



Headache in the international cohort study of mobile phone use and health (COSMOS) in the Netherlands and the United Kingdom

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ABSTRACT

Headache is a common condition with a substantial burden of disease worldwide. Concerns have been raised over the potential impact of long-term mobile phone use on headache due to radiofrequency electromagnetic fields (RF-EMFs). We explored prospectively the association between mobile phone use at baseline (2009–2012) and headache at follow-up (2015–2018) by analysing pooled data consisting of the Dutch and UK cohorts of the Cohort Study of Mobile Phone Use and Health (COSMOS) (N = 78,437). Frequency of headache, migraine, and information on mobile phone use, including use of hands-free devices and frequency of texting, were self-reported. We collected objective operator data to obtain regression calibrated estimates of voice call duration. In the model mutually adjusted for call-time and text messaging, participants in the high category of call-time showed an adjusted odds ratio (OR) of 1.04 (95 % CI: 0.94–1.15), with no clear trend of reporting headache with increasing call-time. However, we found an increased risk of weekly headache (OR = 1.40, 95 % CI: 1.25–1.56) in the high category of text messaging, with a clear increase in reporting headache with increasing texting. Due to the negligible exposure to RF-EMFs from texting, our results suggest that mechanisms other than RF-EMFs are responsible for the increased risk of headache that we found among mobile phone users.

1. Introduction

Over the past few decades, wireless technology has rapidly proliferated throughout society, revolutionising how we interact worldwide. As a result, frequency and duration of use of wireless devices have increased over time, while the intensity of exposure to radiofrequency electromagnetic fields (RF-EMFs) has seen a reduction following the

progression and evolution of new network generations (Iyare et al., 2021). With the expanding uptake of wireless devices and the advancements in mobile technologies, concerns regarding the potential health consequences of long-term exposure to RF-EMFs have been raised. Several experimental and epidemiological cross-sectional and case-control studies have explored the possible link between RF-EMF exposure and symptoms such as headache and migraine. Results

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showed no consistent evidence of adverse health effects at the exposure levels typically encountered in the population (Augner et al., 2012; Oftedal et al., 2007; Cinel et al., 2008; Durusoy et al., 2017; Wang et al., 2017; Cerutti et al., 2016). However, results from cohort studies are still scarce.

The Cohort Study of Mobile Phone Use and Health (COSMOS) is a large prospective cohort study of mobile phone users comprising more than 300,000 adults who will be followed up for over 25 years. COSMOS was established in six European countries (Denmark, Finland, France, Sweden, the Netherlands, and the United Kingdom (UK)) to prospectively investigate possible health effects associated with long-term use of mobile phones and other wireless technologies (Schüz et al., 2011). Several health outcomes are being investigated, including headache and migraine. These represent important causes of disability worldwide with a high public health relevance (GBD, 2016 Headache Collaborators, 2018), and the possible association with RF-EMF exposure among mobile phone users has yet to be clarified.

A study conducted in Sweden and Finland as part of COSMOS found limited evidence for an association between weekly headache and the highest level of mobile phone use and no clear trend with increasing call-time (Auvinen et al., 2019). The association of headache with call-time appeared stronger for calls via the Universal Mobile Telecommunication System (UMTS) (3G) network than via the older Global System for Mobile (GSM) (2G) telecommunications technology, despite the latter involving higher RF-EMF exposure levels to the head (van Wel et al., 2021).

In this study, we assessed the relationship between mobile phone use at baseline and headache at follow-up by exploring two mobile phone use activities: voice calling and texting. Calling, depending on the technology and other usage characteristics, such as the position of the device relative to the body and the use of hands-free devices, exposes the head to different levels of RF-EMFs. Texting produces negligible RF-EMF exposure. Therefore, any association is hypothesized to have other underlying mechanisms than RF-EMF exposure.

2. Methods

2.1. Study participants

In this prospective study, we pooled data from the Dutch and UK cohorts of COSMOS comprising more than 180,000 participants who completed the baseline questionnaire providing information on mobile phone use, health, environmental exposures, lifestyle, and demographics.

In the Netherlands, 88,466 participants were enrolled in three cohort studies between 2011 and 2012, constituting the LIFEWORK cohort, representing the Dutch contribution to COSMOS. LIFEWORK was designed as a federated study integrating the Nightingale Study, the Occupational and Environmental Health Cohort Study (AMIGO), and the European Prospective Investigation into Cancer and Nutrition in the Netherlands (EPIC-NL). In LIFEWORK, a follow-up questionnaire was completed between 2015 and 2017 by 53,697 participants. Compared to the general adult population in the Netherlands, there is a higher proportion of women (89.2 %) and the average age is older (around 50 years old). The rationale, study design, and participant recruitment in LIFEWORK were discussed in detail elsewhere (Beulens et al., 2010; Pijpe et al., 2014; Slottje et al., 2014; Reedijk et al., 2018).

In the UK, 99,424 participants were recruited from across the country between 2009 and 2012 and filled in the baseline questionnaire. Recruitment was from mobile phone subscriber lists (65 %) and the UK edited electoral register (35 %). A follow-up questionnaire was completed by 45,308 UK participants between 2015 and 2018. UK COSMOS participants seem to enjoy better health than the general adult population in the UK, as evidenced by a lower current smoking rate and lower prevalence of obesity. The rationale, study design, and participant recruitment of UK COSMOS were discussed in detail elsewhere

(Toledano et al., 2017).

After exclusions, the pooled cohort of Dutch and UK participants with baseline and follow-up data consisted of 78,437 individuals (Fig. 1).

2.1.1. Exposure assessment

In this study, the exposure information was collected prospectively in relation to the health outcome being analysed. Participants self-reported information on their mobile phone use for the 3 months before baseline, via questionnaire. This included weekly call-time, the proportion of use with hands-free devices, frequency of text messages, use of multiple mobile phones, and whether other people used the participants' mobile phone(s). Call-time on cordless phones was also reported.

In addition to self-reported mobile phone use, outgoing and incoming voice call durations were obtained during the same 3-month period at baseline from network operators for participants (with consent) who had a subscription under their own name. The proportion of participants for whom complete data from network operators at baseline was available was 3 % (the Netherlands) and 58 % (the UK). Information on 2G and 3G networks, technologies that were in use at the time of this study, was not available for these two cohorts.

Self-reported duration of voice calling on a mobile phone is considered an error-prone proxy for mobile phone use (Aydin et al., 2011; Berg et al., 2005; Heinävaara et al., 2011; Vrijheid et al., 2009). We leveraged self-reported and objective operator-recorded mobile phone use data available in the subset of participants with complete network operator data to deal with measurement error in self-reported mobile phone data and improve the estimation of exposure-outcome relationships in COSMOS. Country-specific regression-calibrated estimates based on operator data for both incoming and outgoing mobile phone calls (the average operator-recorded value per category per country) were applied to self-reported weekly mobile phone call-time categories, for all participants (Reedijk et al., 2023).

We adjusted call-time according to the proportion of hands-free use the participant reported (response options "hardly ever", "less than half of the time", "about half of the time", "more than half of the time", "always or nearly always"), reducing voice call duration by 5 %, 10 %, 25 %, 35 %, and 50 %, respectively, for each hands-free use category (Goedhart et al., 2015).

To assess the potential effects of RF-EMF exposure on headache accounting for co-exposure from multiple sources, we estimated the RF-EMF dose to the brain using an organ-specific integrated exposure model (IEM). The IEM uses specific absorption rate transfer algorithms to provide RF-EMF weekly dose estimates (mJ/kg/week) using source-specific attributes (e.g. output power, distance), personal characteristics (e.g. height and weight) and usage patterns. Exposure input data for the IEM included call-time on mobile phones and cordless phones as these were identified as primary contributors to the brain dose (van Wel et al., 2021).

Finally, call-time and RF-EMF dose exposure metrics were categorised into four exposure categories ("very low", "low", "medium", and "high") based on the pooled exposure distribution, with cut-offs aligned as close as possible to predefined percentiles ("lowest 30 %", "30th–69th percentile", "70th–89th percentile", "90th–100th percentile") (Supplementary Table 1). "Low" was selected as the referent exposure category in regression models as it had the highest proportion of both Dutch and UK participants.

The number of text messages sent on a mobile phone at baseline was used as a proxy for use with negligible RF-EMF exposure. It was categorised into three exposure categories ("low", "medium", and "high") corresponding to the response options "never/less than 1 text message per week/1–6 text messages per week", "1–9 text messages per day", "10–29 text messages per day/30 or more text messages per day". For clarity, text messages here refer to Short Message Service (SMS) via the mobile cellular network, and does not include instant messaging via the

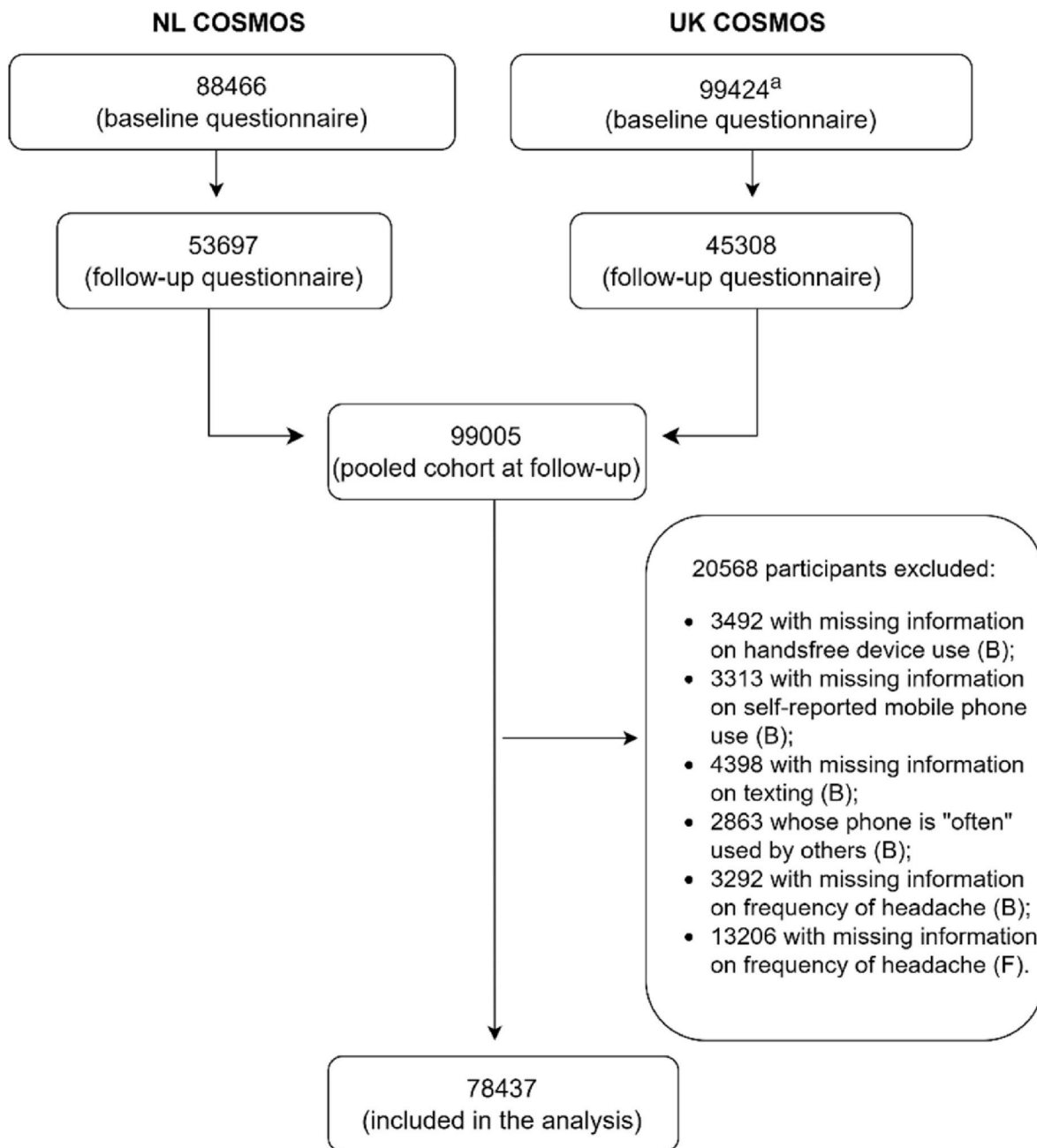


Fig. 1. Flowchart of the COSMOS study data.

^aIn the UK, 99,424 participants provided baseline questionnaire information and 101,540 consented to operator data matching out of 105,028 participants recruited at baseline (Slottje et al., 2014).

B = baseline questionnaire; F = follow-up questionnaire.

internet. An overview of the exposure metrics used in this study is provided in [Supplementary Table 2](#).

2.1.2. Headaches and migraine

Headaches were self-reported at baseline and follow-up. The primary outcome was weekly headache at follow-up. The secondary outcomes were severe weekly headache, daily headache, and migraine diagnosis at follow-up. Headaches were defined according to the question “How often do you get headache at the moment?”, with response categories of “almost every day”, “5 or 6 days a week”, “3–4 days a week”, “once or twice a week” “1–2 days per month”, and “less often”. The Headache Impact Test (HIT-6) score with a cut-off of 56 points defined severe weekly headache. The HIT-6 is a tool used to measure the impact

headaches have on one’s ability to function in various aspects of daily life, including work, school, home, and social contexts. The score, ranging from 36 to 78 points, provides a measure of the degree to which headaches affect daily life and functioning, with higher scores indicating a more significant impact on the participant’s overall life (Kosinski et al., 2003). Migraine diagnosis at follow-up was defined based on the question “Have you ever been diagnosed by a medical doctor with migraine?”. To avoid potential reverse causation, we restricted all analyses to participants who did not report weekly or more frequent headaches at baseline (N = 66,858) and likewise for migraine diagnosis (N = 53,576) (Auvinen et al., 2019).

2.1.3. Covariates

We identified the following potential confounders of the associations between mobile phone use and headaches a priori based on previous studies (Wang et al., 2017; Auvinen et al., 2019; Farashi et al., 2022): sex, age group (18–29, 30–39, 40–49, 50–59, 60+), country (the Netherlands, the UK), highest level of education attained (elementary, secondary and higher), body mass index (BMI) group (normal or underweight, overweight or obese), general health indicator (good, poor), sleep disturbance index, painkiller use (yes, no), depression diagnosis (yes, no), high blood pressure diagnosis (yes, no), smoking status (never, former, current), alcohol consumption (never, former, current). Models were adjusted for these factors, as measured at baseline, a priori.

2.2. Statistical analysis

Missing values were imputed on covariates only through multivariate imputation by chained equations (complete-case data set including 58,229 participants), performed separately for each cohort. All covariates (except country), exposures, and study outcomes were used as predictors, and Rubin’s rule was used to combine the regression parameters over 30 imputed data sets (Buuren and Groothuis-Oudshoorn, 2011; White et al., 2011).

Descriptive statistics of the study population were calculated overall, by country, and by exposure level. Correlation between exposure metrics was evaluated using Spearman’s rank correlation coefficients.

To evaluate the exposure-outcome associations, we estimated multivariable logistic regression models. We first assessed call-time and texting exposures separately, and then mutually adjusted for both exposures in one model. Weekly minutes of call-time at baseline (country-specific regression calibrated estimates adjusted by the proportion of hands-free use (RC-hfa)) was the primary exposure metric.

We calculated a p-value for linear trend across exposure categories as an ordered factor, to test for dose-response relationships between exposure and outcome.

We performed stratified analyses for sex, age group, and country. To examine interactions between call-time and texting and potential modifiers (sex, age group, and country) on the risk of weekly headache, we tested for significance of interaction terms added to the models using a likelihood ratio test.

As secondary analyses, we analysed self-reported mobile phone call-time adjusted by the proportion of hands-free use (SR-hfa), operator-recorded call-time adjusted by the proportion of hands-free use (OP-hfa), and the RF-EMF estimated dose to the brain with the IEM (IEM_{RC-hfa}, IEM_{DECT}) as exposure metrics at baseline, respectively.

We performed the following sensitivity analyses: first, we used country-specific regression calibrated call-time estimates without adjustment for hands-free use (RC) as the exposure metric. Second, we excluded painkiller use as a model covariate, in case use results from headaches. Third, we lowered the cut-off for the “high” exposure category to approximate the 80th percentile of the pooled exposure distribution - for comparison with the main analyses in which the top 10th percentile was used to define highly exposed participants. Fourth, we replicated the analyses by categorising the RC-hfa exposure into quartiles for comparison with the main findings. Last, we performed a complete-case analysis to compare with results obtained on imputed datasets.

All analyses were performed using R Statistical Software (v4.2.3; R Core Team, 2023) . Computing code for all analyses presented is available on request.

3. Results

Baseline characteristics of the study population by categories of call-time and texting are presented in Table 1 and Supplementary Table 3 (baseline characteristics by country in Supplementary Tables 4–7), respectively. No relevant differences in the distribution of baseline

Table 1

Characteristics of the participants by amount of mobile phone use at baseline (weekly minutes of call-time, country-specific regression calibrated estimates adjusted by the proportion of hands-free use (RC-hfa)).

	Amount of mobile phone use at baseline (call-time in categories ^a)				
	Very low (N = 23,211)	Low (N = 31,310)	Medium (N = 14,475)	High (N = 9441)	Overall (N = 78,437)
Sex, n (%)					
Men	3420 (14.7)	7648 (24.4)	5665 (39.1)	4344 (46.0)	21,077 (26.9)
Women	19,791 (85.3)	23,662 (75.6)	8810 (60.9)	5097 (54.0)	57,360 (73.1)
Age group (years), n (%)					
18-29	578 (2.5)	2750 (8.8)	1703 (11.8)	1582 (16.8)	6613 (8.4)
30-39	1868 (8.0)	4305 (13.7)	2293 (15.8)	1719 (18.2)	10,185 (13.0)
40-49	5103 (22.0)	6982 (22.3)	2838 (19.6)	1813 (19.2)	16,736 (21.3)
50-59	7108 (30.6)	10,322 (33.0)	4820 (33.3)	2802 (29.7)	25,052 (31.9)
60+	8554 (36.9)	6951 (22.2)	2821 (19.5)	1525 (16.2)	19,851 (25.3)
Country, n (%)					
The Netherlands	19,462 (83.8)	20,401 (65.2)	4780 (33.0)	0 (0)	44,643 (56.9)
UK	3749 (16.2)	10,909 (34.8)	9695 (67.0)	9441 (100)	33,794 (43.1)
Highest level of education attained, n (%)					
Elementary	3641 (15.7)	2558 (8.2)	871 (6.0)	663 (7.0)	7733 (9.9)
Secondary and higher	19,431 (83.7)	28,379 (90.6)	13,255 (91.6)	8465 (89.7)	69,530 (88.6)
Missing	139 (0.6)	373 (1.2)	349 (2.4)	313 (3.3)	1174 (1.5)
BMI group, n (%)					
Normal or underweight	12,727 (54.8)	16,296 (52.0)	6891 (47.6)	3996 (42.3)	39,910 (50.9)
Overweight or obese	10,241 (44.1)	14,386 (45.9)	6988 (48.3)	4831 (51.2)	36,446 (46.5)
Missing	243 (1.0)	628 (2.0)	596 (4.1)	614 (6.5)	2081 (2.7)
General health indicator, n (%)					
Good	20,307 (87.5)	28,296 (90.4)	13,274 (91.7)	8734 (92.5)	70,611 (90.0)
Poor	2798 (12.1)	2901 (9.3)	1175 (8.1)	707 (7.5)	7581 (9.7)
Missing	106 (0.5)	113 (0.4)	26 (0.2)	0 (0)	245 (0.3)
Sleep disturbance index, mean (SD)	27.9 (18.8)	26.2 (18.7)	25.3 (19.4)	26.1 (21.5)	26.5 (19.2)
Missing, n (%)	26 (0.1)	41 (0.1)	43 (0.3)	38 (0.4)	148 (0.2)
Painkiller use, n (%)					
No	17,691 (76.2)	25,918 (82.8)	12,819 (88.6)	8702 (92.2)	65,130 (83.0)
Yes	2832 (12.2)	3803 (12.1)	1331 (9.2)	671 (7.1)	8637 (11.0)
Missing	2688 (11.6)	1589 (5.1)	325 (2.2)	68 (0.7)	4670 (6.0)
Depression diagnosis, n (%)					
No	18,044 (77.7)	25,994 (83.0)	11,981 (82.8)	7496 (79.4)	63,515 (81.0)
Yes	2400 (10.3)	3709 (11.8)	2195 (15.2)	1881 (19.9)	10,185 (13.0)
Missing	2767 (11.9)	1607 (5.1)	299 (2.1)	64 (0.7)	4737 (6.0)
High blood pressure diagnosis, n (%)					
No	15,971 (68.8)	24,463 (78.1)	11,837 (81.8)	7969 (84.4)	60,240 (76.8)
Yes	5430 (23.4)	5633 (18.0)	2368 (16.4)	1407 (14.9)	14,838 (18.9)
Missing	1810 (7.8)	1214 (3.9)	270 (1.9)	65 (0.7)	3359 (4.3)
Smoking status, n (%)					

(continued on next page)

Table 1 (continued)

Amount of mobile phone use at baseline (call-time in categories ^a)					
	Very low (N = 23,211)	Low (N = 31,310)	Medium (N = 14,475)	High (N = 9441)	Overall (N = 78,437)
Never	11,703 (50.4)	15,096 (48.2)	6929 (47.9)	4618 (48.9)	38,346 (48.9)
Former	9255 (39.9)	13,135 (42.0)	6027 (41.6)	3729 (39.5)	32,146 (41.0)
Current	2085 (9.0)	2944 (9.4)	1417 (9.8)	1002 (10.6)	7448 (9.5)
Missing	168 (0.7)	135 (0.4)	102 (0.7)	92 (1.0)	497 (0.6)
Alcohol consumption, n (%)					
Never	1393 (6.0)	1136 (3.6)	304 (2.1)	118 (1.2)	2951 (3.8)
Former	662 (2.9)	738 (2.4)	314 (2.2)	226 (2.4)	1940 (2.5)
Current	20,665 (89.0)	28,667 (91.6)	13,169 (91.0)	8295 (87.9)	70,796 (90.3)
Missing	491 (2.1)	769 (2.5)	688 (4.8)	802 (8.5)	2750 (3.5)
Weekly headache^b, n (%)					
No	20,461 (88.2)	26,831 (85.7)	12,041 (83.2)	7525 (79.7)	66,858 (85.2)
Yes	2750 (11.8)	4479 (14.3)	2434 (16.8)	1916 (20.3)	11,579 (14.8)
Severe weekly headache^b, n (%)					
No	21,859 (94.2)	29,345 (93.7)	13,552 (93.6)	8728 (92.4)	73,484 (93.7)
Yes	1084 (4.7)	1743 (5.6)	866 (6.0)	705 (7.5)	4398 (5.6)
Missing	268 (1.2)	222 (0.7)	57 (0.4)	8 (0.1)	555 (0.7)
Daily headache^b, n (%)					
No	22,914 (98.7)	30,882 (98.6)	14,238 (98.4)	9225 (97.7)	77,259 (98.5)
Yes	297 (1.3)	428 (1.4)	237 (1.6)	216 (2.3)	1178 (1.5)
Migraine diagnosis^b, n (%)					
No	13,611 (58.6)	21,614 (69.0)	10,862 (75.0)	7489 (79.3)	53,576 (68.3)
Yes	2108 (9.1)	3388 (10.8)	1924 (13.3)	1513 (16.0)	8933 (11.4)
Missing	7492 (32.3)	6308 (20.1)	1689 (11.7)	439 (4.7)	15,928 (20.3)

^a Very low: RC-hfa <19.1 (min/week); Low: RC-hfa ≥19.1 & RC-hfa <58.6 (min/week); Medium: RC-hfa ≥58.6 & RC-hfa <107.8 (min/week); High: RC-hfa ≥107.8 (min/week), (max = 256.8 min/week).

^b At baseline.

characteristics of the study participants were observed when including those who did not complete a follow-up questionnaire (Supplementary Tables 8–9). There was a greater proportion of women than men across all levels of exposures, as almost 90 % of the Dutch cohort were women. Individuals in the high call-time (RC-hfa) category were all UK participants. The baseline distribution of RC-hfa was skewed towards low values, with Dutch participants on average reporting less call-time than the UK participants (Fig. 2).

Call-time exposure metrics were strongly correlated with the RF-EMF estimated dose (Spearman's correlation coefficient ρ : $0.63 \leq \rho \leq 0.99$). We observed weak to moderate correlations between texting and call-time metrics and RF-EMF estimated dose (Spearman's correlation coefficient ρ : $0.24 \leq \rho \leq 0.54$) (Fig. 3).

Of 66,858 participants who were free of weekly headache at baseline and included in analysis of call-time and texting, 5452 (8.2 %) reported weekly headache at follow-up, and 382 (0.6 %) reported daily headache. 1660 (2.5 %) individuals were classified as having severe weekly headache out of 66,234 with complete information on the HIT-6 score at follow-up. Of 53,576 participants free of migraine at baseline, 1812 (3.4 %) reported migraine at follow-up.

In adjusted single exposure models, we found an increased risk of weekly headache at follow-up (OR = 1.10, 95 % CI: 1.01–1.22) in the

high category of regression calibrated call-time at baseline (RC-hfa), with a clear increase of reporting headache with increasing call-time (P trend = 0.002) (Table 2).

Similarly, we found an increased risk in weekly headache at follow-up (OR = 1.42, 95 % CI: 1.28–1.58) in the high category of texting, also with a clear trend of increasing risk with increasing texting (P trend < 0.001) (Table 3).

Results from two-exposure models mutually adjusting for both call-time and texting at baseline, showed substantially lower risk estimates for weekly headache in the high call-time (RC-hfa) category (OR = 1.04, 95 % CI: 0.94–1.15), and no evidence of a trend (P trend = 0.292) (Table 2). Associations with texting were robust to adjustment for call-time: we observed an increased risk of weekly headache in the high category of texting (OR = 1.40, 95 % CI: 1.25–1.56) and a trend of increasing risk with increasing texting frequency (P trend < 0.001), in line with results from the single-exposure model (Table 3).

Regarding secondary health outcomes, we found consistent patterns of results for severe weekly headache and migraine at follow-up in terms of increased risk estimates and significant trends. Increasing risk of daily headache was associated with increasing texting (P trend < 0.001) but not with increasing call-time (P trend = 0.448) (Tables 2 and 3).

We did not detect interactions between call-time and texting, respectively, and potential modifiers (sex, age group, and country) on the risk of weekly headache, and results showed that the exposure-response associations were remarkably consistent across sex, age groups and countries, particularly with regard to texting (Supplementary Tables 10–11).

Secondary analyses, including self-reported mobile phone call-time and operator-recorded call-time as exposure metrics in the separate regression models produced compatible results with the main analysis of regression calibrated call-time (Supplementary Tables 12–15). Results using the RF-EMF estimated brain dose as exposure metric in the models were consistent with those using regression calibrated call-time (Supplementary Tables 16–17). The models using the hands-free unadjusted regression calibrated call-time exposure metric showed no further increase in risk among users compared to the main analyses (Supplementary Tables 18–19). Results from sensitivity analyses were compatible with the main findings (Supplementary Tables 20–29).

4. Discussion

In this large international prospective cohort of mobile phone users in the Netherlands and the UK, mobile phone use for calling and texting at baseline was associated with headaches at follow-up. Mutually adjusting for both call-time and texting considerably attenuated risk estimates for call-time, while associations with texting were still strong and robust to adjustment, with a clear exposure-outcome gradient.

Headache has been linked to excessive mobile phone use, but the mechanism by which mobile phone use may cause symptoms is not properly understood (Wang et al., 2017; Cerutti et al., 2016; Frey, 1998; Hocking, 1998; Oftedal et al., 2000; Schoeni et al., 2015). Previous research in adolescents has suggested that other exposures related to mobile phone use, but not exposure to RF-EMFs, should be considered the causal factor for various symptoms, as the strongest associations were found with activities that cause minimal RF-EMF exposure to the head, such as texting or gaming (Schoeni et al., 2017). Other studies have indicated that stress or unfavourable usage, such as late-night use, may be associated with an increase in reported health symptoms, such as headache (Szyjkowska et al., 2014; Röösl, 2008; Thomée et al., 2011). It is therefore crucial to distinguish between using a mobile phone for calling and other activities that expose the brain to RF-EMFs at lower levels, such as Internet browsing (Cabrè-Riera et al., 2022a; SSM's Scientific Council on Electromagnetic Fields, 2020).

Our study attempted to disentangle the exposure-outcome gradient by considering call-time as a proxy for RF-EMF exposure and texting as a proxy for usage with negligible RF-EMF exposure to the brain (Wall

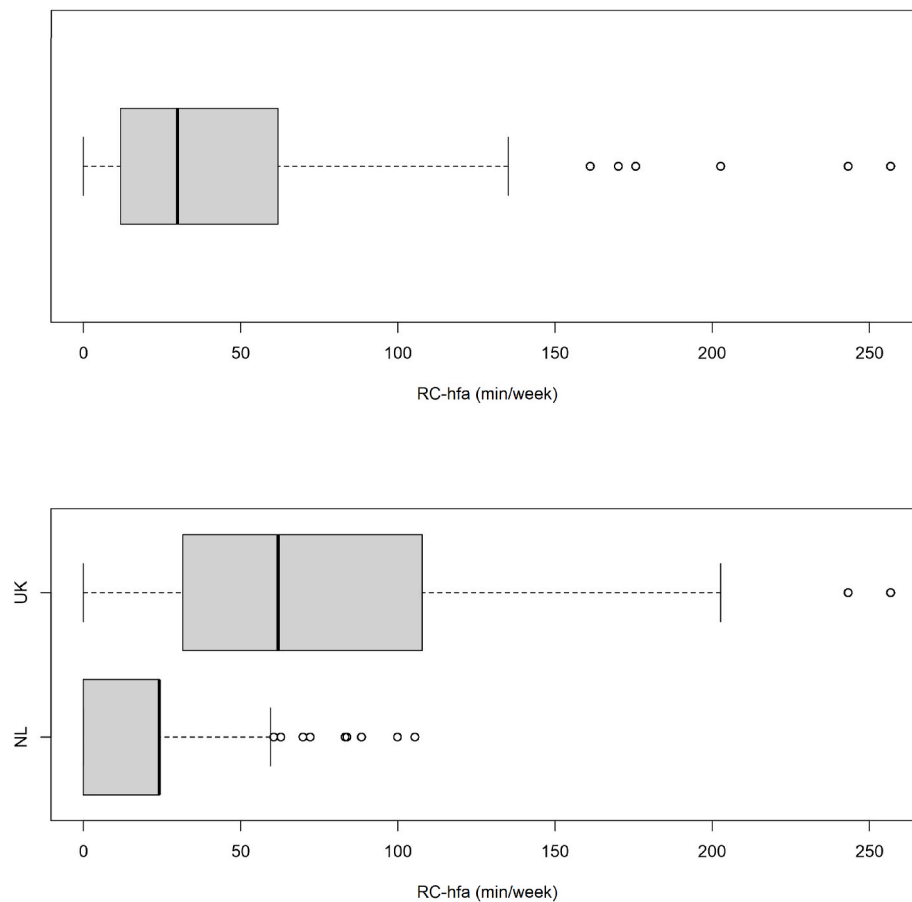


Fig. 2. Distribution of the amount of mobile phone use at baseline (weekly minutes of call-time, country-specific regression calibrated estimates adjusted by the proportion of hands-free use (RC-hfa) in the pooled cohort, and in the Dutch (The Netherlands (NL)) and UK sub-cohorts of COSMOS.

et al., 2019). This study's mobile phone usage data was gathered between 2009 and 2012. During those years, texting was the most popular activity unrelated to RF-EMF exposure.

In both scenarios, we found an increased risk of headache in the high exposure category of mobile phone use with a positive exposure-outcome gradient confirmed by the test for trend. The attenuated risk estimates for call-time in the mutually adjusted model argue against an effect of exposure to RF-EMFs due to the negligible exposure attributed to texting. This conclusion is also supported by comparing call-time analyses with and without hands-free adjustment, where no risk reduction was found among users for the adjusted exposure metrics.

In this study, the distribution of the exposure, specifically regarding call-time, differed between Dutch and UK participants. Mobile phone usage behaviour across countries cannot be assumed to be identical due to various factors such as cultural, economic, technological, and market dynamics (Böhm, 2015). To assess the consistency of our findings, we showed that defining the top exposure category for call-time based on the 80th percentile cut-off, thereby ensuring the inclusion of Dutch participants in the "high" exposure category, yielded results consistent with those obtained using the 90th percentile as a cut-off. These findings suggested that the association we found between call-time and headache was driven not only by UK but also Dutch participants. Of note, all analyses were adjusted for country of residence.

Our study has several strengths. This is the largest prospective study to explore the relationship between mobile phone use and headache using a prospective study design and several exposure metrics, including the regression calibrated estimates where operator-recorded and self-reported call-time were combined to improve the estimation of the exposure by reducing recall bias resulting in more informative exposure-outcome relations (Reedijk et al., 2023).

Furthermore, the RF-EMF estimated dose to the participant's brain calculated with the IEM provided detailed estimates of exposure levels by considering multiple sources of exposure and the intensity of RF-EMFs associated with specific functions (such as the specific absorption rate) (van Wel et al., 2021).

An accurate exposure assessment of RF-EMFs from the use of mobile phones has proved difficult as the dose of exposure depends on several factors, which include source-specific attributes (output power), characteristics of the subject (age, sex, body mass), and the way devices are used (position relative to the body, type of use, duration of use) (van Wel et al., 2021; Lönn et al., 2004). Nevertheless, the quantity and quality of data collected in COSMOS allowed us to characterise mobile phone use for calling and texting in detail.

Given the speed at which technology is developing and the need to assess RF-EMF exposure more thoroughly, we used the IEM to estimate the integrative RF-EMF dose to the brain of participants. The IEM represents the most complete RF-EMF dose estimation tool to date. It can estimate RF-EMF dose to different anatomical sites, including the brain as target organ for headache (van Wel et al., 2021; Cabré-Riera et al., 2022b).

Our study also has limitations. First, we did not have information about "true" RF-EMF exposure. Exposure to RF-EMFs emitted by wireless devices is difficult to quantify, particularly in large populations and over extended periods, as it depends on different factors, such as reception quality or other factors influencing signal strength. In our study, we calculated several exposure metrics as proxies for RF-EMF exposure, which allowed us to estimate the average individual RF-EMF exposure in the population. Additionally, information on other aspects of usage, such as screen time, blue light exposure or unfavourable use at night, may be helpful to include in future studies.

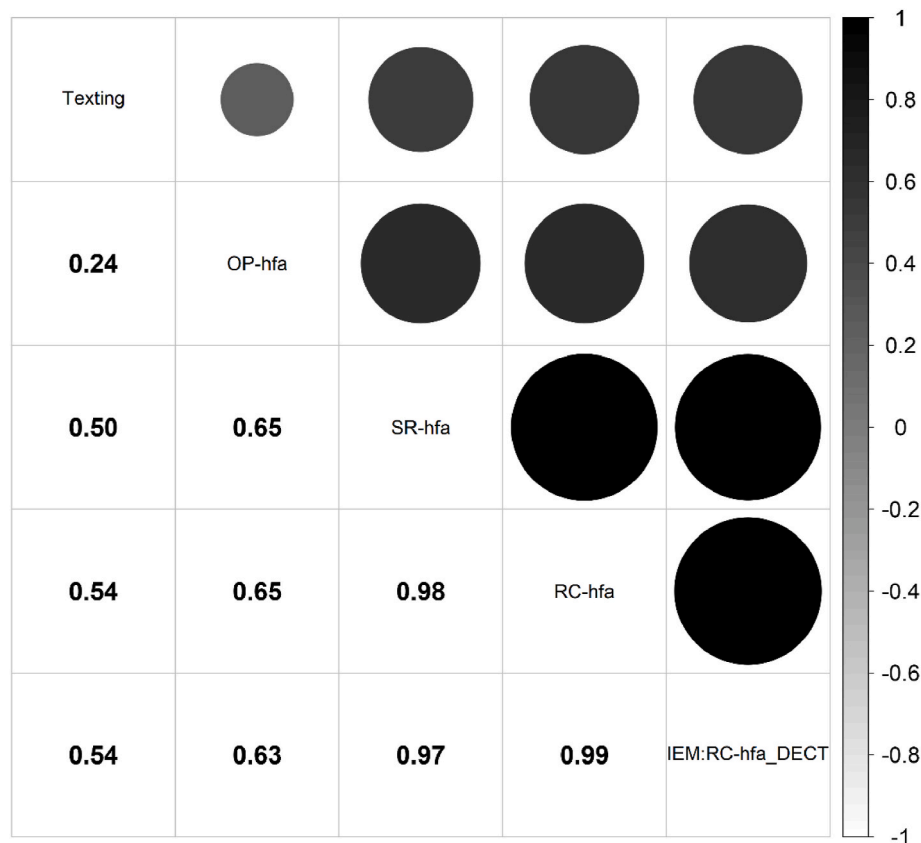


Fig. 3. Spearman rank correlation coefficients and correlation plot of the exposure metrics at baseline. Darker colors and larger circles indicate higher positive correlation levels.

Texting = frequency of text messages; OP-hfa = operator-recorded call-time adjusted by the proportion of hands-free use; SR-hfa = self-reported mobile phone call-time adjusted by the proportion of hands-free use; RC-hfa = country-specific regression calibrated call-time estimates adjusted by the proportion of hands-free use; IEM:RC-hfa_DECT = RF-EMF dose (mJ/kg/week) to the brain of the participants calculated with an integrated exposure model (IEM), including country-specific regression calibrated estimates adjusted by the proportion of hands-free use (minutes/week) and cordless phone use (minutes/week).

Table 2

Odds ratio (OR) with 95 % CI for weekly headache, severe weekly headache, daily headache, and migraine diagnosis at follow-up by amount of mobile phone use at baseline (weekly minutes of call-time, country-specific regression calibrated estimates adjusted by the proportion of hands-free use (RC-hfa)) without (A) and with (B) mutual adjustment for the number of text messages sent with a mobile phone at baseline. Number of participants with the outcome indicated in square brackets.

	Amount of mobile phone use at baseline (call-time in categories ^a)					P trend
	No. of participants	Very low	Low	Medium	High	
Weekly headache ^b (A)	66,858 [5452]	0.94 (0.88–1.01) [1432]	1 (reference) [2160]	1.08 (1.00–1.17) [1086]	1.10 (1.01–1.22) [774]	0.002
Weekly headache ^b (B)	66,858 [5452]	0.99 (0.92–1.07) [1432]	1 (reference) [2160]	1.05 (0.96–1.13) [1086]	1.04 (0.94–1.15) [774]	0.292
Severe weekly headache ^b (A)	66,234 [1660]	0.97 (0.86–1.10) [465]	1 (reference) [671]	1.08 (0.93–1.25) [299]	1.36 (1.13–1.63) [225]	0.001
Severe weekly headache ^b (B)	66,234 [1660]	0.99 (0.87–1.13) [465]	1 (reference) [671]	1.05 (0.90–1.21) [299]	1.25 (1.04–1.51) [225]	0.035
Daily headache ^b (A)	66,858 [382]	1.04 (0.79–1.38) [94]	1 (reference) [136]	0.98 (0.73–1.31) [75]	1.23 (0.90–1.67) [77]	0.448
Daily headache ^b (B)	66,858 [382]	1.09 (0.82–1.46) [94]	1 (reference) [136]	0.93 (0.69–1.24) [75]	1.09 (0.79–1.50) [77]	0.900
Migraine diagnosis ^c (A)	53,576 [1812]	0.93 (0.82–1.06) [396]	1 (reference) [725]	0.97 (0.85–1.11) [355]	1.19 (1.02–1.39) [336]	0.013
Migraine diagnosis ^c (B)	53,576 [1812]	0.97 (0.85–1.11) [396]	1 (reference) [725]	0.94 (0.82–1.08) [355]	1.12 (0.96–1.30) [336]	0.247

^a Very low: RC-hfa <19.1 (min/week); Low: RC-hfa ≥19.1 & RC-hfa <58.6 (min/week); Medium: RC-hfa ≥58.6 & RC-hfa <107.8 (min/week); High: RC-hfa ≥107.8 (min/week), (max = 256.8 min/week).

^b Adjusted for sex, age group, country, highest level of education attained, BMI group, general health indicator, sleep disturbance index, painkiller use, depression diagnosis, high blood pressure diagnosis, smoking status, and alcohol consumption at baseline. Excluding participants with (weekly, severe weekly, daily) headache at baseline.

^c Adjusted for sex, age group, country, highest level of education attained, BMI group, general health indicator, sleep disturbance index, painkiller use, depression diagnosis, high blood pressure diagnosis, smoking status, and alcohol consumption at baseline. Excluding participants with migraine diagnosis at baseline.

For highly transient and acute symptoms such as headache, using the peak of RF-EMF exposure might be theoretically preferable over the weekly exposure assessed in our study. However, adopting this approach would require substantially different exposure assessment methods that are impractical for large cohort studies, such as asking participants to regularly fill in a detailed usage diary. Given the study design and

methodology used to assess RF-EMF exposure in COSMOS, the analysis of the association between RF-EMF peak exposure and reporting of headache symptoms was precluded. In light of the transient nature of headaches, future research may explore the potential effect of peak RF-EMF exposure on symptom onset more thoroughly.

The composition of the Dutch cohort is not representative of the

Table 3

Odds ratio (OR) with 95% CI for weekly headache, severe weekly headache, daily headache, and migraine diagnosis at follow-up by number of text messages sent with a mobile phone at baseline without (A) and with (B) mutual adjustment for the amount of mobile phone use at baseline (weekly minutes of call-time, country-specific regression calibrated estimates adjusted by the proportion of hands-free use (RC-hfa)). Number of participants with the outcome indicated in square brackets.

Number of text messages sent with a mobile phone at baseline (frequency of texting in categories ^a)					
	No. of participants	Low	Medium	High	P trend
Weekly headache ^b (A)	66,858 [5452]	1 (reference) [2770]	1.17 (1.10–1.26) [2012]	1.42 (1.28–1.58) [670]	<0.001
Weekly headache ^b (B)	66,858 [5452]	1 (reference) [2770]	1.16 (1.08–1.25) [2012]	1.40 (1.25–1.56) [670]	<0.001
Severe weekly headache ^b (A)	66,234 [1660]	1 (reference) [868]	1.06 (0.94–1.20) [553]	1.63 (1.37–1.94) [239]	<0.001
Severe weekly headache ^b (B)	66,234 [1660]	1 (reference) [868]	1.04 (0.91–1.19) [553]	1.55 (1.29–1.87) [239]	<0.001
Daily headache ^b (A)	66,858 [382]	1 (reference) [181]	1.08 (0.84–1.40) [131]	1.86 (1.33–2.61) [70]	<0.001
Daily headache ^b (B)	66,858 [382]	1 (reference) [181]	1.12 (0.85–1.47) [131]	1.89 (1.33–2.69) [70]	<0.001
Migraine diagnosis ^c (A)	53,576 [1812]	1 (reference) [791]	1.12 (1.00–1.26) [727]	1.51 (1.29–1.78) [294]	<0.001
Migraine diagnosis ^c (B)	53,576 [1812]	1 (reference) [791]	1.11 (0.99–1.26) [727]	1.47 (1.24–1.75) [294]	<0.001

^a Low: Never/Less than 1 text message per week/1–6 text messages per week; Medium: 1–9 text messages per day; High: 10–29 text messages per day/30 or more text messages per day.

^b Adjusted for sex, age group, country, highest level of education attained, BMI group, general health indicator, sleep disturbance index, painkiller use, depression diagnosis, high blood pressure diagnosis, smoking status, and alcohol consumption at baseline. Excluding participants with (weekly, severe weekly, daily) headache at baseline.

^c Adjusted for sex, age group, country, highest level of education attained, BMI group, general health indicator, sleep disturbance index, painkiller use, depression diagnosis, high blood pressure diagnosis, smoking status, and alcohol consumption at baseline. Excluding participants with migraine diagnosis at baseline.

adult population of the Netherlands with respect to sex and age. In fact, the majority of participants in LIFEWORK were over the age of 50 years and the Nightingale study source population comprised women who were registered as having completed training to be a nurse in the nationwide register for healthcare professionals in the Netherlands. Furthermore, the EPIC study source population was based on women participating in a regional breast cancer screening program (Reedijk et al., 2018). We, a priori, had no indications that the effects of RF-EMFs on the occurrence of headaches would be different between men and women, or across age groups. In any case, these characteristics in the study population are unlikely to have hampered the ability to detect and estimate exposure–outcome associations, given the adequate control of confounding variables that were included in our analyses.

Finally, participants reported headache at baseline and follow-up, and no information was available in between. Therefore, these evaluations might not accurately reflect symptoms between these two time points, particularly for a transient condition such as headache. However, secondary analyses on migraine diagnosis, which should be less likely to change over time, were conducted, and results were consistent with those on headaches.

According to the Global Burden of Disease study, headaches are among the most common nervous system disorders, with migraine being the second among the world's causes of disability (Steiner et al., 2020; Stovner et al., 2022). These conditions are identified as a major public health concern, given the deleterious impact on the personal pain burden, the resulting impairment in the quality of life of those affected, and the related societal costs (Stovner et al., 2006).

Our results showed that the associations with headache and migraine found with call-time were largely explained by texting, and this suggests that the mechanism may be related to lifestyle, other exposures, or behavioural factors associated with the usage of mobile devices. Given the ubiquity of mobile phone use worldwide, more research is warranted to understand the exact underlying mechanism generating headaches and migraines among mobile phone users to develop options for prevention. Future research should also encompass the rapid technological advances and changes in mobile phone usage habits among the population and the associated possible health consequences.

5. Conclusions

In summary, we found that the use of mobile phones, particularly texting, is associated with headaches and migraines, and the associations with call-time were largely explained by texting. As the associations are driven more by text messaging than call-time, they do not

appear to be explained by RF-EMF exposure from the mobile device but are likely to reflect lifestyle, other exposures, or behavioural factors associated with mobile phone use.

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Financial interests

None.

Expert committee work

M.F. has served as advisor to several national and international public advisory and research steering groups concerning the potential health effects of exposure to non-ionizing radiation, including the WHO (ongoing), Public Health England Advisory Group on Non-ionizing Radiation - AGNIR (2009–17), the Norwegian Public Health Institute (2010–12), the Swedish Council for Working Life and Social Research (2003–2012), Swedish Radiation Safety Authority's independent scientific expert group on electromagnetic fields (2003–11). She was member of the International Commission on Non-Ionizing Radiation Protection (ICNIRP), an independent body setting guidelines for non-ionizing radiation protection (2008–May 2020), and vice chairman of the Commission May 2016–May 2020. A.H.P. is a member of the Swedish Radiation Safety Authority's independent scientific expert group on electromagnetic fields since 2018. A.A. has been a member in expert panels on health effects of radiofrequency electromagnetic fields for International Commission on Non-Ionizing Radiation Protection (ICNIRP), Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) of the European Commission, Swedish Radiation Safety Authority (SSM), and World Health Organization (WHO). A. H. is a member of the Swedish Radiation Safety Authority's independent scientific expert group on electromagnetic fields since 2012, and since 2021 serves as chair of the group. She is a member of ICNIRP since 2020; and a board member of the BioEM society (2021–2023). She was member of the EMF committee of the Health Council of the Netherlands from 2015 to 2022. From 2014 to 2023, she was a member of the Swiss Research Foundation for Electricity and Mobile Communication (FSM) scientific council, a non-profit foundation. H.K. was the chair of the EMF committee of the Health Council of the Netherlands from 2017 to 2022. He is currently a member of the WHO Task Group on Radiofrequency Fields and Health Risks. M.B.T. is a member of the expert UK Committee on Medical Aspects of Radiation in the Environment (COMARE). All other authors have declared no conflict of interest.

CRedit authorship contribution statement

Eugenio Traini: Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation. **Rachel B. Smith:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Roel Vermeulen:** Writing – review & editing, Supervision, Resources, Conceptualization. **Hans Kromhout:** Writing – review & editing, Supervision, Resources, Conceptualization. **Joachim Schüz:** Writing – review & editing, Supervision, Resources, Conceptualization. **Maria Feychting:** Writing – review & editing, Supervision, Resources, Conceptualization. **Anssi Auvinen:** Writing – review & editing, Supervision, Resources, Conceptualization. **Aslak Harbo Poulsen:** Writing – review & editing, Supervision, Resources, Conceptualization. **Isabelle Deltour:** Writing – review & editing, Supervision, Resources, Conceptualization. **David C. Muller:** Writing – review & editing, Methodology. **Joël Heller:** Writing – review & editing, Data curation. **Giorgio Tettamanti:** Writing – review & editing, Methodology, Supervision. **Paul Elliott:** Writing – review & editing, Supervision, Resources, Conceptualization. **Anke Huss:** Writing – review & editing,

Supervision, Resources, Conceptualization. **Mireille B. Toledano:** Writing – review & editing, Supervision, Resources, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2024.118290>.

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