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Review

Effect of mobile telephones on sperm quality: A systematic review and meta-analysis ☆

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ABSTRACT

Mobile phones are owned by most of the adult population worldwide. Radio-frequency electromagnetic radiation (RF-EMR) from these devices could potentially affect sperm development and function. Around 14% of couples in high- and middle-income countries have difficulty conceiving, and there are unexplained declines in semen quality reported in several countries. Given the ubiquity of mobile phone use, the potential role of this environmental exposure needs to be clarified. A systematic review was therefore conducted, followed by meta-analysis using random effects models, to determine whether exposure to RF-EMR emitted from mobile phones affects human sperm quality. Participants were from fertility clinic and research centres. The sperm quality outcome measures were motility, viability and concentration, which are the parameters most frequently used in clinical settings to assess fertility.

We used ten studies in the meta-analysis, including 1492 samples. Exposure to mobile phones was associated with reduced sperm motility (mean difference −8.1% (95% CI −13.1, −3.2)) and viability (mean difference −9.1% (95% CI −18.4, 0.2)), but the effects on concentration were more equivocal. The results were consistent across experimental *in vitro* and observational *in vivo* studies. We conclude that pooled results from *in vitro* and *in vivo* studies suggest that mobile phone exposure negatively affects sperm quality. Further study is required to determine the full clinical implications for both sub-fertile men and the general population.

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Abbreviations: CI, confidence interval; RF-EMR, radiofrequency electromagnetic radiation, SAR, specific absorption rate; EEG, electroencephalography; ROS, reactive oxygen species; FEM, fixed effect model; REM, random effects model.

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1. Introduction

Most men of reproductive age in high- or middle-income countries now own mobile (cell) telephones. Accompanying this increase in mobile phone ownership, there is concern over the potential effects of mobile phone exposure on human health. Mobile phones emit electromagnetic radiation (EMR), a low-level radiofrequency (RF), at a frequency of between 800 and 2200 MHz (Agarwal et al., 2011), that can be absorbed by the human body. Mobile phones are legally limited to a specific absorption rate (SAR) of 2.0 W/kg (ICNIRP, 1998), and currently, most have a SAR of ~1.4 W/kg (Agarwal et al., 2011). At this low frequency EMR is unlikely to ionise atoms or molecules (Erogul et al., 2006). However, there is some evidence of potential adverse effects including headaches (Oftedal et al., 2000), increased resting blood pressure (Braune et al., 1998), and disturbances to electroencephalographic (EEG) activity during sleep (Huber et al., 2000). It has also been suggested that mobile phones, and other electromagnetic devices that emit RF-EMR radiation, are detrimental to human fertility (La Vignera et al., 2012).

Around 14% of couples in industrialized countries experience difficulty with conception at some point in their lives (Wilkes et al., 2009). Male factor infertility is involved approximately 40% of the time (Fleming et al., 1995), and a high proportion of cases are unexplained. The oscillating current and transfer of energy generated by the RF electric field can result in rapid heating (Challis, 2005), which could influence sperm quality. There are also non-thermal interactions, including changes to protein conformations and binding properties, and an increase in the production of reactive oxygen species (ROS) that may lead to DNA damage (Challis, 2005; La Vignera et al., 2012). Animal studies have suggested that RF-EMR can affect the cell cycle of sperm (Kesari and Behari, 2010), increase sperm cell death (Yan et al., 2007) and produce histological changes in the testes (Dasdag et al., 1999).

Mobile phone exposure has been linked in some animal studies to a reduction in sperm count (Kesari et al., 2010) and motility (Mailankot et al., 2009), suggesting an impairment of male fertility, although these effects are not consistently reported (Dasdag et al., 2003). In humans, the prolonged use of mobile phones has been associated with decreased motility, sperm concentration, morphology and viability (Agarwal et al., 2008), suggesting a likely impact on fertility. However, the evidence is mixed. Some studies have found an effect on sperm motility but not on sperm concentration (Erogul et al., 2006; Fejes et al., 2005), whilst no effect on sperm quality has also been found (Feijo et al., 2011). We therefore conducted a systematic review and aggregated the available published data on the effect of mobile phone exposure on sperm quality using meta-analysis. The aim was to summarise the evidence on RF-EMR exposure from mobile phones and male fertility indices.

2. Methods

2.1. Search strategy

We conducted a systematic search using Web of Knowledge and MEDLINE to identify all relevant studies published from 2000 to 2012. The MESH search terms used were '*phone*' OR 'electromagnetic' AND 'semen' or 'sperm*' OR '*fertil*'. We limited the search to studies using human subjects and those that reported information on basic semen parameters including motility, viability and concentration. Hand searches were carried out of review articles and reference lists. Authors of unpublished or incomplete datasets were contacted to request that they provide information for this meta-analysis. Insufficient information meant that some studies were excluded (Gutschi et al., 2011; Van-Gheem et al., 2011; Wdowiak et al., 2007). Articles were only included if they were written in English, reported on human participants, did not use workplace RF-EMR exposure and were not review articles. We incorporated both *in vitro* and *in vivo* studies, provided they met with our inclusion criteria (max SAR 2.0 W/kg, frequency 800–2200 MHz, based on previous literature Agarwal et al., 2011). We adhered to PRISMA guidelines and provide the PRISMA checklist in the supporting information. Studies were analysed for inclusion independently by two of the authors, any discrepancies were resolved by discussion. Sixty articles were identified from the title. This was reduced to twenty-three potentially suitable articles using the abstract, largely due to the presence of animal and non-mobile phone related EMR exposure studies. From these, ten studies fulfilled all criteria and were included in the meta-analyses (Table 1).

We specified the primary outcome measures *a priori* as sperm motility (mean %); viability (mean %); and concentration ($\times 10^6$/ml). In clinical settings, these parameters are some of the most frequent measures used for investigations of male fertility. Some of the studies provided data on all three of these outcome measures, and others on just some of them. The following characteristics were assessed for each study: (a) Study design (*in vitro versus in vivo*), (b) data collection methods (*e.g.* semen analysis according to WHO guidelines), and (c) sample size.

2.2. Analysis

Statistical analysis was undertaken using *R* (i386 2.15.1) (RCoreTeam, 2012) with the package 'Meta' (Schwarzer, 2012). Both fixed effects models (FEM) and random effects models (REM) were fitted, to permit

Table 1
Study characteristics from mobile phone exposure and sperm quality meta-analyses. (– denotes information not provided).

Sperm parameters										
Reference	Sample size	Study design	Participant group	Motility	Viability	Concentration	Radio-frequency (MHz)	SAR (W/kg)	Exposure time	Comments
Agarwal et al. (2008)	361	*In vivo*	Fertility clinic	✓	✓	✓	–	–	–	Exposed to commercially available mobile phones
Agarwal et al. (2009)	64	*In vitro*	Fertility clinic	✓	✓	✓	850	1.46	60 min	Exposed to Sony Ericsson w300i
Ahmed and Baig (2011)	44	*In vitro*	Population	✓			900	1.3	60 min	Exposed to Nokia 112 in talk mode
Dkhil et al. (2011)	40	*In vitro*	Population		✓		850	1.46	60 min	Nokia 73 in talk mode
De Iuliis et al. (2009)	8	*In vitro*	Population	✓	✓		1800	1	16 h	Exposed using a waveguide, connected to a function generator and RF amplifier.
Erogul et al. (2006)	54	*In vitro*	Population	✓		✓	900	–	5 min	Exposed to commercially available mobile phones
Falzone et al. (2008)	24	*In vitro*	Population	✓			900	2	60 min	RF-EMR chamber
Feijo et al. (2011)	343	*In vivo*	Fertility clinic	✓	✓	✓	–	–	–	Exposed to commercially available mobile phones
Fejes et al. (2005)	254	*In vivo*	Fertility clinic	✓		✓	–	–	–	Exposed to commercially available mobile phones
Sajeda and Al-Watter (2011)	300	*In vivo*	Fertility Clinic	✓		✓	–	–	–	Exposed to commercially available mobile

assessment of which model-types were most suited to the data. FEMs were based on the inverse variance method and REMs on the DerSimonian and Laird method. Mean differences (MD) between exposed and non-exposed groups were calculated to determine the effect size. The heterogeneity of the studies was assessed using I^2 (Higgins and Thompson, 2002) and associated confidence intervals (CI). Where heterogeneity was high, subgroup analyses were carried out to identify potential sources of the heterogeneity. Sensitivity analyses were conducted to assess the leverage of individual studies on the results (see Supplementary Information Figs. 1–3). Assessment of potential publication bias is also provided in the Supplementary Information (Figs. 4–5).

3. Results

All semen analyses were carried out according to WHO guidelines applicable at the time of publication (WHO, 1999, 2010). Overall, 10 suitable studies were identified, and these included data on 1492 samples. The number of papers included in each meta-analysis varied according to the sperm parameters reported: 9 provided data on motility, 6 provided data on concentration and 5 provided data on viability. All *in vitro* studies were experimental and all *in vivo* studies were observational. Two studies of healthy donors included only normozoospermic individuals, that is men with all semen parameters within normal ranges according to the WHO criteria (WHO, 1999). The exposure rates for the *in vitro* studies are reported in Table 1. All used frequencies of 850–900 MHz, with the exception of one study (De Iuliis et al., 2009); SAR, where reported was in the range 1–2; and duration of exposure ranged from 5 min to 16 h, with four of the studies using a duration of 1 h. Exposure rates were not assessed or reported in the epidemiological studies conducted *in vivo*.

3.1. Motility

Nine studies, which included 1448 samples from 1353 men, were used in this analysis (Fig. 1a.). Mean total motility (%) ranged from 36.6 to 86.8%. Six studies (Agarwal et al., 2008, 2009; Ahmed and Baig, 2011; De Iuliis et al., 2009; Erogul et al., 2006; Sajeda and Al-Watter, 2011) reported a significant negative effect of mobile phone exposure on human sperm motility. Overall, both the FEM and REM indicated that mobile phone exposure was linked to reduced sperm motility, FEM −12.2 (95% CI −13.6, −10.7), and REM −8.1 (95% CI −13.1, −3.2). Given the high heterogeneity (89.5% (95% CI 82.2%, 93.7%)), the REM is likely to provide the most appropriate representation of the data. The consistency in the direction of the effect, and overlap of the confidence intervals across studies, increases confidence in the results. Sensitivity analyses (Supplemental Fig. 1) indicate that removing the paper by (De Iuliis et al., 2009) slightly reduced the mean difference to −6.65. When any of the other studies were removed in turn, the observed pooled effect size was not materially affected (range of mean effect sizes seen using REM −6.65; −9.43).

To assess the causes of the heterogeneity, three subgroup analyses were undertaken (Table 2.). The heterogeneity estimates were not materially affected by performing analyses separately according to study type (*in vivo versus in vitro*) or donor type (population *versus* fertility clinic donors). The effect of how long the samples/participants were exposed to the mobile phone radiation was then assessed (Fig. 2), with the studies being split equally into short exposure (≤60 min) and long exposure (>60 min) groups. All but one of the *in vitro* studies, but none of the *in vivo* studies (De Iuliis et al., 2009), were in the short exposure group. Heterogeneity in the short exposure group was reduced to 35.8%, compared to 90.7% for the long exposure group (Table 2), suggesting that some of the differences between studies are explained by exposure time. The results for the short-exposure treatment were consistent whether a FEM or REM model was used, and suggested that mobile phone exposure reduced motility (Table 2). The observed pooled effect size was larger for the long exposure studies, with a greater reduction in motility compared to the short exposed groups.

3.2. Viability

Five studies, which assayed 816 samples, were analysed (Fig. 1b). Mean viability ranged from 52.3 to 89.0%. Four of the five studies reported a significant negative association between mobile phone exposure and sperm viability. The estimated pooled mean reduction in sperm viability was −5.6% (95% CI −6.4, −4.8) by the FEM, and −9.1% (95% CI −18.4, 0.2) by the REM. Heterogeneity (98.0% (95% CI 96.9%, 98.7%)) was high, and the REM is therefore likely to provide a better representation of the data. In subgroup analyses neither the study type, population group nor duration of exposure explained the heterogeneity between studies (Table 3). Sensitivity analyses showed that, as with motility, the work of De Iuliis et al. (2009) had a large influence on the results: when this study was removed, the effect size reduced to −5.52 (Supplementary Fig. 2). In contrast, the removal of Feijo et al. (2011) increased the mean difference to −12.10. These results are therefore consistent in suggesting a negative association between mobile phone exposure and sperm viability, but also indicate the need for further studies to elucidate size of this association.

3.3. Concentration

Six studies, including 1376 samples, were pooled in this meta-analysis (Fig. 1c). Mean sperm concentration (10^6/ml) ranged from 22.4 to 85.9. There was inconsistent evidence for a reduction in concentration in relation to mobile phone exposure: the FEM, but not the REM, suggested a strong effect on concentration after exposure (FEM MD −12.5 (95% CI −14.5, −10.5); REM MD −3.2 (95% CI −16.6, 10.2)). As heterogeneity was again high (I^2 89.1% (95% CI 79.0%, 94.4%)), the REM is a more suitable analysis, suggesting that there is no effect of mobile phone exposure on concentration (Fig. 1c). Due to the small number of studies, subgroup analysis was only possible for study type (Table 4). Heterogeneity was reduced to 0% in the *in vitro* groups (n = 2) compared to 93% in the *in vivo* groups (n = 4), suggesting the majority of the difference between studies is explained by the study type. Sensitivity analyses (Supplementary Fig. 3) demonstrated that the removal of Feijo et al. (2011) dramatically increased the effect size (to −10.01 from −3.19), as it had for the viability analyses. The removal of any other study from the analyses had no material effect on the results. The overall effect size estimated by the analysis of all the studies may therefore be conservative, due to the influence of Feijo et al.'s study.

4. Discussion

With evidence of a decline in semen quality in recent years (Rolland et al., 2013; Swan et al., 2000), there is a need to clarify the relationships between environmental exposures and sperm quality parameters. Studies on the effect of mobile phones on male fertility indices have been contradictory. This meta-analysis summarises the evidence currently available. Mobile phone exposure was associated with reduced sperm motility and viability, whereas the effect on sperm concentration was less clear. The consistency in the direction of overall effects estimated for all outcomes using both *in vitro* and *in vivo* studies adds confidence to the findings.

The biological plausibility for an effect of mobile phones on sperm quality needs to be considered. RF-EMR may have both thermal and non-thermal effects on biological tissue. Nonthermal interactions are suggested to increase the production of reactive oxygen species (ROS) and this may lead to DNA damage (Challis, 2005). A small amount of ROS has an important functional role in sperm capacitation, the acrosome reaction, and binding to the oocyte (Garrido et al., 2004). Experimental disruption of the flow of electrons through the mitochondrial

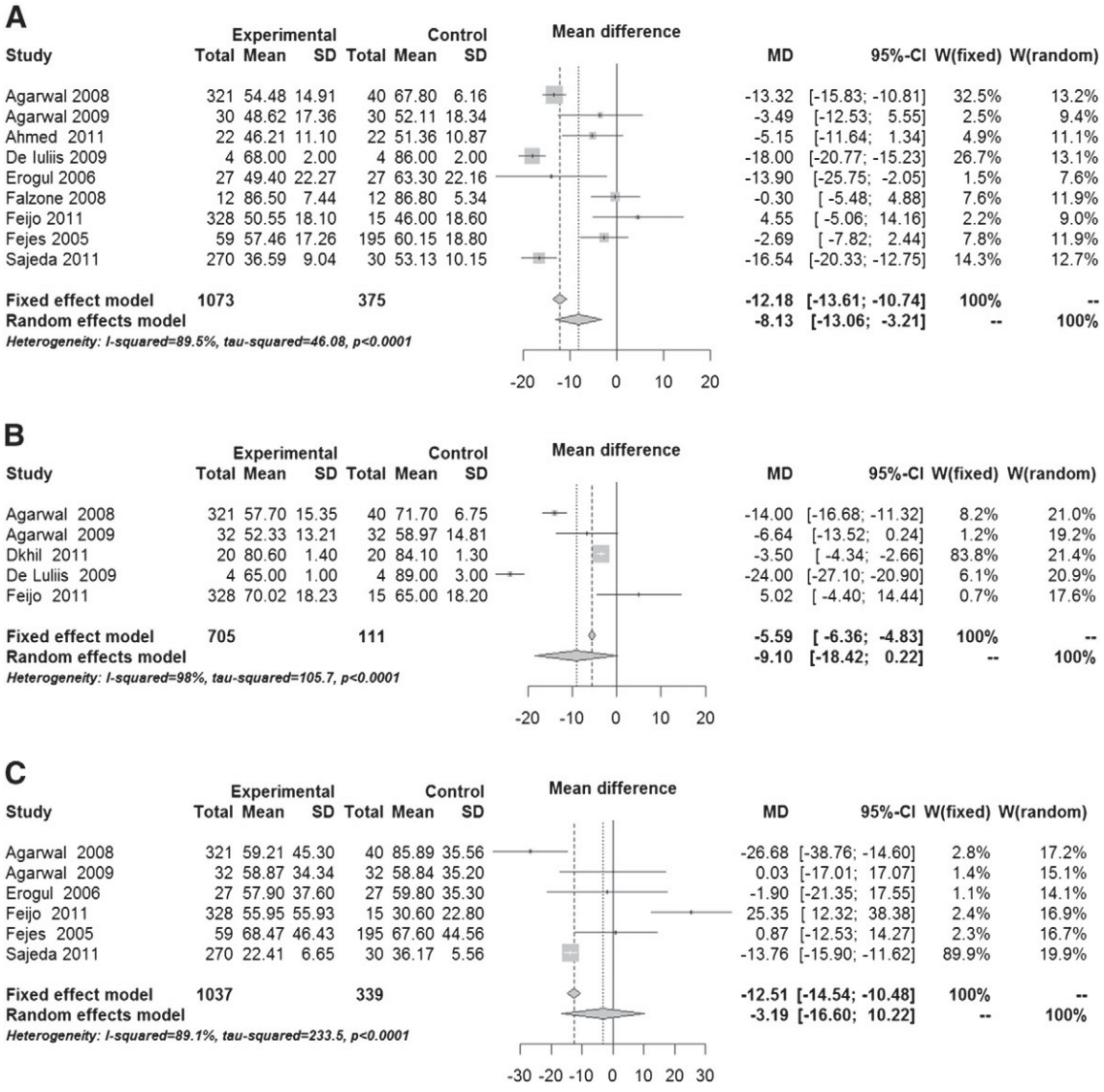


Fig. 1. Forest plot showing the effect of mobile phone exposure on human sperm motility (A), viability (B) and concentration (C). A. FEM −12.2 (95% CI −13.6, −10.7) REM −8.1 (95% CI −13.1, −3.2); B. FEM −5.6 (95% CI −6.4, −4.8) REM −9.1 (95% CI −18.4, 0.2); C. FEM −12.5 (95% CI −14.5, −10.5) REM −3.2 (95% CI −16.6, 10.2).

electron transport chain has been shown to increase ROS production significantly, with negative consequences for sperm motility (Koppers et al., 2008). *In vitro* evidence found EMR emitted at the same frequency as mobile phones increased mitochondrial ROS production and DNA fragmentation in sperm, and decreased motility and viability (De Iuliis et al., 2009). The trends seen in this meta-analysis are consistent with these effects.

Thermal effects could increase the temperature of the testes – since mobile phones are often carried in trouser pockets near the reproductive organs – hampering spermatogenesis and sperm production (Agarwal et al., 2011). Skin surface temperatures on the face have been reported to rise by up to 2.3 °C after 6 min of mobile phone use (Anderson and Rowley, 2007). These thermal effects may be largely due to the heat generated by the handsets rather than the RF-EMR, since the frequencies of EMR released from mobile phones are thought to have negligible heating effects (Agarwal et al., 2011; Challis, 2005; La Vignera et al., 2012). If the impact of mobile phones was mainly due to heating rather than radiation, an effect on sperm concentration rather than parameters such as viability and motility, which are linked with DNA integrity, would be expected.

Table 2
Subgroup analyses for motility.

Motility subgroup analyses	Subgroup	Number of studies (k)	Mean difference, (95% CI)	I^2 (%)	Statistical model
Study Design	*In vivo* groups	4	−8.1, (−15.14, −1.03)	90.2	REM
	In vitro groups	5	−8.1, (−17.08, 0.78)	91.2	REM
Participant group	Fertility Clinic	5	−7.3, (−13.74, −0.94)	88.2	REM
	Population	4	−9.2, (−19.48, 1.03)	92.7	REM
Time of exposure	Short	4	−3.4, (−6.95, 0.10)	35.8	FEM
		4	−4.1, (−8.80, 0.57)	35.8	REM
	Long	5	−10.5, (−16.10, −4.8)	90.7	REM

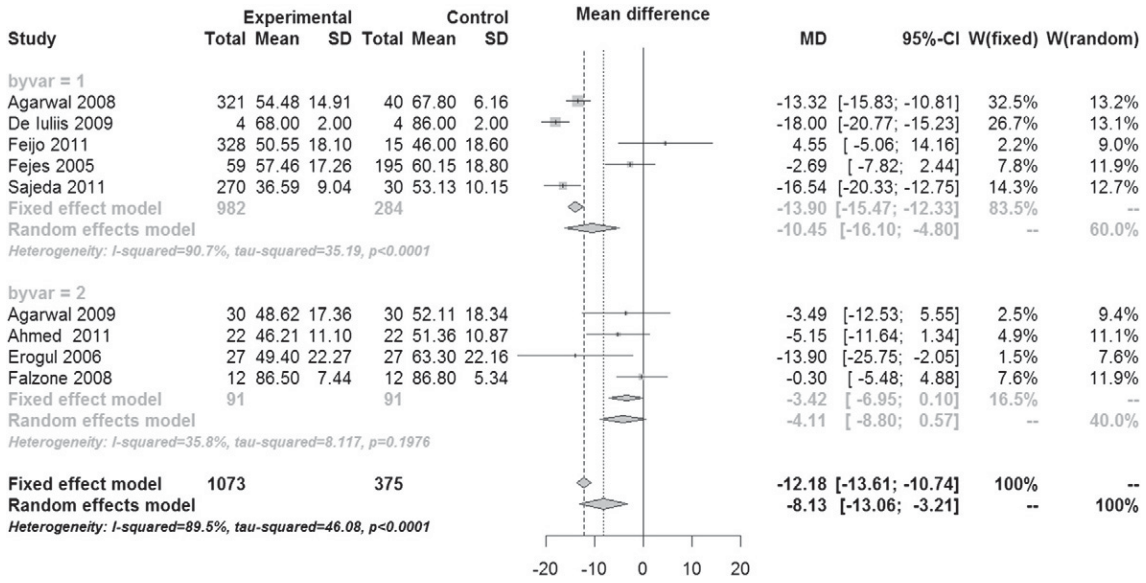


Fig. 2. Exposure time subgroup analyses on the effect of mobile phone exposure on sperm motility. Long exposure (byvar = 1), short exposure (byvar = 2).

There are some limitations to this study. Heterogeneity, that is variation between studies that is greater than expected due to sampling error (Higgins and Thompson, 2002), is an issue in most meta-analyses. Heterogeneity was high in all our meta-analyses ($I^2 > 88\%$). This may partly be due to the inflation of I^2 associated with low study numbers (Huedo-Medina et al., 2006). However, our meta-analysis did include nearly 1500 samples, which increases confidence in the results. The heterogeneity in the motility meta-analysis was partially due to the differences in mobile phone exposure times, as the subgroup analyses demonstrated. The high heterogeneity and relatively low number of studies also precluded meaningful assessment of publication bias (Peters et al., 2007; Ruzni and Idris, 2012; Terrin et al., 2003). However, sensitivity analyses demonstrated minimal differences when individual studies were excluded, with a tendency for our results to be conservative.

The possibility of confounding variables influencing the results of the observational studies cannot be ruled out. For example, participant age and smoking status were not consistently reported, so it is possible that these affected the observational studies since they are known to affect some semen quality parameters, including concentration (smoking only) and motility (Kidd et al., 2001; Ramlau-Hansen et al., 2007). Nevertheless, the inclusion of *in vivo* as well as observational studies, and the consistency of the results between the study types, provides evidence that the observed effects were causal. However, study populations taken from fertility clinics, as used in many studies on male fertility, may not be representative of the general population, as they are likely to contain a higher proportion of men with sperm parameters outside the WHO reference range. This is difficult to assess because even men classified as fertile have high heterogeneity in their semen parameters (Cooper et al., 2010). Nonetheless, in all but two of our studies, the mean values were above the lower reference values given for fertile men (motility (40%, 95% CI (38, 42)); concentration (15, 95% CI (12, 16)); viability (58%, 95% CI (55, 63))) (Cooper et al., 2010), suggesting no marked bias in the study populations. In addition, WHO guidelines for the analysis of the sperm samples were applied consistently across the studies (WHO, 1999) (WHO, 2010), meaning that standardised methodology and presentation were used, facilitating the pooling of data.

4.1. Future research

Mobile phone exposure appears to affect at least two of the most widely-used indices for assessing sperm quality (WHO, 2010). Sperm motility is estimated to be approximately 8% lower in exposed than non-exposed groups. Alone, the clinical importance of an effect of this size may be limited to subfertile men or those at the lower-end of the normal spectrum. However, mobile phone exposure may form part of a cumulative effect of modern day environmental exposures, that collectively reduce sperm quality and explain current trends in infertility. For example, recent evidence found wi-fi from laptops also negatively affected sperm quality (Avendano et al., 2012). A better understanding of the collective influence of environmental factors on sperm quality, and subsequently fertility, will help to improve treatment, advice and support for individuals seeking fertility treatment.

Although the subject of high-profile media attention, the number of available studies on mobile phone exposure and sperm quality is limited. Additional studies, particularly those which assess viability and other sperm parameters, including morphology and subcellular sperm damage such as sperm DNA integrity (not assessed during conventional semen analyses), are required. This would improve the precision of the estimated effect sizes, and allow better judgement of the likely clinical importance of the findings.

Table 3
Subgroup analyses for viability.

Viability Subgroup analyses	Subgroup	Number of studies (k)	Mean difference, (95% CI)	I^2 (%)	Statistical model
Study Design	*In vivo* groups	2	−5.1, (−23.66, 13.56)	93.1	REM
	In vitro groups	3	−11.4, (−26.52, 3.66)	98.7	REM
Participant group	Fertility Clinic	3	−6.0, (−16.26, 4.23)	88.2	REM
	Population	2	−13.7, (−33.78, 6.40)	99.4	REM
Time of exposure	Short	2	−15.6, (−32.61, 1.40)	95.1	REM
	Long	3	−5.1, (−13.82, 3.64)	96.5	REM

Table 4
Subgroup analyses for concentration.

Concentration subgroup analyses	Subgroup	Number of studies (k)	Mean difference, (95% CI)	I^2 (%)	Statistical model
Study Design	*In vivo* groups	4	−4.0, (−21.81, 13.77)	93.0	REM
	In vitro groups	2	−0.8, (−13.63, 12.01)	0.0	REM

The period of exposure is likely to affect semen quality, as has been demonstrated in other species (Mailankot et al., 2009), and the intensity of exposure is also likely to be important. The exposures observed in the *in vivo* studies are constrained by the legal limits placed on SARs for mobile phones (ICNIRP, 1998), and data on the maximum SARs for each phone model are available. However, every device has fluctuating SARs, so better methods of monitoring participant exposure levels are urgently required. Long term *in vivo* studies using standardised levels and periods of exposure, ideally a randomized controlled trial in the general population, is needed to assess the importance of mobile phone exposure to public health. The hypotheses of different thermal and non-thermal effects of RF-EMR on sperm quality also need to be tested. It would be helpful to compare the effects of intermittent exposure (where thermal effects are likely to be small) with continuous exposure to the same total amount of RF-EMR, as has been previously investigated in work on damage to DNA in human fibroblasts from mobile phones (Diem et al., 2005).

5. Conclusions

Our analyses indicate negative associations between mobile phone exposure on sperm viability and motility. The effects on concentration are more equivocal. Further research is required to quantify these effects more precisely and to evaluate the clinical importance of the risk to both sub-fertile men and the general population.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2014.04.015.

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