Differences in Health at Age 100 According to Sex: Population-Based Cohort Study of Centenarians Using Electronic Health Records

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OBJECTIVES: To use primary care electronic health records (EHRs) to evaluate the health of men and women at age 100.

DESIGN: Population-based cohort study.

SETTING: Primary care database in the United Kingdom, 1990–2013.

PARTICIPANTS: Individuals reaching the age of 100 between 1990 and 2013 (N = 11,084, n = 8,982 women, n = 2,102 men).

MEASUREMENTS: Main categories of morbidity and an index of multiple morbidities, geriatric syndromes and an index of multiple impairments, cardiovascular risk factors.

RESULTS: The number of new female centenarians per year increased from 16 per 100,000 in 1990–94 to 25 per 100,000 in 2010–13 ($P < .001$) and of male centenarians from four per 100,000 to six per 100,000 ($P = .06$). The most prevalent morbidities at the age of 100 were musculoskeletal diseases, disorders of the senses, and digestive diseases. Women had greater multiple morbidity than men (odds ratio (OR) = 1.64, 95% confidence interval (CI) = 1.42–1.89, $P < .001$). Geriatric syndromes, including falls, fractures, hearing and vision impairment, and dementia, were frequent; 30% of women and 49% of men had no recorded geriatric syndromes. Women had greater likelihood of having multiple geriatric syndromes (OR = 2.14, 95% CI = 1.90–2.41, $P < .001$).

CONCLUSION: Fewer men than women reach the age of 100, but male centenarians have lower morbidity and fewer geriatric syndromes than women. Research using EHRs offers opportunities to understand the epidemiology of aging and improve care of the oldest old. **J Am Geriatr Soc 63:1331–1337, 2015.**

Key words: centenarians; epidemiology; aging; general practice; primary care

The number of individuals reaching advanced ages is growing rapidly. Recent estimates indicate that the number of centenarians in the United Kingdom has quintupled over the past three decades;[1] in the United States, the number of centenarians increased from 32,194 in 1980 to 53,364 in 2010.[2] This trend is projected to continue over the coming years, to approximately 1 million centenarians worldwide by 2030[3] and 3 million by 2050.[4] Older age is the single most important risk factor for chronic diseases and long-term conditions, including cardiovascular disease (CVD), cancer, diabetes mellitus, and chronic respiratory disease. There is an expectation that population aging will place a substantial burden on the healthcare system, but population-based evidence concerning the epidemiology of chronic illnesses in centenarians is scarce.

Existing studies of centenarians are highly heterogeneous, often relying on self-reported illness and including small and highly selected samples of participants, often healthy centenarians. This limits their generalization to more-diverse centenarian populations.[5,6] Estimates of the prevalence of common morbidities among centenarians vary greatly,[7,8] with the prevalence of dementia estimated to range from 27% [9,10] to 89%,[11] congestive heart failure from 27% [9] to 60%,[12,13] and diabetes mellitus from 1% [14] to 12%.[13,15]

Differences in health according to sex are important throughout the life-course, with generally greater morbidity in women but higher mortality in men up to younger old age. The extent to which differences persist into extreme old age has not been investigated in large population-based samples.[16] Most evidence derives from studies of voluntary participants, potentially underestimating the

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extent of physical and mental health conditions in centenarian populations. Often these studies rely on self-reported information of uncertain validity. Existing studies on differences in centenarians according to sex in Italy,[17,18] Greece,[19] and the United States [20] have used modest sample sizes of less than 2,000 (commonly ~200–400 participants) or focused on limited geographical areas, raising the question of the generalizability and reliability of their findings.

Electronic health records (EHRs), which collect complete clinical and pharmacological data from clinical consultations, have been identified as an important resource for research into the population effect of changing demography on the epidemiology of chronic illnesses.[21] The present study aimed to use primary care EHR data from the Clinical Practice Research Datalink (CPRD) to evaluate the health status of a nationally representative sample of centenarians in the United Kingdom. The study included a population-based cohort of people registered in primary care who reached the age of 100 between 1990 and 2013 and contrasted the health status of men and women at age 100 and older.

METHODS

Data Source

The study examined a population-based cohort of centenarians drawn from the CPRD between 1990 and 2013. The CPRD is one of the world's largest longitudinal anonymized primary care electronic databases, containing comprehensive and validated EHR data[22,23] from approximately 680 family practices in the United Kingdom. Data elements include demographic characteristics, pharmacological and nonpharmacological treatments, clinical events and diagnoses, referrals to specialist services, laboratory tests, and deaths. Diagnoses recorded in the CPRD have been shown to have high predictive value for capturing a correct doctor's diagnosis in several validation studies.[22] For entry into the CPRD, practice data must contribute research-quality data, according to quality criteria set out by the CPRD group.[24] This study received scientific and ethical approval from the Independent Scientific Advisory Committee for CPRD studies (ISAC Protocol 13_151).

Study Population

The study included participants aged 100 and older registered at general practices providing research quality data to CPRD between January 1, 1990, and September 30, 2013. The start of record for each participant was defined as the later of the person's registration date at a CPRD practice or the date the practice joined CPRD and provided up-to-standard data. The end of record was defined as the earliest of the death date, the end of registration date, or the last data collection date. All participant records between study start date and end date were included in the study. Individuals were eligible if they were registered with a CPRD practice during the year in which they turned 100. The year when participants turned 100 was determined using birth year information, because day and month of birth for adults are not available for analysis in CPRD. There were 11,084 individuals who turned 100 between 1990 and 2013.

Study Measures

The prevalence of main categories of morbidity recorded by the age of 100 was determined by evaluating relevant medical codes within clinical and referral records associated with broad categories of chronic disease. Subdivisions of the Read medical code classification were used to identify diabetes mellitus, coronary heart disease, stroke, hypertension, neoplasms, chronic obstructive pulmonary disease, musculoskeletal and connective tissue diseases, digestive diseases, and nervous system diseases in female and male centenarians. Product codes for antidiabetic drugs prescribed were also used to identify diabetes mellitus because of their specificity for this diagnosis. Centenarians were considered to have had a particular morbidity if a relevant code was recorded before June 30 of their 100th year or before the end of record when this was earlier in the 100th year.

The recording of common geriatric or frailty syndromes by the age of 100 was also evaluated according to sex. These included a range of impairments including depression, dementia, cognitive impairment or memory problems, falls, fractures, mobility or gait problems, incontinence, hearing impairment, visual impairment, confusion or delirium, pressure sores, and debility or weakness. Each syndrome was identified from Read medical codes in participants' clinical and referral records. Depression was identified if a participant was diagnosed with depression during their 100th year or if they had ever been diagnosed with depression and were prescribed depression drugs during their 100th year. Prescribing of other, less-specific drugs was not used to identify other medical and geriatric conditions.

Cardiovascular risk factors were contrasted according to sex. Body mass index (BMI) is presented based on the frequency of participants in different weight categories: underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), and obese (≥ 30.0 kg/m^2). The BMI value recorded closest to age 100 was used where available. Height and weight measurements were used to calculate BMI for participants with no recorded value. Mean total cholesterol and mean cholesterol ratios (total:high-density lipoprotein) were determined when information was available in participant records, and the frequency with undesirable levels is presented and contrasted according to sex. High blood pressure was defined as systolic blood pressure of 140 mmHg or greater or diastolic blood pressure of 90 mmHg or greater, and hypertension was evaluated as high blood pressure or prescribed antihypertensive medications. The study evaluated smoking status using medical and product codes related to smoking, as well as additional information on smoking status recorded in the CPRD. Smoking status closest to the age of 100 was coded as nonsmoker, former smoker, or current smoker.

Statistical Analysis

Stata version 13.0 was used to conduct all statistical analysis (Stata Corp., College Station, TX). All centenarians

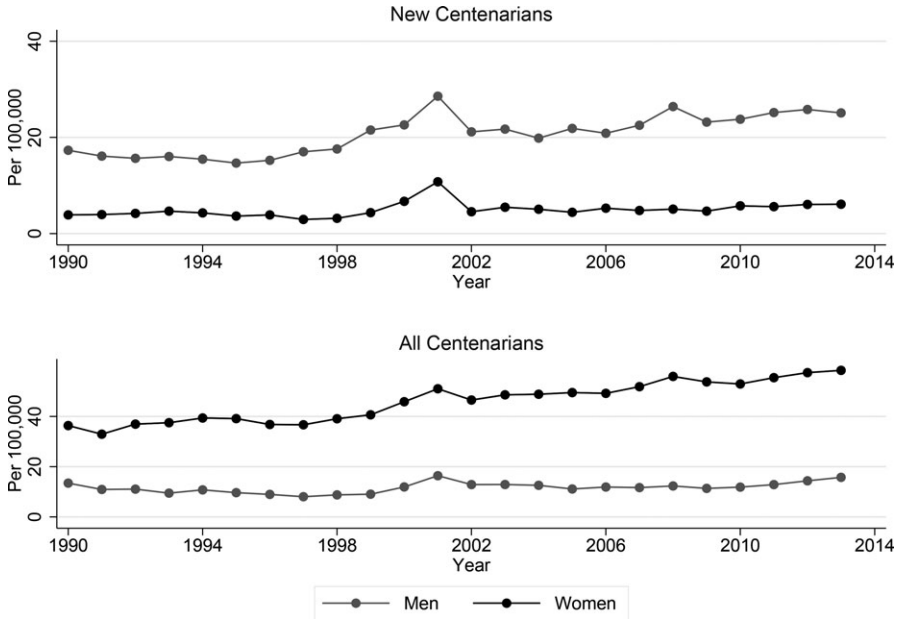

Figure 1. Proportion of population reaching age 100 each year (new centenarians) and proportion of population aged 100 and older (all centenarians).

were individuals aged 100 and older in a given year, and new centenarians were those who reached the age of 100 in a given year. Incidence and prevalence rates for new and all centenarians were estimated using midyear counts for all acceptable individuals in the CPRD population as the denominator. Confidence intervals were estimated using the Poisson distribution. Linear regression was used to evaluate the linear trend in new and all centenarians, using estimated rates as observations. A multiple morbidity score was estimated for each participant as the sum of each category of morbidity. Similarly, a multiple impairment score was estimated by summing all categories of geriatric syndromes. Ordered logistic regression models were fitted to compare the odds of greater impairment in women with the odds in men. Robust variance estimates were used to account for clustering according to practice.

RESULTS

A cohort of 11,048 centenarians (8,982 women, 2,102 men) reaching age 100 between 1990 and 2013 was included in the analysis. The number of participants turning 100 each year increased from 85 in 1990 to 684 in 2013, but the CPRD registered population also increased over the period. The average number of new centenarians per year in this population increased in women from 15.99 per 100,000 in 1990–94 to 24.95 per 100,000 in 2010–13 and for men from 4.25 to 5.88 per 100,000 over the same period (Figure 1). The number of new centenarians increased by 4.74 (95% confidence interval (CI) = 3.28–6.20) per 100,000 per decade in women ($P < .001$) and by 0.87 (95% CI = −0.003 to 1.74) per 100,000 per decade in men ($P = .06$). In absolute terms, the number of all centenarians increased by 10.72 (95% CI = 9.33–12.10) per 100,000 per decade in women ($P < .001$) and by 1.49 (95% CI = 0.35–2.64) per 100,000 per decade in men ($P = .01$).

The most-prevalent morbidities at the age of 100 were musculoskeletal and connective tissue diseases, sensory deficits affecting the eye and ear, and digestive diseases (Table 1). Diabetes mellitus and stroke were observed in fewer than 10% of men and women, although each form of morbidity was more frequent in women than men. The frequency of women with recorded hypertension (27%) was almost double the frequency of men (16%). Figure 2 shows the distribution of multiple morbidities (excluding dementia) in men and women at age 100. More men were free of these selected morbidities (excluding dementia) at age 100, with 37% of men and 21% of women experiencing none of the morbidities (excluding dementia) in

Table 1. Categories of Prevalent Morbidity at Age 100 According to Sex

	Women	Men
Morbidity	n (%)	
Diabetes mellitus	478 (5)	130 (6)
Coronary heart disease	1,376 (15)	328 (16)
Stroke	770 (9)	137 (7)
Neoplasms	1,396 (16)	341 (16)
Hypertensive diseases	2,458 (27)	343 (16)
Chronic obstructive pulmonary disease	974 (11)	246 (12)
Musculoskeletal and connective tissue diseases	5,315 (59)	915 (44)
Arthropathies and related disorders	2,347 (44)	316 (35)
Vertebral column syndromes	1,097 (21)	246 (27)
Rheumatism, excluding the back	1,393 (26)	308 (34)
Digestive diseases	3,755 (42)	773 (37)
Disorders of the nervous system and senses	5,620 (63)	1,033 (49)
Disorders of the eye	3,372 (38)	567 (27)
Cataracts	1,027 (11)	157 (7)
Macular degeneration	332 (4)	50 (2)
Disorders of the ear	1,705 (19)	368 (18)

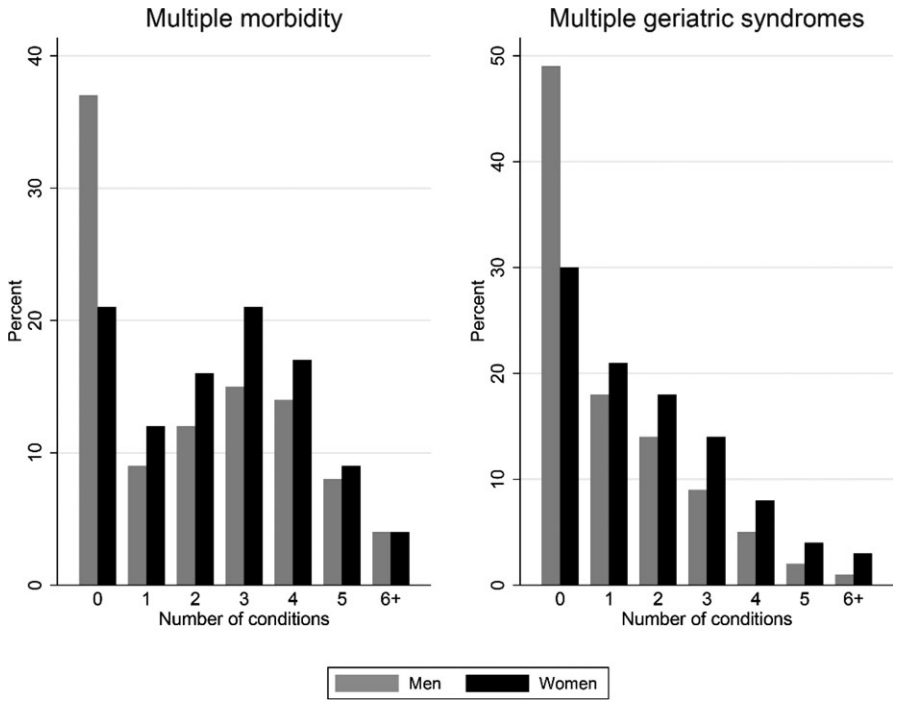

Figure 2. Distribution of multiple morbidities (excluding dementia) and multiple geriatric syndromes for men and women.

Table 1 before the age of 100. Conversely, there were more women than men in each category of multiple morbidity (excluding dementia). In an ordered logistic regression model, the odds of greater multiple morbidity (excluding dementia) in women than in men were 1.64 (95% CI = 1.42–1.89, $P < .001$).

Geriatric syndromes (Table 2) tended to be less frequently recorded than the chronic morbidities in Table 1. Hearing impairments were present in 30% of women and 25% of men, and more women (30%) than men (19%) experienced at least one fall before the age of 100. Dementia was recorded in 12% of women and 6% of men, and cognitive impairment or memory problems, debility or weakness, pressure ulcers, and depression were present in approximately 5% of women and men. Approximately 10% of the cohort was recorded to have incontinence, and 1% was recorded with social isolation. In general, female centenarians had more geriatric syndromes than men. Figure 2 shows the frequency of centenarians with multiple geriatric impairments; 30% of women and 49% of men experienced no geriatric syndromes before the age of 100. The relative odds of a higher category of impairment for women than for men were 2.14 (95% CI = 1.90–2.41, $P < .001$).

Cardiovascular risk factors are described according to sex in Table 3. Most men and women were of normal weight (59%), with a small proportion being obese (6%) or underweight (11%). Women (16%) and men (14%) had similar frequencies of undesirable cholesterol ratios (total:high-density lipoprotein), although more women (53%) were found to have undesirable total cholesterol levels (>5 mmol/L) than men (27%). Forty-six percent of women and 33% of men had high blood pressure (≥140/90 mmHg) or were taking antihypertensive medication at the age of 100. Eighty-one percent of centenarians with smoking records were classified as nonsmokers overall (85% of women, 61% of men). Six percent of centenarians were considered current smokers.

Table 2. Geriatric Syndromes at Age 100 According to Sex

	Women	Men
Syndrome	n (%)	
Depression	500 (6)	68 (3)
Dementia	1,044 (12)	125 (6)
Cognitive impairment or memory	433 (5)	82 (4)
Falls	2,666 (30)	403 (19)
Fractures	3,146 (35)	299 (14)
Mobility or gait	933 (10)	177 (8)
Incontinence	969 (11)	150 (7)
Hearing impairment	2,708 (30)	531 (25)
Visual impairment	1,470 (16)	260 (12)
Confusion or delirium	1,103 (12)	169 (8)
Pressure sores	346 (4)	66 (3)
Debility or weakness	574 (6)	90 (4)

DISCUSSION

Summary

In this primary care–based study, the proportion of new and total centenarians increased by some 50% in women and approximately 30% in men over 2 decades. This is slightly lower than other recent growth estimates of centenarians.[25,26] The most-frequent chronic morbidities observed in centenarians were musculoskeletal disorders, digestive diseases, and disorders of the senses. The frequencies of diabetes mellitus, cancer, stroke, and coronary heart disease tended to be lower than reported in adults aged 75 and older, suggesting that individuals surviving to

Table 3. Cardiovascular Risk Factors in Male and Female Centenarians. Figures are Frequencies (Column Percent) Except Where Indicated

Risk Factor	Female	Male	*P*-Value
Body mass index, kg/m^2			
Records available, n	3,456	780	
Mean ± SD	23.1 ± 4.3	23.8 ± 3.8	<0.001
Underweight (<18.5), n (%)	407 (12)	46 (6)	<0.001
Normal (18.5–24.9), n (%)	2,009 (58)	474 (61)	
Overweight (25.0–29.9), n (%)	824 (15)	211 (27)	0.37
Obese (≥30.0), n (%)	216 (6)	49 (6)	0.81
Cholesterol ratio (total:high-density lipoprotein)			
Records available, n	1,754	362	
Mean ± SD	3.5 ± 1.0	3.5 ± 1.0	0.28
Undesirable level (>4.5), n (%)	280 (16)	52 (14)	0.46
Total cholesterol, mg/dL			
Records available, n	2,388	492	
Mean ± SD	201.1 ± 42.5	174.0 ± 34.8	<0.001
Undesirable levels (>193), n (%)	1,271 (53)	133 (27)	<0.001
Blood pressure, mmHg			
Records available, n	3,280	603	
Systolic, mean ± SD	133 ± 19	131 ± 20	0.12
Diastolic, mean ± SD	73 ± 10	72 ± 11	0.01
High blood pressure (systolic ≥ 140 or diastolic ≥ 90), n (%)	1,271 (39)	207 (34)	0.17
Hypertension			
Records available, n	8,982	2,102	
Hypertension, n (%)[a]	4,153 (46)	685 (33)	<0.001
Smoking status			
Records available, n	6,101	1,142	
Nonsmoker, n (%)	5,186 (85)	696 (61)	<0.001
Former smoker, n (%)	581 (10)	316 (28)	<0.001
Current smoker, n (%)	334 (5)	130 (11)	<0.001

[a]High blood pressure (≥140/90 mmHg) or taking antihypertensive medication during year of turning 100.

the age of 100 might have a lower propensity for these more serious conditions. Nevertheless, 63% of men and 79% of women had one or more categories of morbidity (excluding dementia), and half to two-thirds had one or more geriatric syndromes.

Although fewer men than women reached 100 years old, men who survived tended to be healthier, with fewer geriatric syndromes and sometimes lower risk factor values, than women. This finding confirms earlier evidence in a more-representative sample of centenarians. A greater proportion of men (37%) than of women (21%) were disease free at 100. Men tended to have lower rates of geriatric syndromes than women, although medical records are likely to underrecord dementia and other conditions such as incontinence in very old people. This may be because a greater proportion of men diagnosed with chronic illness die before reaching 100 than of women with similar chronic conditions, for various reasons (e.g., poorer treatment adherence, potential sex differences in functional reserve).[27] Thus, "survival of the fittest" describes the smaller number of generally healthier men who survive to 100 than the larger number of generally less-healthy women reaching this age.

Strengths and Limitations

This study had the strengths of a large sample drawn from a representative population of U.K. general practices. Previous centenarian studies have generally used smaller sample sizes. Use of primary care EHRs allowed for characterization of chronic morbidities, geriatric impairments, and mortality in the oldest individuals. In the United Kingdom, approximately 98% of individuals (healthy and unhealthy) are registered with a family practice, ensuring that the present results are population based. Regular medical surveillance of centenarians is required in the United Kingdom. According to the Department of Health National Service Framework for Older People,[28] individuals aged 75 and older will attend an annual review of medicines, and those with four or more medicines will be reviewed every 6 months, although this review was only introduced in 2002 and may be performed by general practitioners, pharmacists, or nurses. There is a possibility of misclassification of birth year because of poor recording practices at time of birth, and this is suggested by the excess of centenarians in 2000–01, suggesting that some missing dates of birth might have been imputed as 1900–01.

Disease recording in the CPRD generally has high predictive value[29] but does not always permit detailed analysis of disease subtype (e.g., ischemic or hemorrhagic stroke, Alzheimer's or vascular dementia). The frequency of health conditions and, in particular, geriatric syndromes such as dementia may be substantially underestimated because these are rates of general practitioner recording, and it is likely that the true rates are higher. A diagnosis requires that individuals consult with their general practitioner and the clinical features be recognized and a diagnosis recorded, but the present study should provide valid estimates of relative rates for men and women if rates of underreporting are similar. A recent review[30] found that approximately 18–44% of people aged 85 and older have dementia, suggesting that the current findings may slightly underestimate the prevalence of dementia in community samples. Mean values for weight and BMI are robust, but there was a high proportion of missing values for each measure. Underweight individuals may include those who are close to the end of life, and height loss will occur with age because of vertebral osteoporosis.

Comparison with Existing Literature

Previous studies with centenarians from Europe[7,9,12,31] and the United States[32,33] have generally focused on specific conditions, tending to be heterogeneous in sampling strategy and use of assessment instruments. Results have been inconsistent but mostly indicating that centenarians tolerate age-related diseases well and compress the majority of their disability toward the end of their lives,[34] although these studies tended to recruit healthier centenarians, and their generalizability to a more-heterogeneous centenarian population is questionable, as documented in this study.

In a population-based survey of 207 centenarians in Denmark, in which participants were visited at home for an interview and clinical examination, levels of cardiovascular disease (72%), hypertension (52%), and dementia (51%) were higher than the current study, and levels of osteoarthritis (54%) were similar.[12] The rate of cancer-free individuals identified in this study is similar to the rates (80–85%) published in the New England Centenarian Study.[32,33,35] A study[10] that compared cognitive functioning of centenarians in Japan and Sweden found higher levels of dementia (40–63%), although the participants were not representative in terms of random sampling, which calls into question the robustness of their findings. The present study findings on BMI are consistent with those from smaller observational studies conducted in Italy[31] and Sweden.[9] A recent population-based study in England[36] used death registration data to examine trends in place of death and cause of death in centenarians. This study revealed that subjects were more likely to die of pneumonia and less likely to die of cancer and ischemic heart disease than younger elderly adults. This is consistent with the current study, which found low frequencies of cancer and heart disease in centenarians, although there are often concerns about the accuracy of causes of death from death certificates.

Two Italian studies[17,18] examined differences according to sex and geographical variations among centenarians from three regions in Italy, but neither study reported on specific chronic diseases or geriatric disabilities.[18] A study of Greek centenarians focused on the differences according to sex in personality traits and sociodemographic variables, with no reference to medical conditions.[19] Finally, the New England Centenarian Study[20] reported that male centenarians, similar to the present findings, had better cognitive and physical function than female centenarians.

Implications for Research and Practice

Large population-based epidemiological studies reporting trends in incidence and the health of centenarians according to sex are scarce. This is the first study to use primary care EHR data to describe trends in U.K. male and female centenarians and the extent of several chronic diseases and geriatric syndromes. This information allows for a better understanding of sex differences in extreme old age and may provide direction for sex-specific areas of centenarian research. The study has highlighted important differences between men and women with respect to the prevalence of diverse chronic illnesses, geriatric syndromes, and related risk factors. This information can help inform future planning for the provision of healthcare needs in an increasingly large proportion of the U.K. population, with limited healthcare-related information available. The findings concerning prevalence of different chronic conditions and geriatric impairments of centenarians also provide valuable data for improved modelling of future healthcare costs in the United Kingdom. There is potential for future research regarding contrasting patterns of prescription drug use, health care use, and lifestyle factors such as exercise and alcohol use in men and women at extreme old age. It will also be important to investigate further changes in the prevalence of morbidities and geriatric syndromes over time to predict future needs for old age care and disability.

CONCLUSION

This study reports on the contrasting epidemiology and health status of a representative sample of male and female centenarians in a family practice context. The findings underscore a rapid increase in people aged 100 and older. In this group, there is a higher frequency of age-related chronic disease and disability in women than men. The study also provides proof of concept for research using EHRs to understand the epidemiology of aging and improve care of the oldest adults.

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Conflict of Interest: This research was supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' National Health Service Foundation Trust and King's College London.

The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

Author Contributions: All authors were involved in drafting the article and revising it critically for intellectual content, and all authors approved the final version to be published. Martin C. Gulliford (guarantor), Nisha C. Hazra, and Alex Dregan had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Jackson, Gulliford. Acquisition of data: Hazra, Dregan, Gulliford. Analysis and interpretation of data: Hazra, Dregan, Jackson, Gulliford.

Sponsor's Role: The study is based in part on data from the CPRD obtained under license from the U.K. Medicines and Healthcare products Regulatory Agency, although the interpretation and conclusions contained in this report are those of the authors alone.

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