PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Economic inequalities in burden of illness, diagnosis and treatment of five long-term conditions in England: panel study.
AUTHORS	Steel, Nicholas; Hardcastle, Antonia; Bachmann, Max; Richards, Suzanne; Mounce, Luke; Clark, Allan; Lang, Iain; Melzer, David; Campbell, John

VERSION 1 - REVIEW

REVIEWER	Gerry McCartney NHS Health Scotland Scotland
REVIEW RETURNED	16-May-2014

GENERAL COMMENTS	Thank you for the opportunity to review this paper. I think the paper should go forward for publication, but there are few amendments that I recommend to (hopefully) make it a bit clearer. In the abstract: 1. make it clear in the design section that you do not use the longitudinal nature of the data, and just use it as cross sectional data 2. in the outcomes measures section you say that you adjust for wealth. In fact, as I understand it, you stratify by wealth in most of your results. 3. In the results section it didn't make much sense to me to lump all the 5 conditions together. We would expect the inverse care law to operate differently for different conditions. You should also make clear whether you are talking about type I and/or type II diabetes. In the strengths and limitations section, you say that you look at 'the same population over time'. I think it would be more accurate to delete that, given that you can't use the longitudinal data as you note elsewhere. In the main text, you refer at times to cataract, diabetes and osteoarthritis (e.g. line 48) - I think you need to consistently say throughout the text that you only have proxies of these (e.g. self-reported pain and blindness). You do note these limitations elsewhere, but it needs explained throughout. In the methods, you need to make clear if the ELSA cohort is a proportionate sample or some other sampling method. I wasn't clear what you meant by 'slope order of inequality' and whether this differed from 'slope index of inequality'. In the results, it would be good to rephrase the sentence, "over half were women..." which is unclear.

	In figure 1, it would be useful to have a horizontal line at an OR of 1. You could also colour code burden, diagnosis and treatment across conditions to make reading easier. In the discussion, you make the point about longitudinal data - but you (understandably) couldn't use these. So, it isn't really an advantage of this study. You also make a big claim that this is the first study to look at illness burden, diagnosis and treatment. I don't know of a study that does, but it isn't evidenced here. You state that the lack of specificity in condition definition will not be important as it won't vary by wealth between conditions. I don't think this is necessarily true - there are many conditions that are strongly patterned by socioeconomic status whilst others are not. So, I think this should be taken out. I'm not sure if the Sen reference supports the claim that self report is the best measure of pain. All of that said (!), I think this is a very good and helpful paper and is worthy of publication.

REVIEWER	Peter Watson Medical Research Council Cognition and Brain Sciences Unit, UK
REVIEW RETURNED	26-Jun-2014

GENERAL COMMENTS	A few aspects of the analysis could be clarified. For example, how is the dichotomy of wealth derived from the quintiles and used in the logistic regressions? I suspect wealth is a binary predictor but slope order of inequality (a seemingly five rather than two level variable) is described as the independent variable in line 17 on page 6. The proportion and nature of missing values excluded from analyses (page lines 14-15) should be described and any implications discussed. One usually would fit an outcome group by medical condition interaction term to compare the odds ratios in Table 3 (page 9) and as discussed in the first two paragraphs of page 7 which is not done here. I also wonder about power issues with the statistical comparisons of the odds ratios in Table 3 given a consistent difference between odds ratios which nevertheless have overlapping confidence intervals particularly in the case of comparing angina illness burden with both medical diagnosis and treatment with the latter two odds ratios being smaller but still all have overlapping confidence intervals with that of illness burden possibly suggesting they are not statistically different. My main concern would be the overlapping confidence intervals of the odds ratios in Table 3 despite the point estimate odds ratios upon which these are based seemingly being a lot different. An interaction test would clarify if these odds ratios do really differ. I think the fact we are consistently seeing the same direction of differences suggest there may be power issues with the logistic analyses comparing odds ratios in Table 3 as well as in the acknowledged small sample size issues mentioned in lines 26-31 on page 7 but if there is no interaction between medical condition and outcome group (defined as whether a response is a illness burden or medical diagnosis or treatment) and no main effect of outcome

	group it is difficult to motivate individual odds ratio comparisons of each group at each medical condition as is done in this paper on page 7 and in Table 3 on page 9. In broad terms a mean of 1,000,000 may be greater than a mean of '1' but if one or both of these means are imprecisely estimated there is no evidence to suggest the means differ which is why we have to take the precision (standard errors) of odds ratios into account when comparing them which is done through applying a statistical test and obtaining a p-value usually using a test of an interaction or main effect. A series of logistic regressions have been carried out in this study to assess diagnoses on a range of medical conditions to the wealth or participants. A strength of this paper is that the odds ratios in Table 3 on page 9 consistently show a pattern whereby medical diagnosis and treatment have lower odds ratios than the illness burden although these may not always be statistically significantly different (see later) which given the consistency may suggest a lack of power or high variability within or between participants. I have a few queries on explaining exactly how the wealth dichotomy is used in these regressions to yield the odds ratios in Table 3 and also invite comments on how serious the deletion of missing values on the generalizability of the results and wonder if generalized linear mixed models might instead be used which can incorporate incomplete information and use participants with missing covariates. I also query a conclusion in lines 2-9 on page 7 which leads me to wonder if interaction terms involving medical diagnosis by outcome group (representing illness burden or medical diagnosis or treatment) could be fitted to directly compare the odds ratios in Table 3 upon which results are based in the first two paragraphs on page 7. I think you need to compare all three outcome groups together (the three separate responses forming the rows for each wave in Table 3) and see they differ overall before performing pairwise contrasts on them as discussed in the first two paragraphs on page 7 and presented in Table 3 on page 9. Page 6. I am not clear what is a 'Multivariable binomial regression'(line 5). Is this, as I suspect from the later mention of odds ratios, just a series of logistic regressions each with a different present/not present response? To clarify one might add to the description in the first analysis paragraph that the outcomes (line 6) correspond to the presence or absence of the outcome variables. I am also not clear how you convert the wealth quintiles (page 6, line 21) to an odds ratio so an extra sentence or two explaining this would be welcome. My understanding from the description in the second analysis paragraph on page 6 (based upon lines 20-25) is that the odds ratio of wealth for each individual appears to be estimated from a set of quintiles PRIOR to the logistic regression and used as a continuous predictor (line 23 saying modelled as a continuous variable). I suspect wealth is entered as a binary predictor but slope order of inequality (a seemingly five rather than two level variable) is described as the independent variable for wealth (line 17 of page 6) and this is a five-level variable. The usual way of computing odds ratios such as those in Table 3 is for the odds ratio (in this case least to most wealthy) to be either the outcome or a two category predictor. I also notice (page 6, lines 14-15) that missing data was excluded from the analysis. What effect do you think this may have had on the results? I am not sure what percentage of people or variables had missing values. Are different people therefore involved in the

	different logistic regressions depending upon whether they had a missing response? By excluding the missing data we are I assume, therefore, looking at subjects where all predictors and the outcome of interest were observed. Generalized linear mixed models can be fitted which incorporate information even from subjects with incomplete cases assuming missingness is related to the observed values. This would use a combined data set combining the three medical diagnoses and looking at them simultaneously using the one model. Pages 7 and 9 (Table 3). Some conclusions are drawn in lines 2-9 on page 7 concerning differences in odds ratios in Table 3 claiming that the lower odds ratios suggest less wealthy people were not given diagnoses of angina however the 95% confidence intervals for the corresponding odds ratios in Table 3 on page 9 overlap e.g. Overall Illness burden for angina has CI (5.4,10.8) with a overall medical diagnosis CI for angina of (3.3,6.0) even though the conclusion in lines 2-9 on page 7 suggests the odds ratios differ to which these intervals refer. The overlap of the confidence intervals would suggest that there is statistically no difference between these odds ratios. We need to take the variance of the odds ratios into account as well as their value when deciding whether they differ. This is done using a statistical test and obtaining a p-value. One could, for example, fit an interaction term in a logistic regression of the medical condition factor by outcome group factor where the outcome group factor is defined as being one of illness burden, medical diagnosis or treatment and directly test the difference in the odds ratios in Table 3? One might argue that one should only look at separate odds ratios as in Table 3 for different medical conditions split by illness burden/medical diagnosis/treatment type if there is an interaction of medical condition with outcome group. By not doing so we may also be inflating type I error in doing a lot of comparisons without first checking for an overall interaction effect. One might also argue that since all five medical and treatment diagnoses odds ratios are less than their illness burden odds ratios for the five medical conditions show a consistent effect across medical conditions in addition to, or instead of, any possible magnitude differences in odds ratios. If there is no interaction between medical condition and outcome group (defined as whether a response is a illness burden or medical diagnosis or treatment) and no main effect of group it is difficult to motivate individual odds ratio comparisons of each group at each medical condition as we are effectively contrasting groups without having found an overall outcome group effect. Page 8. The percentages for each wave in Table 2 (summed across columns) do not sum to 100%. Is this because we are only looking at five of the possible medical conditions? E.g. Looking at the first row in Table 2, only 46% of participants in wave 2 have illness burdens with the five medical conditions. What about the other 54% - it is not clear in Table 2 if the missing 54% are healthy people or those diagnosed with other conditions? Page 10. Figure 1 appears to be plotting the 15 odds ratios already presented in the overall section of Table 3 on page 9. Since this appears repetitious I wonder if Figure 1 could be dropped.

VERSION 1 – AUTHOR RESPONSE

Reviewer Name Gerry McCartney

In the abstract:

1. make it clear in the design section that you do not use the longitudinal nature of the data, and just use it as cross sectional data – WE USED TWO APPROACHES TO ANALYSIS, EXPLAINED IN THE 'ANALYSIS' SECTION AS FOLLOWS: 'A MAIN ANALYSIS USING SERIAL CROSS SECTIONAL DATA AND THEN A SUBSIDIARY ANALYSIS USING LONGITUDINAL DATA'

2. in the outcomes measures section you say that you adjust for wealth. In fact, as I understand it, you stratify by wealth in most of your results. WE STRATIFIED BY WEALTH IN TABLE 1 (PARTICIPANT CHARACTERISTICS), BUT IN ALL ANALYSES WE ADJUSTED FOR WEALTH (EG TABLE 3)

3. In the results section it didn't make much sense to me to lump all the 5 conditions together. We would expect the inverse care law to operate differently for different conditions. You should also make clear whether you are talking about type I and/or type II diabetes. WE PRESENT THE RESULTS FOR EACH CONDITION SEPARATELY, AND DISCUSS THE SIMILAR PATTERNS SEEN ACROSS CONDITIONS. ALL CONDITIONS AND VARIABLES ARE DEFINED INN THE 'VARIABLES' SECTION

In the strengths and limitations section, you say that you look at 'the same population over time'. I think it would be more accurate to delete that, given that you can't use the longitudinal data as you note elsewhere.

WE HAVE REPLACED THIS WITH: 'IN A LONGITUDINAL PANEL STUDY'

In the main text, you refer at times to cataract, diabetes and osteoarthritis (e.g. line 48) - I think you need to consistently say throughout the text that you only have proxies of these (e.g. self-reported pain and blindness). You do note these limitations elsewhere, but it needs explained throughout.

WE HAVE AMENDED THE TEXT THROUGHOUT TIO REFER TO 'SELF-REPORTED MEDICAL DIAGNOSES'. THE END OF THE INTRODUCTION EXPLAINS THAT WE COMPARED 'THE BURDEN OF ILLNESS (ESTIMATED BY VALIDATED SCALES, BIOMARKER, AND REPORTED SYMPTOMS) OF ANGINA, CATARACT, DEPRESSION, DIABETES AND OSTEOARTHRITIS, TO… SELF-REPORTED MEDICAL DIAGNOSIS'. WE DESCRIBE HOW THE BURDEN OF ILLNESS FOR EACH CONDITION, AND THE SELF-REORTED MEDICAL DIAGNOSES, WERE CLASSIFIED IN THE 'VARIABLES' SECTION

In the methods, you need to make clear if the ELSA cohort is a proportionate sample or some other sampling method. I wasn't clear what you meant by 'slope order of inequality' and whether this differed from 'slope index of inequality'.

WE HAVE ADDED THE FOLLOWING EXPLANATION OF THE SAMPLE TO THE START OF THE METHODS SECTION: 'THE SAMPLE WAS SELECTED FROM HOUSEHOLDS THAT HAD PREVIOUSLY RESPONDED TO THE HEALTH SURVEY FOR ENGLAND, AND DRAWN FROM SELECTED POSTCODE SECTORS STRATIFIED BY HEALTH AUTHORITY AND DEPRIVATION TO BE REPRESENTATIVE OF ADULTS AGED 50 OR MORE LIVING IN PRIVATE HOUSEHOLDS IN ENGLAND'.

WE HAVE ADDED THE FOLLOWING EXPLANATION OF SLOPE ORDER OF INEQUALITY TO THE 'ANALYSIS' SECTION: 'THE SLOPE ORDER OF INEQUALITY WAS MODELLED AS A CONTINUOUS VARIABLE, SO THAT THE SLOPE OR COEFFICIENT OF A LOGIT LINEAR REGRESSION LINE ACROSS ALL FIVE QUINTILES REPRESENTS THE DIFFERENCE IN OUTCOME BETWEEN THE HYPOTHETICALLY WEALTHIEST AND LEAST WEALTHY PARTICIPANT. EXPONENTIATING THIS SLOPE COEFFICIENT RESULTS IN AN ODDS RATIO, WHICH IS THE RATIO OF THE ODDS OF THE OUTCOME IN THE WEALTHIEST COMPARED WITH THE LEAST WEALTHY PARTICIPANT'

In the results, it would be good to rephrase the sentence, "over half were women..." which is unclear.

WE HAVE REPHRASED THIS SENTENCE

In figure 1, it would be useful to have a horizontal line at an OR of 1. You could also colour code burden, diagnosis and treatment across conditions to make reading easier.

WE HAVE DONE THIS

In the discussion, you make the point about longitudinal data - but you (understandably) couldn't use these. So, it isn't really an advantage of this study. You also make a big claim that this is the first study to look at illness burden, diagnosis and treatment. I don't know of a study that does, but it isn't evidenced here.
WE REPORT THE RESULTS OF THE SUBSIDIARY LONGITUDINAL ANALYSIS IN THE MAIN PAPER AND SUPPLEMENTAL FILE 1
You state that the lack of specificity in condition definition will not be important as it won't vary by wealth between conditions. I don't think this is necessarily true - there are many conditions that are strongly patterned by socioeconomic status whilst others are not. So, I think this should be taken out.
WE AGREE THAT MANY CONDITIONS ARE STRONGLY PATTERNED BY WEALTH AND OTHERS ARE NOT, AND MENTION THIS IN THE DISCUSSION. HERE WE REFER TO THE SPECIFICITY OF THE SYMPTOMS THAT WE USED TO ESTIMATE ILLNESS BURDEN FOR OSTEOARTHRITIS AND CATARACT, AND THAT ANY LACK OF SPECIFICITY IS UNLIKELY TO VARY WITH WEALTH
I'm not sure if the Sen reference supports the claim that self report is the best measure of pain.
WE HAVE CHECKED THE REFERENCE AND REPHRASED THIS TO READ: 'THIS IS….LESS OF A PROBLEM WITH SENSORY ASSESSMENT FOR MEASURES OF PAIN, WHICH IS ESSENTIALLY SELF-PERCEIVED, AND WHERE SELF-REPORT IS THE BEST MEANS OF ASSESSMENT'
All of that said (!), I think this is a very good and helpful paper and is worthy of publication.
THANKYOU FOR THE HELPFUL COMMENTS

Reviewer Name Peter Watson
A few aspects of the analysis could be clarified. For example, how is the dichotomy of wealth derived from the quintiles and used in the logistic regressions? I suspect wealth is a binary predictor but slope order of inequality (a seemingly five rather than two level variable) is described as the independent variable in line 17 on page 6.
WE HAVE ADDED THE FOLLOWING EXPLANATION OF SLOPE ORDER OF INEQUALITY TO THE 'ANALYSIS' SECTION: 'THE SLOPE ORDER OF INEQUALITY WAS MODELLED AS A CONTINUOUS VARIABLE, SO THAT THE SLOPE OR COEFFICIENT OF A LOGIT LINEAR REGRESSION LINE ACROSS ALL FIVE QUINTILES REPRESENTS THE DIFFERENCE IN OUTCOME BETWEEN THE HYPOTHETICALLY WEALTHIEST AND LEAST WEALTHY PARTICIPANT. EXPONENTIATING THIS SLOPE COEFFICIENT RESULTS IN AN ODDS RATIO, WHICH IS THE RATIO OF THE ODDS OF THE OUTCOME IN THE WEALTHIEST COMPARED WITH THE LEAST WEALTHY PARTICIPANT'
The proportion and nature of missing values excluded from analyses (page lines 14-15) should be described and any implications discussed.
THE NUMBER AND % OF MISSING DATA IS GIVEN IN TABLE 1 – IE 145 PARTICIPANTS WERE MISSING DATA ON WEALTH, AND 5.5% (N=8) OF THOSE HAD ANGINA. AS THE NUMBERS OF MISSING DATA ARE SMALL THE IMPLICATIONS ARE MINIMAL.
One usually would fit an outcome group by medical condition interaction term to compare the odds ratios in Table 3 (page 9) and as discussed in the first two paragraphs of page 7 which is not done here. I also wonder about power issues with the statistical comparisons of the odds ratios in Table 3 given a consistent difference between odds ratios which nevertheless have overlapping confidence intervals particularly in the case of comparing angina illness burden with both medical diagnosis and treatment with the latter two odds ratios being smaller but still all have overlapping confidence intervals with that of illness burden possibly suggesting they are not statistically different.
WE DID NOT DO INTERACTION TESTS TO COMPARE DIFFERENT CONDITIONS BECAUSE THE AIM OF THE ANALYSIS WAS TO DESCRIBE TRENDS FOR DIFFERENT CONDITIONS, NOT TO TEST THE HYPOTHESIS THAT TREATMENT DIFFERED STATISTICALLY SIGNIFICANTLY BETWEEN CONDITIONS. THE OUTCOMES WERE DEFINED DIFFERENTLY FOR DIFFERENT CONDITIONS, SO IT WOULD NOT MAKE SENSE TO POOL ALL OUTCOMES FOR ALL

CONDITIONS AS THOUGH THEY WERE THE SAME. THE LARGE NUMBER OF CONDITIONS, WAVES AND TYPES OF INDICATOR REPORTED IN TABLE 3 MEANS THAT THERE WOULD BE A HIGH PROBABILITY OF TYPE 1 ERROR, THAT IS, STATISTICALLY SIGNIFICANT ASSOCIATIONS BEING DETECTED DUE TO CHANCE ALONE.

My main concern would be the overlapping confidence intervals of the odds ratios in Table 3 despite the point estimate odds ratios upon which these are based seemingly being a lot different. An interaction test would clarify if these odds ratios do really differ. I think the fact we are consistently seeing the same direction of differences suggest there may be power issues with the logistic analyses comparing odds ratios in Table 3 as well as in the acknowledged small sample size issues mentioned in lines 26-31 on page 7 but if there is no interaction between medical condition and outcome group (defined as whether a response is a illness burden or medical diagnosis or treatment) and no main effect of outcome group it is difficult to motivate individual odds ratio comparisons of each group at each medical condition as is done in this paper on page 7 and in Table 3 on page 9. In broad terms a mean of 1,000,000 may be greater than a mean of '1' but if one or both of these means are imprecisely estimated there is no evidence to suggest the means differ which is why we have to take the precision (standard errors) of odds ratios into account when comparing them which is done through applying a statistical test and obtaining a p-value usually using a test of an interaction or main effect.

PLEASE SEE RESPONSE ABOVE ON INTERACTION

A series of logistic regressions have been carried out in this study to assess diagnoses on a range of medical conditions to the wealth or participants. A strength of this paper is that the odds ratios in Table 3 on page 9 consistently show a pattern whereby medical diagnosis and treatment have lower odds ratios than the illness burden although these may not always be statistically significantly different (see later) which given the consistency may suggest a lack of power or high variability within or between participants. I have a few queries on explaining exactly how the wealth dichotomy is used in these regressions to yield the odds ratios in Table 3 and also invite comments on how serious the deletion of missing values on the generalizability of the results and wonder if generalized linear mixed models might instead be used which can incorporate incomplete information and use participants with missing covariates. I also query a conclusion in lines 2-9 on page 7 which leads me to wonder if interaction terms involving medical diagnosis by outcome group (representing illness burden or medical diagnosis or treatment) could be fitted to directly compare the odds ratios in Table 3 upon which results are based in the first two paragraphs on page 7. I think you need to compare all three outcome groups together (the three separate responses forming the rows for each wave in Table 3) and see they differ overall before performing pairwise contrasts on them as discussed in the first two paragraphs on page 7 and presented in Table 3 on page 9.

PLEASE SEE RESPONSES ABOVE ON MISSING DATA AND INTERACTION

Page 6. I am not clear what is a ‘Multivariable binomial regression’(line 5). Is this, as I suspect from the later mention of odds ratios, just a series of logistic regressions each with a different present/not present response? To clarify one might add to the description in the first analysis paragraph that the outcomes (line 6) correspond to the presence or absence of the outcome variables.

WE HAVE CHANGED THIS TO READ: ‘MULTIVARIABLE LOGISTIC REGRESSION’

I am also not clear how you convert the wealth quintiles (page 6, line 21) to an odds ratio so an extra sentence or two explaining this would be welcome. My understanding from the description in the second analysis paragraph on page 6 (based upon lines 20-25) is that the odds ratio of wealth for each individual appears to be estimated from a set of quintiles PRIOR to the logistic regression and used as a continuous predictor (line 23 saying modelled as a continuous variable). I suspect wealth is entered as a binary predictor but slope order of inequality (a seemingly five rather than two level variable) is described as the independent variable for wealth (line 17 of page 6) and this is a five-level variable. The usual way of computing odds ratios such as those in Table 3 is for the odds ratio (in this case least to most wealthy) to be either the outcome or a two category predictor.

PLEASE SEE RESPONSE ABOVE WITH NEW ADDED EXPLANATION OF THE SLOPE INDEX OF INEQUALITY

I also notice (page 6, lines 14-15) that missing data was excluded from the analysis. What effect do you think this may have had on the results? I am not sure what percentage of people or variables had missing values. Are different people therefore involved in the different logistic regressions depending upon whether they had a missing response? By excluding the missing data we are I assume, therefore, looking at subjects where all predictors and the outcome of interest were observed. Generalized linear mixed models can be fitted which incorporate information even from subjects with incomplete cases assuming missingness is related to the observed values. This would use a combined data set combining the three medical diagnoses and looking at them simultaneously using the one model.

PLEASE SEE RESPONSE ABOVE ON MISSING DATA

Pages 7 and 9 (Table 3). Some conclusions are drawn in lines 2-9 on page 7 concerning differences in odds ratios in Table 3 claiming that the lower odds ratios suggest less wealthy people were not given diagnoses of angina however the 95% confidence intervals for the corresponding odds ratios in Table 3 on page 9 overlap e.g. Overall Illness burden for angina has CI (5.4,10.8) with a overall medical diagnosis CI for angina of (3.3,6.0) even though the conclusion in lines 2-9 on page 7 suggests the odds ratios differ to which these intervals refer. The overlap of the confidence intervals would suggest that there is statistically no difference between these odds ratios. We need to take the variance of the odds ratios into account as well as their value when deciding whether they differ. This is done using a statistical test and obtaining a p-value. One could, for example, fit an interaction term in a logistic regression of the medical condition factor by outcome group factor where the outcome group factor is defined as being one of illness burden, medical diagnosis or treatment and directly test the difference in the odds ratios in Table 3? One might argue that one should only look at separate odds ratios as in Table 3 for different medical conditions split by illness burden/medical diagnosis/treatment type if there is an interaction of medical condition with outcome group. By not doing so we may also be inflating type I error in doing a lot of comparisons without first checking for an overall interaction effect. One might also argue that since all five medical and treatment diagnoses odds ratios are less than their illness burden odds ratios for the five medical conditions show a consistent effect across medical conditions in addition to, or instead of, any possible magnitude differences in odds ratios.

If there is no interaction between medical condition and outcome group (defined as whether a response is a illness burden or medical diagnosis or treatment) and no main effect of group it is difficult to motivate individual odds ratio comparisons of each group at each medical condition as we are effectively contrasting groups without having found an overall outcome group effect.

PLEASE SEE RESPONSE ABOVE ON INTERACTION

Page 8. The percentages for each wave in Table 2 (summed across columns) do not sum to 100%. Is this because we are only looking at five of the possible medical conditions? E.g. Looking at the first row in Table 2, only 46% of participants in wave 2 have illness burdens with the five medical conditions. What about the other 54% - it is not clear in Table 2 if the missing 54% are healthy people or those diagnosed with other conditions?

YES THIS IS CORRECT, AND WE HAVE AMENDED THE TITLE FOR TABLE 2 TO REFER TO PREVALENCE TO CLARIFY THAT WE DO NOT EXPECT THE PERCENTAGES TO ADD TO 100%

Page 10. Figure 1 appears to be plotting the 15 odds ratios already presented in the overall section of Table 3 on page 9. Since this appears repetitious I wonder if Figure 1 could be dropped.

YES THIS IS CORRECT BUT WE WOULD LIKE THE FIGURE TO STAY AS WE THINK IT SHOWS THE PATTERN ACROSS CATEGORIES AND CONDITIONS BETTER THAN THE DATA IN THE TABLES DO, AND THIS PATTERN IS ONE OF THE KEY POINTS OF THE PAPER.

THANKYOU FOR THE HELPFUL COMMENTS.

VERSION 2 – REVIEW

REVIEWER	Gerry McCartney NHS Health Scotland Scotland
REVIEW RETURNED	18-Aug-2014

GENERAL COMMENTS	This remains an important issue and this paper can add to our collective knowledge and understanding. However, I am a little disappointed by the authors responses to my earlier comments few of the suggested amendments have been made. To reiterate: 1. In the abstract the reported results are from cross sectional data but the reported data are longitudinal. It is good that you have done subsidiary analyses on these, but they are subsidiary and it is misleading to report in this way. 2. You have not adjusted for wealth as you state, or if you have, your reporting is very confused indeed. For example, in Table 3 which you cite, your outcome measure is the ratio between wealth quintiles. It is not a putative confounder for which you are adjusting. This point still needs addressed. 3. You are still reporting across all conditions in the first 2 paragraphs of the results section and draw general points out before then going on to say the pattern is quite different for the different conditions. I still think it would be better for you to avoid lumping conditions in your reporting as you would expect different things to happen for different conditions. 4. You have still not addressed the point about diabetes. 5. My point about the description of the data source as longitudinal still stands, your change still has the potential to mislead. 6. Thank you for making clearer the self-reported nature of the illness data and the sampling method - this is now fine. 7. Your description of the 'slope order of inequality' should still be changed to the more familiar slope index of inequality. It also emphasises that you are not adjusting for wealth as you claim. 8. You have changed the sentence starting 'Over half with women...' (second sentence of results). It is still not clear which group(s) you are referring to when you say 'over half'. As stated earlier, this is a good paper and the comments I make above are easy to address and do not change the thrust of what you have found or concluded. But you need to make these changes or it is not publishable in my view. I now reviewed this twice. It is up to the authors to make the changes I have suggested or for the editors to judge if these are necessary before publication. I think they are, but they won't take the authors long at all.

REVIEWER	Peter Watson MRC Cognition and Brain Sciences Unit
REVIEW RETURNED	04-Aug-2014

GENERAL COMMENTS	Economic inequalities in burden of illness, diagnosis and treatment of five long-term conditions in England: panel study. Bmjopen-2014-005530.R1

	The authors have now clarified the method of analysis which is I believe is actually a random effects binomial regression with random subject intercepts. They could even give the STATA code they used in an appendix to absolutely clarify this and a reference to the technique. They also show how the quintiles which ranges from 0-1 can be interpreted as an odds ratio in that the regression estimate represents the change in a single unit in the odds of the presence or absence of a response with a unit increase in the wealth variable which represents a change from least wealthy to most wealthy. The exponential of the regression coefficients for the particular predictor giving the odds ratios quoted in Table 3 on page 9. It would be worth adding in a footnote to Table 3 that the odds ratios in bold represent statistically significant relationships. I would also replace the word 'binomial' with 'logistic' on line 46 of page 15 as it emphasises precisely that a logit link is used to model the binomial probability.

VERSION 2 – AUTHOR RESPONSE

Reviewer Name: Peter Watson
The authors have now clarified the method of analysis which is I believe is actually a random effects binomial regression with random subject intercepts. They could even give the STATA code they used in an appendix to absolutely clarify this and a reference to the technique.
WE STATE IN METHODS: "Intra-person correlation of outcomes was accounted for using robust adjustment with Stata, with each participant's unique identifier included in the regression equation as a cluster variable." WE THINK THAT THERE IS NO NEED TO ADD CODE IN AN APPENDIX, AS ALL WE DID WAS ADD THE OPTION cluster (ID) TO THE REGRESSION COMMANDS.

They also show how the quintiles which ranges from 0-1 can be interpreted as an odds ratio in that the regression estimate represents the change in a single unit in the odds of the presence or absence of a response with a unit increase in the wealth variable which represents a change from least wealthy to most wealthy. The exponential of the regression coefficients for the particular predictor giving the odds ratios quoted in Table 3 on page 9.
YES.

It would be worth adding in a footnote to Table 3 that the odds ratios in bold represent statistically significant relationships.
WE HAVE AMENDED THE FOOTNOTE TO TABLE 3 AS FOLLOWS: 'Statistically significant odds ratios (where the 95% confidence intervals do not include 1 before rounding to one decimal place) are shown in bold'.

I would also replace the word 'binomial' with 'logistic' on line 46 of page 15 as it emphasises precisely that a logit link is used to model the binomial probability.
WE HAVE DONE THIS (IN THE TITLE FOR FIGURE 1).
THANKYOU FOR THE HELPFUL COMMENTS.

Reviewer Name: Gerry McCartney
This remains an important issue and this paper can add to our collective knowledge and understanding.

1. In the abstract the reported results are from cross sectional data but the reported data are longitudinal. It is good that you have done subsidiary analyses on these, but they are subsidiary and it is misleading to report in this way.
WE HAVE REMOVED THE WORD ‘LONGITUDINAL’ WHERE IT APPEARED TWICE IN THE ‘STRENGTHS AND LIMITATIONS OF THIS STUDY’ SECTION AFTER THE ABSTRACT, AND AGAIN IN THE SECOND PARAGRAPH OF THE DISCUSSION, AND ADDED THE WORDS ‘OVER TIME’.
THE RESULTS REPORTED IN THE ABSTRACT ARE THE RESULTS OF THE MAIN ANALYSIS USING SERIAL CROSS SECTIONAL DATA, AND ARE FROM THE FINAL ‘OVERALL’ ROW OF TABLE 3. THE RESULTS OF THE SUBSIDIARY ANALYSIS USING LONGITUDINAL DATA ARE NOT MENTIONED IN THE ABSTRACT AND ARE GIVEN IN A TABLE IN SUPPLEMENTARY FILE 1. WE ARE CLEAR ABOUT THE DIFFERENCE BETWEEN THE SERIAL CROSS SECTIONAL AND LONGITUDINAL ANALYSES IN THE METHODS SECTION OF THE MAIN PAPER: "We used two approaches to analysis, a main analysis using serial cross sectional data and then a subsidiary analysis using longitudinal data." THEN "For the subsidiary analysis using longitudinal data, we estimated the odds ratio of receiving a diagnosis by a subsequent wave only for those who had met the criteria for ‘illness burden’ in a previous wave, and then the likelihood of receiving treatment only for those who had received a diagnosis in a previous wave. This was a subsidiary analysis as the numbers of participants that could be followed over time in this manner was small, particularly for treatment in angina and depression."

2. You have not adjusted for wealth as you state, or if you have, your reporting is very confused indeed. For example, in Table 3 which you cite, your outcome measure is the ratio between wealth quintiles. It is not a putative confounder for which you are adjusting. This point still needs addressed.
WE HAVE ADJUSTED FOR WEALTH BY INCLUDING THE SLOPE ORDER OF INEQUALITY AS A COVARIATE, AND HAVE EXPLAINED IN THE METHODS THAT: "The independent variables were age group, sex and slope order of inequality." WEALTH COULD POTENTIALLY CONFOUND THE ODDS RATIOS FOR AGE AND SEX.

3. You are still reporting across all conditions in the first 2 paragraphs of the results section and draw general points out before then going on to say the pattern is quite different for the different conditions. I still think it would be better for you to avoid lumping conditions in your reporting as you would expect different things to happen for different conditions.
WE AGREE THAT THERE ARE OBVIOUS DIFFERENCES BETWEEN THE CONDITIONS, BUT WOULD VERY MUCH LIKE TO DRAW OUT THE INTERESTING SIMILAR PATTERN ACROSS CONDITIONS, WHICH SUPPORTS OUR CONCLUSION THAT: ‘The substantially higher illness burden in less wealthy participants [in all five conditions at all four time points] was not matched by appropriately higher levels of diagnosis and treatment.’ WE HOPE THAT FIGURE 1 SHOWS THE PATTERN ACROSS CONDITIONS GRAPHICALLY.

4. You have still not addressed the point about diabetes.
WE STATE IN THE ‘VARIABLES’ SECTION THAT: ‘Illness burden for diabetes was defined as a fasting HbA1c level of >7.5%’ AND ‘a medical diagnosis was considered to exist if a participant answered ‘yes’ when asked whether a doctor had ever told them they had the condition of interest.’ FOR DIABETES, THE QUESTION ASKED TO PARTICIPANTS IN THE SURVEY WAS: ‘HAS A DOCTOR EVER TOLD YOU THAT YOU HAVE DIABETES?’

5. My point about the description of the data source as longitudinal still stands, your change still has the potential to mislead.
WE STATED UNAMBIGIOUSLY HOW THE DATA WERE COLLECTED AND ANALYSED. WE MADE IT CLEAR THAT THE PRIMARY ANALYSES WERE CROSS-SECTIONAL, AND THAT LONGITUDINAL ANALYSES WERE LIMITED BECAUSE OF THE SMALL NUMBERS OF

PARTICIPANTS WITH REPEATED OBSERVATIONS OF OUR MAIN OUTCOMES. PLEASE SEE OUR FULLER RESPONSE TO POINT ONE ABOVE.

6. Thank you for making clearer the self-reported nature of the illness data and the sampling method - this is now fine.
THANKYOU

7. Your description of the 'slope order of inequality' should still be changed to the more familiar slope index of inequality. It also emphasises that you are not adjusting for wealth as you claim.
IN KEEPING WITH WAGSTAFF AND VAN DOORSLAYER, THE SLOPE ORDER OF INEQUALITY IS THE VARIABLE, DEFINED BY US, AND THE SLOPE INDEX OF INEQUALITY IS THE ODDS RATIO, ESTIMATED BY MULTIPLE REGRESSION. WE DID ADJUST FOR WEALTH, AS EXPLAINED IN THE METHODS AND IN OUR RESPONSE TO POINT 2 ABOVE.

8. You have changed the sentence starting 'Over half with women...' (second sentence of results). It is still not clear which group(s) you are referring to when you say 'over half'.
WE HAVE DELETED THIS SENTENCE.
As stated earlier, this is a good paper and the comments I make above are easy to address and do not change the thrust of what you have found or concluded.
THANKYOU.