

Mobile and cordless phones, serum transthyretin and the blood-cerebrospinal fluid barrier: a cross-sectional study

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Abstract

Background: Whether low-intensity radiofrequency radiation damages the blood-brain barrier has long been debated, but little or no consideration has been given to the blood-cerebrospinal fluid barrier.

Objective: To test whether long-term and/or short-term use of wireless phones was associated with changes in the serum transthyretin level, indicating altered transthyretin concentration in the cerebrospinal fluid, possibly reflecting an effect of radiation.

Methods: One thousand subjects, 500 of each sex aged 18-65 years, were randomly recruited using the population registry. Data on wireless phone use were assessed by a postal questionnaire and blood samples were analyzed for serum transthyretin concentrations by an immunonephelometric technique using commercially-available reagents from Dade Behring GmbH on a BN Prospec instrument.

Results: The response rate was 31.4%. Gender-specific logistic regression analyses adjusted for age yielded statistically insignificant results for short and long-term use of wireless phones. Linear regression gave significant findings for men: a positive β coefficient for latency of analogue phone and for mobile and cordless desktop phone use combined, and in contrast, a significant negative β coefficient for UMTS phones. For women, linear regression gave a significant association for short-term use of mobile and cordless phones combined, indicating that the sooner blood was withdrawn after the most recent phone call, the higher the expected transthyretin concentration.

Conclusion: This hypothesis-generating descriptive study gave some support for an association between latency of use of certain wireless phones and the serum transthyretin concentration. Too short a latency or confounding may explain the contradictory results for latency with regard to the associations between transthyretin level and different phones.

Introduction

The use of wireless phones has reached one hundred percent prevalence in many countries. Studies on the potentially harmful biological effects of the radiofrequency fields (RF) emanating from these devices are thus pertinent. Dysfunction of the blood-brain barrier (BBB) is one such effect that has long been debated (for reviews, see Nittby et al. [1] and Orendacova et al. [2]). A barrier that has received much less attention, though it also serves to maintain brain homeostasis by separating the central nervous system from the blood stream, is the so-called blood-cerebrospinal fluid barrier (BCSFB). These brain barriers should be given equal importance as both are implicated in chronic neurodegenerative brain diseases [3]. While the BBB separates or controls the traffic of molecules from the blood to the cerebral interstitial fluid, the BCSFB is a discontinuity in the circulation between the blood and cerebrospinal fluid (CSF). The former is made of endothelial cells and the latter of epithelial cells. A leakage or an alteration in the turnover of brain-derived proteins may be used to evaluate the integrity of these barriers, possibly reflecting an effect of RF.

We previously reported on a possible association between serum concentrations of the calcium-binding protein S100B and self-reported use of wireless telephones among healthy Swedish adults [4]. Mainly synthesized by the end-feet of astrocytes, S100B has been described as a suitable marker of integrity of the BBB [5-8]. In the present paper, using the same data, we report the results of analysis of serum levels of transthyretin (TTR), a key CSF protein. TTR could potentially serve as marker of BCSFB dysfunction.

TTR, also known as prealbumin, is a plasma and CSF carrier of thyroxin and retinol and is also described as sequestering amyloid beta peptide in the brain [9]. Its major sites of synthesis are the liver, the choroid plexus (CP) and the retinal pigment epithelium. TTR is used in clinical practice as a marker in several conditions, such as predicting outcome for

critically ill patients [10], in Alzheimer's disease [11, 12], amyloidosis [13], inflammation and malnutrition [14].

With regard to synthesis in the brain, TTR, unlike S100B, is not expressed by perivascular astrocytes [15]. It is mainly produced by the epithelial cells of the CP located in the four ventricles, representing about 25% of the CSF protein [16]. CP expands to fill nearly all the cerebral ventricles and has brush-type borders, microvilli, on the apical side. Once filtered by these brushes of microvilli, the CSF flows from the lateral ventricles through the third and fourth ventricles to the subarachnoid space. From there the fluid spreads over the entire surfaces of the brain and spinal cord.

Most of the CSF is emptied into the blood in the venous sinuses by way of arachnoid granulations. These protrusions are particularly abundant in the superior sagittal sinuses. The passage of CSF into the venous sinuses is caused by hydrostatic pressure, which is higher in the subarachnoid space, about 15 cm H₂O, than in the sinuses, 7-8 cm H₂O [17]. Concentrations of TTR in healthy adults have been reported to be in the range 0.017-0.025 g/l in the CSF [18-20] and 0.20-0.40 g/l in the plasma [21].

Several features make the BCSFB and TTR secretion by the CP particularly interesting for studying a possible effect of RF. Firstly, owing to the enlarged area of microvilli, the CP has a total surface within the same order of magnitude as the BBB [22]. Secondly, it has a rapid blood supply, about 10-fold faster than other regions of the brain [23], with extremely fenestrated endothelial cells that are also quite leaky [24]. Thus, large molecules can readily pass into the connective tissue, but are prevented from further entering the CSF by the tight junctions between epithelial cells. Thirdly, however, these junctions in the BCSFB are leakier than those between the endothelial cells of the BBB [25, 26], which would increase the likelihood of insult to the choroidal tissue by toxic materials originating from the blood.

Finally, the CP, especially in the lateral ventricles, may be associated with the effects of neurotoxic agents owing to its anatomical location close to several brain structures, among them the hippocampus.

In the present report we tested whether long-term and/or short-term use of wireless phones was associated with changed concentrations of TTR in the serum as a marker of alterations in CSF TTR, possibly reflecting an effect of RF. The study was approved by the local ethics committee.

Materials and methods

Data collection

One thousand subjects, 500 of each sex, aged 18-65 years and living in the municipality of Örebro in Sweden, were randomly recruited using the population registry. They received a letter of information and were asked to give informed consent to leave blood and have it stored in a so-called Biobank. Respondents who chose to take part then received further information about the purpose of the study. They were asked to complete a postal questionnaire that covered different topics such as background characteristics including employment history, use of wireless phones (mobile phones (analogue NMT, digital GSM, UMTS) and DECT), various other exposures such as X-rays, chemicals or radiation therapy and finally health- and lifestyle-related questions such as physical exercise and diseases. The first invitations were sent out in March 2007 and data collection was completed by the end of November 2007. A more detailed description of the study design was presented in the publication about S100B based on the same data [4].

Chemical analysis

Participants were asked if possible to leave blood samples at Örebro University Hospital in the afternoon at the end of a working week. All samples were centrifuged and the supernatant was decanted and frozen immediately. Serum TTR concentrations were determined by an immunonephelometric technique using commercially-available reagents from Dade Behring GmbH (Marburg, Germany) on a BN Prospec instrument also from Dade Behring. The total coefficients of variation were 3.4% and 5.5% at concentrations of 0.13 and 0.28 g/l respectively. All results are expressed in g/l.

Statistical Analysis

Frequency tables were produced and explanatory factors were analyzed by the Wilcoxon rank-sum test for one-way comparisons and a Kruskal-Wallis test for multiple comparisons. In all tests the significance level was set at 0.05. Following log-transformation of TTR values to normalize the distribution, linear regression was used to test an association between long- or short-term trends in wireless phone use and serum concentrations of TTR. Short-term use of wireless phones and serum concentrations of TTR were examined by comparing use on the day the blood sample was left; long-term use by comparing average use per day (since the start), cumulative use and latency. The Kruskal-Wallis test was used to analyze the frequencies of use in calls per day and the Wilcoxon rank-sum test to analyze usage in minutes (min) per day. Unconditional logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CI). As far as we are aware there is no established cut-off for determining 'normal' and 'elevated' levels of TTR in current use in clinical practice. We therefore chose the third quartile as cut-off (0.31 g/l serum) so that a sufficient number (n) of subjects would be included in the group with 'elevated' concentrations. Because of the low number of users who were literally unexposed (n=3), definitions of exposed and unexposed in

the logistic regression differed depending on the endpoint of interest. The 'unexposed' in the analysis of serum TTR and short-term use were those who reported not having used any type of wireless phone on the day the blood was drawn; the 'unexposed' in the analyses of long-term use were those with non-use and the quartile with the lowest overall use of mobile phones and DECT. All analyses were done using StataSE 10.1 (Stata/SE 10.1 for Windows; StataCorp., College Station TX).

Results

Descriptive analysis

One thousand persons were invited to take part in the study and 314 participated by answering the questionnaire and giving blood. TTR data were missing for one subject so the final analysis included 313 persons. Descriptive analysis showed that women were more likely than men to participate (χ^2 -test, probability (p) = 0.001) and that the mean age was higher among participants than non-participants (χ^2 -test, p = 0.0001) (Table 1).

Age and gender predicted TTR levels whereas time, day or month of drawing blood did not (Table 2). Men had higher concentrations than women and participants >47 years age had higher serum levels than younger ones, though when stratification was done on gender a significant difference only remained for women (p=0.02; p=0.72 for men). Explanatory factors assessed by the self-administered questionnaire such as hypertension, body mass index (BMI), smoking and use of oral snuff were all statistically significantly related to TTR concentrations, though they had little or no effect when adjusted for in the analyses. Use of detergents was of borderline significance (p=0.049) in women but was based on only 5 subjects, so no adjustment was made. Occupation, workload, head or neck X-ray, external radiation, physical activity, and various disease conditions did not predict serum TTR. In

further analysis, we either adjusted for age and gender or stratified on gender with age adjustment only.

Serum transthyretin levels and use of wireless phones

Logistic regression analysis of serum TTR and long-term total use of wireless phones yielded OR = 1.2, CI = 0.6 – 2.4 (Table 3). Latency analysis of overall use of wireless phones for periods of more than 5 and 10 years both yielded statistically insignificant results; OR = 1.2, CI = 0.6-2.5 and OR = 1.5, CI = 0.7-3.1, respectively. For mobile phones the highest OR was found in the > 10 year latency group, whereas OR for DECT did not change with latency. Also, higher ORs were found for men than for women.

The linear regression analysis of cumulative hours of use gave a somewhat lower p-value for the analogue phone type (p=0.07) than for other phone types (Table 4). Significantly positive β coefficients were found for latency for use of analogue phones (p=0.01) and for mobile phones and DECT combined (p=0.03). Stratification on gender gave significant findings for men and use of mobile phones (p=0.04), analogue phones (p=0.045) and mobile phones and DECT combined (p=0.04), but not for women. Stratification on gender for latency of use of UMTS, on the other hand, gave statistically significant associations in the opposite direction; that is, a significant negative β coefficient (p= 0.02) for men and a significant positive β coefficient (p=0.047) for women.

Further analysis yielded a statistically significant difference for serum TTR concentrations in relation to different frequencies of use in calls per day for digital (GSM) phones (p=0.01; Kruskal-Wallis test) but not for any of the other phone types (data not shown). Stratification on gender gave no significant difference, however (p=0.12 for men, p=0.57 for women).

Participants reporting ≤ 15 min average long-term total use per day were compared with those reporting > 15 min per day (Wilcoxon rank-sum test). Here we found a statistically significant difference in TTR concentrations for digital phones ($p=0.01$, higher TTR for >15 min) and DECT ($p=0.002$, lower TTR for >15 min). Again, the significances disappeared once stratification was done on gender (data not shown). However, for men, there was a tendency towards higher TTR concentrations for those who reported use of a digital phone > 15 min per day ($p=0.06$).

Logistic regression analysis of serum TTR and short-term use of wireless phones (i.e. same day as leaving blood) yielded statistically insignificant results (Table 5). In the linear regression analysis of use of wireless phones on the same day as giving blood, mobile phones and DECT combined gave a low p-value with a negative β coefficient for time since most recent use ($p=0.06$; Table 6), and this was significant for mobile phone use by women ($p=0.03$).

Discussion

There is a need to study the possible physiological effects of RF that might relate to increased risk of chronic disease in humans. Because most of the near-field RF exposure emanating from a wireless phone is absorbed in the head of the person using the device [27], the brain is one of the main organs of interest to study. In this cross-sectional study we investigated the possible association between serum TTR concentrations and self-reported use of wireless phones.

Logistic regression analyses of long-term use yielded statistically insignificant results, though with regard to latency, most ORs increased with years since first use. Linear regression

analysis, on the other hand, gave significant findings for latency both for use of analogue phones and for mobile phones and DECT combined, which after stratification on gender only remained for men. Stratification on gender also gave statistically significant associations for latency of UMTS, but with β coefficients going in opposite directions: for men, TTR concentrations decreased significantly with increasing latency, whereas for women the concentrations increased. What stands out in this group is that it consisted of significantly younger persons than the participants as a whole, see Table 1 (median age for men = 41.0 vs. 50.0; for women = 35.5 vs. 46.0). However, it is the result for men, the negative β coefficient that deviates from the general trend. Adjusting the gender-specific analysis for age, hypertension, BMI, smoking and intake of oral snuff did not change the results. Possibly the maximum latency of four years is too short, and that in combination with the low numbers makes the analysis sensitive to single deviant values. In women, for example, one subject with a high TTR concentration contributed strongly to the significantly positive β coefficient (included=0.087; excluded=0.040), and when this value was omitted the significance disappeared ($p=0.49$). There was no such obvious outlier for men, so the association is either real or more likely confounded by some unknown factor possibly associated with age (median UMTS = 41 years, mobile phones and DECT combined = 50, analogue phones = 54).

Linear regression analysis for cumulative use of analogue phones gave a lower p-value than for other phone types. Analyzing men and women separately gave no significant findings. With regard to a possible long-term effect, the results for analogue phones might be of interest since this phone type has been used longest in Sweden.

Regarding the analysis of long-term average digital phone use, higher TTR concentrations were found for those who reported > 15 min per day. When we stratified on gender these significances disappeared, but there was still a tendency towards higher concentrations in men. The corresponding results for use of DECT, however, showed significantly decreased

concentrations of TTR in the group who reported > 15 min use per day. That significance also disappeared when men and women were analyzed separately. The result was most probably explained by the fact that the group who used DECT > 15 min per day was dominated by women (81 out of 117), who had lower TTR concentrations than men in general.

Analysis of short-term use of mobile phone and DECT combined (min since last call) yielded a negative β coefficient, significantly so for women, indicating that the sooner blood was withdrawn after the most recent phone call, the higher the expected TTR concentration. Since TTR has a biological half-life of 48 hours [20] it should be a reliable marker of a short-term effect. By that we mean that its rate of metabolism would not obviate the possibility of detecting an effect.

In summary, we have somewhat intriguing results for latency and use of mobile phones, found only in men, and for time since last use of a mobile phone, found only in women. These differences between men and women might (except for latency of UMTS) be explained by the fact that men had higher TTR concentrations than women in general, which was significantly associated with latency. Thus, a weak short-term effect might be obscured. The results might also have been influenced by uncontrolled confounding, possibly intake of hormonal drugs, especially by women, which was not assessed in this study. Estrogen use is common among the elderly and estrogens have been reported to up-regulate TTR synthesis in CP and liver in mice [28, 29]. Elevated levels of TTR have also been reported in women using hormonal contraceptive drugs [30].

Another possible source of confounding, which was not assessed in this study, is nutritional status. Most of the TTR in the blood is produced by the liver and is regulated independently of production by the CP. TTR from the liver is a marker of malnutrition and inflammatory processes [20]. However, our study comprised healthy population-based subjects so it is

rather unlikely that malnutrition influenced the results significantly. Moreover, for hormonal contraceptives and nutritional status - or any other factor – to confound the results, those factors would have to covary with wireless phone use (or start of use).

To avoid potential confounding, gender-specific analyses adjusted for age were performed throughout. Because the results were not changed, no additional adjustment was made for hypertension, BMI, smoking or use of oral snuff, even though they were statistically significantly related to TTR concentrations. Interestingly, we found higher concentrations of TTR in subjects who had ever smoked or used oral snuff. As nicotine has been reported to up-regulate the synthesis and secretion of TTR in the CP [31], these results support our choice of method using serum TTR as a marker of TTR in CSF.

Another shortcoming of our study could be that the serum TTR concentration is expected to be 10-fold higher than the CSF level. Nevertheless, the highly vascularised CP and the CSF turnover of four times per 24 hours [23], together with the 13 times faster synthetic rate of TTR in CP than in liver [32], would make alterations of TTR in the CSF detectable in the serum. If we assume that these alterations were caused by RF exposure, there are at least a couple of potential mechanisms. One is up-regulation of the TTR gene in epithelial cells; the other is dysfunction of the BCSFB leading to increased leakage or turnover of TTR in either the CP and/or the superior sagittal sinuses due to the higher pressure in the subarachnoid space [17].

Ideally, TTR should be analyzed in both CSF and serum. For ethical reasons this is obviously not possible unless an opportunity is provided by patients undergoing CSF analysis for medical purposes. Another possibility would be proteomics to distinguish TTR from CP and CSF. Alternatively, use of the ratios between TTR and albumin, TTR and retinol binding

protein, and TTR and thyroxin in the blood could be used to determine the origin of the TTR. We are now considering how these alternatives may be explored in further studies.

The initial aim of the present study was to analyze serum S100B levels as a marker of BBB dysfunction and use of wireless phones. The more general shortcomings related to weaknesses in exposure assessment, study design and low response rate have been discussed more in detail in our previous publication [4]. Briefly, use of wireless phones was self-reported and not validated by operator records; exposure misclassification would thus be expected to some extent, although this error is unlikely to have been different with respect to serum TTR concentration since exposure was assessed beforehand. Therefore, misclassification would most likely be random, leading to a weaker association – given that there is an association. While it is a strength that the study was population-based, the low response rate of 31.4% makes the findings less valid for generalization to the whole population. Possibly it also reduces the power of the study.

In conclusion, this hypothesis-generating descriptive study gave some support for an association between latency of use of certain wireless phones and serum TTR concentration. Too short a latency or confounding may explain the conflicting results for latency with regard to different phones and TTR.

List of abbreviations

BBB, Blood-brain barrier; BCSFB, Blood-cerebrospinal fluid barrier; BMI, Body Mass Index; CSF, Cerebrospinal fluid; CI, Confidence Interval; DECT, Digital Enhanced Cordless Telecommunications; GSM, Global system for mobile communication; min, Minutes; NMT, Nordic Mobile Telephone System; N, Number; OR, Odds Ratio; p, Probability; RF,

Radiofrequency fields; TTR, Transthyretin; UMTS, Universal Mobile Telecommunication System.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FS was the principal investigator responsible for design, conduct, analysis, interpretation of data and writing the manuscript.

MC participated as statistician and in the compilation and interpretation of the data for this publication

LH made contributions to conception and design and also to analysis and drafting the manuscript.

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Table 1. Descriptive data for the study

	Men	Women	Total
Total included	500	500	1 000
-Age: mean, median	41.8, 41.0	41.6, 42.0	41.7, 42.0
Range	18-65	18-65	18-65
Declined to participate	127	156	283
Did not answer inquiry	196	116	312
Answered yes to participation	177	228	405
-Did not give blood	44	44	88
Participated	133	184	317
-Did not answer the questionnaire	0	2	2
-Unknown date for drawing blood	0	1	1
-Missing data, transthyretin	0	1	1
Final participants	133	180	313
-Age: mean, median	47.1, 50.0	44.4, 46.0	45.6, 47.0
Range	18-65	18-64	18-65

Table 2. Descriptive data for serum transthyretin ($\mu\text{g/l}$) for men, women and total

	n	Mean	Median	Min	Max	p
Transthyretin, total	313	0.277	0.270	0.170	0.480	-
Age (median)						
≤ 47 years	158	0.271	0.260	0.170	0.480	0.02
> 47 years	155	0.284	0.280	0.180	0.470	
Gender						
Men	133	0.307	0.300	0.180	0.480	<0.0001
Women	180	0.256	0.250	0.170	0.400	
Time (hour) when blood was drawn						
06:00-12:00	65	0.286	0.270	0.170	0.420	0.12
12:01-16:00	248	0.275	0.270	0.170	0.480	
Day when blood was drawn						
Mon-Thur	174	0.276	0.260	0.170	0.440	0.77
Fri-Sun	139	0.279	0.270	0.170	0.480	
Month when blood was drawn						
March-June	228	0.278	0.270	0.170	0.480	0.94
July-October	85	0.277	0.270	0.170	0.400	

The Wilcoxon rank-sum was used to calculate p-values.

Table 3. Logistic regression analysis with OR and 95% CI for serum transthyretin and use of wireless telephones

Group	Total			> 5 year latency			> 10 year latency		
	H/L ^a	OR	95 % CI	H/L ^a	OR	95 % CI	H/L ^a	OR	95 % CI
Mobile phones + DECT	56/177	1.2	0.6 – 2.4	56/170	1.2	0.6 – 2.5	40/80	1.5	0.7 – 3.1
-Men	46/58	1.5	0.6 – 3.5	46/57	1.5	0.6 – 3.6	34/39	1.6	0.6 – 3.9
-Women	10/119	0.8	0.3 – 2.6	10/113	0.8	0.3 – 2.7	6/41	1.3	0.4 – 4.6
-Mobile phones	55/176	1.2	0.6 – 2.4	53/152	1.2	0.6 – 2.5	35/58	1.5	0.7 – 3.3
-Men	45/58	1.4	0.6 – 3.5	45/53	1.6	0.7 – 3.8	32/34	1.7	0.7 – 4.2
-Women	10/118	0.8	0.3 – 2.6	8/99	0.8	0.2 – 2.5	3/24	1.2	0.3 – 5.8
-Analogue	19/33	1.4	0.6 – 3.4	19/32	1.5	0.6 – 3.6	18/29	1.4	0.6 – 3.6
-Men	17/25	1.2	0.5 – 3.3	17/25	1.2	0.5 – 3.3	17/23	1.4	0.5 – 3.7
-Women	2/8	2.4	0.4 – 15	2/7	3.2	0.5 – 22	1/6	2.0	0.2 – 22
-Digital	55/173	1.2	0.6 – 2.5	53/150	1.3	0.6 – 2.6	32/52	1.6	0.7 – 3.6
-Men	45/56	1.5	0.6 – 3.6	45/52	1.6	0.7 – 3.9	29/29	1.8	0.7 – 4.6
-Women	10/117	0.8	0.3 – 2.6	8/98	0.8	0.2 – 2.5	3/23	1.3	0.3 – 6.0
-UMTS	13/30	1.0	0.4 – 2.9	0/0	-	-	0/0	-	-
-Men	13/17	1.6	0.5 – 5.0	0/0	-	-	0/0	-	-
-Women	0/13	-	-	0/0	-	-	0/0	-	-
-DECT	54/165	1.3	0.6 – 2.6	44/127	1.3	0.7 – 2.7	17/46	1.3	0.6 – 3.1
-Men	44/51	1.6	0.7 – 3.9	35/38	1.6	0.7 – 4.1	13/17	1.4	0.5 – 4.0
-Women	10/114	0.9	0.3 – 2.7	9/89	0.9	0.3 – 3.0	4/29	1.2	0.3 – 4.9

^aH: Transthyretin > 0.31; L: Transthyretin ≤ 0.31.

Adjustments were made for age and gender.

'Unexposed' were those with non-use and the quartile with the lowest overall use of mobile phones and DECT.

Persons with missing information about use of wireless phones were excluded from the analysis.

Table 4. Linear regression analysis based on log-transformation of serum transthyretin and cumulative hours of use and latency for use of wireless telephones

Group	n	β coefficient	95 % CI	p
<i>Cumulative use (hours), mobile phone/DECT</i>				
Mobile phones + DECT	308	0.0000049	-0.0000012 to 0.000011	0.11
-Men	132	0.0000068	-0.0000045 to 0.000018	0.24
-Women	176	0.0000041	-0.0000029 to 0.000011	0.25
-Mobile phones	305	0.0000087	-0.0000020 to 0.000019	0.11
-Men	131	0.000011	-0.0000012 to 0.000024	0.08
-Women	174	-0.0000033	-0.000028 to 0.000022	0.80
-Analogue	58	0.00011	-0.0000082 to 0.00022	0.07
-Men	45	0.00010	-0.000019 to 0.00022	0.10
-Women	13	0.00011	-0.00036 to 0.00059	0.61
-Digital	302	0.0000086	-0.0000026 to 0.000020	0.13
-Men	130	0.000011	-0.0000020 to 0.000025	0.10
-Women	172	-0.0000024	-0.000028 to 0.000023	0.85
-UMTS	49	-0.000031	-0.00010 to 0.000043	0.41
-Men	31	-0.000035	-0.00010 to 0.000033	0.31
-Women	18	0.00079	-0.00071 to 0.0023	0.28
-DECT	279	0.0000027	-0.0000051 to 0.000011	0.50
-Men	117	-0.000017	-0.000042 to 0.000077	0.17
-Women	162	0.0000054	-0.0000025 to 0.000013	0.18
<i>Latency (years), mobile phone /DECT</i>				
Mobile phones + DECT	309	0.0052	0.00065 to 0.0097	0.03
-Men	133	0.0076	0.00029 to 0.015	0.04
-Women	176	0.0038	-0.0020 to 0.0097	0.20
-Mobile phones	306	0.0034	-0.0010 to 0.0078	0.13
-Men	132	0.0070	0.00044 to 0.014	0.04
-Women	174	0.00038	-0.0057 to 0.0064	0.90
-Analogue	59	0.013	0.0029 to 0.024	0.01
-Men	46	0.013	0.00033 to 0.026	0.045
-Women	13	0.014	-0.0054 to 0.034	0.14
-Digital	302	0.0031	-0.0026 to 0.0088	0.29
-Men	130	0.0075	-0.0024 to 0.017	0.14
- Women	172	0.0012	-0.0058 to 0.0082	0.74
-UMTS	49	-0.0065	-0.052 to 0.039	0.78
-Men	31	-0.056	-0.10 to -0.0085	0.02
-Women	18	0.087	0.0014 to 0.17	0.047
-DECT	279	0.0022	-0.0022 to 0.0066	0.33
-Men	117	0.00070	-0.0068 to 0.0082	0.85
-Women	162	0.0031	-0.0023 to 0.0086	0.26

Adjustments were made for age and gender.

Data for cumulative use of mobile phone/DECT are missing for two persons (one had used only a mobile phone, the other had used both a mobile phone and DECT).

Data for latency of mobile phone/DECT are missing for one person (a user of both mobile phone and DECT).

Table 5. Logistic regression analysis with OR and 95% CI of serum transthyretin and short-term use of wireless phones

Group	H/L^a	OR	95 % CI
Mobile phones + DECT	55/156	1.4	0.7 – 2.8
-Men	47/55	1.8	0.8 – 4.3
-Women	8/101	0.9	0.3 – 2.8
-Mobile phones	46/117	1.5	0.7 – 3.0
-Men	42/43	2.1	0.9 – 5.1
-Women	4/74	0.6	0.2 – 2.3
-DECT	20/79	1.2	0.5 – 2.5
-Men	15/26	1.2	0.5 – 3.3
-Women	5/53	1.0	0.3 – 3.6

^aH: Transthyretin > 0.31; L: Transthyretin ≤ 0.31.

Adjustments were made for age and gender.

Table 6. Linear regression analysis based on log-transformation of serum transthyretin and use of wireless telephones on the same day as giving blood

Group	n	β coefficient	95 % CI	p
<i>Minutes of use</i>				
Mobile phones	163	0.000055	-0.0014 to 0.0015	0.94
-Men	85	0.0000085	-0.0017 to 0.0017	0.99
-Women	78	0.00035	-0.0027 to 0.0034	0.82
DECT	99	-0.00036	-0.0024 to 0.0016	0.72
-Men	41	0.000067	-0.0034 to 0.0036	0.97
-Women	58	-0.00066	-0.0031 to 0.0018	0.59
<i>Minutes from last use – blood sampling</i>				
Mobile phones + DECT	205	-0.00023	-0.00047 to 0.000014	0.06
-Men	98	-0.00013	-0.00051 to 0.00025	0.51
-Women	107	-0.00036	-0.00067 to -0.000038	0.03
-Mobile phones	159	-0.00016	-0.00044 to 0.00012	0.25
-Men	82	0.000074	-0.00033 to 0.00048	0.72
-Women	77	-0.00043	-0.00082 to -0.000047	0.03
-DECT	97	-0.00024	-0.00061 to 0.00013	0.20
-Men	40	-0.00025	-0.00086 to 0.00035	0.40
-Women	57	-0.00023	-0.00071 to 0.00024	0.33

Adjustments were made for age and gender.

Data for minutes from last use of mobile phone/DECT to blood sampling are missing for six persons (four had used a mobile phone, two had used DECT).

Additional files provided with this submission:

Additional file 1: söderqvist et al - science of the total environment 2009.pdf,
479K

<http://www.ehjournal.net/imedia/1976416690254554/supp1.pdf>