and can be categorized according to the severity of depressive symptoms (12).

Outcome measures

The primary outcome was clinical remission at 6 months, defined as an IDS-SR score ≤13. Secondary outcomes were quality of life and patients' satisfaction with the medical interview.

To assess quality of life, patients were administered the World Health Organization Quality of Life-BREF (WHOQOL-BREF) at baseline and 6 months. This self-report instrument measures four domains of quality of life: physical health, psychological, social relationships and environment. de Girolamo *et al.* validated the Italian version in a sample of 379 people attending health care services and the tool proved to have good internal consistency (from 0.65 for social relationships to 0.80 for physical health), good test–retest reliability (from 0.63 for environment to 0.88 for the psychological domain) and a satisfactory concurrent validity with medical outcomes scale-short form-36 for physical health and psychological domains (13).

The Medical Interview Satisfaction Scale (MISS-21) was administered only at 6 months. This instrument is designed to assess patients' satisfaction with individual doctor–patient consultations and consists of four domains: Distress Relief, Communication Comfort, Rapport and Compliance Intent. It was validated in a UK general practice population and proved to have good acceptability and construct validity (14).

Power analysis

We estimated that a sample of 180 patients (90 per arm) would be required to test a 20% difference in the percentage of remission between the TG and CG groups with a power of 80% and a level of significance $\alpha = 0.05$. Moreover, to take into account the 'clustered' nature of the data, a correction to the original sample size was applied, assuming an intra-class correlation coefficient equal to 0.03. This leads to a total of 240 subjects to be recruited, that is, 15 patients for each of the 16 GPs.

Statistical analyses

Descriptive statistics were used to summarize all variables. Means and standard deviations were used for quantitative variables, absolute frequency and percentage for categorical variables. The percentage of remitters and other categorical variables was compared between the experimental (TG) and the control (CG) groups using χ^2 test; and quantitative variables were compared between groups using *t*-test or Mann–Whitney test as appropriate.

Multiple logistic regression was used to compare the proportion of remission at 6 months between groups, adjusting for the potential confounding effect of age, gender, ongoing psychotherapy and

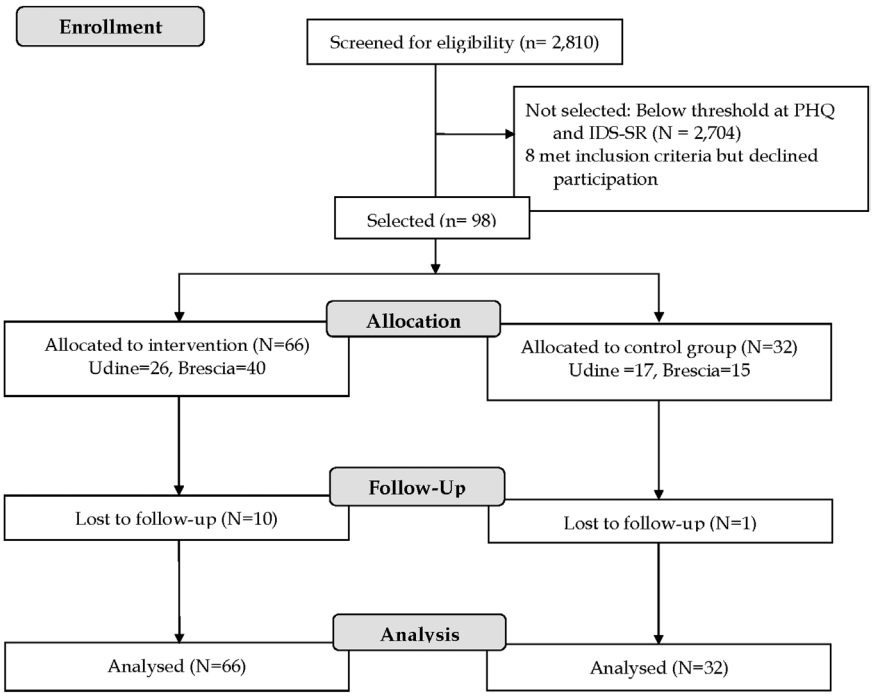

Figure 2. CONSORT study diagram.

Table 1. Socio-demographic and clinical features of study participants ($n = 98$).

	TG $n = 66$	CG $n = 32$	χ^2 (P)
	n (%)	n (%)	
Female gender	52 (78.8)	23 (71.9)	0.57 (0.45)
Education (≤8 years)	23 (34.8)	15 (46.9)	1.31 (0.25)
Employed	27 (40.9)	15 (46.9)	0.31 (0.06)
Single	18 (27.3)	6 (18.8)	0.85 (0.36)
Past history of depression	26 (39.4)	14 (43.8)	0.17 (0.68)
Past history of self-harm	5 (7.9)	3 (9.7)	0.08 (0.78)
Ongoing psychotherapy and/or counselling	11 (16.7)	1 (3.1)	3.68 (0.055)
	Mean (SD)	Mean (SD)	t-test (P)
Age	44.9 (12.0)	49.4 (11.9)	1.77 (0.09)
PHQ-9	15.4 (4.5)	15.2 (2.5)	0.34 (0.74)
IDS-SR	37.9 (8.7)	37.6 (8.6)	0.17 (0.87)

Data were collected in the framework of a cluster randomized trial carried out in 2014 in four GP units.

SD, standard deviation.

severity of depression at baseline. Repeated measures analysis of variance was used to compare the change of the quality of life domain scores from baseline to 6 months between groups. The significance level was set at $P < 0.05$, and tests were two tailed. All analyses were conducted using IBM SPSS, version 25.0.

Results

Overall, 2810 patients were screened at the four GP clinics (Fig. 2). The distribution of PHQ-9 scores stratified by age groups and gender is provided in Supplementary Table 1S). Overall, only 3.5% of patients passed the two steps of evaluation.

Ninety-eight (66 in the experimental units and 32 in the control units) patients agreed to fill out the IDS-SR and achieved a score greater than 26 at this second stage of evaluation. No significant differences were found between the two groups on socio-demographic and clinical characteristics (Table 1). At baseline, 21/66 (31.8%) patients in the TG groups and 8/30 (27.6%) patients in the CG group started antidepressant treatment. The 21 TG patients continued their antidepressant treatment for 6 months and four more started treatment during the study. Of the eight CG patients who started antidepressants at baseline, four continued their treatment until the end of the study and the other four discontinued it.

About one-fourth of patients (17/66, 25.8%) in the TG group received SMS (median = 73). The most frequent reminder was about doing regular exercise (median = 57).

The percentage of remitters (i.e. patients achieving an IDS-SR score ≤13 at 6 months) was significantly higher in the TG group than in the CG group (27.6% versus 9.4%, $\chi^2 = 4.1$, $P = 0.043$). After adjusting for age, gender, any psychotherapy and IDS-SR score at baseline in a multiple logistic regression model, the difference between groups remained significant and the TG group had an odd ratio (OR) of remission more than four times as high as the CG group (OR = 4.6, 95% CI = 1.2–18.8; Table 2).

As to quality of life, no significant differences were found between the TG and the CG groups at baseline and 6 months. However, we found that WHOQOL physical and psychological scores increased significantly from baseline to 6 months, irrespective of the study group, while the social relationship score remained stable over time and the environment domain increased significantly only in the TG group (Table 3).

Concerning satisfaction with the medical interview, we found that MISS-21 scores were high in the subset of 64 patients who filled out the instrument at 6 months, pointing to good satisfaction for the doctor–patient relationship, high communication comfort, high compliance and distress relief. Domain scores did not differ significantly between the TG and CG groups; however, communication comfort was higher among TG than CG patients ($P = 0.054$).

Discussion

To our knowledge, this is the first Italian study to test the effectiveness of CCDSS in patients with depression recruited in general practice. Our study shows that an intervention based on CCDSS and including elements of telemedicine is more effective than TAU in the management of PC patients with depression. The percentage of remitters at 6 months was significantly higher in the TG group (27.6%) than in the CG group (9.4%). This is an encouraging result, since most experiences in this latter field are not positive, similar to what happens in other fields of medicine (5). In a first study, Trivedi *et al.* had demonstrated the effectiveness of the non-computerized version of the TMAP algorithm (6). On the other hand, a subsequent randomized clinical trial in primary care showed no differences between CCDSS and controls (15). In a further trial, the use of computerized guidelines led to a statistically but not clinically significant improvement compared to usual care after 6 weeks (16). So far, only Kurian *et al.* demonstrated the efficacy of a CCDSS-based treatment in a small sample of patients using a system similar to ours (17).

If we consider the process components that may have contributed to the greater efficacy of treatment in patients with TG, the literature provides some examples of variables associated with the effectiveness of treatments conducted with electronic or telecommunication technology. In the study carried out by Simon *et al.*, an improvement of depressive symptoms was present only if algorithm-based telephone recommendations to the GPs on drug strategies to adopt in case of poor efficacy or tolerability of therapies were provided (18). In the US multi-centre trial conducted on 364 depressed primary care patients by Fortney *et al.*, telemedicine-based collaborative care treatment proved to be more effective than practice-based collaborative care (19). Improved outcomes were associated with higher adherence to the care manager protocol in the telemedicine-based model, which, however, did not lead to improvements in the quality of pharmacotherapy or telepsychotherapy. Quality of life in any case improved in the TG. Kurian *et al.* reported that the better outcomes of CCDSS patients were unrelated to quality of antidepressant treatment (e.g., adequacy of dosage, augmentation or switch strategies), while they were related to the number of physician visits (17).

In our study, improved outcomes were unrelated to age, gender and IDS-SR score at baseline. The proportion of patients starting antidepressant at baseline was also similar, around 30% in each group. However, if we take into account that other four patients in the experimental group started an antidepressant during the trial and that half of the patient in the CG discontinued antidepressant treatment, the proportions of patients on antidepressants at 6 months were 37.9% in the experimental group and 13.3% in the CG. Treatment adherence is probably an important reason for the better outcome of patients receiving the CCDSS/telemedicine approach. Another reason is that it helped physicians understand for whom treatment was appropriate and facilitated shared decisions with the patients.

Table 2. OR of remission in the TG and CG groups, adjusted for age, gender, severity of depression and ongoing psychotherapy at baseline.

	B	SE (*B*)	OR	95% CI	*P*
Group (TG versus CG)	1.529	0.716	4.613	1.134–18.763	0.033
Baseline IDS-SR	−0.056	0.041	0.946	0.873–1.024	0.169
Age	0.019	0.025	1.019	0.969–1.071	0.465
Gender	−0.625	0.664	1.869	0.509–6.865	0.346
Ongoing psychotherapy	−0.456	0.904	0.634	0.108–3.726	0.614
Constant	−1.407	2.300	0.245		0.982

Results of multiple logistic regression analysis (n = 98). Data were collected in the framework of a cluster randomized trial carried out in 2014 in four GP units.

SE, standard error.

Table 3. WHOQOL-BREF and MISS-21 domain scores in the two groups.

WHOQOL-BREF scores[a]								
	Baseline				6 months			
	CG (n = 32)		TG (n = 66)		CG (n = 24)		TG (n = 45)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Physical	12.3	2.6	12.2	2.1	13.4	2.4	13.6	2.8
Psychological	10.2	2.0	10.5	2.4	11.6	2.4	12.4	2.8
Social relationships	11.8	2.4	12.5	3.0	12.1	3.2	13.2	3.0
Environment	12.7	2.2	13.1	1.8	13.4	2.3	13.7	2.0
MISS-21 domain scores								
					CG (n = 22)		TG (n = 42)	
					Mean	SD	Mean	SD
Distress relief[b]					31.6	9.4	31.9	8.3
Rapport^					46.7	7.2	48.2	6.9
Compliance intent°					14.4	4.4	15.7	4.3
Communication comfort§					19.7	4.6	21.9	4.8

Data were collected in the framework of a cluster randomized trial carried out in 2014 in four GP units. No significant differences on WHOQOL-BREF domains were found between the TG and CG groups at baseline and 6 months.

[a]Within-group comparisons using paired samples t-test CG: physical: P = 0.037; psychological: P = 0.007; social relationships: P = 0.547; environment: P = 0.087; TG: physical P = 0.002; psychological: P < 0.001; social relationships: P = 0.125; environment: P < 0.05.

[b]Between-group comparisons at 6 months using Mann–Whitney test: P = 0.788; ^P = 0.368; °P = 0.204; §P = 0.054

Our study also suggests that the subjective experience of patients about the treatment received might be associated with the effectiveness of the TG intervention. All patients reported a good satisfaction with the GPs at 6 months, but communication satisfaction was higher, albeit not significantly, among TG patients. Further studies on larger samples are needed to explore satisfaction with the GPs in depressed patients using MISS-21.

A further comment is related to the fact that, in our study, telemedicine (i.e. the SMS) was used only to a limited extent, in line with the low algorithm adherence reported in the trial by Trivedi *et al*. (6). In our investigation, about one-fifth of patients refused to be contacted with SMS and, in some cases, the GP themselves partially used the algorithm. Our study was conducted in areas where Continuing Medical Education programs among GPs are carried forward in a regular manner. This means that, in general, the GPs' competence in the management of common mental disorders, such as depression, can be considered good. In this situation, the GP may be little motivated to add another tool to his/her professional armamentarium, especially because of time constraints and crowded clinics.

Limitations

The first limitation of our study is that the sample size was lower than anticipated. This was largely due to the low percentage of patients who passed the two-stage screening procedure: only 3.5% of patients met the inclusion criteria for the study. Even if this percentage can be considered fairly low, it is actually higher than that found in their large study by Fortney *et al*.: from an initial pool of 19 285 patients screened for depression with the PHQ-9 (score threshold of 10), they found only 364 patients eligible and able to complete the baseline telephone interview (19). The main implication of the small sample is that the precision of the estimate of the proportion remitting is low, with a large confidence interval (CI).

The second limitation is that we relied only on self-reported measures. However, evidence from the literature suggests that a clinician-based assessment of depressive symptoms would not produce relevant differences from self-report measures, as shown by Trivedi *et al*., which obtained similar scores using the IDS clinician-rated scale and the IDS self-report scale (6). We chose to use a PHQ-9 score ≥11, although the most common cut-off for the PHQ-9 is 10. However, it was shown that cut-offs between 8 and 11 have similar sensitivity and specificity (20).

A third limitation might be that the four GP clinics are not representative of the Italian practices. However, group practices are the most common form of association of GPs in Italy and they are similar to those of the other Italian GP practices, both in size and type of training. Thus, there are no reasons to believe that our results cannot be generalized to general practice in Italy. Lastly, the results may not be generalizable to many depressive patients in GP who have relatively mild illness with PHQ-9 score <11.

Conclusions

Our results indicate that a combined CCDSS and telemedicine approach to the treatment of depression may be superior to the usual care offered by GPs. These results can support the idea that information technology tools might be useful when some obstacles hinder the delivery of optimal care, for example, when GPs' knowledge of the best practice in mental health is low, when there are considerable geographical distances between GPs and their patients or under exceptional circumstances such, as the current COVID-19 outbreak.

Supplementary material

Supplementary material is available at *Family Practice* online.

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Declarations

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Ethical approval: ethical approval was granted by the Comitato Etico Istituzioni Ospedaliere Cattoliche belonging to the IRCCS Istituto Centro San Giovanni di Dio Fatebenefratelli, Brescia, and by the Comitato Etico Regionale Unico of the Azienda Ospedaliera Universitaria 'Santa Maria della Misericordia' di Udine. Written informed consent was obtained from all the study participants.

Conflict of interest: all authors declare that they have no competing interests.

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