PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study
AUTHORS	Dahlgren, Cecilia; Geary, Lukas; Hasselström, Jan; Rehnberg, Clas; Schenck-Gustafsson, Karin; Wändell, Per; von Euler, Mia

VERSION 1 - REVIEW

| REVIEWER | John Edwards Research Institute for Primary Care and Health Sciences Keele University Keele Staffordshire ST5 5BG UK

JJE provides primary medical care under a General Medical Services contract and has been an invited speaker to the EULAR Congress on primary care quality indicators for osteoarthritis. |
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| REVIEW RETURNED | 18-Jan-2017 |

| GENERAL COMMENTS | Thank you very much for the opportunity to read this manuscript. I share the view that the making and recording of a correct diagnosis is important to consider as a possible quality indicator in primary care.

General point
If possible, it would be helpful to have sight of a study protocol? Is there a completed STROBE checklist as it seemed not to have been included in the manuscript?
"Detection of diagnosis in primary care" might more precisely be specified as "diagnosis recorded in the primary care health records." Can I check that it was as stated the inclusion of a relevant diagnosis in the record, rather than a consultation regarding the relevant diagnosis that was required?

Methods
Please can you elaborate on the reasons for excluding patients who had received a discharge diagnosis more than once during their index year rather than stratifying by one or more-than-one event? Is it possible to define just how common is it for hospitals to retain prescribing responsibility for up to a year after an index event? Additionally, the use of two filled prescriptions in the second year after the index event (so presumably in the first year of GP |
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responsibility for prescribing) would benefit from clarification. If each period covers only short period, the clinical benefit of two prescriptions may be only marginally better than that from one, so defining how long a period of treatment this cover would cover would help. I assume this definition was set before the analysis but the rationale for its use should be explained.

Statistical analysis

A design/analysis issue needs some clarification: exposure has been defined as "receiving a primary care diagnosis…during the two years following the index year". Outcome is defined as medication adherence in the second of these years. As written, I am not completely reassured that outcomes as measured (potentially occurring at the start of the second year after the index year) cannot predate exposure as measured (potentially recorded at the end of the second year after the exposure year) and would be grateful for your comment on this.

You highlight private specialists as a potential confounding factor. I wondered to what extent clustering of patients within providers may have affected the assessment of outcomes in general. It may be helpful to either include adjustment for clustering or at least undertake a sensitivity analysis to determine if this would have affected the results.

Discussion

I didn't quite follow the comment that selecting a diagnosis cannot have an effect on drug prescription. Although the act of recording a diagnosis may come at the end of a consultation and follow after a prescription, this is not always the case (at least in the UK) and furthermore the diagnosis may have been made even if not recorded (and in fact one would hope that a physician has made a working diagnosis before deciding on the treatment plan). It may be that this comment refers to prompt systems, in which case some expansion of the text would help.

If the requirement about diagnosis "detection" implies a consultation, could it be that the association between a diagnosis and medication adherence as defined is due to a common third factor, such as a recall system potentially instigated by an earlier code entry (such as within the index year), rather than it being the presence of a diagnostic code per se that is the cause of the increased adherence?

Ideally there should be some brief discussion about additional confounders that could explain the results that were not (or were only partly) accounted for in the model.

A comment about the clinical benefit expected from the level of medication adherence measured could usefully be included.

Consideration of generalisability to other healthcare jurisdictions should be included.

REVIEWER	Gary Abel University of Exeter Medical School, UK
REVIEW RETURNED	27-Jan-2017

| GENERAL COMMENTS | This paper presents an analysis looking at the association between a recording of TIA, stroke or acute coronary syndrome in primary care records following a discharge from hospital with one of these diagnosis and dispensation of recommended medications. Whilst the analysis within the paper is reasonably sound I am left very uncomfortable with the framing of the paper in terms of assessing a potential quality indicator as well as use of the term "detection of |

diagnosis".

The title of the paper is "Is "Detection of Diagnosis" a Useful Quality Indicator in Primary Care? - A Registry Based Prospective Cohort Study". This would suggest that the paper is going to consider the usefulness of "Detection of Diagnosis" as a quality indicator, whereas in fact it does no such thing. This paper simply looks at the predictive validity of the measure. This is only one aspect of validity and as the authors point out in the discussion section "Implications for Policy", validity is only one requirement of a serviceable quality indicator. Rather frustratingly the authors point out the requirements without then discussing how they have contributed to this. I have no issue with the authors discussing the potential use of "Detection of Diagnosis" as a quality indicator and what they have done to start to establish its suitability, however to frame the whole paper around this question seems rather disingenuous. I think the study stands on its own simply asking the question as to whether a recorded diagnosis in primary care is associated with dispensation of recommended medications. I recommend that title be changed along with alterations to the introduction and conclusions to change the framing of the paper.

The term "Detection of Diagnosis" is used to mean a recording of a related diagnosis in primary care records in the two years following hospital discharge with one of the diagnoses of interest. This does not tell us whether the hospital diagnosis has been detected or not. It may be that the primary care physician is well aware of the diagnosis, but not formally recorded it. It may also be that a recorded diagnosis in primary care records relates to a secondary event which may not have been recorded in hospital records. A study by Payne et al (A retrospective cohort study assessing patient characteristics and the incidence of cardiovascular disease using linked routine primary and secondary care data, BMJOpen 2012) showed that apparent incidence of cardiovascular disease was lower when using only hospital records that when using combined hospital and primary care records. This indicates that a number of events will be missed when using hospital only records and that the exclusion of people with multiple hospital discharges will not exclude these cases. I think it would be much better to use a term such as "recorded diagnosis in primary care". Of course it may be that "Detection of Diagnosis" is an established term. However, I am not aware of this term being used elsewhere, and if it is references should be given.

Similarly I have some concerns over the use of the term "medication adherence". In the methods sections the authors do point out that dispensation is a marker of adherence, but their analyses use dispensation as an outcome and so it should be labelled as such in the results. These results may then be interpreted in terms of adherence, but the results should relate to what is actually measured.

Technical points

There is no reason given for the stratification of analyses by gender. Potentially this may lead to loss of power and may be why fewer significant effects are seen for antihypertensives.

As these data are being proposed as a quality indicator one would hope that there is clustering of results by primary care organisation of physician. However, the analysis does not allow for this,

potentially giving rise to confidence intervals which are too narrow. Some adjustment should be made, however, not with a random effect as this will lead to within cluster comparisons and potentially adjust away the association of interest.

Details are not given as to how the age adjustment was made (linear term, categorical etc.)

Interpretation of results is only done on the basis of their significance rather than a discussion of effect sizes.

No numerical results are given in the abstract.

No mention is made of the fact that antihypertensives are less common in women with a recorded TIA than women where it is not recorded. Given this result is opposite to all others I would consider it worthy of mention.

Whilst not in this context, the paper mentioned above by Payne et al and another by Herrett et al (Completeness and diagnostic validity of recording acute myocardial infarction events in primary care, hospital care, disease registry, and national mortality records: cohort study, BMJ 2013) have both looked at the difference between hospital and primary care coding of diagnoses and should be cited.

The review form asks about the STROBE checklist. This does not seem to have been supplied, however, having submitted to BMJ Open myself I would be surprised if it has not been completed, just not made available with the submission.

REVIEWER	Kees van Boven Department of Primary and Community Care Radboud University Nijmegen, The Netherlands
REVIEW RETURNED	29-Jan-2017

GENERAL COMMENTS	Ad 2 and 9: In my opinion you could say that following guidelines is a quality indicator but the research is about if the detection of diagnosis could serve as indicator for the adharence to guidelines. Striking is the low percentage of detected diagnoses (for the whole group less than 40%). Mentioning this percentage in the abstract is advisable. I miss also more outcome data in the abstract (the Odds) Policy implications:Indeed the detection of a diagnosis could serve as an indicator of measuring the quality of information exchange between hospital and primary care.

REVIEWER	Marieke C Visser VU medical centre, Amsterdam, the Netherlands
REVIEW RETURNED	05-Feb-2017

GENERAL COMMENTS	The authors aim to improve compliance after hospital discharge. This is an important topic. Aspects to be considered is transferral of information, clear protocols for the primary health care physician on what to prescribe and how to follow-up, and patient specific aspects such as understanding the indication of medication, adverse effect,

	discipline to get a prescription and to take the medication. Cost aspects may be involved, but apparently not in Sweden. Improving compliance may lead to better outcome, this was not investigated in the study. It was illustrated however, that if the primary physician had not registered a diagnosis, compliance was worse.
	Assuming better compliance leads to better outcome the use of detection of diagnosis as indicator may be useful. It would be interesting to do a pilot study first to see if compliance does improve and leads to better outcome.
	What the paper also shows that for some diagnoses, such as TIA the detection rate was incredibly low (15 en 16%). It would be useful to comment on this a bit more.
	Even though the GPs may not be held fully responsible for not detecting a diagnosis (transferral of information at discharge, patient not showing up, other patient characteristics) it is imaginable that establishing this indicator may lead to better detection and compliance in the whole chain.
	The paper is methodologically sound and has a clear and important message.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: John Edwards
Institution and Country: Research Institute for Primary Care and Health Sciences, Keele University, UK Competing Interests: JJE provides primary medical care under a General Medical Services contract and has been an invited speaker to the EULAR Congress on primary care quality indicators for osteoarthritis.

Thank you very much for the opportunity to read this manuscript. I share the view that the making and recording of a correct diagnosis is important to consider as a possible quality indicator in primary care.

Thank you for your valuable comments! As a result we have made significant improvements to our manuscript.

General point
If possible, it would be helpful to have sight of a study protocol? Is there a completed STROBE checklist as it seemed not to have been included in the manuscript?

We will be happy to provide you with our STROBE checklist. The checklist is attached as a supplementary file (appendix 5) in our revised submission. We have updated the STROBE checklist since the page numbers in the original STROBE were no longer applicable due to revisions, including the addition of a new appendix (subgroup analysis), changes to table 3 etc. The original STROBE checklist and manuscript can be provided upon request.

"Detection of diagnosis in primary care" might more precisely be specified as "diagnosis recorded in the primary care health records." Can I check that it was as stated the inclusion of a relevant diagnosis in the record, rather than a consultation regarding the relevant diagnosis that was required?

Thank you for this comment. We have changed the term "detected diagnosis" to "recorded diagnosis" in the entire manuscript. As a consequence, we have changed the title to "Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study".

The requirements for inclusion were indeed, as you have pointed out in your question, the inclusion of a relevant diagnosis in the record. As this is a registry study we have no way of determining if the recorded diagnosis was the main focus of the consultation in question or not.

Methods
Please can you elaborate on the reasons for excluding patients who had received a discharge diagnosis more than once during their index year rather than stratifying by one or more-than-one event?

This is an important question. The main objective of our study was to ascertain if there is any association between primary care physicians recording a diagnosis related to a hospital discharge diagnosis and dispensation of secondary preventive medication. We had several reasons for excluding patients with multiple diagnoses. We had the issue of patients with both an ischemic and a hemorrhagic event during the study period. In this case the interpretation of results would have been difficult considering the different recommendation regarding antithrombotics. Also patients discharged with the same diagnosis multiple times during the study period (e.g. ischemic stroke during the index year and the year after) were excluded since, in those cases, it would have been difficult to determine if a hospital or a primary care center was in charge of the patients' long term care during the study.

You do however bring up a good point that one option would have been to stratify by one or more-than-one event in the ischemic group of diagnoses (myocardial infarction, ischemic stroke, TIA). In response to your comment, we have analyzed the excluded patients further in a sensitivity analysis which we will supply in a new appendix 2. This analysis showed results similar to the main analysis. Patients in the strata with multiple events had a recorded diagnosis in primary care to a slightly higher extent than those with only one event. In 18 out of 22 groups, the results point in the same direction as in the main analysis, that recorded patients are dispensed two medications to a higher extent than not recorded patients in most groups. When adjusting for confounders, the confidence intervals are wider for the strata with multiple events because of the lower number of included observations. As a consequence, the differences between the recorded and not recorded group are statistically significant to a lesser extent than in the main analysis.

We have also added the following text to the "Study design and participants" section:

"Patients receiving different pre-specified discharge diagnoses during the study period or the same discharge diagnoses during more than one year were excluded from the study ("multiple diagnoses" in Figure 1). By excluding patients with more than one of the diagnoses (e.g. ACS and hemorrhagic stroke) we were able to be more certain of which medications were recommended as secondary prevention for each patient. Patients discharged with the same diagnosis multiple times during the study period (e.g. ischemic stroke during the index year and the year after) were excluded since, in those cases, it would have been difficult to determine if a hospital or a primary care center was in charge of the patients' long term care during the study. As a sensitivity analysis we have followed the excluded patients with multiple diagnoses in the same way as the included patients. These results are presented in appendix 2."

Is it possible to define just how common is it for hospitals to retain prescribing responsibility for up to a year after an index event?

Unfortunately we do not have access to this data. From our clinical experience (two of the authors work in hospitals in Stockholm County and one works in a primary care center) prescribing practice varies from hospital to hospital and also within hospitals. Sometimes a patient may be discharged with prescriptions that will last for a full year, sometimes not. The longest period of time that a hospital

doctor can prescribe for however is one year.

Additionally, the use of two filled prescriptions in the second year after the index event (so presumably in the first year of GP responsibility for prescribing) would benefit from clarification. If each period covers only short period, the clinical benefit of two prescriptions may be only marginally better than that from one, so defining how long a period of treatment this cover would cover would help. I assume this definition was set before the analysis but the rationale for its use should be explained.

Thank you this question. When renewing prescriptions for chronic conditions the routine for primary care doctors in Sweden is to provide prescription that will last for one year. The routine is also that one individual dispensation will last for three months (so a one year prescription will mean four refills for a patient). This means that if a patient is dispensed a certain medication twice in one year they are expected to have in their possession enough of that medication to cover at least 180 days of the year in question. We chose two and not one dispensation as two dispensations more strongly implies use of the medication. There are many ways to study medication adherence and we do not, as yet, have a gold standard for doing so.

In response to your comment we have added the following text in the section "Medication adherence and dispensation":

"In Sweden, every filled prescription for chronic conditions will last for three months and thus two dispensations in one year will last for 180 days. We chose two and not one dispensation as two dispensations more strongly implies use of the medication."

Statistical analysis
A design/analysis issue needs some clarification: exposure has been defined as "receiving a primary care diagnosis.during the two years following the index year". Outcome is defined as medication adherence in the second of these years. As written, I am not completely reassured that outcomes as measured (potentially occurring at the start of the second year after the index year) cannot predate exposure as measured (potentially recorded at the end of the second year after the exposure year) and would be grateful for your comment on this.

You make a valid point. As you have correctly stated some patients may have their prescriptions filled in January of year 3 and again in April year 3 (one prescription lasts three months, see comment above). They may then receive a registered primary care diagnosis in April to December year 3. The problem of outcome predating exposure is thus an important issue. To address your comment we have decided to modify our model. The dispensation period has been pushed forward one year, becoming year 4. In our new model, if the index year is 2011 (year 1), the recording period (previously "detection period") will be 2012-13 (year 2-3) and the dispensation period will be 2014 (year 4). With this modification we no longer run the risk of outcome predating the exposure. We have analyzed our data again using our new model and all results, tables and figures have been updated. There have not been any significant changes to our results from modifying the model. We have revised figure 2 and included it in our re-submitted manuscript.

You highlight private specialists as a potential confounding factor. I wondered to what extent clustering of patients within providers may have affected the assessment of outcomes in general. It may be helpful to either include adjustment for clustering or at least undertake a sensitivity analysis to determine if this would have affected the results.

Again, you bring up an important point. We agree that it is important to adjust for clustering. As a result of your comment we have made changes to the manuscript.

In the "Potential confounders" section we have added the following paragraph:

"Clustering of results by providers may also be a confounder. Some providers may be better than others at prescribing recommended medications and there is most likely also a provider effect in the likelihood of recording a diagnosis."

We have performed further analysis, including "clustering within providers" as a variable that has been adjusted for. In the "Statistical analysis" section we have added the following (changes in red):

"Adjustments were made for age (as a continuous variable), index year, for health care consumption in the form of physician visits to private specialists that may function as a substitute to some patients' primary care provider, and for clustering within providers."

As a consequence we have updated our table 3 to include three models. Model 1 is the unadjusted model. Model 2 is the original adjusted model and model 3 also includes clustering within providers as a variable. We have revised table 3 and included it in our re-submitted manuscript.

Discussion
I didn't quite follow the comment that selecting a diagnosis cannot have an effect on drug prescription. Although the act of recording a diagnosis may come at the end of a consultation and follow after a prescription, this is not always the case (at least in the UK) and furthermore the diagnosis may have been made even if not recorded (and in fact one would hope that a physician has made a working diagnosis before deciding on the treatment plan). It may be that this comment refers to prompt systems, in which case some expansion of the text would help.

The section you are referring to was an attempt at discussing the temporality of prescription (or decision to prescribe) which often happens during the consultation, and the actual computerized recording, which in Sweden happens afterwards. Of course, in most cases the primary care physician will have made the diagnosis during the consultation. We agree that this section does not add much and may be somewhat confusing to readers and as a result of your comment we have decided to remove the following text:

"A diagnosis is chosen by the primary care physician after a patient visit has been completed, when potential medication prescriptions have already been communicated with the patient. The act of selecting a diagnosis cannot therefore, in itself, have any effect on a doctor choosing to prescribe a certain drug as they are not temporally related."

If the requirement about diagnosis "detection" implies a consultation, could it be that the association between a diagnosis and medication adherence as defined is due to a common third factor, such as a recall system potentially instigated by an earlier code entry (such as within the index year), rather than it being the presence of a diagnostic code per se that is the cause of the increased adherence?

In the Stockholm health care system primary care units are obliged to have a system for recalling patients. The way this is carried out however is up to each unit. One of the problems, and a cause for this study, is that recall systems as such are not always used. In some computer systems previous and chronic diagnoses are visible, in others you have to search the system actively. This may limit the generalizability. In response to your comment we added the following text highlighting this issue in the discussion, section "Generalizability":

"The generalizability is also limited to the record system and possible incentive structures used to stimulate recording of diagnoses as well as recall systems, the use of chronic diagnoses, and such factors. Different health care systems are organized differently. In systems where the diagnosis dictates which medications are subsidized, recording of a diagnosis may have a different impact and would need to be interpreted in light of this. If recording a diagnosis were to be used as a quality indicator it would need to be used with caution and adapted to the health care system in question."

Ideally there should be some brief discussion about additional confounders that could explain the results that were not (or were only partly) accounted for in the model.

In the new version of the manuscript we discuss the several different electronic journal systems in use in Stockholm County and the potential for confounding. The following text has been added to the discussion, section "Potential explanations":

"There are several different electronic medical record systems used by primary care centers in Stockholm County. Some of them share systems with the hospitals enabling electronic transfer of information within the system. In these cases the primary care physician often has electronic access to detailed information on a patient's medical history including discharge medication. Theoretically this access could facilitate prescription, thus influencing dispensation. Other centers need to rely on old fashion mailing of patient information and referral notes. However, even those care givers who share the same electronic medical record system are not automatically able to read another care giver's information as informed consent from the patient is needed if a referral note has not been sent. Our registries do not allow us to know which centers use which electronic medical record systems. Thus we have not been able to determine if use of certain systems increases or decreases the likelihood of recording of a diagnosis. This could be a confounding factor."

Also we have added "clustering within providers" as a potential confounder (earlier comment).

A comment about the clinical benefit expected from the level of medication adherence measured could usefully be included.

Thank you for this relevant comment. Previous studies have shown clinical benefit related to better adherence. To address your comment we have added the following to the "Strengths and limitations" section:

"The absolute clinical benefits of our results are difficult to approximate in the present study since we have only studied dispensation of recommended secondary preventive medication and not actual clinical outcomes. Improved adherence to recommendations may be seen as a surrogate marker for clinical benefit since the clinical benefits of good adherence to medical therapy in cardiovascular conditions has been shown in multiple studies.[30-36] Further study is needed to determine if recording of diagnosis is associated with any improvements in patient outcomes such as mortality,

recurrence of disease etc."

The newly added references cited are:

30. Burke JP, Sander S, Shah H, Zarotsky V, Henk H. Impact of persistence with antiplatelet therapy on recurrent ischemic stroke and predictors of nonpersistence among ischemic stroke survivors. Curr. Med. Res. Opin. 2010;26(5):1023-30 doi: 10.1185/03007991003670563[published Online First: Epub Date]|.

31. Chen PS, Cheng CL, Kao Yang YH, Li YH. Statin Adherence After Ischemic Stroke or Transient Ischemic Attack Is Associated With Clinical Outcome. Circ. J. 2016;80(3):731-7 doi: 10.1253/circj.CJ-15-0753[published Online First: Epub Date]|.

32. Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. Eur. Heart J. 2013;34(38):2940-8 doi: 10.1093/eurheartj/eht295[published Online First: Epub Date]|.

33. Colivicchi F, Bassi A, Santini M, Caltagirone C. Discontinuation of statin therapy and clinical outcome after ischemic stroke. Stroke 2007;38(10):2652-7 doi: 10.1161/strokeaha.107.487017[published Online First: Epub Date]|.

34. Ho PM, Spertus JA, Masoudi FA, et al. Impact of medication therapy discontinuation on mortality after myocardial infarction. Arch. Intern. Med. 2006;166(17):1842-7 doi: 10.1001/archinte.166.17.1842[published Online First: Epub Date]|.

35. Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. JAMA 2007;297(2):177-86 doi: 10.1001/jama.297.2.177[published Online First: Epub Date]|.

36. Wei L, Wang J, Thompson P, Wong S, Struthers AD, MacDonald TM. Adherence to statin treatment and readmission of patients after myocardial infarction: a six year follow up study. Heart 2002;88(3):229-33.

Consideration of generalisability to other healthcare jurisdictions should be included.

We have added the following text in the section "Generalizability" (changes in red):

"In order to utilize recording of a diagnosis in a diverse primary care population with a wide range of diagnoses, many of which are recorded in primary care only, the model used for recording of diagnosis would have to be altered and further studied. The generalizability is also limited to the record system and possible incentive structures used to stimulate recording of diagnoses as well as recall systems, the use of chronic diagnoses and such factors. Different health care systems are organized differently. In systems where the diagnosis dictates which medications are subsidized, recording of a diagnosis may have a different impact and would need to be interpreted in light of this. If recording a diagnosis were to be used as a quality indicator it would need to be used with caution and adapted to the health care system in question.

Reviewer: 2
Reviewer Name: Gary Abel
Institution and Country: University of Exeter Medical School, UK Competing Interests: None declared

This paper presents an analysis looking at the association between a recording of TIA, stroke or acute coronary syndrome in primary care records following a discharge from hospital with one of these diagnosis and dispensation of recommended medications. Whilst the analysis within the paper is reasonably sound I am left very uncomfortable with the framing of the paper in terms of assessing a potential quality indicator as well as use of the term "detection of diagnosis".

The title of the paper is "Is "Detection of Diagnosis" a Useful Quality Indicator in Primary Care? - A Registry Based Prospective Cohort Study". This would suggest that the paper is going to consider the usefulness of "Detection of Diagnosis" as a quality indicator, whereas in fact it does no such thing. This paper simply looks at the predictive validity of the measure. This is only one aspect of validity and as the authors point out in the discussion section "Implications for Policy", validity is only one requirement of a serviceable quality indicator. Rather frustratingly the authors point out the requirements without then discussing how they have contributed to this. I have no issue with the authors discussing the potential use of "Detection of Diagnosis" as a quality indicator and what they have done to start to establish its suitability, however to frame the whole paper around this question seems rather disingenuous. I think the study stands on its own simply asking the question as to whether a recorded diagnosis in primary care is associated with dispensation of recommended medications. I recommend that title be changed along with alterations to the introduction and conclusions to change the framing of the paper.

We agree with your comment. We have made significant revisions to our manuscript. Several sections have been changed including the introduction and the discussion as well as the abstract. The focus of the paper has been changed to the association between recording a diagnosis and the dispensation of recommended medications as you suggest. Also, the title has been changed to "Recording a Diagnosis of Stroke, TIA, or Myocardial Infarction in Primary Health Care and the Association with Dispensation of Secondary Preventive Medication – a Registry Based Prospective Cohort Study" from the previous "Is "Detection of Diagnosis" a Useful Quality Indicator in Primary Care? - A Registry Based Prospective Cohort Study". We have decided to change the term "detection of diagnosis" to "recording a diagnosis" for better clarity.
In response to your comment regarding the use of "recording a diagnosis" as a quality indicator we have made significant changes to the introduction, putting less emphasis on the potential use of recording as a quality indicator. We do however discuss the potential use in the section "Policy implications" where the following text has been added (some of the text from the previous version has been retained):

"The results show that recording a diagnosis is associated with higher utilization of recommended medications. What does this mean for clinical practice? Could recording of a diagnosis be used as a quality indicator? We do not know of any other established quality indicators which target the lack of communication between hospitals and primary care. Previously published requirements for quality indicators are acceptability, feasibility, reliability, sensitivity to change, and validity.[23] Future research would need to confirm that these requirements are met in which case "recording a diagnosis" could potentially be used as an indicator of both physician adherence to recommended treatment, and the quality of the chain of care from hospital to primary care. Information about degree of recording of diagnosis at each primary health care center could also be useful from the health care center's perspective as it provides information about their patient population which could be used to improve the provided care."

The cited reference [23] is "Campbell SM, Braspenning J, Hutchinson A, Marshall MN. Research methods used in developing and applying quality indicators in primary care. BMJ 2003;326(7393):816-9 doi: 10.1136/bmj.326.7393.816[published Online First: Epub Date]|."

The term "Detection of Diagnosis" is used to mean a recording of a related diagnosis in primary care records in the two years following hospital discharge with one of the diagnoses of interest. This does not tell us whether the hospital diagnosis has been detected or not. It may be that the primary care physician is well aware of the diagnosis, but not formally recorded it. It may also be that a recorded diagnosis in primary care records relates to a secondary event which may not have been recorded in hospital records. A study by Payne et al (A retrospective cohort study assessing patient characteristics and the incidence of cardiovascular disease using linked routine primary and secondary care data, BMJOpen 2012) showed that apparent incidence of cardiovascular disease was lower when using only hospital records that when using combined hospital and primary care records. This indicates that a number of events will be missed when using hospital only records and that the exclusion of people with multiple hospital discharges will not exclude these cases.

Again, thank you for relevant input. To address your comment we have included "Payne et al" in our references section and added the following text in the "Strengths and limitations" section:

"Furthermore, we only included patients where there was an initial hospital diagnosis recorded since the main focus of our study was communication between hospitals and primary care. However it should be noted that in some cases a cardiovascular event may only be recorded in primary care and not in hospital.[28, 29] This means that we will not have included all patients with a stroke/TIA or acute coronary syndrome in the population during the study period."

The newly added references cited are:

28. Herrett E, Shah AD, Boggon R, et al. Completeness and diagnostic validity of recording acute myocardial infarction events in primary care, hospital care, disease registry, and national mortality records: cohort study. BMJ 2013;346:f2350 doi: 10.1136/bmj.f2350[published Online First: Epub Date]|.

29. Payne RA, Abel GA, Simpson CR. A retrospective cohort study assessing patient characteristics and the incidence of cardiovascular disease using linked routine primary and secondary care data. BMJ open 2012;2(2):e000723 doi: 10.1136/bmjopen-2011-000723[published Online First: Epub Date]|.

I think it would be much better to use a term such as "recorded diagnosis in primary care". Of course it may be that "Detection of Diagnosis" is an established term. However, I am not aware of this term being used elsewhere, and if it is references should be given.

Thank you for this valuable comment. We have changed the term "detection of diagnosis" to "recording a diagnosis" in the entire manuscript.

Similarly I have some concerns over the use of the term "medication adherence". In the methods sections the authors do point out that dispensation is a marker of adherence, but their analyses use dispensation as an outcome and so it should be labelled as such in the results. These results may then be interpreted in terms of adherence, but the results should relate to what is actually measured.

Thank you for making a good point. We have made revisions to the results section using the label

dispensation instead of adherence. We exemplify our changes by providing the legend for tables 2 and 3 in our original and revised version:

Original table 2 legend: "Absolute number and proportion of men and women adherent to medications by medication class, detection status, and diagnosis."

Revised table 2 legend: "Absolute number and proportion of men and women dispensed two prescriptions in the dispensation period, by medication class, recorded/not recorded status, and diagnosis."

Original table 3 legend: "Crude and adjusted odds ratios for medication adherence according to detection status by sex and diagnosis. Undetected patients are the reference group. OR >1 means detected patients are more adherent. Adjustments made for age, visit to private specialist, and index year."

Revised table 3 legend: "Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by sex and diagnosis. Not recorded patients are the reference group. OR >1 means recorded patients are more likely to have two dispensations in the dispensation period."

Technical points

There is no reason given for the stratification of analyses by gender. Potentially this may lead to loss of power and may be why fewer significant effects are seen for antihypertensives.

We believe stratifying by gender to be important. The reason to stratify by gender is that there may be important differences between men and women, either in the biology or in the society which will influence morbidity and mortality and other health parameters.

As these data are being proposed as a quality indicator one would hope that there is clustering of results by primary care organisation of physician. However, the analysis does not allow for this, potentially giving rise to confidence intervals which are too narrow. Some adjustment should be made, however, not with a random effect as this will lead to within cluster comparisons and potentially adjust away the association of interest.

Thank you for this most relevant comment. We agree that it is important to adjust for clustering. As a result of your comment we have made changes to the manuscript.

In the "Potential confounders" section we have added the following paragraph:

"Clustering of results by providers may also be a confounder. Some providers may be better than others at prescribing recommended medications and there is most likely also a provider effect in the likelihood of recording a diagnosis."

We have performed additional analysis, including "clustering within providers" as a variable that has been adjusted for. In the "Statistical analysis" section we have added the following (changes in red):

"Adjustments were made for age (as a continuous variable), index year, for health care consumption in the form of physician visits to private specialists that may function as a substitute to some patients'

primary care provider, and for clustering within providers."

As a consequence we have updated our table 3 to include three models. Model 1 is the unadjusted model. Model 2 is the original adjusted model and model 3 also includes clustering within providers as a variable. We have revised table 3 and included it in our re-submitted manuscript.

Also in the "Strengths and limitations" section, we have added the following text:
"In table 3 when results are corrected for clustering within providers (model 3), the association between recorded primary care diagnosis and dispensed medications is strengthened. However, as some diagnostic groups are small (i.e. hemorrhagic stroke) some confidence intervals become wide and these results must be interpreted with caution."

Details are not given as to how the age adjustment was made (linear term, categorical etc.)

To clarify we have added the following text in the "Statistical analysis" section (changes in red):

"Adjustments were made for age (as a continuous variable)…"

Interpretation of results is only done on the basis of their significance rather than a discussion of effect sizes.

We have attempted to address this by including data from table 2 in the abstract. The results section in the abstract has been significantly revised. Please see comment below concerning abstract.

No numerical results are given in the abstract.

We agree that more numerical results are needed in the abstract. As a result we have made the following changes:

Original results section in abstract: "With the exception for antihypertensives, detection of diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups."

Revised results section in abstract: "Recording a diagnosis was associated with higher utilization of recommended medications with the exception of antihypertensives in men and women with TIA/ischemic stroke and women with hemorrhagic stroke.
Dispensation of antithrombotics was high overall, 80-90% in patients without a recorded diagnosis and 90-94% for those with a diagnosis. Statins were dispensed less, 46-59% of women and 57-77% of men without and 56-71% of women and 68-83% of men, respectively, with a recorded diagnosis of ischemic stroke/TIA/ACS.
The difference between the groups with and without a recorded diagnosis remained after adjusting for age, index year, visit to private practitioners and clustering within providers. The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16%)."

No mention is made of the fact that antihypertensives are less common in women with a recorded TIA than women where it is not recorded. Given this result is opposite to all others I would consider it worthy of mention.

We agree that it is a result worthy if mention. We have added the following text to the results section:

"In contrast to the other medications and diagnoses, recorded women with TIA were dispensed less

antihypertensives (64%) than those not recorded (70%), a difference which remained significant after adjusting for confounders."

Whilst not in this context, the paper mentioned above by Payne et al and another by Herrett et al (Completeness and diagnostic validity of recording acute myocardial infarction events in primary care, hospital care, disease registry, and national mortality records: cohort study, BMJ 2013) have both looked at the difference between hospital and primary care coding of diagnoses and should be cited.

Thank you, we have also found these references to be important and have included them in our revised manuscript. Please see our reply to your previous comment.

The review form asks about the STROBE checklist. This does not seem to have been supplied, however, having submitted to BMJ Open myself I would be surprised if it has not been completed, just not made available with the submission.

Thank you for all your valuable comments. As a result we believe that we have made significant improvements to our manuscript! We will be happy to provide you with our STROBE checklist, which will be attached as a supplementary file (appendix 5) in our revised submission.

Reviewer: 3
Reviewer Name: Kees van Boven
Institution and Country: Department of Primary and Community Care Radboud University Nijmegen, The Netherlands Competing Interests: None declared

Ad 2 and 9: In my opinion you could say that following guidelines is a quality indicator but the research is about if the detection of diagnosis could serve as indicator for the dherence to guidelines. Striking is the low percentage of detected diagnoses (for the whole group less than 40%). Mentioning this percentage in the abstract is advisable.

Thank you for your comment. We agree that the low percentage is striking. We have changed the terminology from "detection of diagnosis" to "recording a diagnosis" as we believe it to be clearer and more easily grasped by readers. In response to your comment we have added the following text to our abstract:

"The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16%)."

I miss also more outcome data in the abstract (the Odds)

We agree that more outcome data in the abstract is a good suggestion. We have made the following changes:

Original results section in abstract: "With the exception for antihypertensives, detection of diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups."

Revised results section in abstract: "Recording a diagnosis was associated with higher utilization of

recommended medications with the exception of antihypertensives in men and women with TIA/ischemic stroke and women with hemorrhagic stroke.

Dispensation of antithrombotics was high overall, 80-90% in patients without a recorded diagnosis and 90-94% for those with a diagnosis. Statins were dispensed less, 46-59% of women and 57-77% of men without and 56-71% of women and 68-83% of men, respectively, with a recorded diagnosis of ischemic stroke/TIA/ACS.

The difference between the groups with and without a recorded diagnosis remained after adjusting for age, index year, visit to private practitioners and clustering within providers. The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16%)."

Policy implications: Indeed the detection of a diagnosis could serve as an indicator of measuring the quality of information exchange between hospital and primary care.

We appreciate your comment! We are also of this opinion but agree with one of the other reviewers that further study is needed and as such we have added the following text in the "Policy implications" section:

"The results show that recording a diagnosis is associated with higher utilization of recommended medications. What does this mean for clinical practice? Could recording of a diagnosis be used as a quality indicator? We do not know of any other established quality indicators which target the lack of communication between hospitals and primary care. Previously published requirements for quality indicators are acceptability, feasibility, reliability, sensitivity to change, and validity.[23] Future research would need to confirm that these requirements are met in which case "recording a diagnosis" could potentially be used as an indicator of both physician adherence to recommended treatment, and the quality of the chain of care from hospital to primary care. Information about degree of recording of diagnosis at each primary health care center could also be useful from the health care center's perspective as it provides information about their patient population which could be used to improve the provided care."

The cited reference [23] is "Campbell SM, Braspenning J, Hutchinson A, Marshall MN. Research methods used in developing and applying quality indicators in primary care. BMJ 2003;326(7393):816-9 doi: 10.1136/bmj.326.7393.816[published Online First: Epub Date]|."

Reviewer: 4
Reviewer Name: Marieke C Visser
Institution and Country: VU medical centre, Amsterdam, the Netherlands Competing Interests: none

The authors aim to improve compliance after hospital discharge. This is an important topic. Aspects to be considered is transferral of information, clear protocols for the primary health care physician on what to prescribe and how to follow-up, and patient specific aspects such as understanding the indication of medication, adverse effect, discipline to get a prescription and to take the medication. Cost aspects may be involved, but apparently not in Sweden.

Improving compliance may lead to better outcome, this was not investigated in the study. It was illustrated however, that if the primary physician had not registered a diagnosis, compliance was worse.

Assuming better compliance leads to better outcome the use of detection of diagnosis as indicator may be useful. It would be interesting to do a pilot study first to see if compliance does improve and leads to better outcome.

Thank you for your comment! Please note that we have changed the terminology from "detection of diagnosis" to "recording a diagnosis" as we believe it to be clearer and more easily grasped by readers. We have added the following text to the "Strengths and limitations" section which to some extent addresses your comment:

"The absolute clinical benefits of our results are difficult to approximate in the present study since we have only studied dispensation of recommended secondary preventive medication and not actual clinical outcomes. Improved adherence to recommendations may be seen as a surrogate marker for clinical benefit since the clinical benefits of good adherence to medical therapy in cardiovascular conditions has been shown in multiple studies.[30-36] Further study is needed to determine if recording of diagnosis is associated with any improvements in patient outcomes such as mortality, recurrence of disease etc."

The newly added references cited are:

30. Burke JP, Sander S, Shah H, Zarotsky V, Henk H. Impact of persistence with antiplatelet therapy on recurrent ischemic stroke and predictors of nonpersistence among ischemic stroke survivors. Curr. Med. Res. Opin. 2010;26(5):1023-30 doi: 10.1185/03007991003670563[published Online First: Epub Date]|.

31. Chen PS, Cheng CL, Kao Yang YH, Li YH. Statin Adherence After Ischemic Stroke or Transient Ischemic Attack Is Associated With Clinical Outcome. Circ. J. 2016;80(3):731-7 doi: 10.1253/circj.CJ-15-0753[published Online First: Epub Date]|.

32. Chowdhury R, Khan H, Heydon E, et al. Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences. Eur. Heart J. 2013;34(38):2940-8 doi: 10.1093/eurheartj/eht295[published Online First: Epub Date]|.

33. Colivicchi F, Bassi A, Santini M, Caltagirone C. Discontinuation of statin therapy and clinical outcome after ischemic stroke. Stroke 2007;38(10):2652-7 doi: 10.1161/strokeaha.107.487017[published Online First: Epub Date]|.

34. Ho PM, Spertus JA, Masoudi FA, et al. Impact of medication therapy discontinuation on mortality after myocardial infarction. Arch. Intern. Med. 2006;166(17):1842-7 doi: 10.1001/archinte.166.17.1842[published Online First: Epub Date]|.

35. Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. JAMA 2007;297(2):177-86 doi: 10.1001/jama.297.2.177[published Online First: Epub Date]|.

36. Wei L, Wang J, Thompson P, Wong S, Struthers AD, MacDonald TM. Adherence to statin treatment and readmission of patients after myocardial infarction: a six year follow up study. Heart 2002;88(3):229-33.

What the paper also shows that for some diagnoses, such as TIA the detection rate was incredibly low (15 en 16%). It would be useful to comment on this a bit more.

We agree that this is important to mention and we have added the following text to the "Key results" section:

"The rate of diagnosis recording spanned from 15-47% and was especially low in TIA (men 15%, women 16% recorded)."

The low rate of diagnosis recording in TIA has surprised us too and we are not certain why this is the case. Potentially the lack of symptoms contributes to the low rate of recording. We have added the following text in the "Potential explanations" section to address your comment:

"The strikingly low rate of recording of a diagnosis in TIA may partially be explained by the lack of remaining objective symptoms. Primary care physicians caring for a patient with chronic symptoms from a stroke will be reminded of the patient's previous disease and this may influence the likelihood of recording a stroke diagnosis. The same reminder is not provided when physicians see patients with a previous TIA in which case the diagnosis might not be recorded."

Even though the GPs may not be held fully responsible for not detecting a diagnosis (transferral of information at discharge, patient not showing up, other patient characteristics) it is imaginable that establishing this indicator may lead to better detection and compliance in the whole chain.

The paper is methodologically sound and has a clear and important message.

Thank you! We very much appreciate your comments!

VERSION 2 – REVIEW

REVIEWER	John Edwards Research Institute for Primary Care and Health Sciences Keele University Keele Staffordshire ST5 5BG UK JJE provides primary medical care under a General Medical Services contract and has been an invited speaker to the EULAR Congress on primary care quality indicators for osteoarthritis.
REVIEW RETURNED	29-Mar-2017

GENERAL COMMENTS	Thank you for your substantial further analytical and redrafting work. You have thoroughly addressed all of my original questions and concerns. I just have a couple of minor points that are, in my view, optional to consider. You highlight (p. 9, line 54) that Model 3 should be interpreted with caution due to a large number of providers. This may be a fair point but feels somewhat imbalanced as caution is also needed for the other two models due to the use of unadjusted OR in Model 1 and

	lack of adjustment for clustering in Model 2. As a minor point, I see that you offer as a potential explanation (p. 13, line 37) for low levels of TIA recording the lack of objective signs at follow up. How justifiable is this compared to the high levels of acute coronary syndrome recording, which may also lack objective signs at follow up?

REVIEWER	Gary Abel University of Exeter
REVIEW RETURNED	10-May-2017

GENERAL COMMENTS	For the most part the authors have addressed my comments and the paper is much improved. Below are a few remaining issues. Abstract The sentence starting "Statins were dispensed less" is complex and took me a few readings to work out what was being said – this could do with simplification. The conclusions still have a heavy bias toward the use as a quality indicator, and the simple addition of the word "Potentially" does not shift the focus. Given previous comments and changes made to the paper I feel this is still too dominant. Introduction The sentence "In this study we explore if "recording a diagnosis" could be a marker for good communication between hospital and primary care and thus improve utilization of recommended medications." Is inaccurate as this study does make any measurement of good communication. What they actually do is explore if recording a diagnosis has an impact on the utilisation of recommended medications assuming that this is mediated through good communication. Methods I was confused by the sentence "with the provider effect as a fixed effect to avoid controlling for the association of interest." Is this to imply that a random effect for provider would have controlled for the association of interest. Whilst I potentially agree I do not see how a fixed effect would not play the same role as a random effect. My recommendation of not using a random effect was potentially unclear – what I should have said was not using adjustment for cluster as a fixed or random effect, but rather to use something like a sandwich estimator which will give appropriate inference without adjusting for the confounding/mediating effect. Relatedly I would think that provide was a mediator rather than a confounder as it is likely to sit on the causal pathway and so the paragraph where confounding by provider is discussed should be rethought. The reasons given in the response to my comment about stratification by gender are good reasons to adjust for gender rather than to stratify. I stand by my original comments, but acknowledge that such stratification is common (and commonly leads to potentially misleading negative results).

VERSION 2 – AUTHOR RESPONSE

RESPONSE TO REVIEWERS' COMMENTS

Reviewers' Comments to Author:

Reviewer: 1
Reviewer Name: John Edwards
Institution and Country: Research Institute for Primary Care and Health Sciences, Keele University, UK
Competing Interests: JJE provides primary medical care under a General Medical Services contract and has been an invited speaker to the EULAR Congress on primary care quality indicators for osteoarthritis.

Thank you for your substantial further analytical and redrafting work. You have thoroughly addressed all of my original questions and concerns. I just have a couple of minor points that are, in my view, optional to consider.

To the reviewer:
Thank you for valuable comments, they have helped us make significant improvements. Please note that we have decided to include all appendices in one supplementary file, thus changing the names of the appendices to tables S1-S7 and figure S1.

You highlight (p. 9, line 54) that Model 3 should be interpreted with caution due to a large number of providers. This may be a fair point but feels somewhat imbalanced as caution is also needed for the other two models due to the use of unadjusted OR in Model 1 and lack of adjustment for clustering in Model 2.

Thank you for this comment. We have excluded model 3 from our analysis and we have chosen to adjust model 2 for clustering by using a "sandwich" variance estimator instead of adjusting for provider. The effect of using the sandwich estimator has a very small impact on the confidence intervals, which implies that clustering is not a big problem in our data.

As a minor point, I see that you offer as a potential explanation (p. 13, line 37) for low levels of TIA recording the lack of objective signs at follow up. How justifiable is this compared to the high levels of acute

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coronary syndrome recording, which may also lack
objective signs at follow up?
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Thank you for making a good point with which we agree. The low rate of recording of TIA is, as you point out, likely multifactorial and not only explained by the lack of symptoms. It is possible that the public has better knowledge of what a "heart attack" is than what a "TIA" is. This prior knowledge may lead to acute coronary syndrome patients being more aware of what disease they have had making them more likely to remind the primary care provider. This "patient reminder" effect may be less pronounced in TIA. Also there may be other factors at play related to differences in follow up between TIA and acute coronary syndrome leading to differences in how information is transferred between providers etc. However this is only speculation and we do not know of any references in the literature which could clarify. As such we have changed the paragraph you mentioned to better reflect that more research is needed and that the reasons for the low rate of recording are uncertain (changes in red).

The strikingly low rate of recording of a diagnosis in TIA may partially be explained by the lack of remaining objective symptoms. Primary care physicians caring for a patient with chronic symptoms from a stroke will be reminded of the patient's previous disease and this may influence the likelihood of recording a stroke diagnosis. The same reminder is not provided when physicians see patients with a previous TIA in which case the diagnosis might not be recorded. However the low rate of recording in TIA needs further research as the causes are, is in all likelihood, multifactorial. Acute coronary syndrome patients also lack symptoms at follow up in many cases, and still those patients are recorded to a high degree.

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Reviewer: 2
Reviewer Name: Gary Abel
Institution and Country: University of Exeter, UK
Competing Interests: None declared
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For the most part the authors have addressed my comments
and the paper is much improved. Below are a few remaining
issues.
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To the reviewer:
Thank you for valuable comments, they have helped us make significant improvements. Please note that we have decided to include all appendices in one supplementary file, thus changing the names of the appendices to tables S1-S7 and figure S1.

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Abstract
The sentence starting "Statins were dispensed less" is
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complex and took me a few readings to work out what was
being said – this could do with simplification.

Again, thank you for your comment. We agree that the sentence needs simplification.
Accordingly we have rewritten it (changes in red):

*Dispensation of antithrombotics was high overall, 80-90% in patients without a
recorded diagnosis and 90-94% for those with a diagnosis. Women with recorded
ischemic stroke/TIA/ACS (56-71%) were dispensed more statins than those with no
recorded diagnosis (46-59%). Similarly 68-83% of men with a recorded diagnosis
were dispensed statins (57-77% in men with no recorded diagnosis).*

The conclusions still have a heavy bias toward the use as
a quality indicator, and the simple addition of the word
"Potentially" does not shift the focus. Given previous
comments and changes made to the paper I feel this is
still too dominant.

We thank you for your comment. In response we have made the following changes to
the abstract and the "Policy implications" sections (changes in red):

Abstract
Conclusion: *Recording a diagnosis of TIA/stroke or acute coronary syndrome in
primary care was found to be associated with higher dispensation of recommended
secondary preventive medications. Further study is necessary in order to determine
the mechanisms underlying our results and to establish the utility of our findings.*

Policy implications
*The results show that recording a diagnosis is associated with higher utilization of
recommended medications. Diagnosis recording is potentially an indicator of
physician adherence to recommended treatment and a marker of an intact chain of
care from hospital to primary care. What does this mean for clinical practice? Could
recording of a diagnosis be used as a quality indicator? Previously published
requirements for quality indicators are acceptability, feasibility, reliability, sensitivity
to change, and validity.[23] Future research needs to confirm that these requirements
are met for "recording a diagnosis" before its utility as a quality indicator can be
considered. Information about degree of recording of diagnosis at each primary
health care center could also be useful from the health care center's perspective as it
provides information about their patient population which could be used to improve
the provided care.*

Introduction

The sentence "In this study we explore if "recording a diagnosis" could be a marker for good communication between hospital and primary care and thus improve utilization of recommended medications." Is inaccurate as this study does make any measurement of good communication. What they actually do is explore if recording a diagnosis has an impact on the utilisation of recommended medications assuming that this is mediated through good communication.

Once again we agree with your comment and have made the following changes (in red):

In this study, we explore if "recording a diagnosis" *has an impact on the utilization of recommended medications.* *In our study, if a primary care physician "records a diagnosis" it means that a patient discharged from hospital care to primary care is diagnosed with their hospital diagnosis, or a corresponding follow-up diagnosis, in primary care at some point. A diagnosis that is not being recorded in primary care could be an indication of lack of communication between the different health care providers which could affect the quality of the subsequent treatment. If there is an association between recording of diagnosis and utilization of recommended medications then "recording a diagnosis" could potentially be used as a quality indicator in primary care.*

Methods

I was confused by the sentence "with the provider effect as a fixed effect to avoid controlling for the association of interest." Is this to imply that a random effect for provider would have controlled for the association of interest. Whilst I potentially agree I do not see how a fixed effect would not play the same role as a random effect. My recommendation of not using a random effect was potentially unclear – what I should have said was not using adjustment for cluster as a fixed or random effect, but rather to use something like a sandwich estimator which will give appropriate inference without adjusting for the confounding/mediating effect. Relatedly I would think that provide was a mediator rather than a confounder as it is likely to sit on the causal pathway and so the paragraph where confounding by provider is discussed should be rethought.

The reasons given in the response to my comment about stratification by gender are good reasons to adjust for gender rather than to stratify. I stand by my original comments, but acknowledge that such stratification is common (and commonly leads to potentially misleading negative results).

Thank you for these comments. We have modified our model by adjusting for sex instead of stratifying (new table 3 below). We will however provide supplementary material which is stratified by sex (table S7 in our supplementary file). As a result of no longer stratifying by sex we have made changes to the results section to reflect our new table 3. The following paragraph has been <u>added</u>:

For antihypertensives, the adjusted results show that recorded patients with stroke and acute coronary syndrome were more likely to be dispensed two prescriptions. However, recorded patients with TIA were less likely to be dispensed antihypertensives than the not recorded group.

We have <u>removed</u> the following paragraph:

In contrast to the other medications and diagnoses, recorded women with TIA were dispensed less antihypertensives (64%) than those not recorded (70%), a difference which remained significant after adjusting for confounders.

Also we include a new sentence in the "Key results" section:

Recording a diagnosis was associated with higher utilization of recommended medications for all studied diagnosis groups, except for antihypertensives in TIA patients.

We have <u>revised</u> the following paragraph in the "Potential explanations" section (changes in red):

In contrast to the overall pattern, TIA patients with a recorded diagnosis were dispensed less antihypertensives than those with no recorded diagnosis.
A potential explanation for the varying associations between dispensation of antihypertensive therapy and recording of the different diagnoses could stem from the fact that treatment of hypertension is well established. As many patients with stroke/TIA and/or ischemic heart disease have established hypertension [21, 22] they would be treated regardless of other diagnoses. This is not the case for

antithrombotics and statins. Hypertension *is also a common condition with a high prevalence of treatment and this diagnosis may be chosen instead of a diagnosis of cardio/cerebrovascular disease. However, it should be noted that the proportion of recorded TIA patients is small and the data concerning this group should be interpreted with caution.*

To improve the goodness-of-fit of the adjusted models, we have also included age as a categorical variable instead of a continuous variable. The chosen age categories are: <51, 51-65, 66-75, and >75. We have clarified this in the text (changes in red):

Adjustments were made for age (age categories <51, 51-65, 66-75, >75), index year, for health care consumption in the form of physician visits to private specialists that may function as a substitute to some patients' primary care provider.

We have adjusted for clustering by basing standard errors on the "sandwich" variance estimator instead of adjusting for provider as a fixed effect. The effect of using the sandwich estimator has a very small impact on the confidence intervals, which implies that clustering is not a big problem in our data. The number of providers is relatively large, over 200, in comparison to the number of patients that are included in the data, which could be a potential explanation for the lack of a cluster effect. Also, in Stockholm, a majority of providers consist of several doctors who may work differently and thus there may be a variation within providers as well. We provide the updated table 3:

Table 3. Crude and adjusted odds ratios for being dispensed two prescriptions in the dispensation period according to recorded/not recorded status, by diagnosis. Not recorded patients are the reference group. Odds Ratios >1 mean recorded patients are more likely to have two dispensations in the dispensation period.

	Crude Odds Ratios (95% Confidence Intervals)	Adjusted Odds Ratios* (95% Confidence Intervals)
TIA		
Statins	1.55 (1.31-1.84)	1.53 (1.28-1.82)
Antithrombotics	2.33 (1.76-3.08)	2.33 (1.74-3.11)
Antihypertensives	0.83 (0.69-0.99)	0.80 (0.66-0.96)
Ischemic stroke		
Statins	1.59 (1.43-1.76)	1.58 (1.42-1.76)
Antithrombotics	1.78 (1.52-2.08)	1.92 (1.63-2.27)
Antihypertensives	1.05 (0.94-1.18)	1.16 (1.03-1.31)
Hemorrhagic stroke		
Antihypertensives	2.21 (1.57-3.12)	2.54 (1.72-3.76)
Acute coronary syndrome		
Statins	1.58 (1.42-1.75)	1.64 (1.47-1.83)
Antithrombotics	1.97 (1.68-2.32)	2.02 (1.72-2.38)

Antihypertensives	1.74 (1.47-2.07)	1.76 (1.48-2.10)
Beta-blockers	1.50 (1.34-1.68)	1.48 (1.32-1.66)

Adjustments made for age, sex, index year, and visits to private specialists. To adjust for clustering, standard errors are based on the "sandwich" variance estimator.

We have <u>removed</u> the following text in the "Potential confounders" section:

Clustering of results by providers may also be a confounder. Some providers may be better than others at prescribing recommended medications and there is most likely also a provider effect in the likelihood of recording a diagnosis.

We have <u>removed</u> the following text in the "Statistical analysis" section (removed text in red):

Adjustments were made for age (age categories <51, 51-65, 66-75, >75), index year, for health care consumption in the form of physician visits to private specialists that may function as a substitute to some patients' primary care provider, and for clustering within providers. To adjust for clustering within providers, a categorical variable for provider was included in the model with the provider effect as a fixed effect to avoid controlling for the association of interest. The results were stratified by sex.

We have <u>removed</u> the following text in the "Results" section:

Adjusting for clustering within primary health care providers with the provider effect as a fixed effect (model 3 in table 3) was found to strengthen the association between recorded primary care diagnosis and dispensed medications. However, model 3 should be interpreted with caution, especially for the smaller patients groups, since the provider variable contains a large number of categories.

We have <u>removed</u> the following text in the "Strenghts and limitations" section:

In table 3 when results are corrected for clustering within providers (model 3), the association between recorded primary care diagnosis and dispensed medications is strengthened. However, as some diagnostic groups are small (i.e. hemorrhagic stroke) some confidence intervals become wide and these results must be interpreted with caution.

We have <u>added</u> the following text in the abstract "Results" section (changes in red):

The difference between the groups with and without a recorded diagnosis remained after adjusting for age, sex, index year, and visits to private practitioners.

We have <u>added</u> the following text in the "Statistical analysis" section:

The patients in our dataset are grouped within different primary health care centers. This implies a risk that the data are cluster-correlated and that the estimated standard errors are not independent. In order to adjust for this, without adjusting for the provider effect, which could be a mediator in the casual pathway, we have based standard errors on the "sandwich" variance estimator.

We have <u>added</u> the following text in the "Results" section:

Adjusting for clustering with the "sandwich" variance estimator only marginally affected the confidence intervals, which implies that the data is not clustered to a high extent.

REVIEWER	Gary Abel
	University of Exeter Medical School
REVIEW RETURNED	15-Jun-2017

GENERAL COMMENTS	I am happy that the authors have responded to all outstanding comments. I would suggest the two words in the new text are changed for readability. My suggestion is to use the word "account" rather than "adjust" when talking about the use of the sandwich estimator as to avoid confusion with issues about confounding. In this case
	"In order to adjust for this, without adjusting for the provider effect, which could be a mediator in the casual pathway, we have based standard errors on the "sandwich" variance estimator"
	would become
	"In order to account for this, without adjusting for the provider effect, which could be a mediator in the casual pathway, we have based standard errors on the "sandwich" variance estimator"
	and
	"Adjusting for clustering with the "sandwich" variance estimator only marginally affected the confidence intervals, which implies that the data is not clustered to a high extent"
	would become
	"Accounting for clustering with the "sandwich" variance estimator only marginally affected the confidence intervals, which implies that the data is not clustered to a high extent"