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Factors driving polypharmacy in primary care: A cross-sectional study

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ABSTRACT:

OBJECTIVES: While older age and ill-health are known to be driving polypharmacy, this paper aims to identify whether wealth, body mass index (BMI), smoking and alcohol consumption are also contributing to polypharmacy (5-9 prescribed medications) and hyper-polypharmacy prevalence (>10 prescribed medications), among older people living in England.

DESIGN: Cross-sectional study

SETTING: The English Longitudinal Study of Ageing (Wave 6)

PARTICIPANTS: 7730 participants aged over 50 years old, in May 2012

DATA SYNTHESIS: Two multivariate models were created. Hazard ratios (HR) with corresponding 95% confidence intervals (CI), for polypharmacy and hyper-polypharmacy, were calculated after adjusting for gender, age, wealth, smoking, alcohol consumption, BMI, self-rated health and the presence of a long-standing condition.

RESULTS: Lower wealth (adjusted HR highest wealth quintile versus lowest wealth quintile, 1.28; 95%CI, 1.04-1.69, p=0.02) and obesity (adjusted HR 1.81; 95%CI, 1.53-2.15, p<0.001) were independently associated with polypharmacy. Increasing age (adjusted HR 50-59 years versus 70-79 years, 3.42; 95% CI, 2.81-4.77, p<0.001) and the presence of a long-standing condition (adjusted HR 2.94;95%CI, 2.55-3.99, p<0.001) were also associated with polypharmacy. No statistically significant association between smoking and polypharmacy (adjusted HR 1.06; 95% CI, 0.86-1.29, p=0.56) was established; whilst, very frequent alcohol consumption (consuming alcohol >5 times per week) was inversely associated with polypharmacy (adjusted HR never versus very frequently, 0.64; 95%CI, 0.52-0.78, p<0.001). The adjusted hazard ratios for hyper-polypharmacy were accentuated, compared to polypharmacy.

CONCLUSION: This study has identified that lower wealth, obesity, increasing age and the presence of long-standing conditions are independently driving polypharmacy and hyper-polypharmacy prevalence. The effect of these factors, on polypharmacy and especially hyper-polypharmacy prevalence, is likely to become more pronounced with the widening gap in UK wealth inequalities, the current obesity epidemic and the growing population of older people. The alcohol findings contribute to the debate on the relationship between alcohol consumption and health.

Keywords: polypharmacy, longitudinal, demography, older people

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This cross-sectional study uses medication data, from over 7000 older individuals, to identify factors which are driving polypharmacy prevalence in primary care.
- In the analysis, a large number of covariates were used to minimise the impact of confounding factors.
- Participants were asked to self-report information about their prescribed medication usage. To verify their responses, participants were asked to show their medication containers to the interviewer.
- Smoking and alcohol consumption data was also collected by asking participants to self-report. This relies on accurate and truthful information recall to prevent bias.

INTRODUCTION

Polypharmacy has been discussed extensively in the literature and media; however, there is no universally accepted definition for the practice of prescribing multiple medications to one individual. [1] At present, polypharmacy is commonly defined as "the use of five or more regular medications", whilst hyper-polypharmacy is defined as "the use of ten or more regular medications". Although polypharmacy prevalence has increased over the past decade, there are relatively few data about the factors driving polypharmacy and hyper-polypharmacy.[2] The aim of this study is to determine whether wealth, body mass index (BMI), smoking, alcohol consumption, age and the presence of long-standing conditions, are currently driving the increase in polypharmacy and hyper-polypharmacy prevalence in primary care.

Previous studies have shown that increasing age and the presence of long-term conditions are independently associated with an increase in polypharmacy prevalence. [3-5] Comparatively fewer studies have examined whether socio-demographic or lifestyle factors, for example wealth and obesity, are independently associated with polypharmacy. The existing studies are limited by their small sample sizes and data collection methods. [6-9] In a study conducted by Haider et al, [6] no statistically significant association between polypharmacy and an individual's socio-economic status was established. The findings from a study by Rajska-Neumann [7] revealed that there was no statistically significant difference in polypharmacy prevalence between smokers and non-smokers; whereas a statistically significant inverse relationship between alcohol consumption and the concomitant administration of medications was detected by Wong et al. [8] Finally, when Bueno et al [9] examined the association between polypharmacy and obesity, an adjusted odds ratio revealed that obese individuals (BMI >30kg/m^2) were 1.6 times more likely to be experiencing polypharmacy, compared to individuals with a BMI less than 30kg/m^2. To advance knowledge on this topic, and to identify the current and future drivers of polypharmacy, a larger-scale, population based study is required.

This study used data from The English Longitudinal Study of Ageing (ELSA) as this provided an opportunity to link polypharmacy and hyper-polypharmacy data to participants' personal data. In particular, this study aimed to determine whether wealth, BMI, smoking and

alcohol consumption, age and the presence of long-standing conditions, are driving polypharmacy (5-9 prescribed medications) and hyper-polypharmacy (>10 prescribed medications) prevalence in a community population of older people living in England.

METHOD

Sample and participants

A cross-sectional study was conducted using Wave 6 data from The English Longitudinal Study of Ageing (ELSA). Data collection took place between May 2012 and June 2013, from a representative sample of the English population who were aged 50 years or above.

Since ELSA began in 2002, participants have been asked to provide personal information about their household finances, health status, lifestyle choices and social interactions, on a bi-annual basis. To be included in ELSA Wave 6, participants must have been successfully interviewed in one or more of the previous ELSA Waves. Also, they must have been aged over 50 at the time of study enrollment and living at private residential addresses in England. [10]

Patient Involvement and Ethics

This study only used data from the ELSA database. No patients were involved in the development of the research question, study design or interpretation of data in this study. Ethical approval was not required for this study.

Data Collection

Face-to-face interviews

The face-to-face interviews were conducted by trained interviewers, who asked participants to provide information about their current lifestyle choices, including smoking habits and alcohol consumption over the past twelve months. Smoking status was recorded as current smoker or non-smoker; whereas, the frequency of alcohol consumption over the past year was recorded as never, rarely, frequently or very frequently. [12] Rarely was defined as drinking alcohol less than twice a month. Frequently was defined as drinking alcohol between one and four times a week; whilst, very frequently was defined as drinking alcohol at least five times a week.

Participants were also asked to describe their current health status. Participants could select one of the following options: “excellent, very good, good, fair or poor”. [13] These responses were converted into a two-level variable: good/fair and poor, with good/fair health status being the sum of responses ranging from “excellent” to “fair”. In a subsequent question, participants were asked whether they had any long-standing illness, disability or infirmity. When the latter question was asked, the interviewers defined long-standing as “anything that has troubled you over a period of time, or that is likely to affect you over a period of time”, and participants could answer this question with either yes or no. [13]

Finally, participants were asked to provide information about their household income, including information about their employment status, personal finances, assets, pensions and other benefits. Participant pension data was excluded when wealth index scores were calculated. Based upon their wealth index scores, participants were allocated to one of five wealth quintiles. Quintile 1 was the most affluent, whilst quintile 5 was the poorest.

Questionnaire

After completion of the face-to-face interview, participants were asked to complete a paper-based questionnaire. The questionnaire was designed to obtain further information about the participants' living arrangements, health status, lifestyle choices and social interactions. [14]

Nurse visit

The nurse visits took place in the participant's home. At the beginning of the visit, the nurse recorded information about participant demographics and their currently prescribed medications. Prescribed medication formulations were defined by the nurses as "pills, syrups, ointments, inhalers or injections". [15] If a participant reported taking one or more prescribed medications, the nurse sought their permission to record the name of their medication, in addition to seeing its container. A nurse could record a maximum of 27 prescribed medications. During the latter part of the visit, the nurse conducted a physical examination and recorded information about the participant's blood pressure, grip strength, height, weight and lung function. [15] Using a participant's height and weight data, it was possible to calculate their body mass index. A BMI <18.5kg/m^2 was recorded as underweight, a BMI value between 18.5 -24.9 kg/m^2 was considered to be normal weight; whereas, a BMI of 25.0-29.9kg/m^2 was recorded as overweight and a BMI >30kg/m^2 was recorded as obese.

Inclusion Criteria

All participants must have completed a face-to-face interview, a paper-based questionnaire and received a nurse visit during ELSA wave 6 to meet the inclusion criteria for this study. [11]

Defining polypharmacy and hyper-polypharmacy

Polypharmacy was defined as the concurrent use of five to nine prescribed medications, whilst hyper-polypharmacy was defined as the concurrent use of ten or more prescribed medications. These definitions have been used previously in other population based studies. [2,16]

Data analysis

Initially, descriptive statistics were used to summarise the prevalence of polypharmacy and hyper-polypharmacy among participants. These data were subsequently stratified according to participant demographics. In the second part of the analysis, a bivariate model was used to assess the relationship between polypharmacy and the following independent variables: frequent alcohol consumption, increasing age, poor wealth, female sex, smoking, raised body mass index (BMI), poor self-rated health and the presence of a long-standing condition.

In the final part of the analysis, two multivariate models were created to identify associations between participant characteristics and polypharmacy prevalence. In both models, ill health was controlled for by using participants taking between one and four prescribed medications. This group of participants formed the control group. Participants taking no prescribed medications were excluded from this part of the analysis. In the first model, participants taking 5 to 9 medications were compared to the control group. In the second model, participants taking 10 or more medications were compared to the control group. Hazard ratios with corresponding 95% confidence intervals (CI), for polypharmacy and hyper-

polypharmacy, were calculated after adjusting for covariates. The following factors were considered as covariates: gender, age, wealth, smoking, alcohol consumption, BMI, self-rated health and the presence of long-standing conditions. The data generated from the models was statistically significant if $p<0.05$. All data analysis was undertaken using SPSS version 24.0.

RESULTS

Participant Characteristics:

A total of 7730 participants' data from ELSA Wave 6 were analysed. Participant characteristics are presented in Table 1. The mean age of participants in Wave 6 was 67.6 years, and 55.4% (n=4282/7730) of the sample were female. Overall, 24.1% (n= 1862/7730) of the participants received polypharmacy and 6.4% (n=494/7730) were receiving hyper-polypharmacy (Table 1). The proportion of individuals receiving polypharmacy and hyper-polypharmacy increased steadily with age. However, the prevalence of polypharmacy and hyper-polypharmacy in males and females was similar. (Table 1)

	No medications	**1-4 medications**	**5-9 medications**	**10+ medications**
Participant Characteristics:			**Polypharmacy**	**Hyper-polypharmacy**
All participants (n=7730)	23.8%	45.7%	24.1%	6.4%
Age:				
50-59 years (n=1695)	43.2%	42.4%	11.7%	2.7%
60-69 years (n=3012)	26.6%	49.2%	19.6%	4.6%
70-79 years (n=2114)	11.8%	45.9%	33.1%	9.2%
80+ years (n=909)	6.4%	39.6%	41.3%	12.7%
Gender:				
Male (n=3448)	24.9%	44.6%	24.4%	6.1%
Female (n=4282)	22.9%	46.6%	23.9%	6.6%
Long-standing condition:				
Yes (n=4289)	9.6%	44.5%	35.2%	10.7%
No (n=3441)	41.6%	47.1%	10.3%	1.0%

Table 1: Polypharmacy versus patient characteristics

Overall, 35.2% (n= 1509/4289) of participants who reported a long-standing condition were receiving polypharmacy; whereas, 10.7% (n=459/4289) were receiving hyper-polypharmacy. Only 10.3% (n=353/3441) and 1.0% (n=35/3441) of participants with no long-standing conditions, received polypharmacy and hyper-polypharmacy respectively (Table 1).

In a bivariate model, moderate positive correlations were detected between polypharmacy and the following variables: the presence of a long-standing condition, poor self-rated health and increasing age. A weak positive correlation between polypharmacy and a high BMI was established. Similarly, there was a weak positive correlation between lower wealth and polypharmacy. No correlation between gender and polypharmacy was established. In addition, there was a weak negative correlation between polypharmacy and smoking. There was also a weak negative correlation between polypharmacy and frequent alcohol consumption. All bivariate correlations are presented in Figure 1.

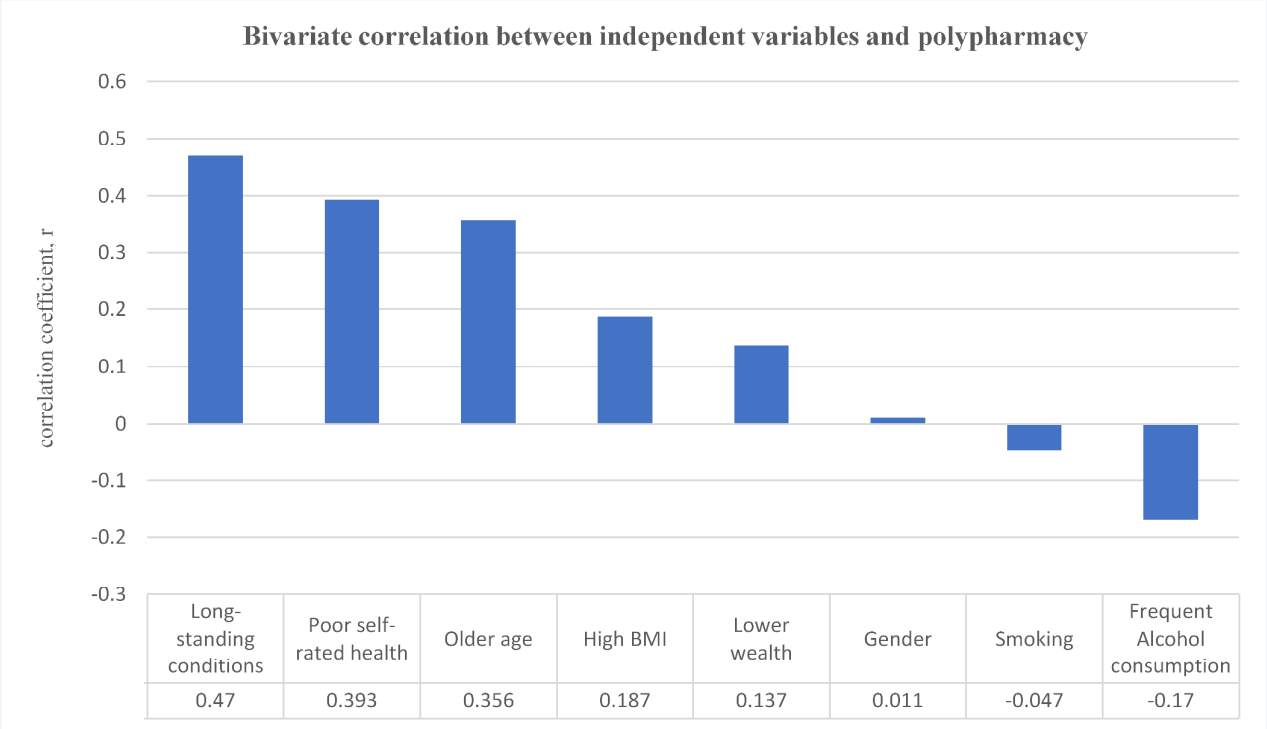

Figure 1: Bivariate correlations between polypharmacy and covariates

To determine whether other variables are driving polypharmacy and hyper-polypharmacy, the results from the two multivariate models (Polypharmacy-1 and Hyper-polypharmacy-2) were analysed and presented in Table 2 and Table 3 respectively.

Independent Variables	**Adjusted HR**	95% CI		**Sig.**
		Lower	Upper	
Age				
50-59 years **(Reference)**	1			
60-69 years	1.66	1.37	2.01	**<0.00**
70-79 years	3.42	2.81	4.77	**<0.00**
80+	4.52	3.58	5.70	**<0.00**
Gender				
Male **(Reference)**	1			
Female	0.92	0.81	1.04	0.21
Long-standing condition				
No **(Reference)**	1			
Yes	2.94	2.55	3.39	**0.00**
Self-rated health				
Self-rated health: Good **(Reference)**	1			
Self-rated health: Poor	2.98	2.61	3.4	**0.00**
Wealth				
Wealth: Quintile 1 (wealthiest) **(Reference)**	1			
Wealth: Quintile 2	1.08	0.9	1.31	0.37
Wealth: Quintile 3	1.13	0.93	1.37	0.19
Wealth: Quintile 4	1.23	1.02	1.5	**0.03**
Wealth: Quintile 5 (poorest)	1.28	1.04	1.69	**0.02**
Body Mass Index (BMI)				
BMI<18.5kg/m^2: underweight	0.93	0.5	1.74	0.83

BMI 18.5 -24.9 kg/m^2: normal **(Reference)**	1			
BMI 25.0-29.9kg/m^2: overweight	1.13	0.96	1.33	0.13
BMI >30kg/m^2: obese	1.81	1.53	2.15	**0.00**
Current smoking habits since last ELSA interview				
Non-smoker **(Reference)**	1			
Smoker	1.06	0.86	1.29	0.56
Alcohol consumption in past 12 months				
Never (**Reference)**	1			
Rarely	0.76	0.61	0.94	**0.01**
Frequently	0.65	0.53	0.79	**0.00**
Very frequently	0.64	0.52	0.78	**0.00**

Table 2: Model 1: Independent variables in polypharmacy (5-9 medications) versus no polypharmacy (1-4 medications)

Independent Variables	**Adjusted HR**	95% CI		**Sig.**
		Lower	Upper	
Age				
50-59 years **(Reference)**	1			
60-69 years	1.79	1.21	2.64	**<0.00**
70-79 years	4.11	2.77	6.09	**<0.00**
80+	5.94	3.79	9.29	**<0.00**
Gender				
Male **(Reference)**	1			
Female	0.94	0.71	1.15	0.41
Long standing condition				
No **(Reference)**	1			
Yes	5.30	3.63	7.73	**0.00**
Self-rated health				
Self-rated health: Good **(Reference)**	1			
Self-rated health: Poor	6.69	5.21	8.58	**0.00**
Wealth				
Wealth: Quintile 1 (wealthiest) **(Reference)**	1			
Wealth: Quintile 2	1.41	0.93	2.13	0.11
Wealth: Quintile 3	1.36	0.90	2.06	0.15
Wealth: Quintile 4	1.75	1.17	2.60	**0.006**
Wealth: Quintile 5 (poorest)	2.04	1.34	3.11	**0.001**
Body Mass Index (BMI)				
BMI<18.5kg/m^2: underweight	0.88	0.26	2.95	0.83
BMI 18.5 -24.9 kg/m^2: normal **(Reference)**	1			
BMI 25.0-29.9kg/m^2: overweight	1.38	0.98	1.95	0.07
BMI >30kg/m^2: obese	2.28	1.63	3.21	**0.00**
Current smoking habits since last ELSA interview				
Non-smoker **(Reference)**	1			
Smoker	0.98	0.68	1.39	0.89

Alcohol consumption in past 12 months				
Never (**Reference)**	1			
Rarely	0.70	0.50	0.99	**0.046**
Frequently	0.40	0.29	0.56	**0.00**
Very frequently	0.39	0.27	0.55	**0.00**

Table 3: Model 2: Independent variables in hyper-polypharmacy (10+ medications) versus no polypharmacy (1-4 medications)

Examining the association between age and polypharmacy

In both models, increasing age was associated with polypharmacy and hyper-polypharmacy. For participants aged between 70 years and 79 years, the adjusted hazard ratio for polypharmacy was 3.42 (2.81 to 4.77, p<0.001) (Table 2). This value increased to 4.52 (3.58 to 5.70, p<0.001) in participants aged above 80 years old (Table 2). Similarly, the adjusted hazard ratios for hyper-polypharmacy increased from 4.11 (2.77 to 6.09, p<0.001) in participants aged between 70 years and 79 years to 5.94 (3.79 to 9.29, p<0.001) in participants aged above 80 years old (Table 3). All findings were statistically significant.

Examining the association between the presence of a long-standing condition and polypharmacy

The adjusted hazard ratio for polypharmacy and the presence of a long-standing condition was 2.94 (2.55 to 3.39, p<0.001) (Table 2); whereas, the adjusted hazard ratio for hyper-polypharmacy and the presence of a long-standing condition was 5.30 (3.63 to 7.73, p<0.001) (Table 3). In both models, statistically significant results were generated.

Examining the association between wealth and polypharmacy

The adjusted hazard ratio for polypharmacy increased from 1.08 (0.9 to 1.31, p=0.37) in wealth quintile 2 to 1.28 (1.04 to 1.69, p=0.02) in wealth quintile 5 (Table 2). Similarly, the adjusted hazard ratio for hyper-polypharmacy increased from 1.41 (0.93 to 2.13, p=0.11) in wealth quintile 2 to 2.04 (1.34 to 3.11, p=0.001) in wealth quintile 5 (Table 3). In both models, statistically significant differences in adjusted hazard ratios for polypharmacy and hyper-polypharmacy were detected in the lower wealth quintiles (quintile 4 and 5).

Examining the association between BMI and polypharmacy

In underweight participants, the adjusted hazard ratio for polypharmacy was 0.93 (0.5 to 1.74, p=0.83) (Table 2); whereas, the adjusted hazard ratios for polypharmacy in participants who were overweight or obese were 1.13 (0.96 to 1.33, p=0.13) and 1.81 (1.53 to 2.15, p<0.001) respectively (Table 2). Adjusted hazard ratios for hyper-polypharmacy produced similar results. In underweight participants, the adjusted hazard ratio for hyper-polypharmacy decreased to 0.88 (0.26 to 2.95, p=0.83) (Table 3); whereas, the adjusted hazard ratio for hyper-polypharmacy in overweight participants was 1.38 (0.98 to 1.95, p=0.07) increasing substantially to 2.28 (1.63 to 3.21, p<0.001) in obese participants (Table 3). Only the adjusted hazard ratios for polypharmacy and hyper-polypharmacy, in relation to obesity, produced statistically significant results.

Examining the association between smoking and polypharmacy

The adjusted hazard ratio for polypharmacy and smoking was 1.06 (0.86 to 1.29, p=0.56) (Table 2) whereas the adjusted hazard ratio for hyper-polypharmacy and smoking was 0.98 (0.68 to 1.39, p=0.89) (Table 3). Both models failed to produce any statistically significant results.

Examining the association between alcohol consumption and polypharmacy

Adjusted hazard ratios for polypharmacy and hyper-polypharmacy were calculated using the participant's alcohol consumption data provided during the face-to-face interview. When compared to individuals who reported never drinking alcohol, the adjusted hazard ratio for participants who reported rarely consuming alcohol was 0.76 (0.61 to 0.94, p=0.01) (Table 2). This value decreased further to 0.64 (0.52 to 0.78, p<0.001) in participants who reported drinking alcohol very frequently (Table 2). The adjusted hazard ratios for hyper-polypharmacy produced similar results. For participants who reported rarely consuming alcohol, the adjusted hazard ratio for hyper-polypharmacy was 0.70 (0.50 to 0.99, p=0.046), when compared to individuals who reported never drinking alcohol (Table 3); whereas the adjusted hazard ratio for hyper-polypharmacy in participants who reported drinking alcohol frequently was 0.39 (0.27 to 0.55, p<0.001) (Table 3). All adjusted hazard ratios for polypharmacy and hyper-polypharmacy, in relation to self-reported alcohol consumption, were statistically significant.

DISCUSSION

This study confirms that increasing age and the presence of long-standing conditions are driving polypharmacy prevalence, but also that obesity and lower wealth are independently associated with polypharmacy. Frequent alcohol consumption is inversely associated with polypharmacy prevalence. Results from previous studies, which have investigated the influence of ageing and long-standing conditions on polypharmacy prevalence, complement our findings. [16,17].

In the existing literature, very few studies have investigated whether polypharmacy prevalence is associated with wealth or BMI. [18,19] One study conducted in Rome, analysed a national prescription database and a multivariate model was used to identify participant characteristics which influenced polypharmacy prevalence. [18] The authors concluded that individuals living in lower socio-economic areas are 33% more likely to experience polypharmacy compared to individuals living in higher socio-economic areas. In our study, participants were allocated to one of five wealth quintiles, based upon their wealth index scores. Participants living in the lowest wealth quintiles were 28% more likely to experience polypharmacy and twice as likely to experience hyper-polypharmacy, when compared to participants living in the highest wealth quintile. Our findings were statistically significant, showing that lower wealth is independently associated with an increase in polypharmacy and hyper-polypharmacy prevalence. This finding is important because the latest figures published by the Office of National Statistics [19] show that wealth inequalities across the United Kingdom (UK) have begun to rise again, after a decade-long decline and thus, a widening gap between the UK's wealthiest and poorest households will further drive polypharmacy and hyper-polypharmacy prevalence.

Our multivariate model also revealed that obesity (body mass index >30kg/m^2) was another independent driver of polypharmacy and hyper-polypharmacy prevalence. This finding was

statistically significant. The same association was identified during another study; however, the authors did not comment on the statistical significance of their results, nor did they conduct any further research into the association. [20] Identifying the association between polypharmacy and obesity is also important because obesity has become a major public health concern in England. Assuming the current obesity epidemic continues as predicted, the prevalence of polypharmacy and hyper-polypharmacy among older people in England, is likely to follow suit. [21]

This study found no statistically significant association between smoking and polypharmacy. Similarly, there were no statistically significant association between smoking and hyper-polypharmacy. Our findings are supported by Rajska-Neumann [7] and Henderson et al [22]. However, another study reports that smoking is inversely associated with polypharmacy (adjusted OR 0.42;95%CI,0.33-0.53). [23]

Frequent alcohol consumption in the past year was inversely associated with polypharmacy and hyper-polypharmacy prevalence. This finding is consistent with previous work, involving ELSA, which reported that self-reported alcohol consumption (even at high levels) was not related to poor self-rated health. [24,25] The alcohol findings in this current study could be explained by the sick quitter hypothesis, where individuals stop or reduce their alcohol consumption due to illness. [26] However, Rimm and Moats [27] conclude that the sick quitter hypothesis has been refuted by a wide range of evidence. The inverse association between alcohol consumption and polypharmacy was also detected by Incalzi et al [23] although they appear to discount a genuine association and rather attribute this to bias (i.e. patients in better health are less motivated to correct unhealthy habits).

Finally, most of the existing literature suggests that females take more medications compared to males; however, our study found that there was no statistically significant difference in polypharmacy and hyper-polypharmacy prevalence between males and females. [28,29,30] Pan et al [31] provides support for our findings and concluded that female sex is not independently associated with an increased polypharmacy prevalence.

To our knowledge this is the first study which has used medication data, from a large representative sample of older adults, to determine whether lower wealth, obesity, smoking, alcohol consumption, in addition to increasing age and the presence of long-standing conditions, are independently driving polypharmacy and hyper-polypharmacy prevalence in primary care. All analysed data was obtained using standardised data collection methods and validated data collection tools. Also, this study used a large number of covariates, which reduced the impact of confounders and minimised study bias.

This study has several limitations though. During the nurse visit, participants were asked about their prescribed medications; however, medications purchased without prescription, for example weak analgesics or antihistamines, were not recorded. In addition, when the nurse enquired about prescribed medications, they asked the following question: “Are you taking or using any medications, pills, syrups, ointments, puffers or injections prescribed to you by a doctor or a nurse?” [16] This question refers to some medicinal formulations, but the list is not exhaustive. Thus, a participant using eye drops or wearing a transdermal patch may not have reported this medication as the formulation was not explicitly stated in the question. Therefore, actual medication use may have been higher than recorded medication use, resulting in an underestimation of polypharmacy and hyper-polypharmacy prevalence. Also,

to obtain data about several covariates including smoking habits and alcohol consumption, participants were asked to self-report. This method of data collection relies on all participants accurately and truthfully recalling information to prevent bias. [32] Finally, it is not possible to determine the direction of causality from our data, due to the cross-sectional nature of the study.

CONCLUSION

This study has identified that lower wealth, obesity, increasing age and the presence of long-standing conditions are all independently driving polypharmacy and hyper-polypharmacy prevalence, among older people in primary care. An inverse relationship between frequent alcohol consumption and polypharmacy prevalence was also established. In the future, the effect of obesity and lower wealth on polypharmacy and hyper-polypharmacy prevalence is likely to become more pronounced, as the gap in UK wealth inequalities begins to widen again and the UK obesity epidemic continues. Future exploratory work is required to determine the causation behind these associations.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

- The prevalence of polypharmacy and hyper-polypharmacy is increasing globally
- Increasing age and the presence of long-term conditions are independently associated with an increase in polypharmacy prevalence.
- Few studies have examined whether socio-demographic or lifestyle factors, for example wealth and obesity, are independently associated with polypharmacy.

WHAT THIS STUDY ADDS

- Obesity and lower wealth have been identified as factors which independently drive polypharmacy and especially hyper-polypharmacy.
- Frequent alcohol consumption is inversely associated with polypharmacy and hyper-polypharmacy prevalence.

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CONTRIBUTORSHIP STATEMENT

All authors contributed to the study idea. MF led the study and conducted all data analysis. All authors had full access to ELSA Wave 6 data, supplied by the UK Data Service and they take full responsibility for the integrity and accurate analysis of data. All authors contributed to data interpretation. NS drafted the manuscript with contributions from MF, RV and SW. NS and MF are the Guarantors for this study.

TRANSPARENCY STATEMENT

NS and MF confirm that the manuscript is an honest, accurate and transparent account of the study being reported. No important aspects of this study have been omitted.

COMPETING INTERESTS All authors have completed the ICMJE form for disclosure of potential conflicts of interest available from www.icmje.org/coi_disclosure.pdf and declare that there is nothing to disclose.

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DATA SHARING STATEMENT No additional data is available

REFERENCES

1. Duerden M, Payne R. Polypharmacy – what is it and how common is it? Prescriber. 2014 Nov
2. Guthrie B, Makubate B, Hernandez-Santiago V, Dreischulte T. The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995–2010.BMC Med 2015;13:74
3. The Dynamics of Ageing. Evidence from the English Longitudinal Study of Ageing (Wave 7) 2002-2015. Available from www.ifs.org.uk/uploads/elsa/docs_w7/report.pdf [Accessed 27/07/2017]
4. Department of Health. Long Term Condition Compendium of Information. Third Edition. 2012www.gov.uk/government/uploads/attachment_data/file/216528/dh_134486.pdf [Accessed 27/07/2017]
5. Silveira EA, Dalastra L, Pagotto V. Polypharmacy, chronic diseases and nutritional markers in community-dwelling older. Revista Brasileira de Epidemiologia. 2014 Dec;17(4):818-29.
6. Haider SI, Johnell K, Thorslund M, Fastbom J. Analysis of the association between polypharmacy and socioeconomic position among elderly aged≥ 77 years in Sweden. Clinical therapeutics. 2008 Feb 1;30(2):419-27.
7. Rajska-Neumann A, Szymański M, Balcer N, Grześkowiak E, Szałek E, Wieczorowska-Tobis K. Is smoking a determinant of polypharmacy among elderly subject?. Przeglad lekarski. 2004 Dec;62(10):1145-7.
8. Wong H, Heuberger R, Logomarsino J, Hewlings S. Associations between alcohol use, polypharmacy and falls in older adults: Helen Wong and colleagues report on a cross-sectional study into alcohol consumption, medication use and falls in the community. Nursing older people. 2016 Jan 28;28(1):30-6.
9. Bueno DR, Monteiro HL, Rosa CS, Codogno JS, Fernandes RA, Marucci MF. Association between physical activity levels and polypharmacy in hypertensive patients. Medicina (Ribeirão Preto. Online). 2016;49(3):240-7.
10. Wade KF, Marshall A, Vanhoutte B, Wu FC, O'Neill TW, Lee DM. Does pain predict frailty in older men and women? Findings from the English Longitudinal Study of Ageing (ELSA). The Journals of Gerontology: Series A. 2017 Mar 1;72(3):403-9.
11. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English longitudinal study of ageing. International journal of epidemiology. 2012 Nov 6;42(6):1640-8.
12. Lee DM, Nazroo J, O'Connor DB, Blake M, Pendleton N. Sexual health and well-being among older men and women in England: findings from the English Longitudinal Study of Ageing. Archives of sexual behavior. 2016 Jan 1;45(1):133-44.

13. Nat Cen Social Research. English Longitudinal Study of Ageing Wave 6 interview questionnaire. Version 3.0 Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/main_questionnaire.pdf [Accessed 5/9/2017]
14. English Longitudinal Study of Ageing Health and Lifestyles of People aged 50 or over. Self-completion questionnaire. Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/self_completion_main.pdf [Accessed 5/9/2017]
15. Nat Cen Social Research. English Longitudinal Study of Ageing Wave 6 Nurse questionnaire. 2012-2013. Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/nurse_documentation.pdf [Accessed 5/9/2017]
16. Bjerrum L, Søgaard J, Hallas J, Kragstrup J. Polypharmacy: correlations with sex, age and drug regimen A prescription database study. European journal of clinical pharmacology. 1998 Jun 1;54(3):197-202
17. The Irish Longitudinal Study of Ageing. Main Questionnaire 2010.Available from http://www.ucd.ie/issda/static/documentation/tilda/tilda-capi-qaire-wave1.pdf [Accessed 5/9/2017]
18. Fano V, Chini F, Pezzotti P, Bontempi K. Estimating the Prevalence and the Determinants of Polypharmacy Using Data from a Health Administrative Database: A Comparison of Results Obtained Employing Different Algorithms. Advances in Pharmacoepidemiology & Drug Safety. 2014;3(151):2167-1052.
19. The Office of National Statistics Report: Chapter 2 Total Wealth, Wealth in GB, 2012-2014. Available from http://webarchive.nationalarchives.gov.uk/20160105170657/http://www.ons.gov.uk/ons/rel/was/wealth-in-great-britain-wave-4/2012-2014/rpt-chapter-2.html
20. Team CP. The impact of obesity on drug prescribing in primary care. The British Journal of General Practice. 2005 Oct 1;55(519):743.
21. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. The Lancet. 2011 Sep 2;378(9793):815-25.
22. Henderson JA, Buchwald D, Manson SM. Relationship of medication use to health-related quality of life among a group of older American Indians. Journal of applied gerontology. 2006 Feb;25(1_suppl):89S-104S.
23. Incalzi RA, Corsonello A, Pedone C, Corica F, Carbonin P. Depression and drug utilization in an elderly population. Therapeutics and clinical risk management. 2005 Mar;1(1):55.
24. Frisher M, Mendonça M, Shelton N, Pikhart H, de Oliveira C, Holdsworth C. Is alcohol consumption in older adults associated with poor self-rated health? Cross-sectional and longitudinal analyses from the English Longitudinal Study of Ageing. BMC public health. 2015 Jul 24;15(1):703.
25. Holdsworth C, Mendonca M, Pikhart H, Frisher M, de Oliveira C, Shelton N. Is regular drinking in later life an indicator of good health? Evidence from the English Longitudinal Study of Ageing. J Epidemiol Community Health 2016 Aug 1;70(8):764-70
26. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men: Explaining the U-shaped curve. Lancet. 1988; 2:1267–1273.
27. Rimm EB, Moats C. Alcohol and coronary heart disease: drinking patterns and mediators of effect. Annals of Epidemiology. 2007. May 31; 17(5): S3-7
28. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. Jama. 2002 Jan 16;287(3):337-44.
29. Schuler J, Dückelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wiener klinische Wochenschrift. 2008 Dec 1;120(23):733-41.
30. Wauters M, Elseviers M, Vaes B, Degryse J, Dalleur O, Vander Stichele R, Van Bortel L, Azermai M. Polypharmacy in a Belgian cohort of community-dwelling oldest old (80+). Acta Clinica Belgica. 2016 May 3;71(3):158-66.
31. Pan HH, Li CY, Chen TJ, Su TP, Wang KY. Association of polypharmacy with fall-related fractures in older Taiwanese people: age-and gender-specific analyses. BMJ open. 2014 Mar 1;4(3): e004428. Depression and drug utilization in an elderly population
32. Barker, C., Pistrang, N. and Elliott, R. (2002) Self-Report Methods, in Research Methods in Clinical Psychology: An Introduction for Students and Practitioners, Second Edition, John Wiley & Sons, Ltd, Chichester, UK. doi: 10.1002/0470013435.ch6

SUPPLEMENTARY MATERIAL:

Bivariate correlations between covariates

	Frequent alcohol intake	Increased age	Low wealth	Smoking	Obesity	poor self-rated health	Presence of long-standing condition	Gender (female)	Polypharmacy
Frequent alcohol intake	1	-0.106	-0.251	-0.108	-0.094	-0.220	-0.137	-0.204	-0.188
Increased age	-0.106	1	-0.049	-0.195	-0.033	0.118	0.141	0.010	0.353
Low wealth	-0.251	-0.049	1	0.205	0.135	0.218	0.107	0.059	0.149
Smoking	-0.108	-0.195	0.205	1	-0.117	0.107	0.000	0.044	-0.040
Obesity	-0.094	-0.033	0.135	-0.117	1	0.142	0.115	-0.030	0.187
Poor self-rated health	-0.220	0.118	0.218	0.107	0.142	1	0.407	-0.010	0.421
Presence of long-standing condition	-0.137	0.141	0.107	0.000	0.115	0.407	1	0.006	0.473
Gender (female)	-0.204	0.010	0.059	0.044	-0.030	-0.010	0.006	1	0.011
Poly pharmacy	-0.188	0.353	0.149	-0.040	0.187	0.421	0.473	0.011	1

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	3-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	9-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-9
		(*b*) Report category boundaries when continuous variables were categorized	8-9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Factors associated with polypharmacy in primary care: A cross-sectional analysis of data from The English Longitudinal Study of Ageing (ELSA)

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Factors associated with polypharmacy in primary care: A cross-sectional analysis of data from The English Longitudinal Study of Ageing (ELSA)

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ABSTRACT:

OBJECTIVES: While older age and ill-health are known to be associated with polypharmacy, this paper aims to identify whether wealth, body mass index (BMI), smoking and alcohol consumption are also contributing to polypharmacy (5-9 prescribed medications) and hyper-polypharmacy prevalence (≥10 prescribed medications), among older people living in England.

DESIGN: Cross-sectional study

SETTING: The English Longitudinal Study of Ageing Wave 6 (2012-2013)

PARTICIPANTS: 7730 participants aged over 50 years old

DATA SYNTHESIS: Two multivariate models were created. Hazard ratios (HR) with corresponding 95% confidence intervals (CI), for polypharmacy and hyper-polypharmacy, were calculated after adjusting for gender, age, wealth, smoking, alcohol consumption, BMI, self-rated health and the presence of a chronic health condition.

RESULTS: Lower wealth (adjusted HR highest wealth quintile versus lowest wealth quintile, 1.28; 95%CI, 1.04-1.69, p=0.02) and obesity (adjusted HR 1.81; 95%CI, 1.53-2.15, p<0.001) were significantly associated with polypharmacy. Increasing age (adjusted HR 50-59 years versus 70-79 years, 3.42; 95% CI, 2.81-4.77, p<0.001) and the presence of a chronic health condition (adjusted HR 2.94;95%CI, 2.55-3.99, p<0.001) were also associated with polypharmacy. No statistically significant association between smoking and polypharmacy (adjusted HR 1.06; 95% CI, 0.86-1.29, p=0.56) was established; whilst, very frequent alcohol consumption (consuming alcohol >5 times per week) was inversely associated with polypharmacy (adjusted HR never drank versus very frequently, 0.64; 95%CI, 0.52-0.78, p<0.001). The adjusted hazard ratios for hyper-polypharmacy were accentuated, compared to polypharmacy.

CONCLUSION: This study has identified that lower wealth, obesity, increasing age and chronic health conditions are significantly associated with polypharmacy and hyper-polypharmacy prevalence. The effect of these factors, on polypharmacy and especially hyper-polypharmacy prevalence, is likely to become more pronounced with the widening gap in UK wealth inequalities, the current obesity epidemic and the growing population of older people. The alcohol findings contribute to the debate on the relationship between alcohol consumption and health.

Keywords: polypharmacy, longitudinal, demography, older people

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This cross-sectional study uses medication data, from over 7000 older individuals, to identify factors which are associated with polypharmacy prevalence in primary care.
- In the analysis, a large number of covariates were used to minimise the impact of confounding factors.
- Participants were asked to self-report information about their prescribed medication usage. To verify their responses, participants were asked to show their medication containers to the interviewer.
- Smoking and alcohol consumption data was also collected by asking participants to self-report. This relies on accurate and truthful information recall to prevent bias.

INTRODUCTION

Polypharmacy has been discussed extensively in the literature and media; however, there is no universally accepted definition for the practice of prescribing multiple medications to one individual. [1] At present, polypharmacy is commonly defined as "the use of five or more regular medications", whilst hyper-polypharmacy, which is sometimes termed as "excessive polypharmacy", is defined as "the use of ten or more regular medications". [2] Although polypharmacy prevalence has increased over the past decade, there are relatively few data about the factors associated with polypharmacy and hyper-polypharmacy in primary care.[3]

Previous studies have shown that increasing age and the presence of chronic conditions are significantly associated with an increase in polypharmacy prevalence. [4-6] Comparatively fewer studies have examined whether socio-demographic or lifestyle factors, for example wealth and obesity, are associated with polypharmacy. In a study conducted by Haider et al, [7] no statistically significant association between polypharmacy and an individual's socio-economic status was established. The findings from a study by Rajska-Neumann [8] revealed that there was no statistically significant difference in polypharmacy prevalence between smokers and non-smokers; whereas a statistically significant inverse relationship between alcohol consumption and the concomitant administration of medications was detected by Wong et al. [9] Finally, when Bueno et al [10] examined the association between polypharmacy and obesity, an adjusted odds ratio revealed that obese individuals (BMI >30kg/m^2) were 1.6 times more likely to be experiencing polypharmacy, compared to individuals with a BMI less than 30kg/m^2. To evaluate the relationship between the aforementioned factors and polypharmacy prevalence in primary care, a large sample study is required.

This study used data from The English Longitudinal Study of Ageing (ELSA) as this provided an opportunity to link polypharmacy and hyper-polypharmacy data to participants' personal data. In particular, this study aimed to determine whether wealth, body mass index (BMI), smoking, alcohol consumption, age and the presence of chronic health conditions, are associated with polypharmacy (5-9 prescribed medications) and hyper-polypharmacy (≥10 prescribed medications) prevalence in a community population of older people living in England.

METHOD

Sample and participants

A cross-sectional study was conducted using Wave 6 data from The English Longitudinal Study of Ageing (ELSA). Data collection took place between May 2012 and June 2013, from a representative sample of the English population who were aged 50 years or above.

Since ELSA began in 2002, participants have been asked to provide personal information about their household finances, health status, lifestyle choices and social interactions, on a bi-annual basis. In Wave 6, information from 10,601 participants was collected, which included 9,169 'core' participants. Members were considered 'core' if they were aged over 50 years old at the time of study enrollment and living at private residential addresses in England. [11] 8,054 nurse visits were completed at Wave 6, of whom 7,730 were carried out with core members. This latter group are the focus of the current study. [11]

Patient Involvement and Ethics

Ethical approval for ELSA Wave 6 was granted from the National Research Ethics Committee under the National Research and Ethics Service (NRES). All participants were required to provide informed written consent. [12] All ELSA data is anonymous and freely accessible from the UK Data Service Discover. [13] Only data contained within the ELSA database was included in the analyses. No patients were involved in the development of the research question, study design or interpretation of the data in this study; therefore, ethical approval was not required for this study.

Data Collection

Face-to-face interviews

The face-to-face interviews were conducted by trained interviewers, who asked participants to provide information about their current lifestyle choices, including smoking habits and alcohol consumption over the past twelve months. Smoking status was recorded as current smoker or non-smoker; whereas, the frequency of alcohol consumption over the past year was recorded as never, rarely, frequently or very frequently. [14] Rarely was defined as drinking alcohol less than twice a month. Frequently was defined as drinking alcohol between one and four times a week; whilst, very frequently was defined as drinking alcohol at least five times a week.

Participants were also asked to describe their current health status. Participants could select one of the following options: "excellent, very good, good, fair or poor". [15] These responses were converted into a two-level variable: good/fair and poor, with good/fair health status being the sum of responses ranging from "excellent" to "fair". In a subsequent question, participants were asked whether they had any chronic health conditions. Participants could answer this question with either yes or no. [15].

Finally, participants were asked to provide information about their household income, including information about their employment status, personal finances, assets, pensions and other benefits. Participant pension data was excluded when wealth index scores were calculated. Based upon their wealth index scores, participants were allocated to one of five wealth quintiles. Quintile 1 was the most affluent, whilst quintile 5 was the poorest.

Questionnaire

After completion of the face-to-face interview, participants were asked to complete a paper-based questionnaire. The questionnaire was designed to obtain further information about the participants' living arrangements, health status, lifestyle choices and social interactions. [16]

Nurse visit

The nurse visits took place in the participant's home. At the beginning of the visit, the nurse recorded information about participant demographics and their currently prescribed medications. Prescribed medication formulations were defined by the nurses as "pills, syrups, ointments, inhalers or injections". [17] If a participant reported taking one or more prescribed medications, the nurse sought their permission to record the name of their medication, in addition to seeing its container. The nurse determined current medication usage by asking the participant to confirm whether they had taken or used each reported medicine within the last seven days. [17] A maximum of 27 prescribed medications could be recorded for each participant. Medication information was coded by the nurse, according to the British National Formulary (Edition 61) chapter and subsection.

During the latter part of the visit, the nurse conducted a physical examination and recorded information about the participant's blood pressure, grip strength, height, weight and lung function. [17] Using a participant's height and weight data, it was possible to calculate their body mass index. A BMI <18.5kg/m^2 was recorded as underweight, a BMI value between 18.5 -24.9 kg/m^2 was considered to be normal weight; whereas, a BMI of 25.0-29.9kg/m^2 was recorded as overweight and a BMI >30kg/m^2 was recorded as obese.

Inclusion Criteria

All participants must have completed a face-to-face interview, a paper-based questionnaire and received a nurse visit during ELSA wave 6 to meet the inclusion criteria for this study. [18]

Defining polypharmacy and hyper-polypharmacy

Polypharmacy was defined as the concurrent use of five to nine currently prescribed medications, whilst hyper-polypharmacy was defined as the concurrent use of ten or more currently prescribed medications. These definitions have been used previously in other population based studies. [3,19]

Data analysis

Initially, descriptive statistics were used to summarise the prevalence of polypharmacy and hyper-polypharmacy among participants. These data were subsequently stratified according to participant demographics. In the second part of the analysis, a bivariate model was used to assess the relationship between polypharmacy and the following independent variables: frequent alcohol consumption, increasing age, poor wealth, female sex, smoking, raised body mass index (BMI), poor self-rated health and the presence of a chronic health condition. Bivariate correlations between other covariates were also examined. Findings were presented as Pearson correlation coefficients (*r*). The strength of each correlation was considered and described as either strong (1.00 – 0.50), moderate (0.49-0.30) or weak (0.29-0.10).[20]

In the final part of the analysis, two multivariate models were created to identify associations between participant characteristics and polypharmacy prevalence. Based upon previous work by Peduzzi et al [21], the minimum sample size required for the first multivariate model (polypharmacy) was 333; whilst the minimum sample size required for the second multivariate model (hyper-polypharmacy) was 1250. In both models, ill health was controlled for by using participants taking between one and four prescribed medications. This group of participants formed the control group. Participants taking no prescribed medications were excluded from this part of the analysis. In the first model, participants taking 5 to 9 medications were compared to the control group (1 to 4 prescribed medications). In the second model, participants taking 10 or more medications were compared to the control group (1 to 4 prescribed medications). Hazard ratios with corresponding 95% confidence intervals (CI), for polypharmacy and hyper-polypharmacy, were calculated after adjusting for covariates. The following factors were considered as covariates: gender, age, wealth, smoking, alcohol consumption, BMI, self-rated health and the presence of a chronic health condition. Missing data was coded as "missing" and presented as a separate category in the multivariate models. The data generated from the models was statistically significant if $p<0.05$. All data analysis was undertaken using SPSS version 24.0.

RESULTS

Participant Characteristics:

A total of 7730 participants' data from ELSA Wave 6 were analysed. Participant characteristics are presented in Table 1. The mean age of participants in Wave 6 was 67.6 years, and 55.4% (n=4282/7730) of the sample were female. Overall, 24.1% (n= 1862/7730) of the participants received polypharmacy and 6.4% (n=494/7730) were receiving hyper-polypharmacy (Table 1). The proportion of individuals receiving polypharmacy and hyper-polypharmacy increased steadily with age. However, the prevalence of polypharmacy and hyper-polypharmacy in males and females was similar. (Table 1)

	No medications	1-4 medications	5-9 medications	≥10 medications
Participant Characteristics:			**Polypharmacy**	**Hyper-polypharmacy**
All participants (n=7730)	23.8%	45.7%	24.1%	6.4%
Age:				
50-59 years (n=1695)	43.2%	42.4%	11.7%	2.7%
60-69 years (n=3012)	26.6%	49.2%	19.6%	4.6%
70-79 years (n=2114)	11.8%	45.9%	33.1%	9.2%
80+ years (n=909)	6.4%	39.6%	41.3%	12.7%
Gender:				
Male (n=3448)	24.9%	44.6%	24.4%	6.1%
Female (n=4282)	22.9%	46.6%	23.9%	6.6%
Chronic health condition:				
Yes (n=4289)	9.6%	44.5%	35.2%	10.7%
No (n=3441)	41.6%	47.1%	10.3%	1.0%

Table 1: Polypharmacy versus patient characteristics

Overall, 35.2% (n= 1509/4289) of participants who reported having a chronic health condition were receiving polypharmacy; whereas, 10.7% (n=459/4289) were receiving hyper-polypharmacy. Only 10.3% (n=353/3441) and 1.0% (n=35/3441) of participants with no chronic health conditions, received polypharmacy and hyper-polypharmacy respectively (Table 1).

In a bivariate model, moderate positive correlations were detected between polypharmacy and the following variables: the presence of a chronic health condition, poor self-rated health and increasing age. A weak positive correlation between polypharmacy and a high BMI was established. Similarly, there was a weak positive correlation between lower wealth and polypharmacy. No correlations between gender and polypharmacy, and smoking and polypharmacy, were established. However, there was a weak negative correlation between polypharmacy and frequent alcohol consumption. All bivariate correlations are presented in Figure 1. Bivariate correlations between other covariates were also examined, and data is available in online supplementary table 1.

To determine whether other variables are associated with polypharmacy and hyper-polypharmacy, the results from the two multivariate models (Polypharmacy-1 and Hyper-polypharmacy-2) were analysed and presented in Table 2 and Table 3 respectively.

Independent Variables	**Adjusted HR**	95% CI		**Sig.**
		Lower	Upper	
Age				
50-59 years **(Reference)** (n=963)	1			
60-69 years (n=2210)	1.66	1.37	2.01	**<0.00**
70-79 years (n=2344)	3.42	2.81	4.77	**<0.00**
80+ (n=371)	4.52	3.58	5.70	**<0.00**
Gender				
Male **(Reference)** (n=2588)	1			
Female (n=3300)	0.92	0.81	1.04	0.21
Chronic health condition				
No **(Reference)** (n=2008)	1			
Yes (n=3879)	2.94	2.55	3.39	**0.00**
Missing chronic health condition data (n=1)				
Self-rated health				
Self-rated health: Good **(Reference)** (n=3907)	1			
Self-rated health: Poor (n=1978)	2.98	2.61	3.4	**0.00**
Missing self-rated health data (n=3)				
Wealth				
Wealth: Quintile 1 (wealthiest) **(Reference)** (n=1237)	1			
Wealth: Quintile 2 (n=1244)	1.08	0.9	1.31	0.37
Wealth: Quintile 3 (n=1196)	1.13	0.93	1.37	0.19
Wealth: Quintile 4 (n=1190)	1.23	1.02	1.5	**0.03**
Wealth: Quintile 5 (poorest) (n=921)	1.28	1.04	1.69	**0.02**
Missing wealth data (n=100)				
Body Mass Index (BMI)				
BMI<18.5kg/m^2: underweight (n=54)	0.93	0.5	1.74	0.83
BMI 18.5 -24.9 kg/m^2: normal **(Reference)** (n=1313)	1			
BMI 25.0-29.9kg/m^2: overweight (n=2272)	1.13	0.96	1.33	0.13

BMI >30kg/m^2: obese (n=1930)	1.81	1.53	2.15	**0.00**
Missing BMI data (n=319)				
Current smoking habits since last ELSA interview				
Non-smoker **(Reference)** (n=3153)	1			
Smoker (n=650)	1.06	0.86	1.29	0.56
Missing smoking data (n=2085)				
Alcohol consumption in past 12 months				
Never (**Reference)** (n=792)	1			
Rarely (n=930)	0.76	0.61	0.94	**0.01**
Frequently (n=1797)	0.65	0.53	0.79	**0.00**
Very frequently (n=1791)	0.64	0.52	0.78	**0.00**
Missing alcohol consumption data (n=578)				

Table 2: Model 1: Independent variables in polypharmacy (5-9 medications, n=2356) versus no polypharmacy (1-4 medications, n=3532)

Independent Variables	**Adjusted HR**	95% CI		**Sig.**
		Lower	Upper	
Age				
50-59 years **(Reference)** (n=765)	1			
60-69 years (n=1620)	1.79	1.21	2.64	**<0.00**
70-79 years (n=1444)	4.11	2.77	6.09	**<0.00**
80+ (n=197)	5.94	3.79	9.29	**<0.00**
Gender				
Male **(Reference)** (n=1748)	1			
Female (n=2278)	0.94	0.71	1.15	0.41
Chronic health condition				
No **(Reference)** (n=1656)	1			
Yes (n=2370)	5.30	3.63	7.73	**0.00**
Self-rated health				
Self-rated health: Good **(Reference)** (n=2944)	1			
Self-rated health: Poor (n=1081)	6.69	5.21	8.58	**0.00**
Missing self-rated health data (n=1)				
Wealth				
Wealth: Quintile 1 (wealthiest) **(Reference)** (n=907)	1			
Wealth: Quintile 2 (n=875)	1.41	0.93	2.13	0.11
Wealth: Quintile 3 (n=797)	1.36	0.90	2.06	0.15
Wealth: Quintile 4 (n=756)	1.75	1.17	2.60	**0.006**
Wealth: Quintile 5 (poorest) (n=611)	2.04	1.34	3.11	**0.001**
Missing wealth data (n=80)				
Body Mass Index (BMI)				
BMI<18.5kg/m^2: underweight (n=38)	0.88	0.26	2.95	0.83
BMI 18.5 -24.9 kg/m^2: normal **(Reference)** (n=959)	1			
BMI 25.0-29.9kg/m^2: overweight (n=1633)	1.38	0.98	1.95	0.07
BMI >30kg/m^2: obese (n=1205)	2.28	1.63	3.21	**0.00**
Missing BMI data (n=191)				

Current smoking habits since last ELSA interview				
Non-smoker **(Reference)** (n=2077)	1			
Smoker (n=424)	0.98	0.68	1.39	0.89
Missing smoking data (n=1525)				
Alcohol consumption in past 12 months				
Never (**Reference)** (n=489)	1			
Rarely (n=619)	0.70	0.50	0.99	**0.046**
Frequently (n=1256)	0.40	0.29	0.56	**0.00**
Very frequently (n=1293)	0.39	0.27	0.55	**0.00**
Missing alcohol consumption data (n=369)				

Table 3: Model 2: Independent variables in hyper-polypharmacy (≥10 medications, n=494) versus no polypharmacy (1-4 medications, n=3532)

Examining the association between age and polypharmacy

In both models, increasing age was associated with polypharmacy and hyper-polypharmacy. For participants aged between 70 years and 79 years, the adjusted hazard ratio for polypharmacy was 3.42 (2.81 to 4.77, p<0.001) (Table 2). This value increased to 4.52 (3.58 to 5.70, p<0.001) in participants aged above 80 years old (Table 2). Similarly, the adjusted hazard ratios for hyper-polypharmacy increased from 4.11 (2.77 to 6.09, p<0.001) in participants aged between 70 years and 79 years to 5.94 (3.79 to 9.29, p<0.001) in participants aged above 80 years old (Table 3). All findings were statistically significant.

Examining the association between the presence of a chronic health condition and polypharmacy

The adjusted hazard ratio for polypharmacy and the presence of a chronic health condition was 2.94 (2.55 to 3.39, p<0.001) (Table 2); whereas, the adjusted hazard ratio for hyper-polypharmacy and the presence of a chronic health condition was 5.30 (3.63 to 7.73, p<0.001) (Table 3). In both models, statistically significant results were generated.

Examining the association between wealth and polypharmacy

The adjusted hazard ratio for polypharmacy increased from 1.08 (0.9 to 1.31, p=0.37) in wealth quintile 2 to 1.28 (1.04 to 1.69, p=0.02) in wealth quintile 5 (Table 2). Similarly, the adjusted hazard ratio for hyper-polypharmacy increased from 1.41 (0.93 to 2.13, p=0.11) in wealth quintile 2 to 2.04 (1.34 to 3.11, p=0.001) in wealth quintile 5 (Table 3). In both models, statistically significant differences in adjusted hazard ratios for polypharmacy and hyper-polypharmacy were detected in the lower wealth quintiles (quintile 4 and 5).

Examining the association between BMI and polypharmacy

In underweight participants, the adjusted hazard ratio for polypharmacy was 0.93 (0.5 to 1.74, p=0.83) (Table 2); whereas, the adjusted hazard ratios for polypharmacy in participants who were overweight or obese were 1.13 (0.96 to 1.33, p=0.13) and 1.81 (1.53 to 2.15, p<0.001) respectively (Table 2). Adjusted hazard ratios for hyper-polypharmacy produced similar results. In underweight participants, the adjusted hazard ratio for hyper-polypharmacy decreased to 0.88 (0.26 to 2.95, p=0.83) (Table 3); whereas, the adjusted hazard ratio for hyper-polypharmacy in overweight participants was 1.38 (0.98 to 1.95, p=0.07) increasing

substantially to 2.28 (1.63 to 3.21, p<0.001) in obese participants (Table 3). Only the adjusted hazard ratios for polypharmacy and hyper-polypharmacy, in relation to obesity, produced statistically significant results.

Examining the association between smoking and polypharmacy

The adjusted hazard ratio for polypharmacy and smoking was 1.06 (0.86 to 1.29, p=0.56) (Table 2) whereas the adjusted hazard ratio for hyper-polypharmacy and smoking was 0.98 (0.68 to 1.39, p=0.89) (Table 3). Both models failed to produce any statistically significant results.

Examining the association between alcohol consumption and polypharmacy

Adjusted hazard ratios for polypharmacy and hyper-polypharmacy were calculated using the participant's alcohol consumption data provided during the face-to-face interview. When compared to individuals who reported never drinking alcohol, the adjusted hazard ratio for participants who reported rarely consuming alcohol was 0.76 (0.61 to 0.94, p=0.01) (Table 2). This value decreased further to 0.64 (0.52 to 0.78, p<0.001) in participants who reported drinking alcohol very frequently (Table 2). The adjusted hazard ratios for hyper-polypharmacy produced similar results. For participants who reported rarely consuming alcohol, the adjusted hazard ratio for hyper-polypharmacy was 0.70 (0.50 to 0.99, p=0.046), when compared to individuals who reported never drinking alcohol (Table 3); whereas the adjusted hazard ratio for hyper-polypharmacy in participants who reported drinking alcohol frequently was 0.39 (0.27 to 0.55, p<0.001) (Table 3). All adjusted hazard ratios for polypharmacy and hyper-polypharmacy, in relation to self-reported alcohol consumption, were statistically significant.

DISCUSSION

This study confirms that increasing age and the presence of chronic health conditions are associated with polypharmacy prevalence, but also that obesity and lower wealth are significantly associated with polypharmacy. Frequent alcohol consumption is inversely associated with polypharmacy prevalence. Results from previous studies, which have investigated the influence of ageing and chronic health conditions on polypharmacy prevalence, complement our findings. [19,22,23].

In the existing literature, few studies have investigated whether polypharmacy prevalence is associated with wealth or BMI. [24,25] One study conducted in Rome, analysed a national prescription database and a multivariate model was used to identify participant characteristics which influenced polypharmacy prevalence. [24] The authors concluded that individuals living in lower socio-economic areas are 33% more likely to experience polypharmacy compared to individuals living in higher socio-economic areas. In our study, participants were allocated to one of five wealth quintiles, based upon their wealth index scores. Participants living in the lowest wealth quintiles were 28% more likely to experience polypharmacy and twice as likely to experience hyper-polypharmacy, when compared to participants living in the highest wealth quintile. Our findings show that lower wealth is significantly associated with an increase in polypharmacy and hyper-polypharmacy prevalence. This finding is important because the latest figures published by the Office of National Statistics [25] show that wealth inequalities across the United Kingdom (UK) have begun to rise again, after a decade-long decline. There is also evidence to suggest that the

incidence of chronic health conditions and multi-morbidities is highest among individuals residing in deprived areas. [26,27] The aforementioned individuals are likely to require multiple medications to manage or treat their chronic conditions and thus, providing support for the association between lower wealth and polypharmacy.

Our multivariate model also revealed that obesity (body mass index >30kg/m^2) was another factor associated with polypharmacy and hyper-polypharmacy prevalence. This finding was statistically significant. The same association was identified during another study; however, the authors did not comment on the statistical significance of their results, nor did they conduct any further research into the association. [28] Identifying the association between polypharmacy and obesity is also important because obesity has become a major public health concern in England. Assuming the current obesity epidemic continues as predicted, the prevalence of polypharmacy and hyper-polypharmacy among older people in England, is likely to follow suit. [29]

This study found no statistically significant association between smoking and polypharmacy. Similarly, there were no statistically significant association between smoking and hyper-polypharmacy. Our findings are supported by Rajska-Neumann [8] and Henderson et al [30]. However, another study reports that smoking is inversely associated with polypharmacy (adjusted OR 0.42;95%CI,0.33-0.53). [31]

Frequent alcohol consumption in the past year was inversely associated with polypharmacy and hyper-polypharmacy prevalence. This finding is consistent with previous work, involving ELSA, which reported that self-reported alcohol consumption (even at high levels) was not related to poor self-rated health. [32,33] The alcohol findings in this current study could be explained by the sick quitter hypothesis, where individuals stop or reduce their alcohol consumption due to illness. [34] However, Rimm and Moats [35] conclude that the sick quitter hypothesis has been refuted by a wide range of evidence. The inverse association between alcohol consumption and polypharmacy was also detected by Incalzi et al [31] although they appear to discount a genuine association and rather attribute this to bias (i.e. patients in better health are less motivated to correct unhealthy habits).

Finally, most of the existing literature suggests that females take more medications compared to males; however, our study found that there was no statistically significant difference in polypharmacy and hyper-polypharmacy prevalence between males and females. [36,37,38] Pan et al [39] provides support for our findings and concluded that female sex is not significantly associated with an increased polypharmacy prevalence.

To our knowledge this is the first study which has used medication data, from a large representative sample of older adults, to determine whether lower wealth, obesity, smoking, alcohol consumption, in addition to increasing age and the presence of chronic health conditions, are associated with polypharmacy and hyper-polypharmacy prevalence in primary care. All analysed data was obtained using standardised data collection methods and validated data collection tools. Also, this study used a large number of covariates, which reduced the impact of confounders and minimised study bias.

This study has several limitations. Actual medication use among participants may have been higher than recorded medication use for several reasons. Firstly, participants were asked about their prescribed medications; however, medications purchased without prescription, for

example weak analgesics or antihistamines, were not recorded. Secondly, prescribed medications were coded according to BNF chapter and subsection. It was assumed that each code presented a single active ingredient; however, several combination drugs, for example co-amilofruse and co-amilozide, were also represented by a single code. Furthermore, when the nurse enquired about prescribed medications, they asked the following question: "Are you taking or using any medications, pills, syrups, ointments, puffers or injections prescribed to you by a doctor or a nurse?" [19] This question refers to some medicinal formulations, but the list is not exhaustive. Thus, a participant using eye drops or wearing a transdermal patch may not have reported this medication as the formulation was not explicitly stated in the question. Consequently, polypharmacy and hyper-polypharmacy prevalence may have been underestimated in this study.

To obtain data about prescribed medications and several other covariates, including smoking habits and alcohol consumption, participants were asked to self-report. This method of data collection relies on all participants accurately and truthfully recalling information to prevent bias. [40] The risk of recall bias associated with prescribed medication information was minimised by the nurse, because participants were asked to show their medication containers to verify their responses. However, it was not possible to minimise the risk of recall bias associated with the other covariates. Finally, it is not possible to determine the direction of causality from our data, due to the cross-sectional nature of the study.

CONCLUSION

This study has identified that lower wealth, obesity, increasing age and the presence of chronic health conditions are all associated with polypharmacy and hyper-polypharmacy prevalence, among older people in primary care. An inverse relationship between frequent alcohol consumption and polypharmacy prevalence was also established. In the future, the effect of obesity and lower wealth on polypharmacy and hyper-polypharmacy prevalence is likely to become more pronounced, as the gap in UK wealth inequalities begins to widen again and the UK obesity epidemic continues. Future exploratory work is required to determine the causation behind these associations.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

- The prevalence of polypharmacy and hyper-polypharmacy is increasing globally
- Increasing age and the presence of chronic health conditions are associated with an increase in polypharmacy prevalence.
- Few studies have examined whether socio-demographic or lifestyle factors, for example wealth and obesity, are associated with polypharmacy.

WHAT THIS STUDY ADDS

- Obesity and lower wealth have been identified as factors which are significantly associated with polypharmacy and especially hyper-polypharmacy. As the gap in UK wealth inequalities widens and the UK obesity epidemic continues, the effect these factors on polypharmacy prevalence is likely to become more pronounced.

- Frequent alcohol consumption is inversely associated with polypharmacy and hyper-polypharmacy prevalence.

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CONTRIBUTORSHIP STATEMENT

All authors contributed to the study idea. MF led the study and conducted all data analysis. All authors had full access to ELSA Wave 6 data, supplied by the UK Data Service and they take full responsibility for the integrity and accurate analysis of data. All authors contributed to data interpretation. NS drafted the manuscript with contributions from MF, RV and SW. NS and MF are the Guarantors for this study.

TRANSPARENCY STATEMENT

NS and MF confirm that the manuscript is an honest, accurate and transparent account of the study being reported. No important aspects of this study have been omitted.

COMPETING INTERESTS All authors have completed the ICMJE form for disclosure of potential conflicts of interest available from www.icmje.org/coi_disclosure.pdf and declare that there is nothing to disclose.

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DATA SHARING STATEMENT No additional data is available; however, anonymous ELSA data is publicly available from https://discover.ukdataservice.ac.uk/ [36]

REFERENCES

1. Duerden M, Payne R. Polypharmacy – what is it and how common is it? Prescriber. 2014 Nov
2. O'Dwyer M, Peklar J, McCallion P, McCarron M, Henman MC. Factors associated with polypharmacy and excessive polypharmacy in older people with intellectual disability differ from the general population: a cross-sectional observational nationwide study. BMJ open. 2016 Apr 1;6(4):e010505.
3. Guthrie B, Makubate B, Hernandez-Santiago V, Dreischulte T. The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995–2010.BMC Med 2015;13:74
4. The Dynamics of Ageing. Evidence from the English Longitudinal Study of Ageing (Wave 7) 2002-2015. Available from www.ifs.org.uk/uploads/elsa/docs_w7/report.pdf [Accessed 27/07/2017]

5. Department of Health. Long Term Condition Compendium of Information. Third Edition. 2012www.gov.uk/government/uploads/attachment_data/file/216528/dh_134486.pdf [Accessed 27/07/2017]
6. Silveira EA, Dalastra L, Pagotto V. Polypharmacy, chronic diseases and nutritional markers in community-dwelling older. Revista Brasileira de Epidemiologia. 2014 Dec;17(4):818-29.
7. Haider SI, Johnell K, Thorslund M, Fastbom J. Analysis of the association between polypharmacy and socioeconomic position among elderly aged≥ 77 years in Sweden. Clinical therapeutics. 2008 Feb 1;30(2):419-27.
8. Rajska-Neumann A, Szymański M, Balcer N, Grześkowiak E, Szałek E, Wieczorowska-Tobis K. Is smoking a determinant of polypharmacy among elderly subject?. Przeglad lekarski. 2004 Dec;62(10):1145-7.
9. Wong H, Heuberger R, Logomarsino J, Hewlings S. Associations between alcohol use, polypharmacy and falls in older adults: Helen Wong and colleagues report on a cross-sectional study into alcohol consumption, medication use and falls in the community. Nursing older people. 2016 Jan 28;28(1):30-6.
10. Bueno DR, Monteiro HL, Rosa CS, Codogno JS, Fernandes RA, Marucci MF. Association between physical activity levels and polypharmacy in hypertensive patients. Medicina (Ribeirão Preto. Online). 2016;49(3):240-7.
11. Wade KF, Marshall A, Vanhoutte B, Wu FC, O'Neill TW, Lee DM. Does pain predict frailty in older men and women? Findings from the English Longitudinal Study of Ageing (ELSA). The Journals of Gerontology: Series A. 2017 Mar 1;72(3):403-9.
12. English Longitudinal Study of Ageing (ELSA) Wave 1 to Wave 6. Available from http://doc.ukdataservice.ac.uk/doc/5050/mrdoc/pdf/5050_elsa_user_guide_waves_1-6_v3.pdf Accessed 8/12/2017
13. UK Data Service Discover. English Longitudinal Study of Ageing. Available from https://discover.ukdataservice.ac.uk/series/?sn=200011 Accessed 8/12/2017
14. Lee DM, Nazroo J, O'Connor DB, Blake M, Pendleton N. Sexual health and well-being among older men and women in England: findings from the English Longitudinal Study of Ageing. Archives of sexual behavior. 2016 Jan 1;45(1):133-44.
15. Nat Cen Social Research. English Longitudinal Study of Ageing Wave 6 interview questionnaire. Version 3.0 Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/main_questionnaire.pdf [Accessed 5/9/2017]
16. English Longitudinal Study of Ageing Health and Lifestyles of People aged 50 or over. Self-completion questionnaire. Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/self_completion_main.pdf [Accessed 5/9/2017]
17. Nat Cen Social Research. English Longitudinal Study of Ageing Wave 6 Nurse questionnaire. 2012-2013. Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/nurse_documentation.pdf [Accessed 5/9/2017]
18. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English longitudinal study of ageing. International journal of epidemiology. 2012 Nov 6;42(6):1640-8.
19. Bjerrum L, Søgaard J, Hallas J, Kragstrup J. Polypharmacy: correlations with sex, age and drug regimen A prescription database study. European journal of clinical pharmacology. 1998 Jun 1;54(3):197-202
20. Statistical correlation. The relationship between two variables. Available from https://explorable.com/statistical-correlation Accessed 8/12/2017
21. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. Journal of clinical epidemiology. 1996 Dec 1;49(12):1373-9.
22. The Irish Longitudinal Study of Ageing. Main Questionnaire 2010.Available from http://www.ucd.ie/issda/static/documentation/tilda/tilda-capi-qaire-wave1.pdf [Accessed 5/9/2017]
23. Tjia J, Velten SJ, Parsons C, Valluri S, Briesacher BA. Studies to reduce unnecessary medication use in frail older adults: a systematic review. Drugs & aging. 2013 May 1;30(5):285-307.
24. Fano V, Chini F, Pezzotti P, Bontempi K. Estimating the Prevalence and the Determinants of Polypharmacy Using Data from a Health Administrative Database: A Comparison of Results Obtained Employing Different Algorithms. Advances in Pharmacoepidemiology & Drug Safety. 2014;3(151):2167-1052.
25. The Office of National Statistics Report: Chapter 2 Total Wealth, Wealth in GB, 2012-2014. Available from http://webarchive.nationalarchives.gov.uk/20160105170657/http://www.ons.gov.uk/ons/rel/was/wealth-in-great-britain-wave-4/2012-2014/rpt-chapter-2.html

26. Kings Fund. Long term conditions. Available from https://www.kingsfund.org.uk/projects/time-think-differently/trends-disease-and-disability-long-term-conditions-multi-morbidity
27. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. The Lancet. 2012 Jul 13;380(9836):37-43.
28. Team CP. The impact of obesity on drug prescribing in primary care. The British Journal of General Practice. 2005 Oct 1;55(519):743.
29. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. The Lancet. 2011 Sep 2;378(9793):815-25.
30. Henderson JA, Buchwald D, Manson SM. Relationship of medication use to health-related quality of life among a group of older American Indians. Journal of applied gerontology. 2006 Feb;25(1_suppl):89S-104S.
31. Incalzi RA, Corsonello A, Pedone C, Corica F, Carbonin P. Depression and drug utilization in an elderly population. Therapeutics and clinical risk management. 2005 Mar;1(1):55.
32. Frisher M, Mendonça M, Shelton N, Pikhart H, de Oliveira C, Holdsworth C. Is alcohol consumption in older adults associated with poor self-rated health? Cross-sectional and longitudinal analyses from the English Longitudinal Study of Ageing. BMC public health. 2015 Jul 24;15(1):703.
33. Holdsworth C, Mendonca M, Pikhart H, Frisher M, de Oliveira C, Shelton N. Is regular drinking in later life an indicator of good health? Evidence from the English Longitudinal Study of Ageing. J Epidemiol Community Health 2016 Aug 1;70(8):764-70
34. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men: Explaining the U-shaped curve. Lancet. 1988; 2:1267–1273.
35. Rimm EB, Moats C. Alcohol and coronary heart disease: drinking patterns and mediators of effect. Annals of Epidemiology. 2007. May 31; 17(5): S3-7
36. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. Jama. 2002 Jan 16;287(3):337-44.
37. Schuler J, Dückelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wiener klinische Wochenschrift. 2008 Dec 1;120(23):733-41.
38. Wauters M, Elseviers M, Vaes B, Degryse J, Dalleur O, Vander Stichele R, Van Bortel L, Azermai M. Polypharmacy in a Belgian cohort of community-dwelling oldest old (80+). Acta Clinica Belgica. 2016 May 3;71(3):158-66.
39. Pan HH, Li CY, Chen TJ, Su TP, Wang KY. Association of polypharmacy with fall-related fractures in older Taiwanese people: age-and gender-specific analyses. BMJ open. 2014 Mar 1;4(3): e004428. Depression and drug utilization in an elderly population
40. Barker, C., Pistrang, N. and Elliott, R. (2002) Self-Report Methods, in Research Methods in Clinical Psychology: An Introduction for Students and Practitioners, Second Edition, John Wiley & Sons, Ltd, Chichester, UK. doi: 10.1002/0470013435.ch6

FIGURE LEGENDS:

Figure 1: Bivariate correlations between polypharmacy and covariates

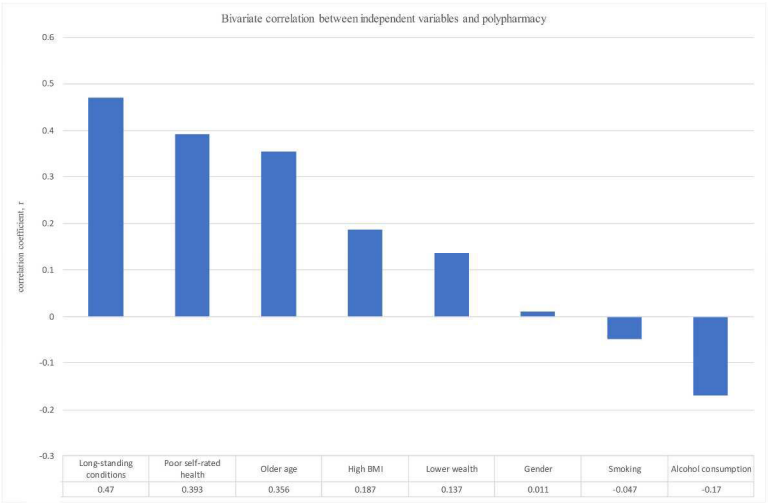

Figure 1: Bivariate correlations between polypharmacy and covariates

338x190mm (300 x 300 DPI)

ONLINE SUPPLEMENTARY TABLE 1:

	Frequent alcohol intake	Increased age	Low wealth	Smoking	Obesity	Poor self-rated health	Presence of a chronic health condition	Gender (female)	Polypharmacy
Frequent alcohol intake	1	-0.106	-0.251	-0.108	-0.094	-0.220	-0.137	-0.204	-0.188
Increased age	-0.106	1	-0.049	-0.195	-0.033	0.118	0.141	0.010	0.353
Low wealth	-0.251	-0.049	1	0.205	0.135	0.218	0.107	0.059	0.149
Smoking	-0.108	-0.195	0.205	1	-0.117	0.107	0.000	0.044	-0.040
Obesity	-0.094	-0.033	0.135	-0.117	1	0.142	0.115	-0.030	0.187
Poor self-rated health	-0.220	0.118	0.218	0.107	0.142	1	0.407	-0.010	0.421
Presence of a chronic health condition	-0.137	0.141	0.107	0.000	0.115	0.407	1	0.006	0.473
Gender (female)	-0.204	0.010	0.059	0.044	-0.030	-0.010	0.006	1	0.011
Poly-pharmacy	-0.188	0.353	0.149	-0.040	0.187	0.421	0.473	0.011	1

Bivariate correlations between covariates

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	7-9
Outcome data	15*	Report numbers of outcome events or summary measures	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(*b*) Report category boundaries when continuous variables were categorized	8-9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Factors associated with polypharmacy in primary care: A cross-sectional analysis of data from The English Longitudinal Study of Ageing (ELSA)

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Factors associated with polypharmacy in primary care: A cross-sectional analysis of data from The English Longitudinal Study of Ageing (ELSA)

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ABSTRACT:

OBJECTIVES: While older age and ill-health are known to be associated with polypharmacy, this paper aims to identify whether wealth, body mass index (BMI), smoking and alcohol consumption are also contributing to polypharmacy (5-9 prescribed medications) and hyper-polypharmacy prevalence (≥10 prescribed medications), among older people living in England.

DESIGN: Cross-sectional study

SETTING: The English Longitudinal Study of Ageing Wave 6 (2012-2013)

PARTICIPANTS: 7730 participants aged over 50 years old

DATA SYNTHESIS: Two multivariate models were created. Hazard ratios (HR) with corresponding 95% confidence intervals (CI), for polypharmacy and hyper-polypharmacy, were calculated after adjusting for gender, age, wealth, smoking, alcohol consumption, BMI, self-rated health and the presence of a chronic health condition.

RESULTS: Lower wealth (adjusted HR highest wealth quintile versus lowest wealth quintile, 1.28; 95%CI, 1.04-1.69, p=0.02) and obesity (adjusted HR 1.81; 95%CI, 1.53-2.15, p<0.001) were significantly associated with polypharmacy. Increasing age (adjusted HR 50-59 years versus 70-79 years, 3.42; 95% CI, 2.81-4.77, p<0.001) and the presence of a chronic health condition (adjusted HR 2.94;95%CI, 2.55-3.99, p<0.001) were also associated with polypharmacy. No statistically significant association between smoking and polypharmacy (adjusted HR 1.06; 95% CI, 0.86-1.29, p=0.56) was established; whilst, very frequent alcohol consumption (consuming alcohol >5 times per week) was inversely associated with polypharmacy (adjusted HR never drank versus very frequently, 0.64; 95%CI, 0.52-0.78, p<0.001). The adjusted hazard ratios for hyper-polypharmacy were accentuated, compared to polypharmacy.

CONCLUSION: This study has identified that lower wealth, obesity, increasing age and chronic health conditions are significantly associated with polypharmacy and hyper-polypharmacy prevalence. The effect of these factors, on polypharmacy and especially hyper-polypharmacy prevalence, is likely to become more pronounced with the widening gap in UK wealth inequalities, the current obesity epidemic and the growing population of older people. The alcohol findings contribute to the debate on the relationship between alcohol consumption and health.

Keywords: polypharmacy, longitudinal, demography, older people

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This cross-sectional study uses medication data, from over 7000 older individuals, to identify factors which are associated with polypharmacy prevalence in primary care.
- In the analysis, a large number of covariates were used to minimise the impact of confounding factors.
- Participants were asked to self-report information about their prescribed medication usage. To verify their responses, participants were asked to show their medication containers to the interviewer.
- Smoking and alcohol consumption data was also collected by asking participants to self-report. This relies on accurate and truthful information recall to prevent bias.

INTRODUCTION

Polypharmacy has been discussed extensively in the literature and media; however, there is no universally accepted definition for the practice of prescribing multiple medications to one individual. [1] At present, polypharmacy is commonly defined as "the use of five or more regular medications", whilst hyper-polypharmacy, which is sometimes termed as "excessive polypharmacy", is defined as "the use of ten or more regular medications". [2] Although polypharmacy prevalence has increased over the past decade, there are relatively few data about the factors associated with polypharmacy and hyper-polypharmacy in primary care.[3]

Previous studies have shown that increasing age and the presence of chronic conditions are significantly associated with an increase in polypharmacy prevalence. [4-6] Comparatively fewer studies have examined whether socio-demographic or lifestyle factors, for example wealth and obesity, are associated with polypharmacy. In a study conducted by Haider et al, [7] no statistically significant association between polypharmacy and an individual's socio-economic status was established. The findings from a study by Rajska-Neumann [8] revealed that there was no statistically significant difference in polypharmacy prevalence between smokers and non-smokers; whereas a statistically significant inverse relationship between alcohol consumption and the concomitant administration of medications was detected by Wong et al. [9] Finally, when Bueno et al [10] examined the association between polypharmacy and obesity, an adjusted odds ratio revealed that obese individuals (BMI >30kg/m^2) were 1.6 times more likely to be experiencing polypharmacy, compared to individuals with a BMI less than 30kg/m^2. To evaluate the relationship between the aforementioned factors and polypharmacy prevalence in primary care, a large sample study is required.

This study used data from The English Longitudinal Study of Ageing (ELSA) as this provided an opportunity to link polypharmacy and hyper-polypharmacy data to participants' personal data. In particular, this study aimed to determine whether wealth, body mass index (BMI), smoking, alcohol consumption, age and the presence of chronic health conditions, are associated with polypharmacy (5-9 prescribed medications) and hyper-polypharmacy (≥10 prescribed medications) prevalence in a community population of older people living in England.

METHOD

Sample and participants

A cross-sectional study was conducted using Wave 6 data from The English Longitudinal Study of Ageing (ELSA). Data collection took place between May 2012 and June 2013, from a representative sample of the English population who were aged 50 years or above.

Since ELSA began in 2002, participants have been asked to provide personal information about their household finances, health status, lifestyle choices and social interactions, on a bi-annual basis. In Wave 6, information from 10,601 participants was collected, which included 9,169 'core' participants. Members were considered 'core' if they were aged over 50 years old at the time of study enrollment and living at private residential addresses in England. [11] 8,054 nurse visits were completed at Wave 6, of whom 7,730 were carried out with core members. This latter group are the focus of the current study. [11]

Patient Involvement and Ethics

Ethical approval for ELSA Wave 6 was granted from the National Research Ethics Committee under the National Research and Ethics Service (NRES). All participants were required to provide informed written consent. [12] All ELSA data is anonymous and freely accessible from the UK Data Service Discover. [13] Only data contained within the ELSA database was included in the analyses. No patients were involved in the development of the research question, study design or interpretation of the data in this study; therefore, ethical approval was not required for this study.

Data Collection

Face-to-face interviews

The face-to-face interviews were conducted by trained interviewers, who asked participants to provide information about their current lifestyle choices, including smoking habits and alcohol consumption over the past twelve months. Smoking status was recorded as current smoker or non-smoker; whereas, the frequency of alcohol consumption over the past year was recorded as never, rarely, frequently or very frequently. [14] Rarely was defined as drinking alcohol less than twice a month. Frequently was defined as drinking alcohol between one and four times a week; whilst, very frequently was defined as drinking alcohol at least five times a week.

Participants were also asked to describe their current health status. Participants could select one of the following options: "excellent, very good, good, fair or poor". [15] These responses were converted into a two-level variable: good/fair and poor, with good/fair health status being the sum of responses ranging from "excellent" to "fair". In a subsequent question, participants were asked whether they had any chronic health conditions. Participants could answer this question with either yes or no. [15].

Finally, participants were asked to provide information about their household income, including information about their employment status, personal finances, assets, pensions and other benefits. Participant pension data was excluded when wealth index scores were calculated. Based upon their wealth index scores, participants were allocated to one of five wealth quintiles. Quintile 1 was the most affluent, whilst quintile 5 was the poorest.

Questionnaire

After completion of the face-to-face interview, participants were asked to complete a paper-based questionnaire. The questionnaire was designed to obtain further information about the participants' living arrangements, health status, lifestyle choices and social interactions. [16]

Nurse visit

The nurse visits took place in the participant's home. At the beginning of the visit, the nurse recorded information about participant demographics and their currently prescribed medications. Prescribed medication formulations were defined by the nurses as "pills, syrups, ointments, inhalers or injections". [17] If a participant reported taking one or more prescribed medications, the nurse sought their permission to record the name of their medication, in addition to seeing its container. The nurse determined current medication usage by asking the participant to confirm whether they had taken or used each reported medicine within the last seven days. [17] A maximum of 27 prescribed medications could be recorded for each participant. Medication information was coded by the nurse, according to the British National Formulary (Edition 61) chapter and subsection.

During the latter part of the visit, the nurse conducted a physical examination and recorded information about the participant's blood pressure, grip strength, height, weight and lung function. [17] Using a participant's height and weight data, it was possible to calculate their body mass index. A BMI <18.5kg/m^2 was recorded as underweight, a BMI value between 18.5 -24.9 kg/m^2 was considered to be normal weight; whereas, a BMI of 25.0-29.9kg/m^2 was recorded as overweight and a BMI >30kg/m^2 was recorded as obese.

Inclusion Criteria

All participants must have completed a face-to-face interview, a paper-based questionnaire and received a nurse visit during ELSA Wave 6 to meet the inclusion criteria for this study. [18]

Defining polypharmacy and hyper-polypharmacy

Polypharmacy was defined as the concurrent use of five to nine currently prescribed medications, whilst hyper-polypharmacy was defined as the concurrent use of ten or more currently prescribed medications. These definitions have been used previously in other population-based studies. [3,19]

Data analysis

Initially, descriptive statistics were used to summarise the prevalence of polypharmacy and hyper-polypharmacy among participants. These data were subsequently stratified according to participant demographics. In the second part of the analysis, a bivariate model was used to assess the relationship between polypharmacy and the following independent variables: frequent alcohol consumption, increasing age, poor wealth, female sex, smoking, raised body mass index (BMI), poor self-rated health and the presence of a chronic health condition. Bivariate correlations between other covariates were also examined. Findings were presented as Pearson correlation coefficients (*r*). The strength of each correlation was considered and described as either strong (1.00 – 0.50), moderate (0.49-0.30) or weak (0.29-0.10).[20]

In the final part of the analysis, two multivariate models were created to identify associations between participant characteristics and polypharmacy prevalence. Based upon previous work by Peduzzi et al [21], the minimum sample size required for the first multivariate model (polypharmacy) was 333; whilst the minimum sample size required for the second multivariate model (hyper-polypharmacy) was 1250. In both models, ill health was controlled for by using participants taking between one and four prescribed medications. This group of participants formed the control group. Participants taking no prescribed medications were excluded from this part of the analysis. In the first model, participants taking 5 to 9 medications were compared to the control group (1 to 4 prescribed medications). In the second model, participants taking 10 or more medications were compared to the control group (1 to 4 prescribed medications). Hazard ratios with corresponding 95% confidence intervals (CI), for polypharmacy and hyper-polypharmacy, were calculated after adjusting for covariates. The following factors were considered as covariates: gender, age, wealth, smoking, alcohol consumption, BMI, self-rated health and the presence of a chronic health condition. Missing data was coded as "missing" and presented as a separate category in the multivariate models. The data generated from the models was statistically significant if $p<0.05$. All data analysis was undertaken using SPSS version 24.0.

RESULTS

Participant Characteristics:

A total of 7730 participants' data from ELSA Wave 6 were analysed. Participant characteristics are presented in Table 1. The mean age of participants in Wave 6 was 67.6 years, and 55.4% (n=4282/7730) of the sample were female. Overall, 24.1% (n= 1862/7725) of the participants received polypharmacy and 6.4% (n=494/7725) were receiving hyper-polypharmacy (Table 1). The proportion of individuals receiving polypharmacy and hyper-polypharmacy increased steadily with age. However, the prevalence of polypharmacy and hyper-polypharmacy in males and females was similar. (Table 1)

	No medications	**1-4 medications**	**5-9 medications**	**≥10 medications**
Participant Characteristics:			**Polypharmacy**	**Hyper-polypharmacy**
All participants (n=7725)	23.8%	45.7%	24.1%	6.4%
Missing medication data (n=5)				
Age:				
50-59 years (n=1695)	43.2%	42.4%	11.7%	2.7%
60-69 years (n=3012)	26.6%	49.2%	19.6%	4.6%
70-79 years (n=2114)	11.8%	45.9%	33.1%	9.2%
80+ years (n=909)	6.4%	39.6%	41.3%	12.7%
Gender:				
Male (n=3448)	24.9%	44.6%	24.4%	6.1%
Female (n=4282)	22.9%	46.6%	23.9%	6.6%
Chronic health condition:				
Yes (n=4289)	9.6%	44.5%	35.2%	10.7%
No (n=3441)	41.6%	47.1%	10.3%	1.0%

Table 1: Polypharmacy versus patient characteristics

Overall, 35.2% (n= 1509/4289) of participants who reported having a chronic health condition were receiving polypharmacy; whereas, 10.7% (n=459/4289) were receiving hyper-polypharmacy. Only 10.3% (n=353/3441) and 1.0% (n=35/3441) of participants with no chronic health conditions, received polypharmacy and hyper-polypharmacy respectively (Table 1).

In a bivariate model, moderate positive correlations were detected between polypharmacy and the following variables: the presence of a chronic health condition, poor self-rated health and increasing age. A weak positive correlation between polypharmacy and a high BMI was established. Similarly, there was a weak positive correlation between lower wealth and polypharmacy. No correlations between gender and polypharmacy, and smoking and polypharmacy, were established. However, there was a weak negative correlation between polypharmacy and frequent alcohol consumption. All bivariate correlations are presented in Figure 1. Bivariate correlations between other covariates were also examined, and data is available in online supplementary table 1.

To determine whether other variables are associated with polypharmacy and hyper-polypharmacy, the results from the two multivariate models (Polypharmacy-1 and Hyper-polypharmacy-2) were analysed and presented in Table 2 and Table 3 respectively.

Independent Variables	**Adjusted HR**	95% CI		**Sig.**
		Lower	Upper	
Age				
50-59 years **(Reference)** (n=963)	1			
60-69 years (n=2210)	1.66	1.37	2.01	**<0.00**
70-79 years (n=2344)	3.42	2.81	4.77	**<0.00**
80+ (n=371)	4.52	3.58	5.70	**<0.00**
Gender				
Male **(Reference)** (n=2588)	1			
Female (n=3300)	0.92	0.81	1.04	0.21
Chronic health condition				
No **(Reference)** (n=2008)	1			
Yes (n=3879)	2.94	2.55	3.39	**0.00**
Missing chronic health condition data (n=1)				
Self-rated health				
Self-rated health: Good **(Reference)** (n=3907)	1			
Self-rated health: Poor (n=1978)	2.98	2.61	3.4	**0.00**
Missing self-rated health data (n=3)				
Wealth				
Wealth: Quintile 1 (wealthiest) **(Reference)** (n=1237)	1			
Wealth: Quintile 2 (n=1244)	1.08	0.9	1.31	0.37
Wealth: Quintile 3 (n=1196)	1.13	0.93	1.37	0.19
Wealth: Quintile 4 (n=1190)	1.23	1.02	1.5	**0.03**
Wealth: Quintile 5 (poorest) (n=921)	1.28	1.04	1.69	**0.02**
Missing wealth data (n=100)				
Body Mass Index (BMI)				
BMI<18.5kg/m^2: underweight (n=54)	0.93	0.5	1.74	0.83
BMI 18.5 -24.9 kg/m^2: normal **(Reference)** (n=1313)	1			
BMI 25.0-29.9kg/m^2: overweight (n=2272)	1.13	0.96	1.33	0.13

BMI >30kg/m^2: obese (n=1930)	1.81	1.53	2.15	**0.00**
Missing BMI data (n=319)				
Current smoking habits since last ELSA interview				
Non-smoker **(Reference)** (n=3153)	1			
Smoker (n=650)	1.06	0.86	1.29	0.56
Missing smoking data (n=2085)				
Alcohol consumption in past 12 months				
Never (**Reference)** (n=792)	1			
Rarely (n=930)	0.76	0.61	0.94	**0.01**
Frequently (n=1797)	0.65	0.53	0.79	**0.00**
Very frequently (n=1791)	0.64	0.52	0.78	**0.00**
Missing alcohol consumption data (n=578)				

Table 2: Model 1: Independent variables in polypharmacy (5-9 medications, n=2356) versus no polypharmacy (1-4 medications, n=3532)

Independent Variables	**Adjusted HR**	95% CI		**Sig.**
		Lower	Upper	
Age				
50-59 years **(Reference)** (n=765)	1			
60-69 years (n=1620)	1.79	1.21	2.64	**<0.00**
70-79 years (n=1444)	4.11	2.77	6.09	**<0.00**
80+ (n=197)	5.94	3.79	9.29	**<0.00**
Gender				
Male **(Reference)** (n=1748)	1			
Female (n=2278)	0.94	0.71	1.15	0.41
Chronic health condition				
No **(Reference)** (n=1656)	1			
Yes (n=2370)	5.30	3.63	7.73	**0.00**
Self-rated health				
Self-rated health: Good **(Reference)** (n=2944)	1			
Self-rated health: Poor (n=1081)	6.69	5.21	8.58	**0.00**
Missing self-rated health data (n=1)				
Wealth				
Wealth: Quintile 1 (wealthiest) **(Reference)** (n=907)	1			
Wealth: Quintile 2 (n=875)	1.41	0.93	2.13	0.11
Wealth: Quintile 3 (n=797)	1.36	0.90	2.06	0.15
Wealth: Quintile 4 (n=756)	1.75	1.17	2.60	**0.006**
Wealth: Quintile 5 (poorest) (n=611)	2.04	1.34	3.11	**0.001**
Missing wealth data (n=80)				
Body Mass Index (BMI)				
BMI<18.5kg/m^2: underweight (n=38)	0.88	0.26	2.95	0.83
BMI 18.5 -24.9 kg/m^2: normal **(Reference)** (n=959)	1			
BMI 25.0-29.9kg/m^2: overweight (n=1633)	1.38	0.98	1.95	0.07
BMI >30kg/m^2: obese (n=1205)	2.28	1.63	3.21	**0.00**
Missing BMI data (n=191)				

Current smoking habits since last ELSA interview				
Non-smoker **(Reference)** (n=2077)	1			
Smoker (n=424)	0.98	0.68	1.39	0.89
Missing smoking data (n=1525)				
Alcohol consumption in past 12 months				
Never (**Reference)** (n=489)	1			
Rarely (n=619)	0.70	0.50	0.99	**0.046**
Frequently (n=1256)	0.40	0.29	0.56	**0.00**
Very frequently (n=1293)	0.39	0.27	0.55	**0.00**
Missing alcohol consumption data (n=369)				

Table 3: Model 2: Independent variables in hyper-polypharmacy (≥10 medications, n=494) versus no polypharmacy (1-4 medications, n=3532)

Examining the association between age and polypharmacy

In both models, increasing age was associated with polypharmacy and hyper-polypharmacy. For participants aged between 70 years and 79 years, the adjusted hazard ratio for polypharmacy was 3.42 (2.81 to 4.77, p<0.001) (Table 2). This value increased to 4.52 (3.58 to 5.70, p<0.001) in participants aged above 80 years old (Table 2). Similarly, the adjusted hazard ratios for hyper-polypharmacy increased from 4.11 (2.77 to 6.09, p<0.001) in participants aged between 70 years and 79 years to 5.94 (3.79 to 9.29, p<0.001) in participants aged above 80 years old (Table 3). All findings were statistically significant.

Examining the association between the presence of a chronic health condition and polypharmacy

The adjusted hazard ratio for polypharmacy and the presence of a chronic health condition was 2.94 (2.55 to 3.39, p<0.001) (Table 2); whereas, the adjusted hazard ratio for hyper-polypharmacy and the presence of a chronic health condition was 5.30 (3.63 to 7.73, p<0.001) (Table 3). In both models, statistically significant results were generated.

Examining the association between wealth and polypharmacy

The adjusted hazard ratio for polypharmacy increased from 1.08 (0.9 to 1.31, p=0.37) in wealth quintile 2 to 1.28 (1.04 to 1.69, p=0.02) in wealth quintile 5 (Table 2). Similarly, the adjusted hazard ratio for hyper-polypharmacy increased from 1.41 (0.93 to 2.13, p=0.11) in wealth quintile 2 to 2.04 (1.34 to 3.11, p=0.001) in wealth quintile 5 (Table 3). In both models, statistically significant differences in adjusted hazard ratios for polypharmacy and hyper-polypharmacy were detected in the lower wealth quintiles (quintile 4 and 5).

Examining the association between BMI and polypharmacy

In underweight participants, the adjusted hazard ratio for polypharmacy was 0.93 (0.5 to 1.74, p=0.83) (Table 2); whereas, the adjusted hazard ratios for polypharmacy in participants who were overweight or obese were 1.13 (0.96 to 1.33, p=0.13) and 1.81 (1.53 to 2.15, p<0.001) respectively (Table 2). Adjusted hazard ratios for hyper-polypharmacy produced similar results. In underweight participants, the adjusted hazard ratio for hyper-polypharmacy decreased to 0.88 (0.26 to 2.95, p=0.83) (Table 3); whereas, the adjusted hazard ratio for hyper-polypharmacy in overweight participants was 1.38 (0.98 to 1.95, p=0.07) increasing

substantially to 2.28 (1.63 to 3.21, p<0.001) in obese participants (Table 3). Only the adjusted hazard ratios for polypharmacy and hyper-polypharmacy, in relation to obesity, produced statistically significant results.

Examining the association between smoking and polypharmacy

The adjusted hazard ratio for polypharmacy and smoking was 1.06 (0.86 to 1.29, p=0.56) (Table 2) whereas the adjusted hazard ratio for hyper-polypharmacy and smoking was 0.98 (0.68 to 1.39, p=0.89) (Table 3). Both models failed to produce any statistically significant results.

Examining the association between alcohol consumption and polypharmacy

Adjusted hazard ratios for polypharmacy and hyper-polypharmacy were calculated using the participant's alcohol consumption data provided during the face-to-face interview. When compared to individuals who reported never drinking alcohol, the adjusted hazard ratio for participants who reported rarely consuming alcohol was 0.76 (0.61 to 0.94, p=0.01) (Table 2). This value decreased further to 0.64 (0.52 to 0.78, p<0.001) in participants who reported drinking alcohol very frequently (Table 2). The adjusted hazard ratios for hyper-polypharmacy produced similar results. For participants who reported rarely consuming alcohol, the adjusted hazard ratio for hyper-polypharmacy was 0.70 (0.50 to 0.99, p=0.046), when compared to individuals who reported never drinking alcohol (Table 3); whereas the adjusted hazard ratio for hyper-polypharmacy in participants who reported drinking alcohol frequently was 0.39 (0.27 to 0.55, p<0.001) (Table 3). All adjusted hazard ratios for polypharmacy and hyper-polypharmacy, in relation to self-reported alcohol consumption, were statistically significant.

DISCUSSION

This study confirms that increasing age and the presence of chronic health conditions are associated with polypharmacy prevalence, but also that obesity and lower wealth are significantly associated with polypharmacy. Frequent alcohol consumption is inversely associated with polypharmacy prevalence. Results from previous studies, which have investigated the influence of ageing and chronic health conditions on polypharmacy prevalence, complement our findings. [19,22,23].

In the existing literature, few studies have investigated whether polypharmacy prevalence is associated with wealth or BMI. [24,25] One study conducted in Rome, analysed a national prescription database and a multivariate model was used to identify participant characteristics which influenced polypharmacy prevalence. [24] The authors concluded that individuals living in lower socio-economic areas are 33% more likely to experience polypharmacy compared to individuals living in higher socio-economic areas. In our study, participants were allocated to one of five wealth quintiles, based upon their wealth index scores. Participants living in the lowest wealth quintiles were 28% more likely to experience polypharmacy and twice as likely to experience hyper-polypharmacy, when compared to participants living in the highest wealth quintile. Our findings show that lower wealth is significantly associated with an increase in polypharmacy and hyper-polypharmacy prevalence. This finding is important because the latest figures published by the Office of National Statistics [25] show that wealth inequalities across the United Kingdom (UK) have begun to rise again, after a decade-long decline. There is also evidence to suggest that the

incidence of chronic health conditions and multi-morbidities is highest among individuals residing in deprived areas. [26,27] The aforementioned individuals are likely to require multiple medications to manage or treat their chronic conditions and thus, providing support for the association between lower wealth and polypharmacy.

Our multivariate model also revealed that obesity (body mass index >30kg/m^2) was another factor associated with polypharmacy and hyper-polypharmacy prevalence. This finding was statistically significant. The same association was identified during another study; however, the authors did not comment on the statistical significance of their results, nor did they conduct any further research into the association. [28] Identifying the association between polypharmacy and obesity is also important because obesity has become a major public health concern in England. Assuming the current obesity epidemic continues as predicted, the prevalence of polypharmacy and hyper-polypharmacy among older people in England, is likely to follow suit. [29]

This study found no statistically significant association between smoking and polypharmacy. Similarly, there were no statistically significant association between smoking and hyper-polypharmacy. Our findings are supported by Rajska-Neumann [8] and Henderson et al [30]. However, another study reports that smoking is inversely associated with polypharmacy (adjusted OR 0.42;95%CI,0.33-0.53). [31]

Frequent alcohol consumption in the past year was inversely associated with polypharmacy and hyper-polypharmacy prevalence. This finding is consistent with previous work, involving ELSA, which reported that self-reported alcohol consumption (even at high levels) was not related to poor self-rated health. [32,33] The alcohol findings in this current study could be explained by the sick quitter hypothesis, where individuals stop or reduce their alcohol consumption due to illness. [34] However, Rimm and Moats [35] conclude that the sick quitter hypothesis has been refuted by a wide range of evidence. The inverse association between alcohol consumption and polypharmacy was also detected by Incalzi et al [31] although they appear to discount a genuine association and rather attribute this to bias (i.e. patients in better health are less motivated to correct unhealthy habits).

Finally, most of the existing literature suggests that females take more medications compared to males; however, our study found that there was no statistically significant difference in polypharmacy and hyper-polypharmacy prevalence between males and females. [36,37,38] Pan et al [39] provides support for our findings and concluded that female sex is not significantly associated with an increased polypharmacy prevalence.

To our knowledge this is the first study which has used medication data, from a large representative sample of older adults, to determine whether lower wealth, obesity, smoking, alcohol consumption, in addition to increasing age and the presence of chronic health conditions, are associated with polypharmacy and hyper-polypharmacy prevalence in primary care. All analysed data was obtained using standardised data collection methods and validated data collection tools. Also, this study used a large number of covariates, which reduced the impact of confounders and minimised study bias.

This study has several limitations. Actual medication use among participants may have been higher than recorded medication use for several reasons. Firstly, participants were asked about their prescribed medications; however, medications purchased without prescription, for

example weak analgesics or antihistamines, were not recorded. Secondly, prescribed medications were coded according to BNF chapter and subsection. It was assumed that each code represented a single active ingredient; however, several combination drugs, for example co-amilofruse and co-amilozide, were also represented by a single code. Furthermore, when the nurse enquired about prescribed medications, they asked the following question: "Are you taking or using any medications, pills, syrups, ointments, puffers or injections prescribed to you by a doctor or a nurse?" [19] This question refers to some medicinal formulations, but the list is not exhaustive. Thus, a participant using eye drops or wearing a transdermal patch may not have reported this medication as the formulation was not explicitly stated in the question. Consequently, polypharmacy and hyper-polypharmacy prevalence may have been underestimated in this study.

To obtain data about prescribed medications, smoking habits and alcohol consumption, participants were asked to self-report. This method of data collection relies on all participants accurately and truthfully recalling information to prevent bias. [40] The risk of recall bias associated with prescribed medication information was minimised by the nurse, because participants were asked to show their medication containers to verify their responses. However, it was not possible to minimise the risk of recall bias associated with the other covariates. Participants also reported information about chronic health conditions; however, the associations between specific health conditions, multi-morbidity and polypharmacy were not examined in this study. Finally, it is not possible to determine the direction of causality from our data, due to the cross-sectional nature of this study.

CONCLUSION

This study has identified that lower wealth, obesity, increasing age and the presence of chronic health conditions are all associated with polypharmacy and hyper-polypharmacy prevalence, among older people in primary care. An inverse relationship between frequent alcohol consumption and polypharmacy prevalence was also established. In the future, the effect of obesity and lower wealth on polypharmacy and hyper-polypharmacy prevalence is likely to become more pronounced, as the gap in UK wealth inequalities begins to widen again and the UK obesity epidemic continues. Future exploratory work is required to determine the causation behind these associations.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC

- The prevalence of polypharmacy and hyper-polypharmacy is increasing globally
- Increasing age and the presence of chronic health conditions are associated with an increase in polypharmacy prevalence.
- Few studies have examined whether socio-demographic or lifestyle factors, for example wealth and obesity, are associated with polypharmacy.

WHAT THIS STUDY ADDS

- Obesity and lower wealth have been identified as factors which are significantly associated with polypharmacy and especially hyper-polypharmacy. As the gap in UK

wealth inequalities widens and the UK obesity epidemic continues, the effect these factors on polypharmacy prevalence is likely to become more pronounced.

- Frequent alcohol consumption is inversely associated with polypharmacy and hyper-polypharmacy prevalence.

ACKNOWLEDGEMENTS

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CONTRIBUTORSHIP STATEMENT

All authors contributed to the study idea. MF led the study and conducted all data analysis. All authors had full access to ELSA Wave 6 data, supplied by the UK Data Service and they take full responsibility for the integrity and accurate analysis of data. All authors contributed to data interpretation. NS drafted the manuscript with contributions from MF, RV and SW. NS and MF are the Guarantors for this study.

TRANSPARENCY STATEMENT

NS and MF confirm that the manuscript is an honest, accurate and transparent account of the study being reported. No important aspects of this study have been omitted.

COMPETING INTERESTS All authors have completed the ICMJE form for disclosure of potential conflicts of interest available from www.icmje.org/coi_disclosure.pdf and declare that there is nothing to disclose.

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DATA SHARING STATEMENT No additional data is available; however, anonymous ELSA data is publicly available from https://discover.ukdataservice.ac.uk/ [36]

REFERENCES

1. Duerden M, Payne R. Polypharmacy – what is it and how common is it? Prescriber. 2014 Nov
2. O'Dwyer M, Peklar J, McCallion P, McCarron M, Henman MC. Factors associated with polypharmacy and excessive polypharmacy in older people with intellectual disability differ from the general population: a cross-sectional observational nationwide study. BMJ open. 2016 Apr 1;6(4):e010505.
3. Guthrie B, Makubate B, Hernandez-Santiago V, Dreischulte T. The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995–2010.BMC Med 2015;13:74

4. The Dynamics of Ageing. Evidence from the English Longitudinal Study of Ageing (Wave 7) 2002-2015. Available from www.ifs.org.uk/uploads/elsa/docs_w7/report.pdf [Accessed 27/07/2017]
5. Department of Health. Long Term Condition Compendium of Information. Third Edition. 2012www.gov.uk/government/uploads/attachment_data/file/216528/dh_134486.pdf [Accessed 27/07/2017]
6. Silveira EA, Dalastra L, Pagotto V. Polypharmacy, chronic diseases and nutritional markers in community-dwelling older. Revista Brasileira de Epidemiologia. 2014 Dec;17(4):818-29.
7. Haider SI, Johnell K, Thorslund M, Fastbom J. Analysis of the association between polypharmacy and socioeconomic position among elderly aged≥ 77 years in Sweden. Clinical therapeutics. 2008 Feb 1;30(2):419-27.
8. Rajska-Neumann A, Szymański M, Balcer N, Grześkowiak E, Szałek E, Wieczorowska-Tobis K. Is smoking a determinant of polypharmacy among elderly subject?. Przeglad lekarski. 2004 Dec;62(10):1145-7.
9. Wong H, Heuberger R, Logomarsino J, Hewlings S. Associations between alcohol use, polypharmacy and falls in older adults: Helen Wong and colleagues report on a cross-sectional study into alcohol consumption, medication use and falls in the community. Nursing older people. 2016 Jan 28;28(1):30-6.
10. Bueno DR, Monteiro HL, Rosa CS, Codogno JS, Fernandes RA, Marucci MF. Association between physical activity levels and polypharmacy in hypertensive patients. Medicina (Ribeirão Preto. Online). 2016;49(3):240-7.
11. Wade KF, Marshall A, Vanhoutte B, Wu FC, O'Neill TW, Lee DM. Does pain predict frailty in older men and women? Findings from the English Longitudinal Study of Ageing (ELSA). The Journals of Gerontology: Series A. 2017 Mar 1;72(3):403-9.
12. English Longitudinal Study of Ageing (ELSA) Wave 1 to Wave 6. Available from http://doc.ukdataservice.ac.uk/doc/5050/mrdoc/pdf/5050_elsa_user_guide_waves_1-6_v3.pdf Accessed 8/12/2017
13. UK Data Service Discover. English Longitudinal Study of Ageing. Available from https://discover.ukdataservice.ac.uk/series/?sn=200011 Accessed 8/12/2017
14. Lee DM, Nazroo J, O'Connor DB, Blake M, Pendleton N. Sexual health and well-being among older men and women in England: findings from the English Longitudinal Study of Ageing. Archives of sexual behavior. 2016 Jan 1;45(1):133-44.
15. Nat Cen Social Research. English Longitudinal Study of Ageing Wave 6 interview questionnaire. Version 3.0 Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/main_questionnaire.pdf [Accessed 5/9/2017]
16. English Longitudinal Study of Ageing Health and Lifestyles of People aged 50 or over. Self-completion questionnaire. Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/self_completion_main.pdf [Accessed 5/9/2017]
17. Nat Cen Social Research. English Longitudinal Study of Ageing Wave 6 Nurse questionnaire. 2012-2013. Available from https://www.elsa-project.ac.uk/uploads/elsa/docs_w6/nurse_documentation.pdf [Accessed 5/9/2017]
18. Steptoe A, Breeze E, Banks J, Nazroo J. Cohort profile: the English longitudinal study of ageing. International journal of epidemiology. 2012 Nov 6;42(6):1640-8.
19. Bjerrum L, Søgaard J, Hallas J, Kragstrup J. Polypharmacy: correlations with sex, age and drug regimen A prescription database study. European journal of clinical pharmacology. 1998 Jun 1;54(3):197-202
20. Statistical correlation. The relationship between two variables. Available from https://explorable.com/statistical-correlation Accessed 8/12/2017
21. Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. Journal of clinical epidemiology. 1996 Dec 1;49(12):1373-9.
22. The Irish Longitudinal Study of Ageing. Main Questionnaire 2010.Available from http://www.ucd.ie/issda/static/documentation/tilda/tilda-capi-qaire-wave1.pdf [Accessed 5/9/2017]
23. Tjia J, Velten SJ, Parsons C, Valluri S, Briesacher BA. Studies to reduce unnecessary medication use in frail older adults: a systematic review. Drugs & aging. 2013 May 1;30(5):285-307.
24. Fano V, Chini F, Pezzotti P, Bontempi K. Estimating the Prevalence and the Determinants of Polypharmacy Using Data from a Health Administrative Database: A Comparison of Results Obtained Employing Different Algorithms. Advances in Pharmacoepidemiology & Drug Safety. 2014;3(151):2167-1052.
25. The Office of National Statistics Report: Chapter 2 Total Wealth, Wealth in GB, 2012-2014. Available from

http://webarchive.nationalarchives.gov.uk/20160105170657/http://www.ons.gov.uk/ons/rel/was/wealth-in-great-britain-wave-4/2012-2014/rpt-chapter-2.html
26. Kings Fund. Long term conditions. Available from https://www.kingsfund.org.uk/projects/time-think-differently/trends-disease-and-disability-long-term-conditions-multi-morbidity
27. Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. The Lancet. 2012 Jul 13;380(9836):37-43.
28. Team CP. The impact of obesity on drug prescribing in primary care. The British Journal of General Practice. 2005 Oct 1;55(519):743.
29. Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic burden of the projected obesity trends in the USA and the UK. The Lancet. 2011 Sep 2;378(9793):815-25.
30. Henderson JA, Buchwald D, Manson SM. Relationship of medication use to health-related quality of life among a group of older American Indians. Journal of applied gerontology. 2006 Feb;25(1_suppl):89S-104S.
31. Incalzi RA, Corsonello A, Pedone C, Corica F, Carbonin P. Depression and drug utilization in an elderly population. Therapeutics and clinical risk management. 2005 Mar;1(1):55.
32. Frisher M, Mendonça M, Shelton N, Pikhart H, de Oliveira C, Holdsworth C. Is alcohol consumption in older adults associated with poor self-rated health? Cross-sectional and longitudinal analyses from the English Longitudinal Study of Ageing. BMC public health. 2015 Jul 24;15(1):703.
33. Holdsworth C, Mendonca M, Pikhart H, Frisher M, de Oliveira C, Shelton N. Is regular drinking in later life an indicator of good health? Evidence from the English Longitudinal Study of Ageing. J Epidemiol Community Health 2016 Aug 1;70(8):764-70
34. Shaper AG, Wannamethee G, Walker M. Alcohol and mortality in British men: Explaining the U-shaped curve. Lancet. 1988; 2:1267–1273.
35. Rimm EB, Moats C. Alcohol and coronary heart disease: drinking patterns and mediators of effect. Annals of Epidemiology. 2007. May 31; 17(5): S3-7
36. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA. Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. Jama. 2002 Jan 16;287(3):337-44.
37. Schuler J, Dückelmann C, Beindl W, Prinz E, Michalski T, Pichler M. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wiener klinische Wochenschrift. 2008 Dec 1;120(23):733-41.
38. Wauters M, Elseviers M, Vaes B, Degryse J, Dalleur O, Vander Stichele R, Van Bortel L, Azermai M. Polypharmacy in a Belgian cohort of community-dwelling oldest old (80+). Acta Clinica Belgica. 2016 May 3;71(3):158-66.
39. Pan HH, Li CY, Chen TJ, Su TP, Wang KY. Association of polypharmacy with fall-related fractures in older Taiwanese people: age-and gender-specific analyses. BMJ open. 2014 Mar 1;4(3): e004428. Depression and drug utilization in an elderly population
40. Barker, C., Pistrang, N. and Elliott, R. (2002) Self-Report Methods, in Research Methods in Clinical Psychology: An Introduction for Students and Practitioners, Second Edition, John Wiley & Sons, Ltd, Chichester, UK. doi: 10.1002/0470013435.ch6

FIGURE LEGENDS:

Figure 1: Bivariate correlations between polypharmacy and covariates

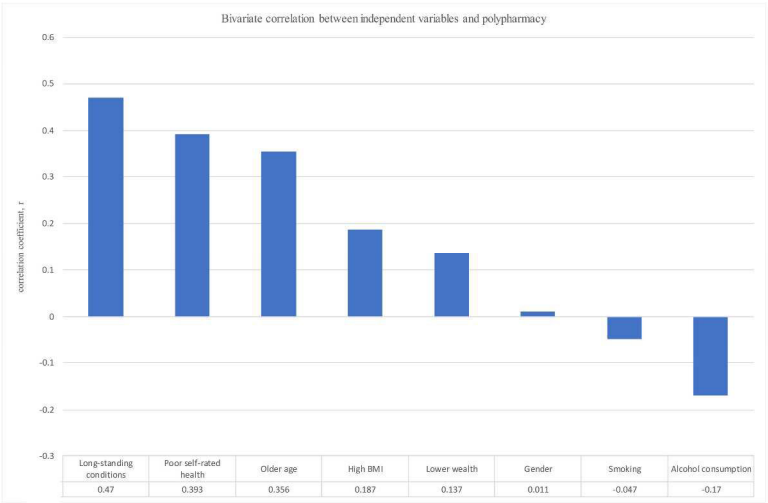

Figure 1: Bivariate correlations between polypharmacy and covariates

338x190mm (300 x 300 DPI)

ONLINE SUPPLEMENTARY TABLE 1:

	Frequent alcohol intake	Increased age	Low wealth	Smoking	Obesity	Poor self-rated health	Presence of a chronic health condition	Gender (female)	Polypharmacy
Frequent alcohol intake	1	-0.106	-0.251	-0.108	-0.094	-0.220	-0.137	-0.204	-0.188
Increased age	-0.106	1	-0.049	-0.195	-0.033	0.118	0.141	0.010	0.353
Low wealth	-0.251	-0.049	1	0.205	0.135	0.218	0.107	0.059	0.149
Smoking	-0.108	-0.195	0.205	1	-0.117	0.107	0.000	0.044	-0.040
Obesity	-0.094	-0.033	0.135	-0.117	1	0.142	0.115	-0.030	0.187
Poor self-rated health	-0.220	0.118	0.218	0.107	0.142	1	0.407	-0.010	0.421
Presence of a chronic health condition	-0.137	0.141	0.107	0.000	0.115	0.407	1	0.006	0.473
Gender (female)	-0.204	0.010	0.059	0.044	-0.030	-0.010	0.006	1	0.011
Poly-pharmacy	-0.188	0.353	0.149	-0.040	0.187	0.421	0.473	0.011	1

Bivariate correlations between covariates

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4-5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	12
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	5-6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6-9
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	7-9
Outcome data	15*	Report numbers of outcome events or summary measures	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-9
		(*b*) Report category boundaries when continuous variables were categorized	8-9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.