ORIGINAL ARTICLE

Mobile phone calls, genetic susceptibility, and new-onset hypertension: results from 212 046 UK Biobank participants

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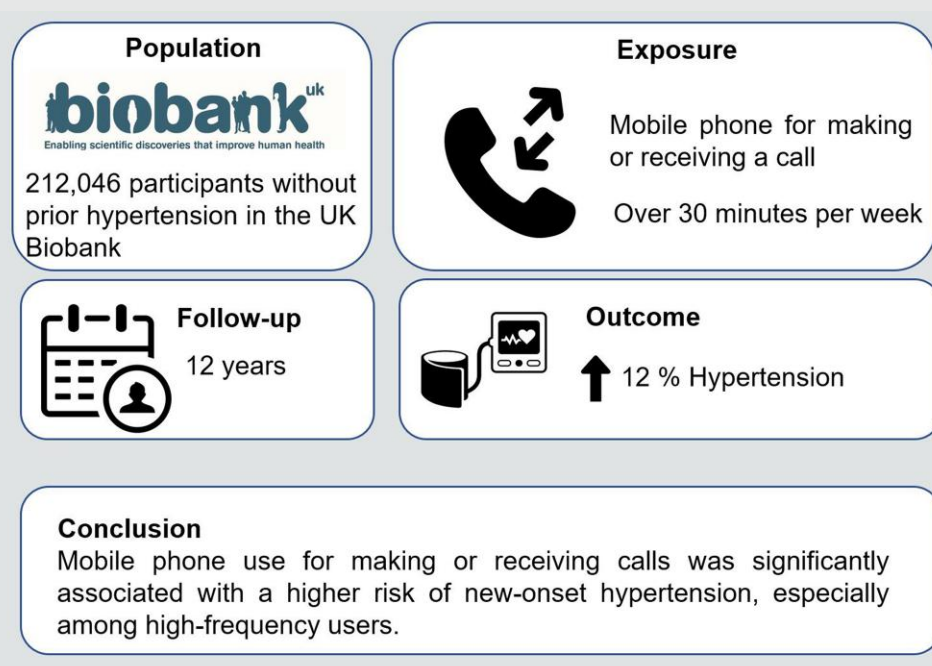|	
Aims	The relationship between mobile phone use for making or receiving calls and hypertension risk remains uncertain. We aimed to examine the associations of mobile phone use for making or receiving calls and the use frequency with new-onset hypertension in the general population, using data from the UK Biobank.
Methods and results	A total of 212 046 participants without prior hypertension in the UK Biobank were included. Participants who have been using a mobile phone at least once per week to make or receive calls were defined as mobile phone users. The primary outcome was new-onset hypertension. During a median follow-up of 12.0 years, 13 984 participants developed new-onset hypertension. Compared with mobile phone non-users, a significantly higher risk of new-onset hypertension was found in mobile phone users [hazards ratio (HR), 1.07; 95% confidence interval (CI): 1.01–1.12]. Among mobile phone users, compared with those with a weekly usage time of mobile phones for making or receiving calls <5 mins, significantly higher risks of new-onset hypertension were found in participants with a weekly usage time of 30–59 mins (HR, 1.08; 95%CI: 1.01–1.16), 1–3 h (HR, 1.13; 95%CI: 1.06–1.22), 4–6 h (HR, 1.16; 95%CI: 1.04–1.29), and >6 h (HR, 1.25; 95%CI: 1.13–1.39) (P for trend <0.001). Moreover, participants with both high genetic risks of hypertension and longer weekly usage time of mobile phones making or receiving calls had the highest risk of new-onset hypertension.
Conclusions	Mobile phone use for making or receiving calls was significantly associated with a higher risk of new-onset hypertension, especially among high-frequency users.

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Graphical Abstract

Introduction

Hypertension is one of the leading preventable risk factors for cardio-vascular diseases and premature death worldwide.[1] The global age-standardized prevalence of raised blood pressure was 24.1% in men and 20.1% in women in 2015.[2] Therefore, it is urgent to identify more modifiable factors to improve the primary prevention of hypertension and reduce its associated severe disease burden.

In recent years, mobile phones have become a device of everyday life around the world, with an estimated 8.2 billion subscriptions worldwide in 2020.[3] This raises important questions about the safety of using a mobile phone to make or receive calls, especially for heavy users. Some studies in animals or human cells, for example, suggested that long-term exposure to radio-frequency electromagnetic fields (RF-EMF) emitted by mobile phones was related to oxidative stress, increased inflammation, and DNA damage,[4,5] all of which could lead to the development of hypertension.[6,7] Accordingly, a previous single-blind placebo-controlled study of seven healthy men and three women reported that exposure of the right hemisphere to an RF-EMF for 35 min was associated with an increase in resting blood pressure between 5 and 10 mmHg.[8] Of note, this study had a relatively small sample size and mainly focused on the effects of short-term RF-EMF exposure on blood pressure levels. Moreover, previous studies,[9–13] which were mainly cross-sectional[9,11–13] or case-control[10] designs, have evaluated the relationship of mobile phone use or mobile phone addiction with the prevalence of hypertension or blood pressure levels but reported inconsistent findings. One of the important reasons for the mixed results may be that the different studies[9–13] included different patterns of mobile phone use, including making or receiving calls, short messaging service (SMS), playing games, chatting, and so on.

Furthermore, the cross-sectional and case-control designs limit conclusions about causation and directionality. As such, although making and receiving calls is one of the most important functions of mobile phones and is closely related to RF-EMF; so far, the relationship between mobile phone use for making and receiving calls and long-term changes in blood pressure and the risk of new-onset hypertension remains uncertain.

To address the above gap in knowledge, our current study aimed to investigate the association of mobile phone use for making or receiving calls and its use duration and frequency with the risk of new-onset hypertension in the general population, using data from the large-scale, observational UK Biobank. Moreover, since genetic factors may be involved in the development of hypertension, we further investigated the joint effect of mobile phone use for making or receiving calls and genetic susceptibility of hypertension with new-onset hypertension and explored the potential gene–behaviour interactions.

Methods

Population and study design

The UK Biobank is a large prospective, observational study designed to examine the role of comprehensive exposures in health and diseases. The UK Biobank recruited about 500 000 adult participants, aged 37–73 years, from 22 assessment centres across the United Kingdom from 2006 to 2010. At enrolment, participants completed a touch-screen questionnaire and a series of physical measurements and provided biological samples. Details of the study design and data collection procedures have been described previously.[14,15] Incident diagnoses were observed through linkage to national health records and follow-up visits.[16]

The current analysis included UK Biobank participants with complete information on mobile phone use behaviours about making or receiving calls, and without prior hypertension at baseline. Finally, a total of 212 046 participants were included in the final analysis (see Supplementary material online, Figure S1).

The UK Biobank was approved by the North West Research Ethics Committee. All participants gave written informed consent before enrolment in the study.

Measurements of mobile phone use behaviours about making or receiving calls

Behaviours of mobile phone use in making or receiving calls (length of mobile phone use, weekly usage of mobile phone, and hands-free device/speakerphone use with mobile phone) were self-reported and assessed through the touch-screen questionnaire at baseline.

Length of mobile phone use was assessed using the following question, 'For approximately how many years have you been using a mobile phone at least once per week to make or receive calls?', and seven options were provided to respond: 'never used a mobile phone at least once per week', '1 year or less', '2–4 years', '5–8 years', 'more than 8 years', 'do not know', and 'prefer not to answer'. Based on the above question, those answering 'Never used mobile phone at least once per week' was defined as mobile phone non-users, and participants who have been using a mobile phone at least once per week to make or receive calls were defined as mobile phone users. And mobile phone users were further asked for weekly usage of a mobile phones, and hands-free device/speakerphone use with mobile phones, while others did not.

Weekly usage of mobile phone for making or receiving calls was obtained using the following question, 'over the last 3 months, on average how much time per week did you spend making or receiving calls on a mobile phone?', and eight options were given to respond: '<5 mins', '5–29 mins', '30–59 mins', '1–3 h', '4–6 h', '>6 h', 'do not know', and 'prefer not to answer'.

Hands-free device/speakerphone uses with mobile phones to make or receive calls was assessed using the following question, 'Over the last 3 months, how often have you used a hands-free device/speakerphone when making or receiving calls on your mobile?', and seven options were given to respond: 'never or almost never', 'less than half the time', 'about half the time', 'more than half the time', 'always or almost always', 'do not know', and 'prefer not to answer'.

Definition of the genetic risk score

Detailed information about genotyping, imputation, and quality control in the UK Biobank study has been described previously.[16] A genetic risk score (GRS) using 118 single-nucleotide polymorphisms (SNPs) which showed a significant association with the risk of hypertension.[17] The hypertension-GRS was calculated with a weighted method[18] as followed: $GRS = \sum_{i=1}^{118} \beta_i \times SNP_i$, where each SNP was recorded as 0, 1, or 2 according to the number of risk alleles. A higher GRS score indicated a higher genetic predisposition to hypertension. Participants were classified into three groups low (the first tertile), intermediate (the second tertile), and high (the third tertile) genetic risk of hypertension.

Measurements of covariates

Procedures for collecting and processing baseline blood and urine samples have previously been reported and validated.[19] Biochemical assays were conducted at a dedicated central laboratory. The estimated glomerular filtration rate (eGFR) was calculated using the chronic kidney disease epidemiology collaboration equation.[20]

Detailed information on covariates was available through standardized questionnaires, including age, sex, race, education, smoking, diet, sleep, mental health, income, and the usage of antihypertensive, cholesterol-lowering, and glucose-lowering medications. Body mass index (BMI) was calculated as weight divided by height squared. Area-based socioeconomic status was derived from the postal code of residence by using the Townsend deprivation score. Baseline prevalent diabetes was identified through multiple procedures considering the type of diabetes and sources of the diagnosis.[21] Blood pressure was measured twice manually (manual sphygmometer) or automatically (Omron HEM-7015IT digital blood

Table 1 Baseline characteristics of the total participants according to the status of mobile phone use (users vs. non-users)

Baseline characteristics	Used a mobile phone at least once per week	
	Non-users	Users
Number of participants	26 250	185 796
Age, years	57.9 ± 7.7	53.1 ± 7.9
Male, n (%)	10 337 (39.4)	69 549 (37.4)
White, n (%)	25 300 (96.9)	175 166 (94.5)
Townsend deprivation index	−1.5 ± 2.9	−1.4 ± 3.0
Education (University), n (%)	10 913 (41.9)	71 173 (38.6)
Smoking status	2577 (9.8)	21 510 (11.6)
Physical activity, n (%)		
Low	3785 (17.8)	28 121 (18.0)
Moderate	9126 (42.9)	63 541 (40.7)
High	8357 (39.3)	64 533 (41.3)
Income (<£18 000), n (%)	6329 (28.4)	36 143 (22.0)
Healthy diet score	3.2 ± 1.4	3.0 ± 1.4
Healthy sleep score	3.1 ± 1.0	3.1 ± 1.0
Total mental health complaints	4.3 ± 3.3	4.6 ± 3.2
BMI, kg/m²	25.3 ± 4.1	26.1 ± 4.1
Systolic blood pressure, mmHg	125.0 ± 9.7	123.6 ± 9.9
Diastolic blood pressure, mmHg	75.9 ± 7.0	76.2 ± 7.0
Triglycerides, mmol/L	1.6 ± 0.9	1.6 ± 0.9
HDL cholesterol, mmol/L	1.5 ± 0.4	1.5 ± 0.4
LDL cholesterol, mmol/L	3.6 ± 0.8	3.6 ± 0.8
C-reactive protein, mg/L	2.2 ± 4.3	2.1 ± 3.9
Glucose, mmol/L	5.0 ± 1.0	4.9 ± 0.9
eGFR, mL/min/1.73 m²	90.6 ± 12.4	93.6 ± 12.5
Cholesterol-lowering medication use, n (%)	2312 (8.8)	11 972 (6.4)
Glucose-lowering medications use, n (%)	417 (1.6)	2317 (1.2)
Diabetes, n (%)	605 (2.3)	3514 (1.9)
Depression, n (%)	1593 (6.1)	10 851 (5.8)
Family history of hypertension	10 011 (38.1)	81 205 (43.7)

BMI, body mass index; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.
[a]The results are presented as Mean ± SD or n (%).

pressure monitor), and the mean value of the two measurements was used to minimize measurement error.

The details about these measurements can be found in the UK Biobank online protocol (www.ukbiobank.ac.uk).

Study outcome

The study outcome was new-onset hypertension, based on medical history and linked to hospital admissions. The website (http://content.digital.nhs.uk/services) showed the linkage procedure in detail. Participants with hypertension were defined according to the International Classification of Diseases edition 10: I10. The duration of follow-up was calculated as the time between the date of attendance and the date of diagnosis of new-onset hypertension, date of death, the date of loss to follow-up, or 28 February

Table 2 Baseline characteristics of mobile phone users according to weekly usage time of mobile phones making or receiving calls

Baseline characteristics[a]	Weekly usage of mobile phone						P values
	<5 min	5–29 min	30–59 min	1–3 h	4–6 h	> 6 h	
Number of participants	34 216	70 594	33 700	29 290	8788	9208	
Age, years	55.8 ± 8.0	54.0 ± 7.9	52.5 ± 7.6	51.0 ± 7.3	49.8 ± 6.9	48.8 ± 6.4	<0.001
Male, n (%)	11 961 (35.0)	23 596 (33.4)	12 818 (38.0)	12 579 (42.9)	4025 (45.8)	4570 (49.6)	<0.001
White, n (%)	32 869 (96.3)	67 289 (95.6)	31 746 (94.4)	27 046 (92.6)	8001 (91.2)	8215 (89.4)	<0.001
Townsend deprivation index	−1.7 ± 2.9	−1.5 ± 3.0	−1.2 ± 3.1	−1.1 ± 3.2	−1.0 ± 3.2	−1.0 ± 3.3	<0.001
Education (university), n (%)	12 972 (38.2)	27 620 (39.4)	13 159 (39.3)	11 236 (38.6)	3150 (36.1)	3036 (33.2)	<0.001
Current smoker, n (%)	2927 (8.6)	7114 (10.1)	4142 (12.3)	4177 (14.3)	1437 (16.4)	1713 (18.7)	<0.001
Physical activity, n (%)							<0.001
Low	5177 (18.3)	10 221 (17.3)	4931 (17.3)	4622 (18.5)	1505 (19.9)	1665 (21.1)	
Moderate	11 900 (42.1)	24 779 (42.1)	11 367 (39.8)	9795 (39.2)	2881 (38.1)	2819 (35.7)	
High	11 156 (39.5)	23 920 (40.6)	12 282 (43.0)	10 586 (42.3)	3180 (42.0)	3409 (43.2)	
Income (<£18 000), n (%)	6102 (20.7)	10 486 (16.8)	4470 (14.9)	3632 (13.8)	1035 (13.0)	1102 (13.2)	<0.001
Healthy diet score	3.2 ± 1.4	3.1 ± 1.4	3.0 ± 1.4	2.9 ± 1.4	2.9 ± 1.4	2.8 ± 1.4	<0.001
Healthy sleep score	3.2 ± 1.0	3.2 ± 1.0	3.1 ± 1.0	3.1 ± 1.0	3.0 ± 1.0	3.0 ± 1.0	<0.001
Total mental health complaints	4.4 ± 3.2	4.5 ± 3.2	4.6 ± 3.2	4.6 ± 3.2	4.7 ± 3.3	4.8 ± 3.3	<0.001
BMI, kg/m^2	25.6 ± 4.0	25.9 ± 4.1	26.2 ± 4.1	26.5 ± 4.2	26.9 ± 4.3	27.1 ± 4.4	<0.001
Systolic blood pressure, mmHg	124.4 ± 9.7	123.8 ± 9.9	123.3 ± 9.9	123.1 ± 9.9	123.1 ± 9.9	122.9 ± 9.8	<0.001
Diastolic blood pressure, mmHg	76.0 ± 6.9	76.1 ± 7.0	76.2 ± 7.0	76.4 ± 7.0	76.6 ± 7.1	76.9 ± 7.0	<0.001
Triglycerides, mmol/L	1.5 ± 0.9	1.5 ± 0.9	1.5 ± 0.9	1.6 ± 1.0	1.6 ± 1.0	1.7 ± 1.1	<0.001
HDL cholesterol, mmol/L	1.5 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	<0.001
LDL cholesterol, mmol/L	3.6 ± 0.8	3.6 ± 0.8	3.6 ± 0.8	3.5 ± 0.8	3.5 ± 0.8	3.5 ± 0.8	<0.001
C-reactive protein, mg/L	2.1 ± 3.9	2.1 ± 3.9	2.2 ± 4.1	2.2 ± 4.0	2.2 ± 3.8	2.3 ± 3.8	0.142
Glucose, mmol/L	4.9 ± 0.9	4.9 ± 0.9	4.9 ± 0.9	4.9 ± 0.9	4.9 ± 0.9	4.9 ± 1.0	<0.001
eGFR, mL/min/1.73 m^2	91.9 ± 12.5	93.0 ± 12.5	94.0 ± 12.4	95.1 ± 12.4	95.7 ± 12.4	96.3 ± 12.4	<0.001
Cholesterol-lowering medications use, n (%)	2590 (7.6)	4743 (6.7)	2065 (6.1)	1607 (5.5)	458 (5.2)	509 (5.5)	<0.001
Glucose-lowering medications use, n (%)	461 (1.3)	798 (1.1)	419 (1.2)	375 (1.3)	111 (1.3)	153 (1.7)	<0.001
Diabetes, n (%)	661 (1.9)	1247 (1.8)	635 (1.9)	579 (2.0)	178 (2.0)	214 (2.3)	0.004
Depression, n (%)	1903 (5.6)	4104 (5.8)	2060 (6.1)	1781 (6.1)	503 (5.7)	500 (5.4)	0.008
Family history of hypertension, n (%)	14 026 (41.0)	30 517 (43.2)	14 998 (44.5)	13 303 (45.4)	4033 (45.9)	4328 (47.0)	<0.001
Length of mobile phone use, n (%)							<0.001
1 year or less	2529 (7.4)	1975 (2.8)	372 (1.1)	181 (0.6)	38 (0.4)	24 (0.3)	
2–4 years	10 636 (31.1)	16 282 (23.1)	5408 (16.0)	3071 (10.5)	708 (8.1)	455 (4.9)	
5–8 years	13 079 (38.2)	28 291 (40.1)	12 696 (37.7)	9700 (33.1)	2507 (28.5)	2017 (21.9)	
More than 8 years	7972 (23.3)	24 046 (34.1)	15 224 (45.2)	16 338 (55.8)	5535 (63.0)	6712 (72.9)	
Hands-free device/speakerphone use, n (%)							<0.001
Never or almost never	32 564 (95.2)	62 527 (88.6)	26 606 (78.9)	19 584 (66.9)	4942 (56.2)	4278 (46.5)	
Less than half the time	879 (2.6)	4873 (6.9)	4058 (12.0)	5357 (18.3)	1879 (21.4)	2062 (22.4)	
About half the time	306 (0.9)	1564 (2.2)	1502 (4.5)	1991 (6.8)	867 (9.9)	1029 (11.2)	
More than half the time	145 (0.4)	690 (1.0)	741 (2.2)	1181 (4.0)	525 (6.0)	757 (8.2)	
Always or almost always	322 (0.9)	940 (1.3)	793 (2.4)	1177 (4.0)	575 (6.5)	1082 (11.8)	

BMI, body mass index; HDL cholesterol, high-density lipoprotein cholesterol; LDL cholesterol, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.
[a]The results are presented as mean ± SD or n (%).

2018, for Wales, and 31 March 2021, for Scotland and England, whichever occurred first.

Statistical analysis

Baseline characteristics, presented as means ± SD for continuous variables or proportions for categorical variables, according to the weekly usage time of mobile phones for making or receiving calls (<5 min, 5–29 min, 30–59 min, 1–3 h, 4–6 h, and >6 h), were compared using χ^2-tests for categorical variables and one-way analysis of variance for continuous variables among mobile phone users.

The relationship of mobile phone uses (*vs.* non-users) with new-onset hypertension in the total population, and the associations of the length of mobile phone use (≤1 year, 2–4 years, 5–8 years, and >8 years), weekly usage time of mobile phones for making or receiving calls, and hands-free device/speakerphone use to make or receive calls (never or almost never,

Table 3 Association between mobile phone uses (users vs. non-users) and new-onset hypertension in total participants, and relations of different mobile phone use behaviours with new-onset hypertension in mobile phone users

Mobile phone use	N	Cases	Model 1[a]		Model 2[b]		Model 3[c]	
			HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Total participants (N = 212 046)								
Mobile phone users (used mobile phone at least once per week)								
No	26 250	2067	Ref	—	Ref	—	—	—
Yes	185 796	11 917	1.15 (1.09, 1.20)	<0.001	1.07 (1.01, 1.12)	0.018	—	—
Mobile phone users (N = 185 796)								
Length of mobile phone use								
≤ 1 year	5119	377	Ref	—	Ref	—	Ref	—
2–4 years	36 560	2488	1.00 (0.90, 1.11)	0.995	1.03 (0.91, 1.15)	0.668	1.01 (0.90, 1.14)	0.828
5–8 years	68 290	4231	0.96 (0.87, 1.07)	0.493	1.00 (0.90, 1.13)	0.934	0.98 (0.87, 1.10)	0.739
> 8 years	75 827	4821	1.05 (0.95, 1.17)	0.324	1.08 (0.96, 1.21)	0.192	1.03 (0.92, 1.16)	0.585
Weekly usage time of mobile phones for making or receiving calls								
< 5min	34 216	2404	Ref		Ref		Ref	
5–29 min	70 594	4466	1.04 (0.99, 1.10)	0.095	1.00 (0.95, 1.06)	0.965	1.00 (0.95, 1.06)	0.981
30–59 min	33 700	2129	1.17 (1.10, 1.24)	<0.001	1.08 (1.02, 1.16)	0.015	1.08 (1.01, 1.16)	0.018
1–3 h	29 290	1802	1.28 (1.20, 1.36)	<0.001	1.14 (1.06, 1.22)	<0.001	1.13 (1.06, 1.22)	0.001
4–6 h	8788	529	1.38 (1.25, 1.51)	<0.001	1.16 (1.05, 1.29)	0.005	1.16 (1.04, 1.29)	0.006
> 6 h	9208	587	1.60 (1.45, 1.75)	<0.001	1.25 (1.13, 1.39)	<0.001	1.25 (1.13, 1.39)	<0.001
P for trend			<0.001		<0.001		<0.001	
Categories								
<30 min	104 810	6870	Ref		Ref		Ref	
≥30 min	80 986	5047	1.23 (1.18, 1.27)	<0.001	1.12 (1.08, 1.17)	<0.001	1.12 (1.07, 1.17)	<0.001
Hands-free device/speakerphone used for making or receiving calls								
Never or almost never	150 501	9805	Ref		Ref		Ref	
Less than half the time	19 108	1108	1.06 (0.99, 1.12)	0.094	1.02 (0.95, 1.10)	0.512	0.98 (0.91, 1.05)	0.515
About half the time	7259	431	1.10 (1.00, 1.21)	0.062	1.06 (0.96, 1.18)	0.268	1.00 (0.90, 1.11)	0.988
More than half the time	4039	232	1.07 (0.94, 1.22)	0.338	0.97 (0.84, 1.12)	0.686	0.90 (0.78, 1.04)	0.173
Always or almost always	4889	341	1.22 (1.10, 1.36)	<0.001	1.04 (0.92, 1.17)	0.503	0.97 (0.86, 1.10)	0.660

[a]Model 1: adjusted for age, and sex.
[b]Model 2: adjusted for covariates in Model 1 plus BMI, race, Townsend deprivation index, family history of hypertension, education, smoking status, systolic blood pressure, triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, C-reactive protein, blood glucose, eGFR, use of cholesterol-lowering medications, and glucose-lowering medications use.
[c]Model 3: adjusted for covariates in Model 2 plus mutual adjustments for the different behaviour of using mobile phones.

less than half the time, about half the time, more than half the time, and always or almost always) with new-onset hypertension in the mobile phone users, were estimated using Cox proportional hazards models [hazards ratio (HR) and 95% confidence interval (CI)]. Model 1 adjusted for age and sex. Model 2 adjusted for age, sex, BMI, race, Townsend deprivation index, family history of hypertension, education, smoking status, systolic blood pressure (SBP), triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, C-reactive protein, blood glucose, eGFR, use of cholesterol-lowering medications, and glucose-lowering medications. Model 3 included all the covariates in Model 2 plus mutual adjustments for different behaviours of mobile phones making or receiving calls. The proportional hazards assumptions for the Cox model were tested using the Schoenfeld residuals method and no violation of this assumption was detected. In the sensitivity analyses, we further adjusted for physical activity, household income, healthy sleep scores,[22] healthy diet scores,[23] self-reported depression, and hypertension-GRS.[17] In addition, we investigated the association between weekly usage time of mobile phones to make or receive calls and differences in SBP at follow-up and baseline in a subset of UK Biobank participants (n = 16 229) who were invited to follow-up in 2012–13.

Moreover, we estimated the joint effect of weekly usage time of mobile phones for making or receiving calls and the genetic risk of hypertension (low, intermediate, high) with new-onset hypertension, using weekly usage

time of mobile phones <30 min (vs. ≥30 min) with low genetic risk as reference. Possible modifications of the relationship of weekly usage time of mobile phone for making or receiving calls (<30 min vs. ≥30 min) with new-onset hypertension were also assessed for the following variables: age (<60 or ≥60 years), sex (female or male), BMI (<30 or ≥30 kg/m²), smoking status (current, previous, or never), SBP (<125 [median] or ≥ 125 mmHg), family history of hypertension (no or yes), eGFR (<60 or ≥60 mL/min/1.73 m²) diabetes (no or yes), length of mobile phone use, and hands-free device/speakerphone use to make or receive calls. Interactions between subgroups and weekly usage time of mobile phone for making or receiving calls categories (<30 or ≥30 min) were examined by likelihood ratio testing.

A two-tailed $P < 0.05$ was considered to be statistically significant in all analyses. Analyses were performed using R software (http://www.R-project.org/).

Results

Baseline characteristics of the participants

As shown in the flow chart (see Supplementary material online, Figure S1), a total of 212 046 participants were included in the final
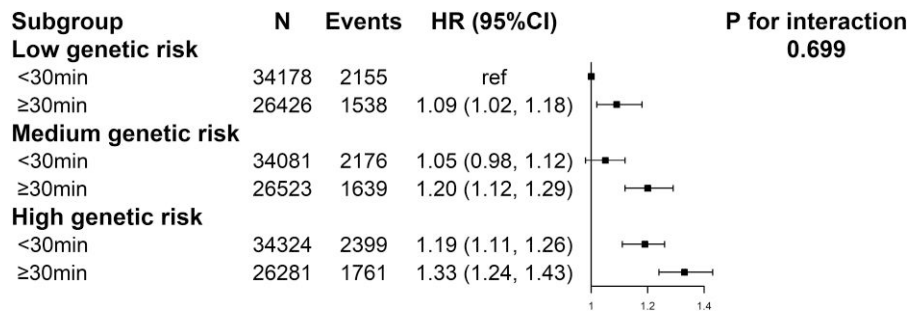
Figure 1 Joint effect of weekly usage time of mobile phones for making or receiving calls (<30 vs. ≥30 min) and the genetic risk of hypertension (low, intermediate, high) on new-onset hypertension among mobile phone users.* *Adjusted for age, sex, body mass index, race, Townsend deprivation index, family history of hypertension, education, smoking status, systolic blood pressure, triglycerides, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, C-reactive protein, blood glucose, eGFR, use of cholesterol-lowering medications, and glucose-lowering medications use., length of mobile phone use, and hands-free device/speakerphone use.

analysis. The mean (SD) age was 53.7 (8.0) years, 79 886 (37.7%) were male, and 185 796 participants (87.6%) were mobile phone users.

Compared with mobile phone non-users, mobile phone users were younger, more likely to be smokers, had higher BMI, lower SBP levels, higher frequency of family history of hypertension, and lower usage of cholesterol-lowering medications and glucose-lowering medications (Table 1). Moreover, among mobile phone users, participants with a longer weekly usage time of mobile phones making or receiving calls were younger, more likely to be male, current smokers, and to use hands-free device/speakerphone; had lower SBP, healthy sleep score, and higher Townsend deprivation index, physical activity, income, healthy diet score, total mental health complaints, BMI, eGFR, C-reactive protein levels, higher frequency of family history of hypertension, and higher length of mobile phone use (Table 2).

Association of mobile phone use and new-onset hypertension in the total population

During a median follow-up period of 12.0 years, 13 984 (6.6%) participants developed new-onset hypertension.

Compared with mobile phone non-users, a significantly higher risk of new-onset hypertension was found in mobile phone users (HR, 1.07; 95%CI: 1.01–1.12) (Table 3).

Association of weekly usage time of mobile phones for making or receiving calls with new-onset hypertension among mobile phone users

Overall, there were no significant relationships between the length of mobile phone use and hands-free device/speakerphone use to make or receive calls with new-onset hypertension among mobile phone users (Table 3).

However, compared with participants with a weekly usage time of mobile phones for making or receiving calls <5mins, significantly higher risks of new-onset hypertension were found in those with a weekly usage time of 30–59 min (HR, 1.08; 95%CI: 1.01–1.16), 1–3 h (HR, 1.13; 95%CI: 1.06–1.22), 4–6 h (HR, 1.16; 95%CI: 1.04–1.29), and >6 h (HR, 1.25; 95%CI: 1.13–1.39) (P for trend <0.001). Accordingly, a significantly higher risk of new-onset hypertension was found in those with a weekly usage time of mobile phones ≥30 min (HR, 1.12; 95%CI: 1.07–1.17), compared with participants with weekly usage time <30 min (Table 3).

Sensitivity analyses

Similar results were found in male and female participants (see Supplementary material online, Table S1). Further adjustments for menopause status and oestradiol levels did not substantially change the results in female participants (see Supplementary material online, Table S1). Moreover, there was a significantly positive association between weekly usage of mobile phones for making or receiving calls and the increase in SBP levels at follow-up (vs. that at baseline) (median follow-up duration: 4.4 years) (see Supplementary material online, Figure S2).

Further adjustments for physical activity, income levels, healthy sleep scores, healthy diet scores, self-reported depression, and GRS of hypertension also did not substantially change the association of weekly usage time of mobile phones for making or receiving calls with new-onset hypertension (see Supplementary material online, Table S2).

Joint effect of weekly usage time of mobile phones for making or receiving calls and genetic risk of hypertension on new-onset hypertension among mobile phone users

Compared with participants with a weekly usage time of mobile phones for making or receiving calls <30 min and low genetic risk of hypertension, those with a weekly usage time of mobile phones ≥30 min and high genetic risk had the highest risk of new-onset hypertension (HR, 1.33; 95%CI: 1.24–1.43) (Figure 1). However, the interaction between the weekly usage time of mobile phones and the genetic risk of hypertension on new-onset hypertension was not significant (P for interaction = 0.699) (Figure 1).

Stratified analyses

Stratified analyses were performed to further assess the association between the weekly usage time of mobile phones for making or receiving calls (<30 vs. ≥30 min) and new-onset hypertension in various subgroups (Figure 2).

None of the variables, including age, sex, BMI, smoking status, SBP, family history of hypertension, eGFR, diabetes, length of mobile phone use, and hands-free device/speakerphone use to make or receive calls, significantly modified the association between weekly usage time of mobile phones making or receiving calls and new-onset hypertension (all P for interaction >0.05).
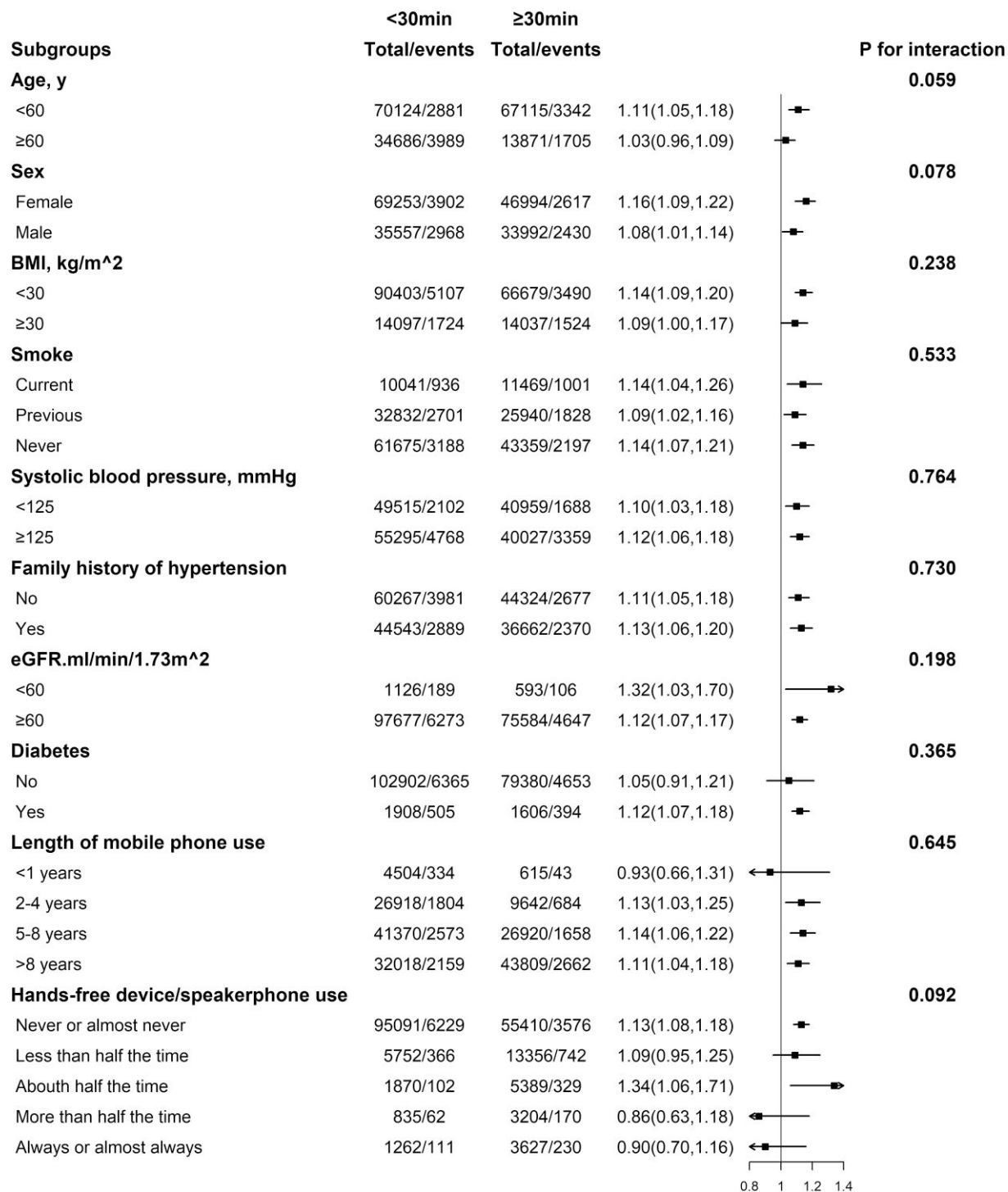
Subgroups	<30min Total/events	≥30min Total/events			P for interaction
Age, y					**0.059**
<60	70124/2881	67115/3342	1.11(1.05,1.18)		
≥60	34686/3989	13871/1705	1.03(0.96,1.09)		
Sex					**0.078**
Female	69253/3902	46994/2617	1.16(1.09,1.22)		
Male	35557/2968	33992/2430	1.08(1.01,1.14)		
BMI, kg/m^2					**0.238**
<30	90403/5107	66679/3490	1.14(1.09,1.20)		
≥30	14097/1724	14037/1524	1.09(1.00,1.17)		
Smoke					**0.533**
Current	10041/936	11469/1001	1.14(1.04,1.26)		
Previous	32832/2701	25940/1828	1.09(1.02,1.16)		
Never	61675/3188	43359/2197	1.14(1.07,1.21)		
Systolic blood pressure, mmHg					**0.764**
<125	49515/2102	40959/1688	1.10(1.03,1.18)		
≥125	55295/4768	40027/3359	1.12(1.06,1.18)		
Family history of hypertension					**0.730**
No	60267/3981	44324/2677	1.11(1.05,1.18)		
Yes	44543/2889	36662/2370	1.13(1.06,1.20)		
eGFR.ml/min/1.73m^2					**0.198**
<60	1126/189	593/106	1.32(1.03,1.70)		
≥60	97677/6273	75584/4647	1.12(1.07,1.17)		
Diabetes					**0.365**
No	102902/6365	79380/4653	1.05(0.91,1.21)		
Yes	1908/505	1606/394	1.12(1.07,1.18)		
Length of mobile phone use					**0.645**
<1 years	4504/334	615/43	0.93(0.66,1.31)		
2-4 years	26918/1804	9642/684	1.13(1.03,1.25)		
5-8 years	41370/2573	26920/1658	1.14(1.06,1.22)		
>8 years	32018/2159	43809/2662	1.11(1.04,1.18)		
Hands-free device/speakerphone use					**0.092**
Never or almost never	95091/6229	55410/3576	1.13(1.08,1.18)		
Less than half the time	5752/366	13356/742	1.09(0.95,1.25)		
Abouth half the time	1870/102	5389/329	1.34(1.06,1.71)		
More than half the time	835/62	3204/170	0.86(0.63,1.18)		
Always or almost always	1262/111	3627/230	0.90(0.70,1.16)		

0.8 1 1.2 1.4

Figure 2 Stratified analyses of the association between weekly usage time of mobile phones for making or receiving calls (<30 vs. ≥30 min) and new-onset hypertension among mobile phone users.* *Adjusted, if not stratified, for age, sex, BMI, race, Townsend deprivation index, family history of hypertension, education, smoking status, systolic blood pressure, triglycerides, LDL cholesterol, HDL cholesterol, C-reactive protein, blood glucose, eGFR, use of cholesterol-lowering medications and glucose-lowering medications use, length of mobile phone use, and hands-free device/speakerphone use to make or receive calls.

Discussion

In this large, population-based prospective cohort study, we first demonstrated that mobile phone use for making or receiving calls was significantly related to a higher risk of new-onset hypertension. More importantly, among mobile phone users, there was a significantly positive association between the weekly usage time of mobile phones for making or receiving calls and new-onset hypertension. In addition, the association between weekly usage of mobile phones for making or receiving calls and the risk of hypertension was strengthened by the genetic susceptibility to hypertension. Nevertheless, there were no significant associations between the length of mobile phone use or hands-free device/speakerphone use to make or receive calls and the risk of new-onset hypertension. These findings suggested that it is the frequency of mobile phone use for making or receiving calls, rather than the length of start using it, that determined the effect of mobile phone use on the risk of hypertension. In other words, long-term healthy mobile phone use for making or receiving calls may not affect the risk of hypertension as long as it is used for no more than 30 min per week to make or receive calls.

Several previous cross-sectional studies have examined the association of mobile phone use with the prevalence of hypertension and blood pressure levels. Amiri *et al.*[9] reported that blood pressure levels and duration of mobile phone use were associated negatively in women who used their phones for at least 8 h. However, no significant association was found in men. Suresh *et al.*[11] classified participants who had working cell phones in the family as cell phone users, and found that cell phone usage was protectively related to the prevalence of self-reported hypertension. Stalin *et al.*[12] reported that there was a negative association between mobile phone usage (including calling, SMS, playing games, listening to music, internet usage, and so on) and the prevalence of hypertension. However, a case-control study suggested a significantly positive association between total call duration per day and the prevalence of hypertension.[10] Another cross-sectional study found that phone addiction was associated with a significantly higher prevalence of hypertension in adolescents.[13] One of the important explanations for the inconsistent results from the above studies[9–13] could be that different studies included different patterns of mobile phone use, including making and receiving calls, SMS, having a working cell phone in the family, and so on. At the same time, cross-sectional and case-control designs preclude the ability to assess causality and directivity. Overall, the above studies[9–13] showed that although making and receiving calls is one of the most important patterns of mobile phone use, to date, the relationship between mobile phone use for making and receiving calls and long-term changes in blood pressure and the risk of new-onset hypertension remains uncertain. Our current study addressed this knowledge gap in a timely manner by considering mobile phone use for making and receiving calls and its use frequency at the same time.

Our study provides some new insights. First, mobile phone use for making or receiving calls was related to a significantly higher risk of new-onset hypertension, especially in those with a longer weekly usage time. The potential mechanisms included, first, the forearm lift, in conjunction with the static handshake exercise, a typical telephoning position, may increase sympathetic activity[24,25] and lead to a short-term increase in plasma adrenomedullin levels,[26] thereby increasing blood pressure levels. However, our study showed that the use of hands-free devices/speakerphones was not significantly related to the risk of new-onset hypertension, suggesting that telephoning position could not fully explain the positive association between a long-term calling and new-onset hypertension. Second, the high frequency of mobile phone use might be linked to adverse mental health[27] and sleep disorders,[28,29] both of which can lead to vascular damage,[30,31] and in turn, result in elevated blood pressure. Third, some previous studies have shown that the RF-EMF of mobile phones can cause a number of harmful effects at the molecular and cellular levels, including DNA damage, oxidative

stress, and inflammation,[4,5] all of which might contribute to the pathogenesis of hypertension.[6,7] Consistently, a previous single-blind placebo-controlled study also observed that exposure of the right hemisphere to an RF-EMF for 35 min was related to an increase in resting blood pressure between 5 and 10 mmHg.[8] Moreover, Chen *et al.*[32] reported that although there was no significant relationship between the daily duration of having the cell phones on with sperm quality parameters, daily talking time on the cell phone was negatively related to sperm concentration and total count, due to increased oxidative stress and DNA fragmentation and apoptosis caused by RF-EMF radiation. Zhang *et al.*[33] also found a similar inverse association between daily talking time on the cell phone and the sperm concentration. A recent meta-analysis in human studies[34] further showed that increased mobile phone use was related to an increased risk of DNA damage. Since the observed harmful effects of calling time and RF-EMF radiation on different health outcomes,[32–34] we speculate that relatively long-term exposure to RF-EMF during making or receiving calls may possibly also have an important role in the occurrence of hypertension. However, the biological mechanisms underlying the positive association between time spent making or receiving calls on a mobile phone and the risk of hypertension still need to be further elucidated.

Second, we first assessed the joint effect of weekly usage of mobile phones for making or receiving calls and the genetic risks of hypertension on new-onset hypertension. Our findings showed that although the genetic risks of hypertension did not show significant modifying effects, those with both longer weekly usage time of mobile phones for making or receiving calls and high genetic risk had the highest risk of new-onset hypertension. On the one hand, these results suggested that the association between mobile phone use for making or receiving calls and the risk of hypertension might be independent of an individual's genetic risk profile. On the other hand, due to the highest absolute risk of new-onset hypertension, those with high genetic risks of hypertension may need to pay more attention to the frequency of mobile phone use for making or receiving calls.

Of note, our study showed that sex did not significantly modify the association between mobile phone calls and the risk of hypertension. Consistently, Suresh *et al.*[11] reported that cell phone use was associated with the prevalence of hypertension, independent of age and sex. However, Amiri *et al.*[9] found that blood pressure levels and duration of mobile phone use were associated negatively in women but not in men. That inconsistency may be due to the difference in study designs and the included covariates. The previous two studies[9,11] were cross-sectional designs, which could not assess causality and directivity. Moreover, our study found that further adjustments for the menopause status and oestradiol levels, two important factors not considered in previous studies, did not materially change the results in women. Nonetheless, future studies are needed to further investigate the possible modifying effect of sex.

Several limitations need to be addressed. First, in the UK biobank, the questionnaire on mobile phone use was limited to the characteristics of making or receiving calls, and other use patterns of mobile phone use, such as SMS, playing games, internet usage, and so on, were not collected. However, making or receiving calls has traditionally been considered an important mobile phone function, and has been widely used as the major mobile phone use characteristic in several large population-based cohort studies, such as the UK Million Women Study[35] and Cohort Study of Mobile Phone Use and Health.[29] Second, based on the available UK Biobank data, our current analysis could not account for some possible confounding factors, such as the type of mobile phone technology used, and other sources of electromagnetic waves. Third, since the study populations were predominantly White middle-aged or older adults and healthier than the UK general population,[36] the results cannot be directly generalized to other populations. Four, in this study, information on mobile phone use for making or receiving calls and other variables were based on questionnaires and bio

samples at baseline. Mobile phone use might have changed over the years, which could have affected the results of this study. However, with the pace of work and life accelerating worldwide, mobile phone users may spend more time making or receiving calls. Therefore, it is possible that our study underestimated the association between weekly usage time making or receiving calls and the risk of new-onset hypertension. In fact, according to the answers to the question 'Is there any difference between your mobile phone use now compared to 2 years ago?', only 12.8% and 13.7% of the participants at baseline and at 2012–13 follow-up in the UK biobank study reported that the mobile phone use was now less frequent. What's more, we also found a significantly positive association between weekly usage of mobile phones for making or receiving calls and an increase in SBP levels at the 2012–13 follow-up (vs. that at baseline) (see Supplementary material online, Figure S2). This result, with a more objective outcome and having direct data indicating relatively stable mobile use during follow-up, further supported our findings of the positive association between weekly usage of mobile phones for making or receiving calls and new-onset hypertension. Fifth, since the proportions of both secondary hypertension and pregnancy at baseline, were very low in UK Biobank, we did not account for these variables in our analysis. Finally, as an observational study, although we have adjusted for a range of important covariates, the possibility of residual confounding due to unknown or unmeasured factors cannot be ruled out. Finally, overall, due to these limitations, our study was just hypothesis-generating and should be confirmed in more studies.

In conclusion, mobile phone use for making or receiving calls was significantly associated with a higher risk of new-onset hypertension, especially in those with a longer weekly usage time, among the general population. Our findings and the underlying mechanisms should be further evaluated in more studies. If further confirmed, our study suggests that reducing the time spent using mobile phones to make or receive calls may play a role in the primary prevention of hypertension in the general population.

Authors' contributions

Xianhui Qin, Ziliang Ye, Yanjun Zhang, and Yuanyuan Zhang designed the research; Xianhui Qin, Ziliang Ye, Yanjun Zhang, and Yuanyuan Zhang conducted the research; Ziliang Ye and Yuanyuan Zhang performed the data management and statistical analyses; Xianhui Qin, Ziliang Ye, Yanjun Zhang, and Yuanyuan Zhang wrote the draft; all authors revised and approved the final manuscript.

Supplementary material

Supplementary material is available at *European Heart Journal – Digital Health*.

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Data availability

The data underlying this article are available in UK Biobank at https://www.ukbiobank.ac.uk/, and can be accessed with reasonable request.

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