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# An Interactive Dynamic Referral Interface (IDRI) Improves quality of referral letters- a randomized cross-over vignette trial

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# ABSTRACT

**Objectives:** We evaluated whether interactive, electronic, dynamic, diagnose-specific checklists improve the quality of referral letters in gastroenterology and assessed the general practitioners (GPs) acceptance of the checklists.

**Design:** Randomized cross-over vignette trial.

**Setting:** Primary care in Norway.

**Participants:** 25 GPs.

**Intervention:** The GPs participated in the trial and were asked to refer eight clinical vignettes in an internet-based electronic health record (EHR)-simulator. A referral support, consisting of dynamic diagnose-specific checklists, was created for the generation of referral letters to gastroenterologists. The GPs were randomized to refer the eight vignettes with- or without the checklists. After a minimum of 3 months they repeated the referral process with the alternative method.

**Main outcome measures:** Difference in quality of the referral letters between referrals with- and without checklists, measured with an objective Thirty Point Score (TPS).
Difference in variance in the quality of the referral letters and GPs' acceptance of the electronic dynamic user interface.

**Results:** The mean TPS was 15.2 (95% Confidence Interval (CI) 13.2 to 16.3) and 22.0 (95% CI 20.6 to 22.8) comparing referrals without and with checklist assistance ($p<0.001$), respectively. The coefficient of variance (CV) was 23.3% for the checklist group and 39.6% for the non-checklist group. Two thirds (16/24) of the GPs thought they had included more relevant information in the referrals with checklists, and considered implementing this type of checklists in their clinical practices if available.

**Conclusions:** Dynamic, diagnose specific checklists improved the quality of referral letters significantly and reduced the variance of the TPS indicating a more uniform quality when checklists were used. The GPs were generally positive to the checklists.

## Strengths and limitations of the study:

- We used vignettes to standardize the setting, making the results objective, quantifiable and comparable.
- The randomized cross-over design makes comparison of individual GPs' changes in referral letter quality possible, regardless of the GPs' initial quality level for referral letters.
- Score for objective measurements of the quality of referral letters developed by our research team
- Vignette design may have appeared unrealistic to the participating GPs, and may have resulted in frustration due to challenges in the virtual communication.
- Appropriateness and structure of the referral letters were not measured.

# INTRODUCTION

High quality, written communication is essential for adequate management of patients referred from primary to secondary care. The referral letter is frequently the only information available to the specialist when deciding the patient's priority and selecting appropriate work-up or treatment.

Referral rates from General Practitioners (GPs) to secondary health care services are increasing[1 2] and challenge the capacity of the secondary care outpatient clinics. A lowered threshold for referral may also potentially cause medical overuse[3] and reduced effectiveness of the health care system. A considerable proportion of referral letters are of low quality or inappropriate.[4-20] Such letters are a challenge for the consultants when assessing the relevance and the priority of the referrals.[15] A discrepancy has also been observed between the general practitioners'(GP) and the specialists' considerations of referral letters in terms of quality and content.[21] The lack of essential information may reduce the quality, safety and cost-effectiveness of the health care system due to the scheduling of potentially erroneous work-up or waiting times, or even unnecessary/redundant procedures.[3 22]

The use of electronic health record (EHR) systems and electronic referrals has increased substantially in the last decade[23], and electronic referrals have improved referral quality.[24 25] This shift to increased digitalization of the health care services has also opened for new solutions to facilitate the referral process. Nevertheless, menu driven structured report generation is neither available in the GPs EHR nor in the hospital EHR. Initiatives to increase appropriateness of referrals have been implemented and tested with varying success.[26-30] According to a Cochrane review, the implementation of structured referral paper templates has been one of few interventions with a documented effect on referral quality,[26] and electronic checklists have been shown to decrease the time spent evaluating referral letters.[27] However, the effect of interactive, electronic, dynamic checklists on the quality of referral letters has to our knowledge never been evaluated, neither in a clinical setting nor in a completely standardized trial, and it would be important to test the solution in a virtual setting before launching expensive development and implementation in the GPs EHR system.

The aim of the present trial was to assess whether interactive, electronic, dynamic, diagnose-specific checklists improved referral quality and reduced the variation in the quality for referral letters in gastroenterology, one of the major specialities in internal medicine and with the majority of patients followed in the out-patient clinic. To avoid bias from clinical and

organizational variation, we wanted to perform the trial in an entirely standardized setting by using vignettes.[31 32]

We further wanted to assess whether the electronic dynamic user interface was well accepted by the GPs.

We hypothesized that referral letters generated with the use of interactive checklists contain more relevant information with less variation than free-text referral letters.

The primary endpoint of the trial was the quality of the referrals measured by a Thirty Point Scale (TPS).[33] The secondary endpoints were the variance in the quality of the referrals, and the user satisfaction of the GPs.

# METHODS

## Study design

Between the 30th of April 2014 and the 6th of October 2014, we recruited GPs to participate in the trial, mainly in groups through already established mandatory educational groups for GPs in Norway. All MDs working in general practice in Norway were eligible for participation in the trial. GPs in the Asker and Bærum region (N=135), as well as some GPs in Oslo (N=9) and Bergen (N=4) were contacted directly and offered to participate in the trial. Additionally an email with information about the trial and invitation to participate was distributed through a national email based debate forum for GPs in Norway (EYR).

We designed the study as a two-armed cross-over trial, where we block-randomized participating GPs to refer eight virtual patients either with an electronic free text referral or with a combination of the free text referral together with electronic checklists as referral support. Drop-outs after randomization, before starting the trial (e.g. those who did not show up on the agreed date for participation), were replaced by new GPs by continuing downwards on the randomization- key. The randomization was done before the day of the participation by using permuted block randomization with different block sizes, generated through the website www.randomization.com.

After a minimum of 3 months the GPs referred the same eight virtual patients again with the alternative referral letter interface, e.g. those who had referred with standard free-text in the first round now referred with the checklist support. We chose the 3 month interval to avoid recollection of the checklist items by the GPs who had used these in the first round.

We instructed the GPs to create the referral letters the same way they normally do with a similar real patient, using the same structure, contents and time.

In the first round of the trial, we gathered groups of GPs (N= 1-7) for participation together in the hospital computer room/other venue with computer/internet access. One investigator from the study team was present to give IT support on how to get started, and also to facilitate the communication with the vignettes when necessary. In the second round, the GPs could choose whether they wanted to complete the trial in the same way, or if they wanted to do it from their offices or homes at a time of their convenience.

## Intervention:

### *Interactive Dynamic Referral Interface (IDRI) program*

We created an EHR-simulator for generating referral letters combined with a virtual patient simulator, in cooperation with Microsoft Norway AS (figure 1). The user-interface resembled common EHR systems for primary care, with a section displaying the patient's previous medical history, current medication, allergies and family history. It was possible to transfer this information directly to the referral letter by clicking an interactive button. The randomization procedure determined whether a section for generating standard free-text referral letters or the semi-structured referral Interactive Dynamic Referral Interface (IDRI) was activated in the user interface.

The patient simulator, based on a chat functionality, was displayed on one side of the interface. An initial statement indicated the patient's reason for seeking medical care, e.g. "Hi, I am really troubled by loose bowels lately, and it is getting worse. What do you think it could be?" Necessary information regarding relevant symptoms and findings could be obtained by chatting with the virtual patient. The GP could write questions to the patient in the dialogue box, either in whole sentences or using keywords, and the simulator would provide with the patient's answer. In addition, it was possible to order relevant laboratory- and radiological examinations. The results of the tests were displayed immediately on the screen and could be transferred to the referral letter. The information provided by the virtual patient during the "consultation" could be written in the referral section using free text or registered by using the checklist-function when activated.

The EHR simulator was set up according to the randomization allocation before the day of the participation by the trial investigator who was also present at the first round of the trial.

The program is available on the IDRI webpage: www.idri.no (username: IDRIopen, password open123).

### *Vignettes*

We created 8 vignettes (virtual patient cases) presenting symptoms and findings within the gastrointestinal field. The symptoms were chosen according to the main clinical situations in the Norwegian Prioritization Guidelines for Gastroenterology (NPGg)[34], namely: dyspepsia, change of bowel habit, diarrhoea, rectal bleeding, longstanding abdominal pain, constipation dysphagia, and jaundice/elevated liver enzymes.

Subsequently, we integrated the 8 vignettes in the virtual patient simulator, with an unique set of answers to anamnestic questions and to laboratory- and radiology test that were made available through using the chat-function or ordering the tests in the EHR-simulator.

### *Interactive dynamic referral checklists/support*

Sending a referral letter from primary care in Norway requires that at least one International Classification of Primary Care (ICPC)- 2[35] diagnosis is stated in the referral letter. We made a selection of relevant ICPC 2 (2005 version)[35] diagnoses for digestive diseases (selected from D01to D99), omitting e.g. diagnoses for acute and paediatric diseases as well as non-GI specific diseases and anal/oropharyngeal diseases. The selection was made based on which diagnoses could be relevant for the 8 vignettes. We also added T08, weight loss, as a potential diagnosis.

When the IDRI functionality was turned on, the GPs selection of ICPC-2 diagnosis activated the corresponding checklist. In total we generated 10 checklists. The list of ICPC-2 codes used and the corresponding checklists can be found in the appendix 1.

The checklists were made based on criteria for referral letters stated respectively in the NPGg,[34] the Norwegian Handbook for doctors (NEL)[36] and UpToDate.[37] After creating an initial draft for the checklists, we adjusted and reduced the content of the checklists based on feedback from experienced gastroenterologists in the study team as well as clinical gastroenterologists.[33] The selection of the checklist items was done based on which clinical information items were considered most valuable for assessing and prioritizing referral letters in gastroenterology. The checklists can be accessed through the IDRI web-page, and a paper-based example can be seen in the appendix 2.

The checklists consisted of drop-down menus with check-boxes or free-text fields with symptom- or finding- specific questions where the GP had the possibility to choose the appropriate variable. Depending on the answers, new checklists-items were activated if relevant. The use of check-lists was not mandated to refer the virtual patient.

## Primary outcome: Quality of the referral letters

We assessed all referral letters generated in the trial by using a pre-developed score, the TPS, for objectively measuring quality of referral letters.[33] The TPS is a symptom-specific score that consists of the 15 most important variables for assessing and prioritizing referrals for nine important gastrointestinal symptoms(dyspepsia, change of bowel habit, diarrhoea, rectal bleeding, longstanding abdominal pain, constipation dysphagia, and jaundice/elevated liver enzymes and weight loss). Points are assigned to the referrals depending on whether the variable/item is described in the referral or not. Both positive (e.g. the patient has seen red blood in the stool) and negative (e.g. the patient has not seen any blood in the stool) findings are assigned points if adequately described. The five most important variables are classified with three points, the next five with two points and the last five with one point, resulting in a maximum score value of 30 points.

One investigator from the study team scored all the referral letters in the present trial.

## Secondary outcomes

As secondary outcomes we also assessed the difference in variance in the quality of the referral letters and compared the frequencies of which important variables were included in referral letters generated with and without checklists.

To give an example of the frequency of individual variables in the referral letters, we did an a priori selection of some variables that we considered relevant for the referrals. We analysed six variables that were relevant for all the referral letters, four variables that were relevant for only the lower-abdomen cases(diarrhoea, change of bowel habit, constipation, long-standing abdominal pain and rectal bleeding) and two variables that were relevant for only the upper-abdomen cases(dyspepsia, dysphagia). For one variable we only used the dyspepsia case as the dysphagia case would have included information of the presence of dysphagia by default in the referral letter.

After completing both rounds of the trial, we asked the GPs to complete a questionnaire where they provided information about age, size of their medical practice, years of experience as a doctor, and their impression of the checklists in terms of usefulness and format.

## Statistics

***Power estimation:***

In our previous paper, we reported a mean TPS of 13.3 (standard deviation (SD) 4.9) for standard referral letters in gastroenterology without the use of a computer-based checklist.[33] We expected an increase in the score of 30%when using the checklist, as well as a smaller variance of the score. The sample size calculation, comparing a mean TPS of 13.3 in the standard referrals with an expected mean of 17.3 in the referrals with checklist, with a two-sided type-1 error probability of 0.05 and a power of 0.80, yielded a minimal sample size of 21 referral pairs needed. In order to secure this quantity of referrals from each indication, we included as many GPs as possible from the local community. This resulted in 25 GPs completing the cross-over study, producing between 21-24 referrals per indication.

***Statistical analysis:***

Descriptive variables are reported as means or proportions with 95% confidence intervals (CI). We compared the mean overall TPS between referral letters with and without checklist using a multilevel linear regression model, adjusting for clinical case and the cluster GP. Paired t-test was used to compare the mean TPS stratified by clinical case. In a sensitivity analysis, we tested whether the differences in the mean TPS in referral letters with or without checklist differed whether the checklist was used in the first or second round by mixed linear regression model, adjusted for clinical case and adding an interaction term between use of checklist and time of use of checklist (first or second round). We also performed a multivariable linear regression analysis to assess whether the scores differed for age, gender and clinical case. To assess the variance of the TPS between referral letters with and without checklist, we calculated the Variance and Coefficient of Variance (CV) (= [SD/mean] * 100%) for all referral letters with and without checklist and displayed box plots showing the median, interquartile range and minimum/maximum values by type of clinical case. We performed multivariable logistic regression models to compare the proportion of single variables in referral letters generated with or without checklist, adjusting for the clinical case and accounting for the cluster GP. A p-value<0.05 was considered statistically significant. The statistical analyses were conducted using SPSS 23.0 and STATA 14 (StataCorp LP).

# RESULTS

## Study population

Between the 30th of April 2014 and the 6th of October 2014, we included 45 GPs in the trial. The inclusion was ended because the targeted N was reached. Of these, 25 (55.6%) participated in both rounds of the cross-over trial. The second round was completed between the 3rd of December 2014 and the 5th of July 2015. One GP was excluded after the first round because he did not activate the ICPC-2 code in the check-list and consequently did not receive the intervention. Some GPs omitted the diagnosis in the individual referral letters, or did not complete all of the eight referral letters in each round, resulting in 21-24 pairs of referral letters per clinical case (flow chart appendix 3). The participating GPs were on average 53 years old and more females (58%) than males participated (Table 1). Sixty-four percent (16/25) of the GPs who completed the trial had 20 years or more of experience as a doctor. Of the 25 GPs completing both rounds of the trial, 24 GPs answered the final questionnaire about the user friendliness of the system.

Table 1: Characteristics of participating GPs.

| Characteristics | All participants (N=45) | Participants who completed both rounds (N=25) |
|---|---|---|
| Age [years], mean (range) | 51,0 (31-72) | 52,3 (33-63) |
| Female, % (n) | 51.1% (23) | 60.0% (15) |
| Checklist first round, % (n) | 48.9 % (22) | 44.0% (11) |
| Time between rounds [days], mean (range) | - | 181.8 (96-371) |

Abbreviations: N/n= number

## Primary outcome: Quality of referral letter by Thirty Point Score (TPS)

The mean Thirty Point Score (TPS) was higher in referral letters with checklist than without checklist overall (mean Δ=6.8, 95%CI 5.1 to 8.5, p<0.001) and across all clinical cases (range of mean Δ= 3.8 to 10.0), but differed significantly for the different cases (global p-value for clinical case<0.001, from multivariable linear regression adjusting for time of checklist and GP cluster) (Table 2 and Figure 2). The smallest difference was observed in the abdominal pain referral letters (Δ=3.8(0.8 to 6.8)) and the biggest difference in the dyspepsia referral letters (Δ=10.0(7.8 to 12.1)). Multivariable regression analysis did not show any influence of gender and age of the GP on the quality of the referral letters. In a sensitivity analysis we

tested whether the increase in score differed between GPs who had the checklist in the first or second round and found no difference (p=0.303 for interaction between use of checklist and time of checklist in a multivariable mixed linear regression model) (Figure 3)

Table 2: TPS for each patient vignette, comparing referral with or without checklist.

| Clinical case | N referral pairs | With checklist (95% CI) | Without checklist (95% CI) | P-value* | Mean TPS difference |
|---|---|---|---|---|---|
| Dyspepsia | 23 | 22.8(20.9-24.7) | 12.9(11.2-14.5) | <0.001 | 10.0(7.8-12.1) |
| Change of bowel habit | 23 | 24.1(22.6-25.6) | 16.2(13.4-18.9) | <0.001 | 7.9(5.6-10.2) |
| Diarrhoea | 24 | 21.9(20.0-23.8) | 15.4(12.9-17.9) | <0.001 | 6.5(3.8-9.1) |
| Rectal bleeding | 24 | 25.3(23.7-27.0) | 17.7(15.3-20.1) | <0.001 | 7.6(5.5-10.7) |
| Abdominal pain | 21 | 19.5(17.1-21.9) | 15.7(12.5-18.8) | 0.016 | 3.8(0.8-6.8) |
| Constipation | 21 | 18.8(17.3-20.2) | 13.3(10.4-16.2) | <0.001 | 5.4(2.7-8.1) |
| Dysphagia | 22 | 22.5(19.7-25.4) | 13.8(11.4-16.1) | <0.001 | 8.8(5.8-11.8) |
| Jaundice/elevated liver enzymes | 22 | 20.3(17.6-22.9) | 16.2(13.3-19.2) | 0.009 | 4.0(1.1-7.8) |
| **Total**** | **180** | **22.0(20.6-23.4)** | **15.2(13.2-17.2)** | **<0.001** | **6.8(5.1-8.5)** |

*P is calculated using paired sample t-test; ** results predicted from multilevel linear regression model adjusting for clinical case and GP cluster. Abbreviations: N=number of referral pairs. CI= Confidence Interval.

## Secondary Outcome: Variance in the quality of referral letters and frequency of specific variables

The variance in the checklist-referral letters was 26.5, with a range from 4-30 points. The variance in the non-checklist referral letters was 36.2, with a range from 0-26 points. The coefficient of variance (CV) was 23.3% for the checklist group and 39.6% for the non-checklist group. The boxplots in figure 4 and line graphs in figure 2 graphically display the larger TPS variance in referral letters without checklist; however, the picture differs by type of clinical case.

When looking at essential clinical variables used to differentiate between serious and less serious conditions, the difference between the checklist-referrals and the non-checklist referrals was also considerable. These variables are shown in table 3.

Table 3: Selected specific clinical variables in the referrals.

| Variable | N vignettes (n referral pairs) | With checklist N (%) | Without checklist N (%) | OR(95% CI)* | p- value* |
|---|---|---|---|---|---|
| Duration | 8 (180) | 156 (86.7) | 121 (67.2) | 3.4 (1.7-6.8) | <0.001 |
| Weight loss | 8 (180) | 156 (86.7) | 93 (51.7) | 6.6 (3.4-12.9) | <0.001 |
| General condition | 8 (180) | 143 (79.4) | 35 (19.4) | 17.7 (6.5-48.1) | <0.001 |
| Current medication | 8 (180) | 150 (83.3) | 124 (69.3) | 2.5 (1.2-5.2) | 0.019 |
| Findings on clinical | 8 (180) | 148 (82.2) | 116 (64.4) | 2.6 (1.4-4.8) | 0.002 |
| Previous medical history | 8 (180) | 168 (93.3) | 159 (88.3) | 1.9 (0.6-5.5) | 0.262 |
| DRE | 5 (113) | 73 (64.6) | 44 (38.9) | 3.1 (1.8-5.1) | <0.001 |
| Rectal bleeding | 5 (113) | 78 (69.0) | 73 (64.6) | 1.3 (0.7-2.3) | 0.422 |
| FOBT | 5 (113) | 103 (91.2) | 86 (76.1) | 3.3 (1.3-8.4) | 0.015 |
| Hb, ferritin/MCV | 5 (113) | 105 (92.9) | 79 (69.9) | 5.7 (2.0-16.6) | 0.001 |
| Hematemesis | 2 (45) | 35 (77.8) | 14 (31.1) | 7.8 (3.3-18.3) | <0.001 |
| Reflux details | 2 (45) | 33 (73.3) | 17 (37.8) | 10.6 (2.3-48.5) | 0.001 |
| Dysphagia | 1 (23) | 19 (82.6) | 3 (13.0) | 31.7 (5.3-189.5) | <0.001 |

*Odds ratios and p-values calculated from multilevel logistic regression model, adjusting for clinical case and the cluster GP. Abbreviations: CI= Confidence Interval, DRE= Digital Rectal Examination, FOBT= Faecal Occult Blood Test, Hb= Haemoglobin, MCV= Mean Corpuscular Volume, N=number, OR=Odds Ratio.

### Secondary Outcome: Acceptance of checklist among GPs

The GPs were generally positive to the check lists/referral support (figure 5). Two thirds, 66.7% (16/24, 95% CI 44.7 to 84.4%), thought they had included more relevant information in the referrals when using the checklists, and that they had included information in the referrals that they would not have included if they had not had access to the checklists. Seventy six percent (76.2%) (16/21, 3 missing, CI 52.8 to 91.8%), reported that they would consider implementing the checklists in their clinical practices if available and 95.5% (21/22, 2 missing, CI 77.2-99.9%) reported that the checklists had potential for improving the collaboration between the primary and the secondary care health services. The GPs largely found the size of the checklists to be appropriate, but 33.3% (8/24, CI 15.6 to 55.3%) found them to contain too many questions. A combination between checkboxes and drop-down menus were preferred by 47.8% (11/23, 1 missing, CI 26.8 to 69.4).

## DISCUSSION

We have evaluated the effect on dynamic diagnose specific checklists on the quality of referral letters in a standardized setting using vignettes.

## Statement of principal findings

We found a significantly higher quality of referral letters with more important clinical variables included when they were written with access to checklists, compared with the ones written using standard free-text templates. The variance in the quality of the referral letters was smaller in the checklist- referral letters than in the non-checklist referral letters. The majority of GPs found the checklists useful and would consider using them in clinical practice. The trial was done using vignettes from the field of gastroenterology, but the results are likely to be transferrable to other medical fields.

## Comparison with existing literature

To our knowledge, no other trials have rigorously evaluated the effect of electronic interactive check-lists on referral letter quality in a standardized virtual setting.

When exploring relevant literature, the general tendency is that studies aiming to improve referral quality and appropriateness have been largely ineffective. The Cochrane review on such interventions published in 2008[26] identified only a few successful studies, but with the main focus on referral rates[38] and referral appropriateness.[39] They concluded that structured referral templates may improve referral practice, but none of the included studies had used electronic referral forms or checklists. Thus, these conclusions may not be valid for comparison with the present trial.

A few important later studies supporting the use of checklists/referral templates should be mentioned. Rokstad et al[27] made a direct implementation of checklists in existing EHR systems of GPs and found that this electronic optional guideline tool for referrals resulted in higher quality of referral letters and 34% less time spent by the specialist on evaluating each referral letter. Wåhlberg et al[29] assessed the effect of paper referral templates distributed to local GP clinics, and observed an 18% improved quality of referral letters compared with a control group. These clinical studies support the findings of the present trial, and the evidence seems to indicate that checklists are in fact useful for both the referring and the receiving clinician.

In a study of gastrointestinal (GI) endoscopy reports, structured electronic check lists increased the quality of the documentation, and concluded that this was likely due to the reminder effect of the check-list.[40] It also concluded that a combination of free text and check lists seem to be the best way to document the procedure.[40] These conclusions form

the basis for the choice of referral design in the present study, also allowing for a combination of free-text and the electronic checklist.

To measure the effect of a checklist on the quality of the referral letter can be challenging because implementation in clinical practice is subject to bias both from patient case mix and from variations in the physicians' time, stress level etc. Vignette studies are validated against standardized patients(gold standard) and medical record extraction as an appropriate way of studying quality and variation of physician practice,[31 32 41 42] and have been used in various studies.[43-51] A virtual solution using clinical vignettes was therefore chosen as the most appropriate way to standardize the setting.[31]

## Strengths and limitations of the trial

The current trial has several strengths. Firstly, we used vignettes to standardize the clinical setting, making the results objective, quantifiable and comparable in a way which would not have been possible using real patients. Additionally, the randomized cross-over design made comparison of individual GPs' changes in referral letter quality possible, regardless of the GPs' initial quality level for referral letters.

However, the study has some weaknesses that we would like to address. Firstly, we used a score (TPS) for objective measurements of the quality of referral letters developed by our research team, which could potentially have influenced the results of the current study. This score was validated in another study,[33] and the results from this study show that the mean TPS for real referrals in gastroenterology is 13.7, thus somewhat lower than the TPS for free-text referrals in the present study. This most likely reflects the study setting, where the participating GPs may have written referrals of higher quality than what they would have done under normal conditions in a clinical setting. However, the cross-over design makes us able to see past this potential bias.

Secondly, the design of the vignettes may not have appeared realistic to the participating GPs, and also may have resulted in frustration due to challenges in the virtual communication. The alternative would have been to use standardized patients[41] or to evaluate the effect of checklists in a clinical setting. However, standardized patients would have been expensive and required much more resources, and real patients would have required implementing our system in existing EHR systems before actually knowing the effect of the intervention.

Thirdly, the TPS does not measure all aspects of referral quality, but rather quantifies the

amount of relevant information covered in each referral letter. Thus, appropriateness and structure of the referral letter is not measured by the score.[33] However, the checklists did not aim to improve these aspects, but rather the amount of relevant information in the referral letters, and the TPS is well suited for this purpose.

### Implications of the study

The findings of the present study support the findings of Rokstad et al[27] and Wahlberg et al,[29] and the evidence supporting the effect checklists on referral letter quality now seems to be well documented. EHR providers should be encouraged to cooperate with both primary- and secondary care specialists in developing appropriate electronic checklists for a wider range of specialities and clinical indications, and implementing these in existing systems. The results from the GP survey indicate that a somewhat shorter checklist may be preferred to the one used in the present study.

### Unanswered questions/future research

The present study have demonstrated an effect of electronic checklists on the quality of the referral letters, but the effect on the clinical management of the referred patients is still unknown.

## CONCLUSION

Dynamic diagnose-specific checklists have a positive effect on the quality of referral letters in gastroenterology. The effect is most likely present also for other medical specialties, and corresponding checklists could be developed. GPs are largely positive to the idea of a checklist for referrals. The impact on the clinical management of the referrals remains unanswered.

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management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

**Contributions of co-authors:**

SLE, TdL and LA designed the study. SLE performed the data- collection. SLE, CB, and CSR performed the power- and data- analysis. SLE drafted the paper. All authors critically reviewed and improved it. SLE is guarantor. All authors had access to all the data and take responsibility for the integrity of the data and the analysis.

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**Ethics approval:**

The study was reported to and approved by the Data Protection Official for research. The Regional Ethics Committee considered the study outside its mandate, and its approval was not required.

**Transparency statement:**

SLE affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

**Declaration of interests:**

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) SLE have support from research grants from the South-East Norway Health Authorities (grant agreement n° 2008040) and the Norwegian Medical Association (grant agreement n° 14/1689) for the submitted work and CSR has received funding from the European Union Seventh Framework Programme (FP7-PEOPLE-2013-COFUND) (grant agreement n° 609020 - Scientia Fellows).; (2) SLE, CB, CSR, LA and TdL have no relationships with companies that might have an interest in the submitted work in the previous

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**Data sharing statement:**

Data sharing: full dataset and statistical code can be made available from the corresponding author. Participants' consent was not obtained in accordance with Norwegian Data Protection legislation, but the presented data are anonymised and risk of identification is low.

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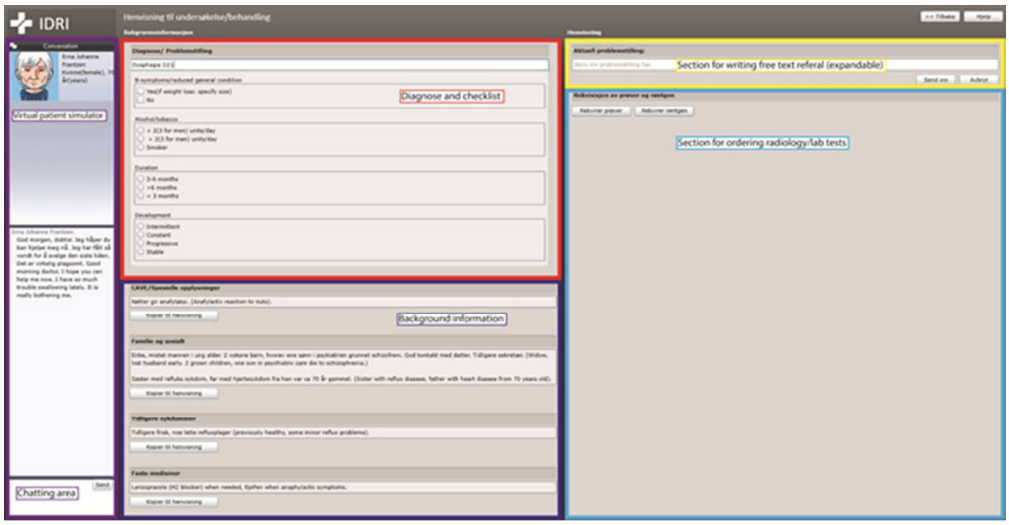
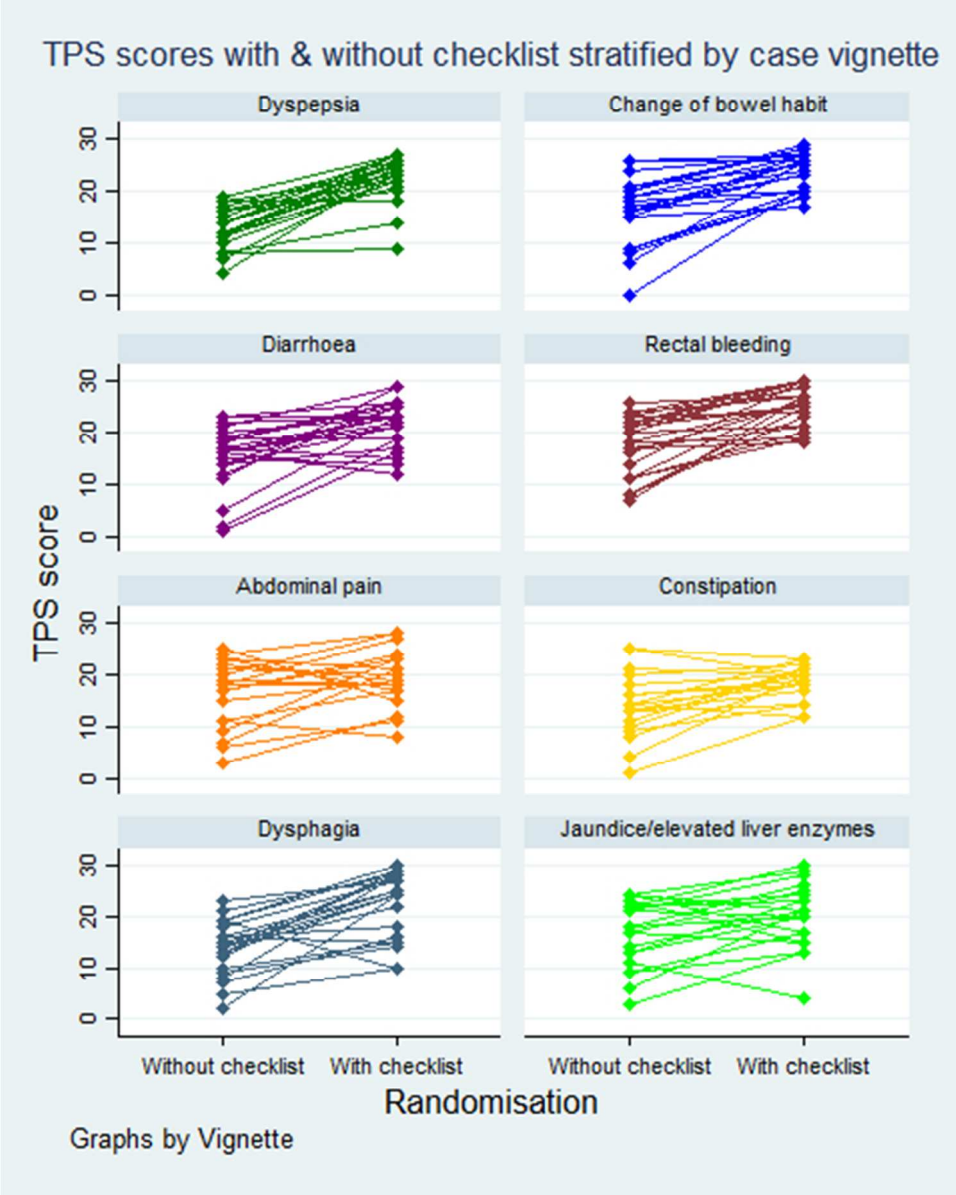


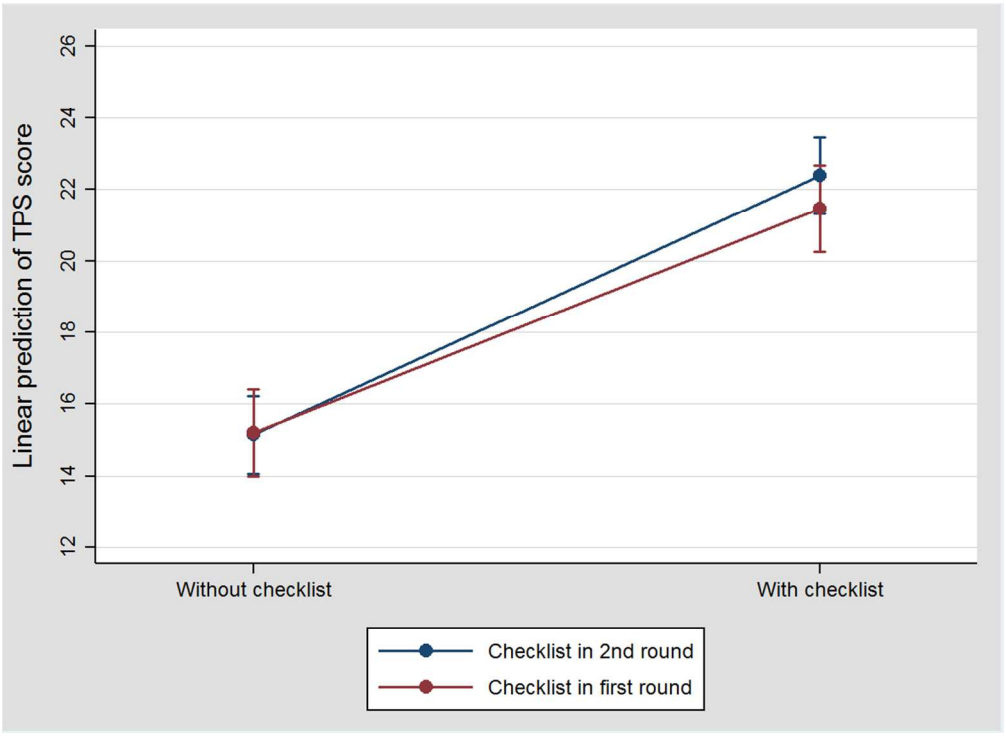

Figure 1: Interface of the virtual EHR/patient simulator

54x27mm (300 x 300 DPI)



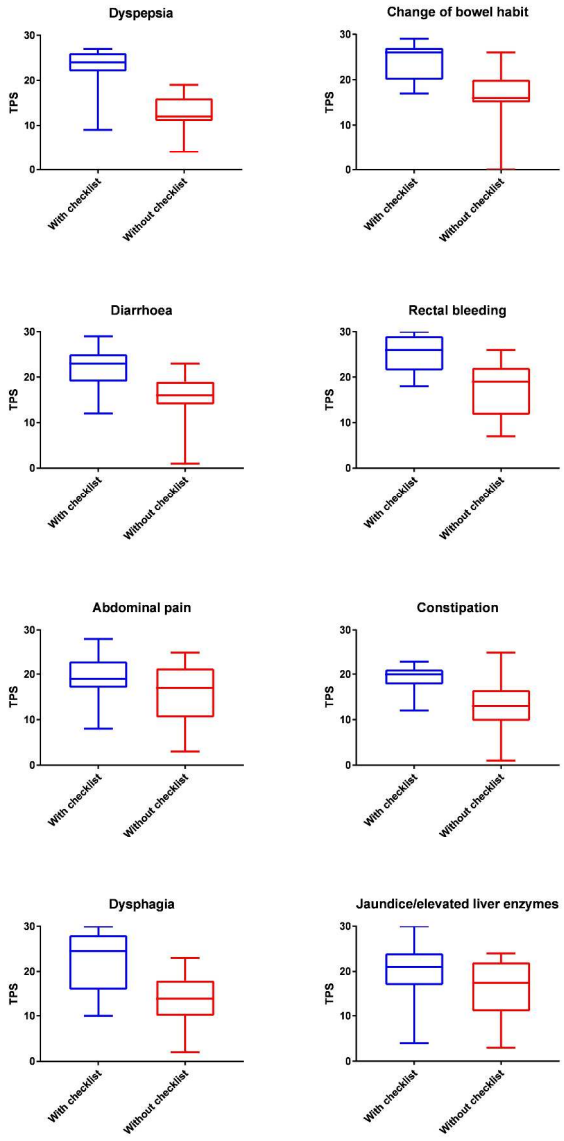

TPS scores for each case with and without checklist, stratified by clinical case

168x210mm (72 x 72 DPI)



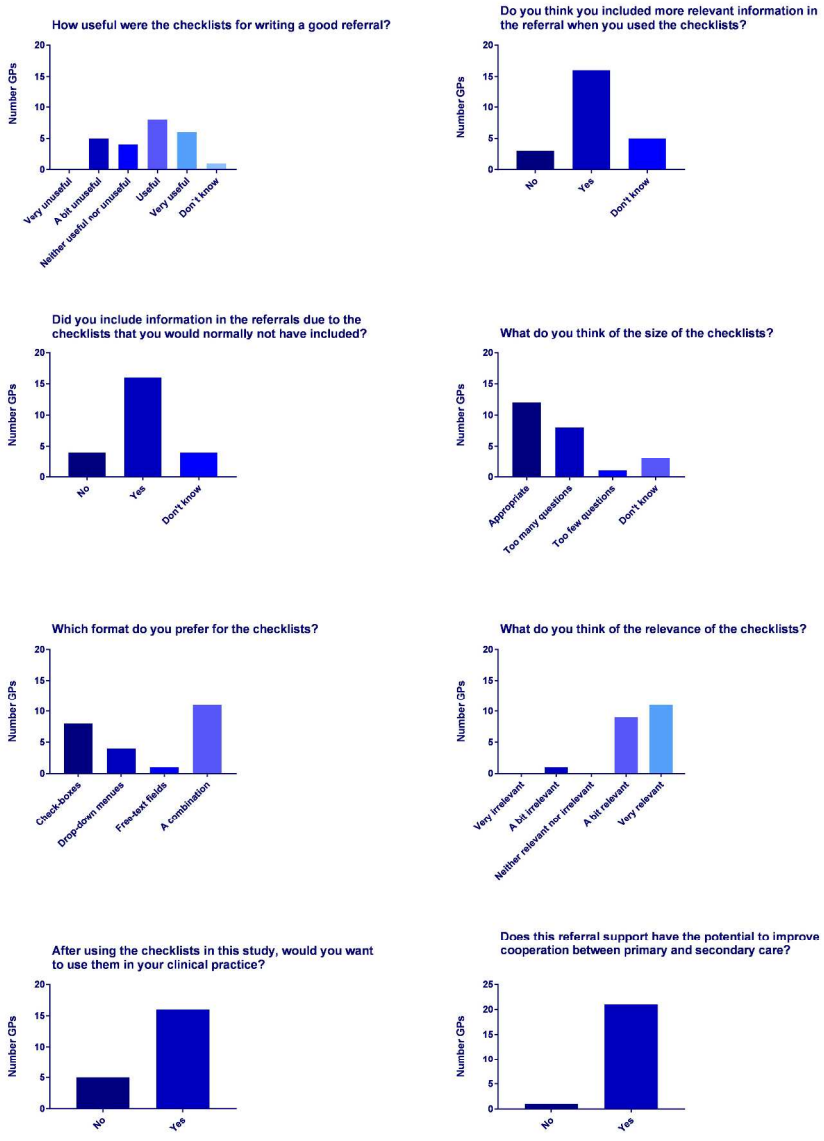

Predicted* mean TPS scores (and 95%CI) of referrals with and without checklist, stratified by time of checklist

415x302mm (72 x 72 DPI)




Boxplot of the TPS stratified by intervention and clinical case

883x1761mm (96 x 96 DPI)




GP opinions after completing the IDRI trial

1125x1559mm (96 x 96 DPI)

| ICPC2 code | ICPC2 text | Checklist |
|---|---|---|
| D01 | Abdominal pain/cramps general | Abdominal pain |
| D01 | Abdominal pain/cramps | Abdominal pain |
| D01 | Abdominal pain/cramps general | Abdominal pain |
| D01 | Abdomen pain | Abdominal pain |
| D01 | Abdominal pain/cramps general | Abdominal pain |
| D01 | Pain abdomen unspecific | Abdominal pain |
| D02 | Abdominal pain epigastric | Dyspagia/reflux/ulcer |
| D02 | Epigastric pain | Dyspagia/reflux/ulcer |
| D02 | Epigastric symptoms/discomfort | Dyspagia/reflux/ulcer |
| D02 | Abdominal pain epigastric | Dyspagia/reflux/ulcer |
| D03 | Heartburn | Dyspagia/reflux/ulcer |
| D03 | Cardialgia | Dyspagia/reflux/ulcer |
| D03 | Reflux | Dyspagia/reflux/ulcer |
| D06 | Abdominal pain pelvis | Abdominal pain |
| D06 | Abdominal pain flank | Abdominal pain |
| D06 | Abdominal pain iliac fossa | Abdominal pain |
| D06 | Abdominal pain hypochondrium | Abdominal pain |
| D06 | Abdominal pain localized other | Abdominal pain |
| D06 | Colonic pain | Abdominal pain |
| D06 | Abdominal pain pelvis | Abdominal pain |
| D06 | Abdominal pain flank | Abdominal pain |
| D06 | Abdominal pain iliac fossa | Abdominal pain |
| D06 | Abdominal pain hypochondrium | Abdominal pain |
| D06 | Abdominal pain localized other | Abdominal pain |
| D07 | Dyspepsia/indigestion | Dyspagia/reflux/ulcer |
| D11 | Bowel frequent/loose | Diarrhoea |
| D11 | Bowel watery | Diarrhoea |
| D11 | Diarrhoea | Diarrhoea |
| D11 | Diarrhoea functional | Diarrhoea |
| D11 | Gastroenteritis non-infectious | Diarrhoea |
| D11 | Colitis non-infectious | Diarrhoea |
| D11 | Loose bowel | Diarrhoea |
| D12 | Constipation | Constipation |
| D12 | Obstipation | Constipation |
| D12 | Constipation | Constipation |
| D13 | Jaundice | Jaundice/elevated liver enzymes |
| D13 | Icterus | Jaundice/elevated liver enzymes |
| D16 | Bowel with fresh blood | Rectal bleeding |
| D16 | Bleeding anal/rectal | Rectal bleeding |
| D16 | Bleeding rectum | Rectal bleeding |
| D16 | Rectal bleeding | Rectal bleeding |
| D18 | Bowel movements changing hard/loose | Change of bowel habit/IBS |
| D18 | Bowel movements changed | Change of bowel habit/IBS |
| D18 | Change faeces/bowel movements | Change of bowel habit/IBS |
| D21 | Dysphagia | Dysphagia |
| D21 | Lump feeling when swallowing | Dysphagia |

| | | |
|---|---|---|
| D21 | Swallowing problem | Dysphagia |
| D21 | Swallowing pain | Dysphagia |
| D84 | Gastroesophageal reflux disease | Dyspepsia/reflux ulcer |
| D84 | GERD (gastro-esophageal reflux disease) | Dyspepsia/reflux ulcer |
| D84 | Reflux oesophagitis | Dyspepsia/reflux ulcer |
| D84 | Oesophagus stricture/stenosis | Dysphagia |
| D84 | Oesophagus disease | Dyspepsia/reflux ulcer |
| D84 | Oesophagitis | Dyspepsia/reflux ulcer |
| D85 | Duodenal ulcer | Dyspepsia/reflux ulcer |
| D85 | Ulcer duodenum | Dyspepsia/reflux ulcer |
| D85 | Ulcus duodeni | Dyspepsia/reflux ulcer |
| D86 | Peptic ulcer other | Dyspepsia/reflux ulcer |
| D86 | Ulcer gastrojejunal | Dyspepsia/reflux ulcer |
| D86 | Ulcer other | Dyspepsia/reflux ulcer |
| D86 | Ulcer chronic | Dyspepsia/reflux ulcer |
| D86 | Ulcer ventricular | Dyspepsia/reflux ulcer |
| D86 | Ulcus ventriculi | Dyspepsia/reflux ulcer |
| D86 | Ventricular ulcer | Dyspepsia/reflux ulcer |
| D87 | Stomach function disorder | Change of bowel habit/IBS |
| D87 | Gastritis chronic | Dyspepsia/reflux ulcer |
| D93 | Colon irritabile | Change of bowel habit/IBS |
| D93 | Irritable colon | Change of bowel habit/IBS |
| D93 | Irritable bowel syndrome | Change of bowel habit/IBS |
| D93 | Irritable bowel syndrome with diarrhoea | Change of bowel habit/IBS |
| D93 | Spastic colon | Change of bowel habit/IBS |
| D97 | Cirrosis alcoholic | Jaundice/elevated liver enzymes |
| D97 | Cirrhose ikke-alkoholisk | Jaundice/elevated liver enzymes |
| D97 | Cirrhose INA | Jaundice/elevated liver enzymes |
| D97 | Fatty liver disease alcoholic | Jaundice/elevated liver enzymes |
| D97 | Fatty liver disease | Jaundice/elevated liver enzymes |
| D97 | Complication from viral hepatitis | Jaundice/elevated liver enzymes |
| D97 | Hepatitis alcoholic | Jaundice/elevated liver enzymes |
| D97 | Hepatitis | Jaundice/elevated liver enzymes |
| D97 | Hepatitis chronic | Jaundice/elevated liver enzymes |
| D97 | Liver failure | Jaundice/elevated liver enzymes |
| D97 | Liver disease NOS | Jaundice/elevated liver enzymes |
| D97 | Liver disease medicine side effect | Jaundice/elevated liver enzymes |
| D97 | Liver disease toxic | Jaundice/elevated liver enzymes |
| D98 | Biliary disease | Jaundice/elevated liver enzymes |
| T08 | Weight loss | Weight loss |

# Checklist dyspepsia/reflux/ulcus

**Frequency reflux/pain**

- ○ Daily
- ○ Several times pr day
- ○ Several times pr week
- ○ 1-4 times pr month

**Duration**

- ○ <3 months
- ○ 3-6 months
- ○ >6 months

**Symptoms**

- ☐ Dysphagia
- ☐ GI-bleeding
  - ○ Melena
  - ○ Hematemesis
  - ○ Positive FOBT
- ☐ Reflux/heartburn
- ☐ Cough
- ☐ Sore throat
- ☐ Worsening when lying down
- ☐ Association with meals
- ☐ Nausea/vomiting
- ☐ Abdominal pain/discomfort
- ☐ Nocturnal reflux symptoms

**B-Symptoms/reduced general condition**

- ☐ No
- ☐ Yes(if weight loss specify size)
  - ○ <5% of body weight the last 6 months
  - ○ >5% of body weight the last 6 months

**Other diseases**

- ☐ Cardiovascular disease
- ☐ Previous ulcus/h.pylori positive
  - ○ Healing of ulcus controlled
  - ○ Treated with PPI
  - ○ H.pylori detected
  - ○ H.pylori eradication completed
- ☐ Previous reflux disease
  - ○ Stage I
  - ○ Stage II
  - ○ Stage III
  - ○ Stage IV

**Current/other relevant medication**

- ☐ Updated list of current medications attached
- ☐ No relief from H2-blockers/PPI
- ☐ Treatment with ASA/NSAIDs
- ☐ Treatment with alendtonate
- ☐ Treatment with steroids

**Lab-analyses attached**

- ☐ Hb, ferritin, MCV
- ☐ CRP, SR, Leuc(with diff)
- ☐ ALAT, ASAT, ALP, GT, bilirubin(conj/unconj), albumine, INR
- ☐ Amylase, lipase, fecal elastase
- ☐ FOBT
- ☐ H.pylori status

**Findings**

- ☐ Abdomen

  Describe:

**Previous upper GI endoscopies**

- ☐ Time

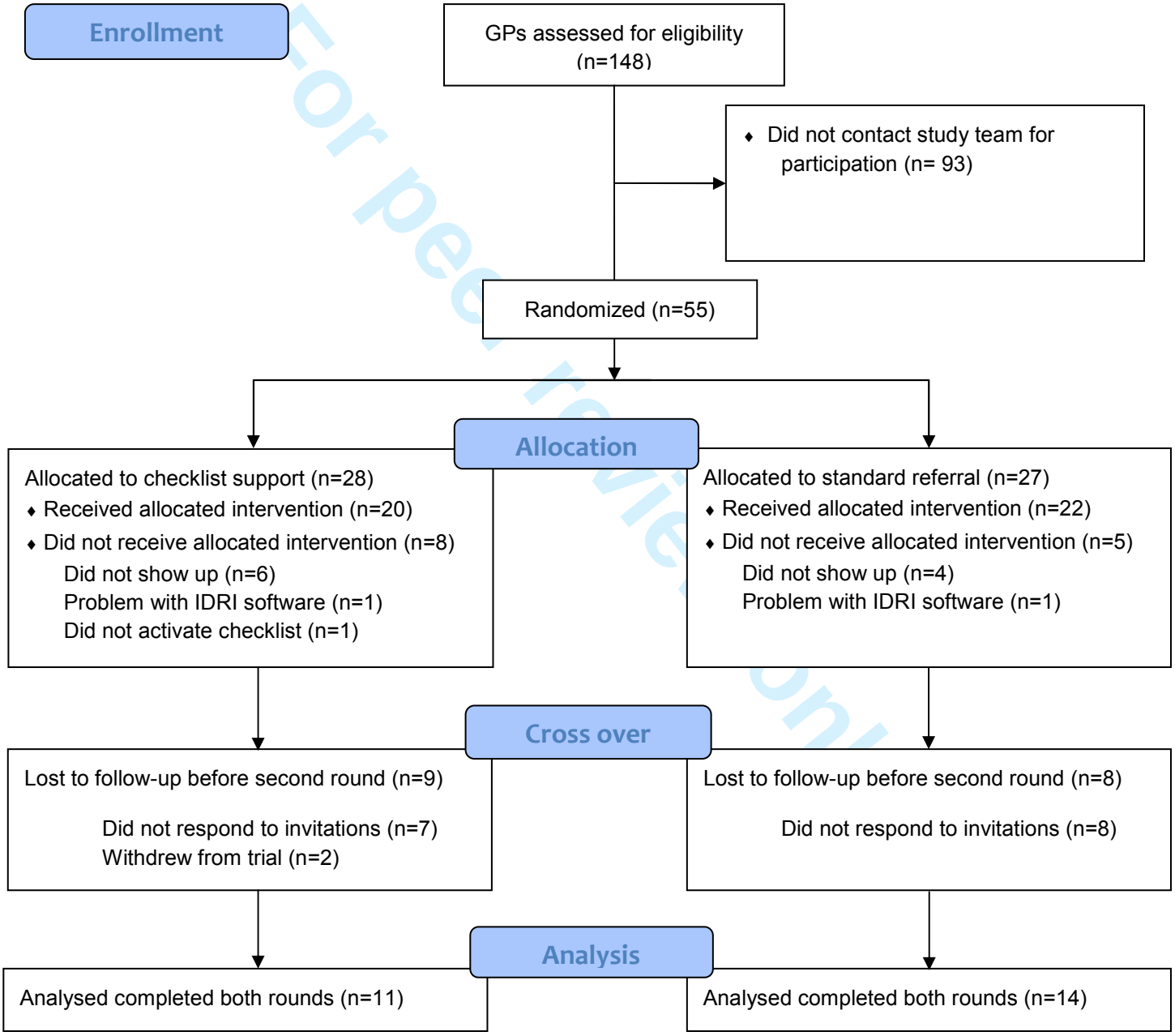
  Describe:

- ☐ Findings

  Describe:

CONSORT
TRANSPARENT REPORTING of TRIALS

## CONSORT 2010 Flow Diagram



BMJ Open

# Assessment of the effect of an Interactive Dynamic Referral Interface (IDRI) on the quality of referral letters from general practitioners to gastroenterologists- a randomized cross-over vignette trial



| | |
|---|---|
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| | |

# Assessment of the effect of an Interactive Dynamic Referral Interface (IDRI) on the quality of referral letters from general practitioners to gastroenterologists- a randomized cross-over vignette trial

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# ABSTRACT

**Objectives:** We evaluated whether interactive, electronic, dynamic, diagnose-specific checklists improve the quality of referral letters in gastroenterology and assessed the general practitioners (GPs) acceptance of the checklists.

**Design:** Randomized cross-over vignette trial.

**Setting:** Primary care in Norway.

**Participants:** 25 GPs.

**Intervention:** The GPs participated in the trial and were asked to refer eight clinical vignettes in an internet-based electronic health record (EHR)-simulator. A referral support, consisting of dynamic diagnose-specific checklists, was created for the generation of referral letters to gastroenterologists. The GPs were randomized to refer the eight vignettes with- or without the checklists. After a minimum of 3 months they repeated the referral process with the alternative method.

**Main outcome measures:** Difference in quality of the referral letters between referrals with- and without checklists, measured with an objective Thirty Point Score (TPS).
Difference in variance in the quality of the referral letters and GPs' acceptance of the electronic dynamic user interface.

**Results:** The mean TPS was 15.2 (95% Confidence Interval (CI) 13.2 to 16.3) and 22.0 (95% CI 20.6 to 22.8) comparing referrals without and with checklist assistance ($p<0.001$), respectively. The coefficient of variance (CV) was 23.3% for the checklist group and 39.6% for the non-checklist group. Two thirds (16/24) of the GPs thought they had included more relevant information in the referrals with checklists, and considered implementing this type of checklists in their clinical practices if available.

**Conclusions:** Dynamic, diagnose specific checklists improved the quality of referral letters significantly and reduced the variance of the TPS indicating a more uniform quality when checklists were used. The GPs were generally positive to the checklists.

## Strengths and limitations of the study:

- We used vignettes to standardize the setting, making the results objective, quantifiable and comparable.
- The randomized cross-over design makes comparison of individual GPs' changes in referral letter quality possible, regardless of the GPs' initial quality level for referral letters.
- Score for objective measurements of the quality of referral letters developed by our research team
- Vignette design may have appeared unrealistic to the participating GPs, and may have resulted in frustration due to challenges in the virtual communication.
- Appropriateness and structure of the referral letters were not measured.

# INTRODUCTION

High quality, written communication is essential for adequate management of patients referred from primary to secondary care. The referral letter is frequently the only information available to the specialist when deciding the patient's priority and selecting appropriate work-up or examinations before the first consultation at the outpatient clinic.

Referral rates from General Practitioners (GPs) to secondary health care services are increasing[1 2] and challenge the capacity of the secondary care outpatient clinics. A lowered threshold for referral may also potentially cause medical overuse[3] and reduced effectiveness of the health care system. A considerable proportion of referral letters are of low quality or inappropriate.[4-20] Such letters are a challenge for the consultants when assessing the relevance and the priority of the referrals.[15] A discrepancy has also been observed between the general practitioners'(GP) and the specialists' considerations of referral letters in terms of quality and content.[21] The lack of essential information may reduce the quality, safety and cost-effectiveness of the health care system due to the scheduling of potentially erroneous work-up or waiting times, or even unnecessary/redundant procedures.[3 22]

The use of electronic health record (EHR) systems and electronic referrals has increased substantially in the last decade,[23] and electronic referrals have improved referral quality.[24 25] This shift to increased digitalization of the health care services has also opened for new solutions to facilitate the referral process. Nevertheless, menu driven structured report generation is neither available in the GPs EHR nor in the hospital EHR. Initiatives to increase appropriateness of referrals have been implemented and tested with varying success.[26-30] According to a Cochrane review, the implementation of structured referral paper templates has been one of few interventions with a documented effect on referral quality,[26] and electronic checklists have been shown to decrease the time spent evaluating referral letters.[27] However, the effect of interactive, electronic, dynamic checklists on the quality of referral letters has to our knowledge never been evaluated, neither in a clinical setting nor in a completely standardized trial, and it would be important to test the solution in a virtual setting before launching expensive development and implementation in the GPs EHR system.

The aim of the present trial was to assess whether interactive, electronic, and dynamic, diagnose-specific checklists improved referral quality and reduced the variation in the quality for referral letters in gastroenterology, one of the major specialities in internal medicine and with the majority of patients followed in the out-patient clinic. To avoid bias from clinical and

organizational variation, we wanted to perform the trial in an entirely standardized setting by using vignettes.[31 32]

We further wanted to assess whether the electronic dynamic user interface was well accepted by the GPs.

We hypothesized that referral letters generated with the use of interactive checklists contain more relevant information with less variation than free-text referral letters.

The primary endpoint of the trial was the quality of the referrals measured by a Thirty Point Scale (TPS).[33] The secondary endpoints were the variance in the quality of the referrals, and the user satisfaction of the GPs.

# METHODS

## Study design

Between the 30th of April 2014 and the 6th of October 2014, we recruited GPs to participate in the trial, mainly in groups through already established mandatory educational groups for GPs in Norway. All MDs working in general practice in Norway were eligible for participation in the trial. GPs in the Asker and Bærum region (N=135), as well as some GPs in Oslo (N=9) and Bergen (N=4) were contacted directly and offered to participate in the trial. Additionally an email with information about the trial and invitation to participate was distributed through a national email based debate forum for GPs in Norway (EYR). The GPs did not receive any material compensation for participating in the trial.

We designed the study as a two-armed cross-over trial, where we block-randomized participating GPs to refer eight virtual patients either with an electronic free text referral or with a combination of the free text referral together with electronic checklists as referral support. Drop-outs after randomization, before starting the trial (e.g. those who did not show up on the agreed date for participation), were replaced by new GPs by continuing downwards on the randomization- key. The randomization was done before the day of the participation by using permuted block randomization with different block sizes, generated through the website www.randomization.com.

After a minimum of 3 months the GPs referred the same eight virtual patients again with the alternative referral letter interface, e.g. those who had referred with standard free-text in the first round now referred with the checklist support. We chose the 3 month interval to avoid recollection of the checklist items by the GPs who had used these in the first round.

We instructed the GPs to create the referral letters the same way they normally do with a similar real patient, using the same structure, contents and time.

In the first round of the trial, we gathered groups of GPs (N= 1-7) for participation together in the hospital computer room/other venue with computer/internet access. One investigator from the study team was present to give IT support on how to get started, and also to facilitate the communication with the vignettes when necessary, e.g. by suggesting alternative phrasing of questions to the vignettes when the simulator failed to give appropriate responses. This was necessary in the beginning as the simulator was sensitive to spelling and did not have a complete natural language. The GPs were quickly accustomed to the form of communication, and mostly required minimal support. In the second round, the GPs could choose whether they wanted to complete the trial in the same way, or if they wanted to do it from their offices or homes at a time of their convenience.

## Intervention:

### *Interactive Dynamic Referral Interface (IDRI) program*

We created an EHR-simulator for generating referral letters combined with a virtual patient simulator, in cooperation with Microsoft Norway AS (figure 1). The user-interface resembled common EHR systems for primary care, with a section displaying the patient's previous medical history, current medication, allergies and family history. It was possible to transfer this information directly to the referral letter by clicking an interactive button. The randomization procedure determined whether a section for generating standard free-text referral letters or the semi-structured referral Interactive Dynamic Referral Interface (IDRI) was activated in the user interface.

The patient simulator, based on a chat functionality, was displayed on one side of the interface. An initial statement indicated the patient's reason for seeking medical care, e.g. "Hi, I am really troubled by loose bowels lately, and it is getting worse. What do you think it could be?" Necessary information regarding relevant symptoms and findings could be obtained by chatting with the virtual patient. The GP could write questions to the patient in the dialogue box, either in whole sentences or using keywords, and the simulator would provide with the patient's answer. In addition, it was possible to order relevant laboratory- and radiological examinations. The results of the tests were displayed immediately on the screen and could be transferred to the referral letter. The information provided by the virtual patient during the "consultation" could be written in the referral section using free text or registered by using the

checklist-function when activated.

The EHR simulator was set up according to the randomization allocation before the day of the participation by the trial investigator who was also present at the first round of the trial.

The program is available on the IDRI webpage: www.idri.no (username: IDRIopen, password open123).

***Vignettes***

We created 8 vignettes (virtual patient cases) presenting symptoms and findings within the gastrointestinal field. The symptoms were chosen according to the main clinical situations in the Norwegian Prioritization Guidelines for Gastroenterology (NPGg)[34], namely: dyspepsia, change of bowel habit, diarrhoea, rectal bleeding, longstanding abdominal pain, constipation dysphagia, and jaundice/elevated liver enzymes.

Subsequently, we integrated the 8 vignettes in the virtual patient simulator, with an unique set of answers to anamnestic questions and to laboratory- and radiology test that were made available through using the chat-function or ordering the tests in the EHR-simulator.

***Interactive dynamic referral checklists/support***

Sending a referral letter from primary care in Norway requires that at least one International Classification of Primary Care (ICPC)- 2[35] diagnosis is stated in the referral letter. We made a selection of relevant ICPC 2 (2005 version)[35] diagnoses for digestive diseases (selected from D01to D99), omitting e.g. diagnoses for acute and paediatric diseases as well as non-GI specific diseases and anal/oropharyngeal diseases. The selection was made based on which diagnoses could be relevant for the 8 vignettes. We also added T08, weight loss, as a potential diagnosis.

When the IDRI functionality was turned on, the GPs selection of ICPC-2 diagnosis activated the corresponding checklist. In total we generated 10 checklists. The list of ICPC-2 codes used and the corresponding checklists can be found in the appendix 1.

The checklists were made based on criteria for referral letters stated respectively in the NPGg,[34] the Norwegian Handbook for doctors (NEL)[36] and UpToDate.[37] After creating an initial draft for the checklists, we adjusted and reduced the content of the checklists based on feedback from experienced gastroenterologists in the study team as well as clinical gastroenterologists.[33] The selection of the checklist items was done based on which clinical information items were considered most valuable for assessing and prioritizing referral letters

in gastroenterology. The checklists can be accessed through the IDRI web-page, and a paper-based example can be seen in the appendix 2.

The checklists consisted of drop-down menus with check-boxes or free-text fields with symptom- or finding- specific questions where the GP had the possibility to choose the appropriate variable. Depending on the answers, new checklists-items were activated if relevant. The use of check-lists was not mandated to refer the virtual patient.

## Primary outcome: Quality of the referral letters

We assessed all referral letters generated in the trial by using a pre-developed score, the TPS, for objectively measuring quality of referral letters. [33] The TPS is a symptom-specific score that consists of the 15 most important variables for assessing and prioritizing referrals for nine important gastrointestinal symptoms (dyspepsia, change of bowel habit, diarrhoea, rectal bleeding, longstanding abdominal pain, constipation dysphagia, and jaundice/elevated liver enzymes and weight loss). Points are assigned to the referrals depending on whether the variable/item is described in the referral or not. Both positive (e.g. the patient has seen red blood in the stool) and negative (e.g. the patient has not seen any blood in the stool) findings are assigned points if adequately described. The five most important variables are classified with three points, the next five with two points and the last five with one point, resulting in a maximum score value of 30 points.

One investigator from the study team scored all the referral letters in the present trial. The investigator was not blinded to the intervention, as the checklists with the GPs answers were displayed together with the referral letters as a supplement to the information in the letters.

## Secondary outcomes

As secondary outcomes we also assessed the difference in variance in the quality of the referral letters and compared the frequencies of which important variables were included in referral letters generated with and without checklists.

To give an example of the frequency of individual variables in the referral letters, we did an a priori selection of some variables that we considered relevant for the referrals. We analysed six variables that were relevant for all the referral letters, four variables that were relevant for only the lower-abdomen cases(diarrhoea, change of bowel habit, constipation, long-standing abdominal pain and rectal bleeding) and two variables that were relevant for only the upper-abdomen cases(dyspepsia, dysphagia). For one variable we only used the dyspepsia case as

the dysphagia case would have included information of the presence of dysphagia by default in the referral letter.

After completing both rounds of the trial, we asked the GPs to complete a questionnaire where they provided information about age, size of their medical practice, years of experience as a doctor, and their impression of the checklists in terms of usefulness and format.

## Statistics

***Power estimation:***

In our previous paper, we reported a mean TPS of 13.3 (standard deviation (SD) 4.9) for standard referral letters in gastroenterology without the use of a computer-based checklist.[33] We expected an increase in the score of 30%when using the checklist, as well as a smaller variance of the score. The sample size calculation, comparing a mean TPS of 13.3 in the standard referrals with an expected mean of 17.3 in the referrals with checklist, with a two-sided type-1 error probability of 0.05 and a power of 0.80, yielded a minimal sample size of 21 referral pairs needed. In order to secure this quantity of referrals from each indication, we included as many GPs as possible from the local community. This resulted in 25 GPs completing the cross-over study, producing between 21-24 referrals per indication.

***Statistical analysis:***

Descriptive variables are reported as means or proportions with 95% confidence intervals (CI). We compared the mean overall TPS between referral letters with and without checklist using a multilevel linear regression model, adjusting for clinical case and the cluster GP. Paired t-test was used to compare the mean TPS stratified by clinical case. In a sensitivity analysis, we tested whether the differences in the mean TPS in referral letters with or without checklist differed whether the checklist was used in the first or second round by mixed linear regression model, adjusted for clinical case and adding an interaction term between use of checklist and time of use of checklist (first or second round). We also performed a multivariable linear regression analysis to assess whether the scores differed for age, gender and clinical case. To assess the variance of the TPS between referral letters with and without checklist, we calculated the Variance and Coefficient of Variance (CV) (= [SD/mean] * 100%) for all referral letters with and without checklist and displayed box plots showing the median, interquartile range and minimum/maximum values by type of clinical case. We performed multivariable logistic regression models to compare the proportion of single

variables in referral letters generated with or without checklist, adjusting for the clinical case and accounting for the cluster GP. A p-value<0.05 was considered statistically significant. The statistical analyses were conducted using SPSS 23.0 and STATA 14 (StataCorp LP).

# RESULTS

## Study population

Between the 30th of April 2014 and the 6th of October 2014, 55 GPs were randomized and 45 GPs were included in the first period of the trial. Ten randomized GPs did not show up at the assigned date for participation and were therefore not included in the study. Of the 45 who attended, 25 (55.6%) participated in both rounds of the cross-over trial. The second round was completed between the 3rd of December 2014 and the 5th of July 2015. The inclusion was ended because the targeted N for paired referrals was reached. One GP was excluded after the first round because he did not activate the ICPC-2 code in the check-list and consequently did not receive the intervention. Some GPs omitted the diagnosis in the individual referral letters, or did not complete all of the eight referral letters in each round, resulting in 21-24 pairs of referral letters per clinical case (flow chart appendix 3). The participating GPs were on average 53 years old and more females (58%) than males participated (Table 1). Sixty-four percent (16/25) of the GPs who completed the trial had 20 years or more of experience as a doctor. Of the 25 GPs completing both rounds of the trial, 24 GPs answered the final questionnaire about the user friendliness of the system. In the counties Asker and Bærum in Norway, the average age of GPs is 50,8 years, with a 47% female GPs.[38]

Table 1: Characteristics of participating GPs.

| Characteristics | All participants (N=45) | Participants who completed both rounds (N=25) |
|---|---|---|
| Age [years], mean (range) | 51,0 (31-72) | 52,3 (33-63) |
| Female, % (n) | 51.1% (23) | 60.0% (15) |
| Checklist first round, % (n) | 48.9 % (22) | 44.0% (11) |
| Time between rounds [days], mean (range) | - | 181.8 (96-371) |

Abbreviations: N/n= number

## Primary outcome: Quality of referral letter by Thirty Point Score (TPS)

The mean Thirty Point Score (TPS) was higher in referral letters with checklist than without checklist overall (mean Δ=6.8, 95%CI 5.1 to 8.5, p<0.001) and across all clinical cases (range of mean Δ= 3.8 to 10.0), but differed significantly for the different cases (global p-value for clinical case<0.001, from multivariable linear regression adjusting for time of checklist and GP cluster) (Table 2 and Figure 2). The smallest difference was observed in the abdominal pain referral letters (Δ=3.8(0.8 to 6.8)) and the biggest difference in the dyspepsia referral letters (Δ=10.0(7.8 to 12.1)). Multivariable regression analysis did not show any influence of gender and age of the GP on the quality of the referral letters. In a sensitivity analysis we tested whether the increase in score differed between GPs who had the checklist in the first or second round and found no difference (p=0.303 for interaction between use of checklist and time of checklist in a multivariable mixed linear regression model) (Figure 3)

Table 2: TPS for each patient vignette, comparing referral with or without checklist.

| Clinical case | N referral pairs | With checklist (95% CI) | Without checklist (95% CI) | P-value* | Mean TPS difference |
|---|---|---|---|---|---|
| Dyspepsia | 23 | 22.8(20.9-24.7) | 12.9(11.2-14.5) | <0.001 | 10.0(7.8-12.1) |
| Change of bowel habit | 23 | 24.1(22.6-25.6) | 16.2(13.4-18.9) | <0.001 | 7.9(5.6-10.2) |
| Diarrhoea | 24 | 21.9(20.0-23.8) | 15.4(12.9-17.9) | <0.001 | 6.5(3.8-9.1) |
| Rectal bleeding | 24 | 25.3(23.7-27.0) | 17.7(15.3-20.1) | <0.001 | 7.6(5.5-10.7) |
| Abdominal pain | 21 | 19.5(17.1-21.9) | 15.7(12.5-18.8) | 0.016 | 3.8(0.8-6.8) |
| Constipation | 21 | 18.8(17.3-20.2) | 13.3(10.4-16.2) | <0.001 | 5.4(2.7-8.1) |
| Dysphagia | 22 | 22.5(19.7-25.4) | 13.8(11.4-16.1) | <0.001 | 8.8(5.8-11.8) |
| Jaundice/elevated liver enzymes | 22 | 20.3(17.6-22.9) | 16.2(13.3-19.2) | 0.009 | 4.0(1.1-7.8) |
| **Total**** | **180** | **22.0(20.6-23.4)** | **15.2(13.2-17.2)** | **<0.001** | **6.8(5.1-8.5)** |

*P is calculated using paired sample t-test; ** results predicted from multilevel linear regression model adjusting for clinical case and GP cluster. Abbreviations: N=number of referral pairs. CI= Confidence Interval.

## Secondary Outcome: Variance in the quality of referral letters and frequency of specific variables

The variance in the checklist-referral letters was 26.5, with a range from 4-30 points. The variance in the non-checklist referral letters was 36.2, with a range from 0-26 points. The coefficient of variance (CV) was 23.3% for the checklist group and 39.6% for the non-checklist group. The boxplots in figure 4 and line graphs in figure 2 graphically display the

larger TPS variance in referral letters without checklist; however, the picture differs by type of clinical case.

When looking at essential clinical variables used to differentiate between serious and less serious conditions, the difference between the checklist-referrals and the non-checklist referrals was also considerable. These variables are shown in table 3.

Table 3: Selected specific clinical variables in the referrals.

| Variable | N vignettes (n referral pairs) | With checklist N (%) | Without checklist N (%) | OR(95% CI)* | p- value* |
|---|---|---|---|---|---|
| Duration | 8 (180) | 156 (86.7) | 121 (67.2) | 3.4 (1.7-6.8) | <0.001 |
| Weight loss | 8 (180) | 156 (86.7) | 93 (51.7) | 6.6 (3.4-12.9) | <0.001 |
| General condition | 8 (180) | 143 (79.4) | 35 (19.4) | 17.7 (6.5-48.1) | <0.001 |
| Current medication | 8 (180) | 150 (83.3) | 124 (69.3) | 2.5 (1.2-5.2) | 0.019 |
| Findings on clinical | 8 (180) | 148 (82.2) | 116 (64.4) | 2.6 (1.4-4.8) | 0.002 |
| Previous medical history | 8 (180) | 168 (93.3) | 159 (88.3) | 1.9 (0.6-5.5) | 0.262 |
| DRE | 5 (113) | 73 (64.6) | 44 (38.9) | 3.1 (1.8-5.1) | <0.001 |
| Rectal bleeding | 5 (113) | 78 (69.0) | 73 (64.6) | 1.3 (0.7-2.3) | 0.422 |
| FOBT | 5 (113) | 103 (91.2) | 86 (76.1) | 3.3 (1.3-8.4) | 0.015 |
| Hb, ferritin/MCV | 5 (113) | 105 (92.9) | 79 (69.9) | 5.7 (2.0-16.6) | 0.001 |
| Hematemesis | 2 (45) | 35 (77.8) | 14 (31.1) | 7.8 (3.3-18.3) | <0.001 |
| Reflux details | 2 (45) | 33 (73.3) | 17 (37.8) | 10.6 (2.3-48.5) | 0.001 |
| Dysphagia | 1 (23) | 19 (82.6) | 3 (13.0) | 31.7 (5.3-189.5) | <0.001 |

*Odds ratios and p-values calculated from multilevel logistic regression model, adjusting for clinical case and the cluster GP. Abbreviations: CI= Confidence Interval, DRE= Digital Rectal Examination, FOBT= Faecal Occult Blood Test, Hb= Haemoglobin, MCV= Mean Corpuscular Volume, N=number, OR=Odds Ratio.

## Secondary Outcome: Acceptance of checklist among GPs

The GPs were generally positive to the check lists/referral support (figure 5). Two thirds, 66.7% (16/24, 95% CI 44.7 to 84.4%), thought they had included more relevant information in the referrals when using the checklists, and that they had included information in the referrals that they would not have included if they had not had access to the checklists. Seventy six percent (76.2%) (16/21, 3 missing, CI 52.8 to 91.8%), reported that they would consider implementing the checklists in their clinical practices if available and 95.5% (21/22, 2 missing, CI 77.2-99.9%) reported that the checklists had potential for improving the collaboration between the primary and the secondary care health services. The GPs largely found the size of the checklists to be appropriate, but 33.3% (8/24, CI 15.6 to 55.3%) found

them to contain too many questions. A combination between checkboxes and drop-down menus were preferred by 47.8% (11/23, 1 missing, CI 26.8 to 69.4).

# DISCUSSION

We have evaluated the effect on dynamic diagnose specific checklists on the quality of referral letters in a standardized setting using vignettes.

## Statement of principal findings

We found a significantly higher quality of referral letters with more important clinical variables included when they were written with access to checklists, compared with the ones written using standard free-text templates. The variance in the quality of the referral letters was smaller in the checklist- referral letters than in the non-checklist referral letters. The majority of GPs found the checklists useful and would consider using them in clinical practice. The trial was set in Norway, using vignettes from the field of gastroenterology. However, we believe that the results are likely to be transferrable to other medical specialties and applicable to other countries with similar referral systems.

## Comparison with existing literature

To our knowledge, no other trials have rigorously evaluated the effect of electronic interactive check-lists on referral letter quality in a standardized virtual setting.

When exploring relevant literature, the general tendency is that studies aiming to improve referral quality and appropriateness have been largely ineffective. The Cochrane review on such interventions published in 2008[26] identified only a few successful studies, but with the main focus on referral rates[39] and referral appropriateness.[40] They concluded that structured referral templates may improve referral practice, but none of the included studies had used electronic referral forms or checklists. Thus, these conclusions may not be valid for comparison with the present trial.

For Clinical Decision Support Systems (CDSS), a review from 2005 stated four important features associated with a beneficial effect, including 1) Automatic provision of the support as a part of clinician workflow, 2) provision of recommendations rather than just assessments, 3) provision of decision support at the time and localization of the decision making, and 4) being computer based.[41] These requirements are probably also valid for our intervention and care

should be taken to integrate checklist solutions in the EHR referral systems to minimize any extra workload on the GPs receiving the support.

A few important later studies supporting the use of checklists/referral templates should be mentioned. Rokstad et al[27] made a direct implementation of checklists in existing EHR systems of GPs and found that this electronic optional guideline tool for referrals resulted in higher quality of referral letters and 34% less time spent by the specialist on evaluating each referral letter. Wåhlberg et al[29] assessed the effect of paper referral templates distributed to local GP clinics, and observed an 18% improved quality of referral letters compared with a control group. These clinical studies support the findings of the present trial, and the evidence seems to indicate that checklists are in fact useful for both the referring and the receiving clinician.

In a study of gastrointestinal (GI) endoscopy reports, structured electronic check lists increased the quality of the documentation, and concluded that this was likely due to the reminder effect of the check-list.[42] It also concluded that a combination of free text and check lists seem to be the best way to document the procedure.[42] These conclusions form the basis for the choice of referral design in the present study, also allowing for a combination of free-text and the electronic checklist.

To measure the effect of a checklist on the quality of the referral letter can be challenging because implementation in clinical practice is subject to bias both from patient case mix and from variations in the physicians' time, stress level etc. Vignette studies are validated against standardized patients (gold standard) and medical record extraction as an appropriate way of studying quality and variation of physician practice,[31 32 43 44] and have been used in various studies.[45-53] A virtual solution using clinical vignettes was therefore chosen as the most appropriate way to standardize the setting[31].

## Strengths and limitations of the trial

The current trial has several strengths. Firstly, we used vignettes to standardize the clinical setting, making the results objective, quantifiable and comparable in a way which would not have been possible using real patients. Additionally, the randomized cross-over design made comparison of individual GPs' changes in referral letter quality possible, regardless of the GPs' initial quality level for referral letters.

However, the study has some weaknesses that we would like to address. Firstly, we used a score (TPS) for objective measurements of the quality of referral letters developed by our research team, which could potentially have influenced the results of the current study. This score was validated in another study,[33] and the results from this study show that the mean TPS for real referrals in gastroenterology is 13.7, thus somewhat lower than the TPS for free-text referrals in the present study. This most likely reflects a volunteer effect, where the participating GPs may have written referrals of higher quality than what they would have done under normal conditions in a clinical setting. However, the cross-over design makes us able to see past this potential bias.

Secondly, we did not achieve blinding of the TPS assessor, due to the very apparent presence of checklist-items in the referrals.

Thirdly, the design of the vignettes may not have appeared realistic to the participating GPs, and also may have resulted in frustration due to challenges in the virtual communication. The alternative would have been to use standardized patients [43] or to evaluate the effect of checklists in a clinical setting. However, standardized patients would have been expensive and required much more resources, and real patients would have required implementing our system in existing EHR systems before actually knowing the effect of the intervention.

Lastly, the TPS does not measure all aspects of referral quality, but rather quantifies the amount of relevant information covered in each referral letter. Thus, appropriateness and structure of the referral letter is not measured by the score.[33] However, the checklists did not aim to improve these aspects, but rather the amount of relevant information in the referral letters, and the TPS is well suited for this purpose.

## Implications of the study

The findings of the present study support the findings of Rokstad et al[27] and Wahlberg et al,[29] and the evidence supporting the effect checklists on referral letter quality now seems to be well documented. EHR providers should be encouraged to cooperate with both primary-and secondary care specialists in developing and implementing appropriate electronic checklists and conduct RCTs to assess whether it also has an impact on patient outcome or health care costs.

The results from the GP survey indicate that a somewhat shorter checklist may be preferred to the one used in the present study.

### Unanswered questions/future research

The present study have demonstrated an effect of electronic dynamic checklists on the quality of the referral letters, but the effect on the clinical management of the referred patients is still unknown.

## CONCLUSION

Dynamic diagnose-specific checklists have a positive effect on the quality of referral letters in gastroenterology. The effect is most likely present also for other medical specialties, and corresponding checklists could be developed. GPs are largely positive to the idea of a checklist for referrals. The impact on the clinical management of the referrals remains unanswered.

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**Contributions of co-authors:**

SLE, TdL and LA designed the study. SLE performed the data- collection. SLE, CB, and CSR performed the power- and data- analysis. SLE drafted the paper. All authors critically reviewed and improved it. SLE is guarantor. All authors had access to all the data and take responsibility for the integrity of the data and the analysis.

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**Ethics approval:**

The study was reported to and approved by the Data Protection Official for research. The Regional Ethics Committee considered the study outside its mandate, and its approval was not required.

**Transparency statement:**

SLE affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

**Declaration of interests:**

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) SLE have support from research grants from the South-East Norway Health Authorities (grant agreement n° 2008040) and the Norwegian Medical Association (grant agreement n° 14/1689) for the submitted work and CSR has received funding from the European Union Seventh Framework Programme (FP7-PEOPLE-2013-COFUND) (grant agreement n° 609020 - Scientia Fellows).; (2) SLE, CB, CSR, LA and TdL have no relationships with companies that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) SLE, CB, CSR, LA and TdL have no non-financial interests that may be relevant to the submitted work.

**Data sharing statement:**

Data sharing: full dataset and statistical code can be made available from the corresponding author. Participants' consent was not obtained in accordance with Norwegian Data Protection legislation, but the presented data are anonymised and risk of identification is low.

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**Figure legends:**

Figure 1: Interface of the virtual EHR/patient simulator

Figure 2: TPS scores for each case with and without checklist, stratified by clinical case

Figure 3: Predicted mean TPS scores (and 95% CI) of referral letters with and without checklist, stratified by time of the checklist.

Figure 4: Boxplot of the TPS stratified by intervention and clinical case

Figure 5: GP opinions after completing the IDRI trial

Appendix 1: ICPC codes and corresponding checklists used

Appendix 2: Checklist for dyspepsia/reflux/ulcus referral

Appendix 3: Consort flowchart for the IDRI trial

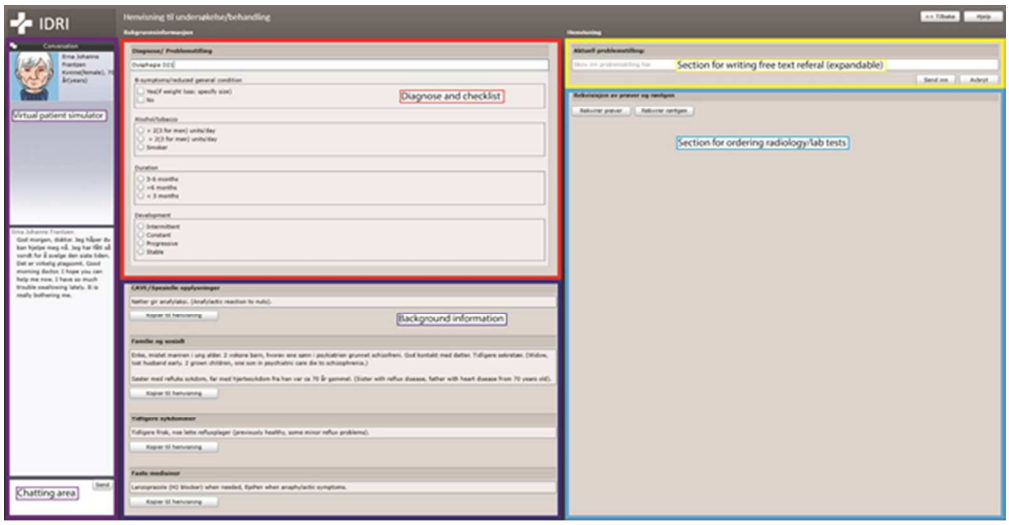



Figure 1: Interface of the virtual EHR/patient simulator

54x27mm (300 x 300 DPI)

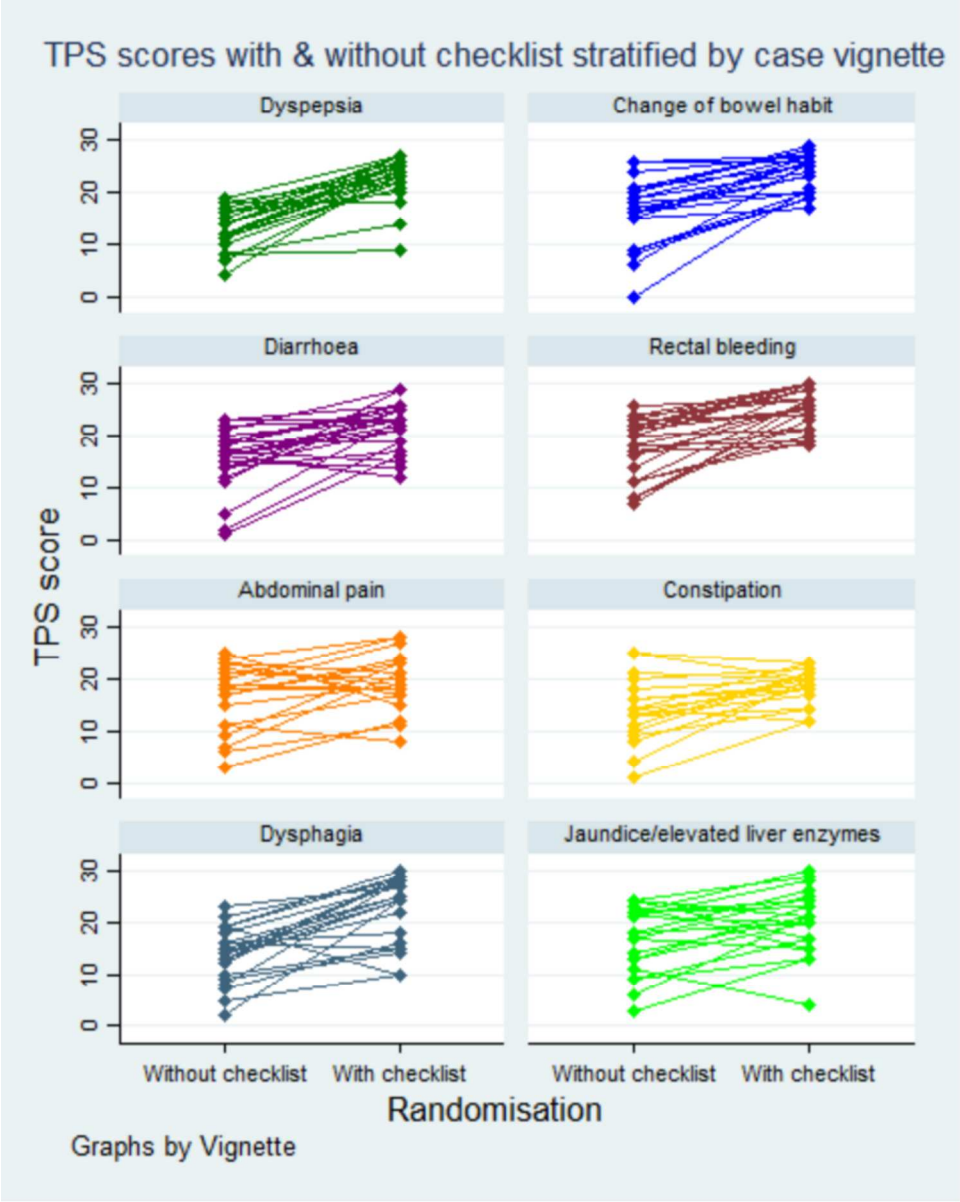



Figure 2: TPS scores for each case with and without checklist, stratified by clinical case

242x303mm (300 x 300 DPI)

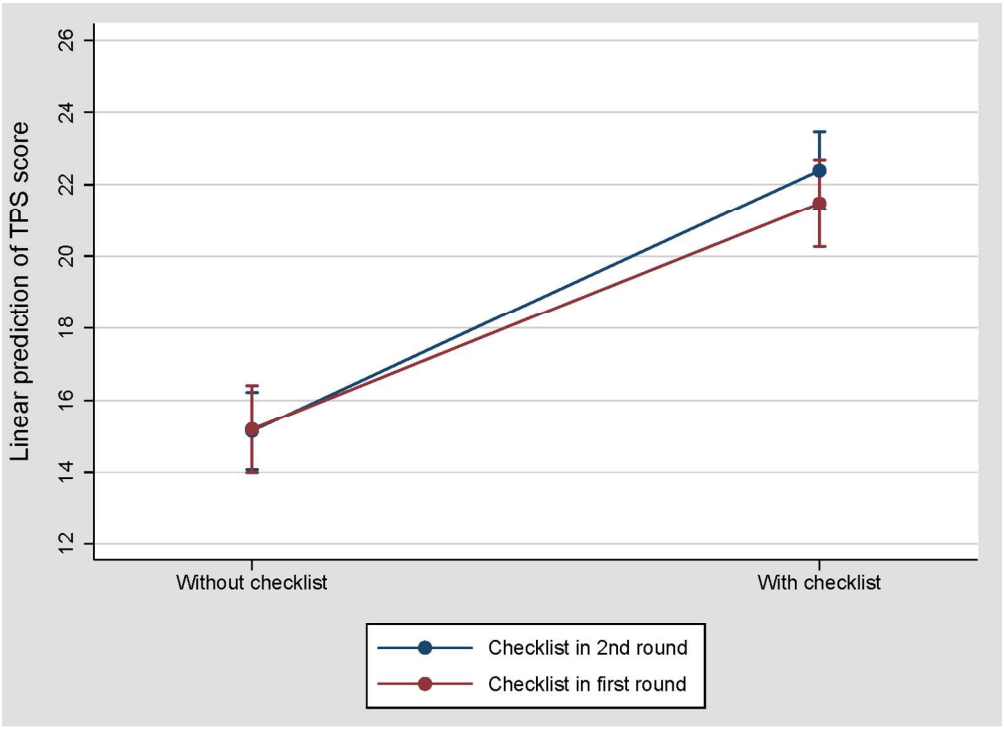



Figure 3: Predicted mean TPS scores (and 95%CI) of referrals with and without checklist, stratified by time of checklist

139x100mm (300 x 300 DPI)

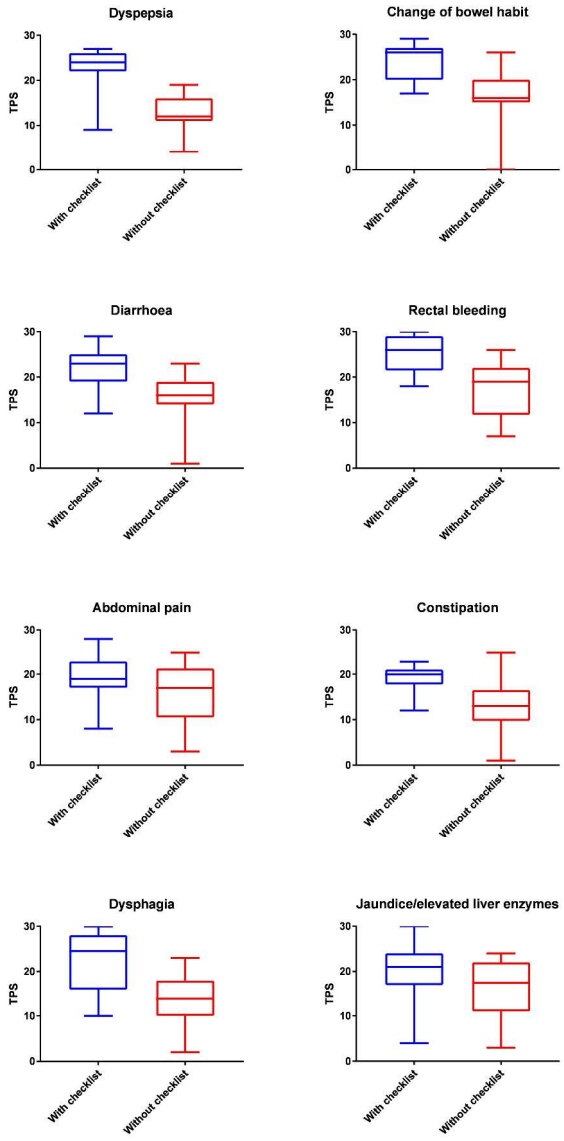



Figure 4: Boxplot of the TPS stratified by intervention and clinical case

282x563mm (300 x 300 DPI)

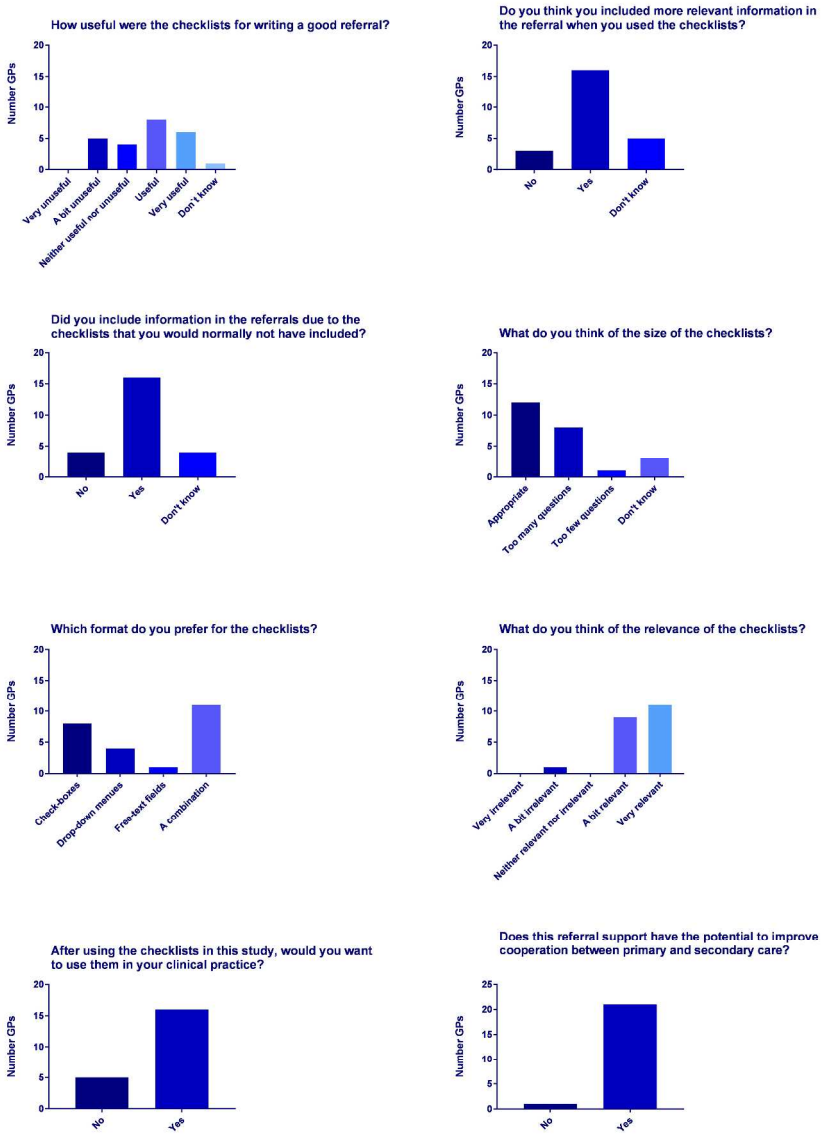



Figure 5: GP opinions after completing the IDRI trial

360x499mm (300 x 300 DPI)

| ICPC2 code | ICPC2 text | Checklist |
|---|---|---|
| D01 | Abdominal pain/cramps general | Abdominal pain |
| D01 | Abdominal pain/cramps | Abdominal pain |
| D01 | Abdominal pain/cramps general | Abdominal pain |
| D01 | Abdomen pain | Abdominal pain |
| D01 | Abdominal pain/cramps general | Abdominal pain |
| D01 | Pain abdomen unspecific | Abdominal pain |
| D02 | Abdominal pain epigastric | Dyspagia/reflux/ulcer |
| D02 | Epigastric pain | Dyspagia/reflux/ulcer |
| D02 | Epigastric symptoms/discomfort | Dyspagia/reflux/ulcer |
| D02 | Abdominal pain epigastric | Dyspagia/reflux/ulcer |
| D03 | Heartburn | Dyspagia/reflux/ulcer |
| D03 | Cardialgia | Dyspagia/reflux/ulcer |
| D03 | Reflux | Dyspagia/reflux/ulcer |
| D06 | Abdominal pain pelvis | Abdominal pain |
| D06 | Abdominal pain flank | Abdominal pain |
| D06 | Abdominal pain iliac fossa | Abdominal pain |
| D06 | Abdominal pain hypochondrium | Abdominal pain |
| D06 | Abdominal pain localized other | Abdominal pain |
| D06 | Colonic pain | Abdominal pain |
| D06 | Abdominal pain pelvis | Abdominal pain |
| D06 | Abdominal pain flank | Abdominal pain |
| D06 | Abdominal pain iliac fossa | Abdominal pain |
| D06 | Abdominal pain hypochondrium | Abdominal pain |
| D06 | Abdominal pain localized other | Abdominal pain |
| D07 | Dyspepsia/indigestion | Dyspagia/reflux/ulcer |
| D11 | Bowel frequent/loose | Diarrhoea |
| D11 | Bowel watery | Diarrhoea |
| D11 | Diarrhoea | Diarrhoea |
| D11 | Diarrhoea functional | Diarrhoea |
| D11 | Gastroenteritis non-infectious | Diarrhoea |
| D11 | Colitis non-infectious | Diarrhoea |
| D11 | Loose bowel | Diarrhoea |
| D12 | Constipation | Constipation |
| D12 | Obstipation | Constipation |
| D12 | Constipation | Constipation |
| D13 | Jaundice | Jaundice/elevated liver enzymes |
| D13 | Icterus | Jaundice/elevated liver enzymes |
| D16 | Bowel with fresh blood | Rectal bleeding |
| D16 | Bleeding anal/rectal | Rectal bleeding |
| D16 | Bleeding rectum | Rectal bleeding |
| D16 | Rectal bleeding | Rectal bleeding |
| D18 | Bowel movements changing hard/loose | Change of bowel habit/IBS |
| D18 | Bowel movements changed | Change of bowel habit/IBS |
| D18 | Change faeces/bowel movements | Change of bowel habit/IBS |
| D21 | Dysphagia | Dysphagia |
| D21 | Lump feeling when swallowing | Dysphagia |

| | | |
|---|---|---|
| D21 | Swallowing problem | Dysphagia |
| D21 | Swallowing pain | Dysphagia |
| D84 | Gastroesophageal reflux disease | Dyspepsia/reflux ulcer |
| D84 | GERD (gastro-esophageal reflux disease) | Dyspepsia/reflux ulcer |
| D84 | Reflux oesophagitis | Dyspepsia/reflux ulcer |
| D84 | Oesophagus stricture/stenosis | Dysphagia |
| D84 | Oesophagus disease | Dyspepsia/reflux ulcer |
| D84 | Oesophagitis | Dyspepsia/reflux ulcer |
| D85 | Duodenal ulcer | Dyspepsia/reflux ulcer |
| D85 | Ulcer duodenum | Dyspepsia/reflux ulcer |
| D85 | Ulcus duodeni | Dyspepsia/reflux ulcer |
| D86 | Peptic ulcer other | Dyspepsia/reflux ulcer |
| D86 | Ulcer gastrojejunal | Dyspepsia/reflux ulcer |
| D86 | Ulcer other | Dyspepsia/reflux ulcer |
| D86 | Ulcer chronic | Dyspepsia/reflux ulcer |
| D86 | Ulcer ventricular | Dyspepsia/reflux ulcer |
| D86 | Ulcus ventriculi | Dyspepsia/reflux ulcer |
| D86 | Ventricular ulcer | Dyspepsia/reflux ulcer |
| D87 | Stomach function disorder | Change of bowel habit/IBS |
| D87 | Gastritis chronic | Dyspepsia/reflux ulcer |
| D93 | Colon irritabile | Change of bowel habit/IBS |
| D93 | Irritable colon | Change of bowel habit/IBS |
| D93 | Irritable bowel syndrome | Change of bowel habit/IBS |
| D93 | Irritable bowel syndrome with diarrhoea | Change of bowel habit/IBS |
| D93 | Spastic colon | Change of bowel habit/IBS |
| D97 | Cirrosis alcoholic | Jaundice/elevated liver enzymes |
| D97 | Cirrhose ikke-alkoholisk | Jaundice/elevated liver enzymes |
| D97 | Cirrhose INA | Jaundice/elevated liver enzymes |
| D97 | Fatty liver disease alcoholic | Jaundice/elevated liver enzymes |
| D97 | Fatty liver disease | Jaundice/elevated liver enzymes |
| D97 | Complication from viral hepatitis | Jaundice/elevated liver enzymes |
| D97 | Hepatitis alcoholic | Jaundice/elevated liver enzymes |
| D97 | Hepatitis | Jaundice/elevated liver enzymes |
| D97 | Hepatitis chronic | Jaundice/elevated liver enzymes |
| D97 | Liver failure | Jaundice/elevated liver enzymes |
| D97 | Liver disease NOS | Jaundice/elevated liver enzymes |
| D97 | Liver disease medicine side effect | Jaundice/elevated liver enzymes |
| D97 | Liver disease toxic | Jaundice/elevated liver enzymes |
| D98 | Biliary disease | Jaundice/elevated liver enzymes |
| T08 | Weight loss | Weight loss |

# Checklist dyspepsia/reflux/ulcus

**Frequency reflux/pain**

- ○ Daily
- ○ Several times pr day
- ○ Several times pr week
- ○ 1-4 times pr month

**Duration**

- ○ <3 months
- ○ 3-6 months
- ○ >6 months

**Symptoms**

- ☐ Dysphagia
- ☐ GI-bleeding
  - ○ Melena
  - ○ Hematemesis
  - ○ Positive FOBT
- ☐ Reflux/heartburn
- ☐ Cough
- ☐ Sore throat
- ☐ Worsening when lying down
- ☐ Association with meals
- ☐ Nausea/vomiting
- ☐ Abdominal pain/discomfort
- ☐ Nocturnal reflux symptoms

**B-Symptoms/reduced general condition**

- ☐ No
- ☐ Yes(if weight loss specify size)
  - ○ <5% of body weight the last 6 months
  - ○ >5% of body weight the last 6 months

**Other diseases**

- ☐ Cardiovascular disease
- ☐ Previous ulcus/h.pylori positive
  - ○ Healing of ulcus controlled
  - ○ Treated with PPI
  - ○ H.pylori detected
  - ○ H.pylori eradication completed
- ☐ Previous reflux disease
  - ○ Stage I
  - ○ Stage II
  - ○ Stage III
  - ○ Stage IV

**Current/other relevant medication**

- ☐ Updated list of current medications attached
- ☐ No relief from H2-blockers/PPI
- ☐ Treatment with ASA/NSAIDs
- ☐ Treatment with alendtonate
- ☐ Treatment with steroids

**Lab-analyses attached**

- ☐ Hb, ferritin, MCV
- ☐ CRP, SR, Leuc(with diff)
- ☐ ALAT, ASAT, ALP, GT, bilirubin(conj/unconj), albumine, INR
- ☐ Amylase, lipase, fecal elastase
- ☐ FOBT
- ☐ H.pylori status

**Findings**

- ☐ Abdomen

  Describe:

**Previous upper GI endoscopies**

- ☐ Time

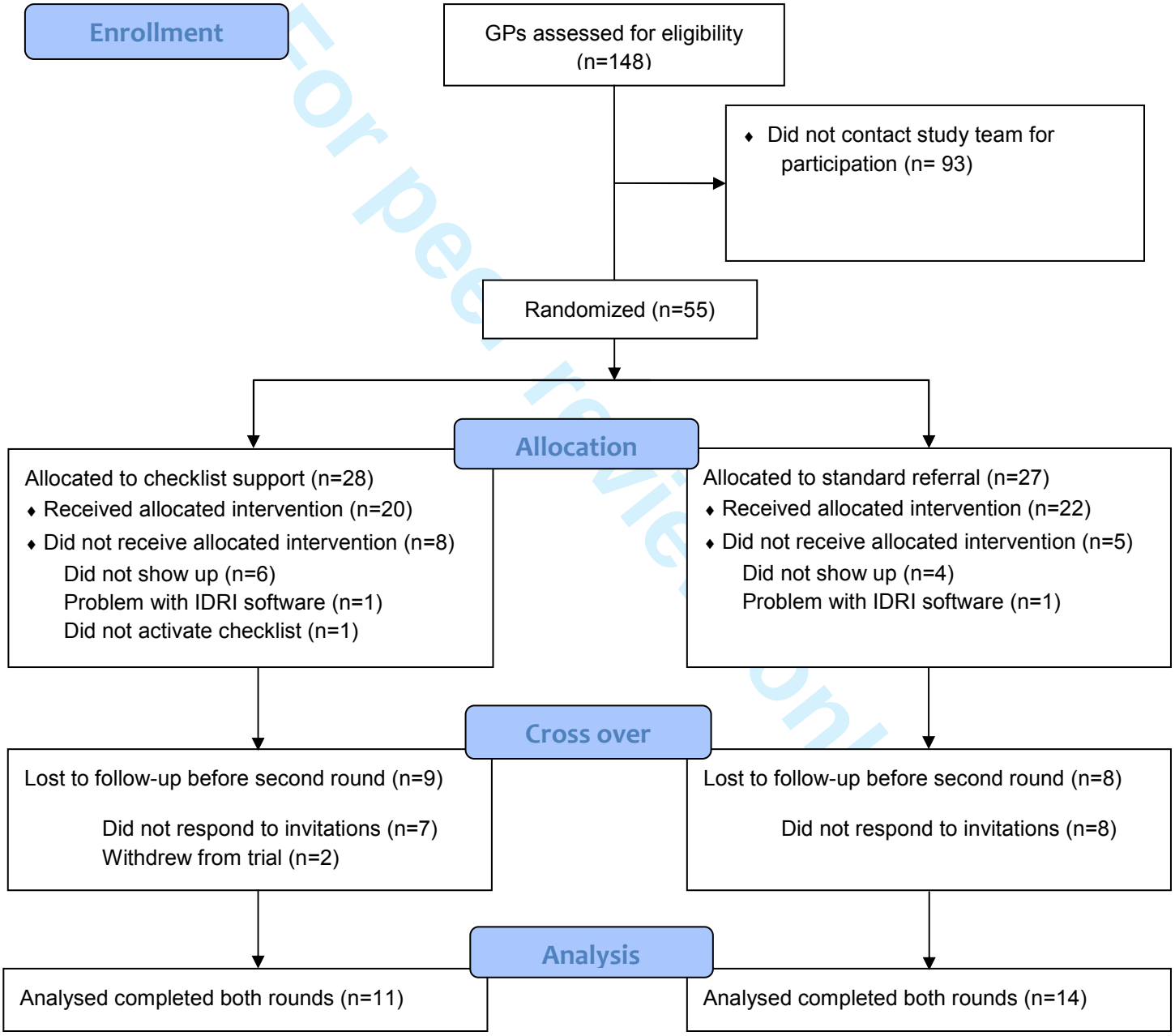
  Describe:

- ☐ Findings

  Describe:

CONSORT
TRANSPARENT REPORTING of TRIALS

## CONSORT 2010 Flow Diagram



# CONSORT 2010 checklist of information to include when reporting a randomised trial*

| Section/Topic | Item No | Checklist item | Reported on page No |
|---|---|---|---|
| **Title and abstract** | | | |
| | 1a | Identification as a randomised trial in the title | 1 |
| | 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | 2 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale | 4 |
| | 2b | Specific objectives or hypotheses | 4,5 |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | 5 |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | NA |
| Participants | 4a | Eligibility criteria for participants | 5 |
| | 4b | Settings and locations where the data were collected | 5 |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 5,6,7 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 8 |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | NA |
| Sample size | 7a | How sample size was determined | 9 |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | NA |
| Randomisation: | | | |
| Sequence generation | 8a | Method used to generate the random allocation sequence | 5 |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | 5 |
| Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | 5 |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | 5 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those | NA |

| | | | |
|---|---|---|---|
| | | assessing outcomes) and how | |
| | 11b | If relevant, description of the similarity of interventions | NA |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | 9 |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 9 |
| **Results** | | | |
| Participant flow (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome | Appendix flow chart. |
| | 13b | For each group, losses and exclusions after randomisation, together with reasons | Appendix flow chart. |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up | 10 |
| | 14b | Why the trial ended or was stopped | 10 |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | Table 1 |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | NA, cross over |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | 11-12 |
| | 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | Table 3 |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | NA |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | NA |
| **Discussion** | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 14,15 |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | 13,15 |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | 13,14 |
| **Other information** | | | |
| Registration | 23 | Registration number and name of trial registry | NA |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | NA |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | 16 |

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.