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ORIGINAL ARTICLE ***Reproductive epidemiology***

Male cellular telephone exposure, fecundability, and semen quality: results from two preconception cohort studies

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STUDY QUESTION: To what extent is exposure to cellular telephones associated with male fertility?

SUMMARY ANSWER: Overall, we found little association between carrying a cell phone in the front pants pocket and male fertility, although among leaner men (BMI $<25\,kg/m^2$), carrying a cell phone in the front pants pocket was associated with lower fecundability.

WHAT IS KNOWN ALREADY: Some studies have indicated that cell phone use is associated with poor semen quality, but the results are conflicting.

STUDY DESIGN, SIZE, DURATION: Two prospective preconception cohort studies were conducted with men in Denmark (n = 751) and in North America (n = 2349), enrolled and followed via the internet from 2012 to 2020.

PARTICIPANTS/MATERIALS, SETTING, METHODS: On the baseline questionnaire, males reported their hours/day of carrying a cell phone in different body locations. We ascertained time to pregnancy via bi-monthly follow-up questionnaires completed by the female partner for up to 12 months or until reported conception. We used proportional probabilities regression models to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs) for the association between male cell phone habits and fecundability, focusing on front pants pocket exposure, within each cohort separately and pooling across the cohorts using a fixed-effect meta-analysis. In a subset of participants, we examined selected semen parameters (semen volume, sperm concentration and sperm motility) using a home-based semen testing kit.

MAIN RESULTS AND THE ROLE OF CHANCE: There was little overall association between carrying a cell phone in a front pants pocket and fecundability: the FR for any front pants pocket exposure versus none was 0.94 (95% CI: 0.0.83–1.05). We observed an inverse association between any front pants pocket exposure and fecundability among men whose BMI was $<25\,kg/m^2$ (FR = 0.72, 95% CI: 0.59–0.88) but little association among men whose BMI was $\geq 25\,kg/m^2$ (FR = 1.05, 95% CI: 0.90–1.22). There were few consistent associations between cell phone exposure and semen volume, sperm concentration, or sperm motility.

LIMITATIONS, REASONS FOR CAUTION: Exposure to radiofrequency radiation from cell phones is subject to considerable non-differential misclassification, which would tend to attenuate the estimates for dichotomous comparisons and extreme exposure categories (e.g. exposure 8 vs. 0 h/day). Residual confounding by occupation or other unknown or poorly measured factors may also have affected the results.

WIDER IMPLICATIONS OF THE FINDINGS: Overall, there was little association between carrying one's phone in the front pants pocket and fecundability. There was a moderate inverse association between front pants pocket cell phone exposure and fecundability among men with BMI $<25\,kg/m^2$, but not among men with BMI $\geq 25\,kg/m^2$. Although several previous studies have indicated associations between cell phone exposure and lower sperm motility, we found few consistent associations with any semen quality parameters.

STUDY FUNDING/COMPETING INTEREST(S): The study was funded by the National Institutes of Health, grant number R03HD090315. In the last 3 years, PRESTO has received in-kind donations from Sandstone Diagnostics (for semen kits), Swiss Precision

Diagnostics (home pregnancy tests), Kindara.com (fertility app), and FertilityFriend.com (fertility app). Dr. L.A.W. is a fibroid consultant for AbbVie, Inc. Dr. H.T.S. reports that the Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to and administered by Aarhus University. None of these studies are related to the current study. Dr. M.L.E. is an advisor to Sandstone Diagnostics, Ro, Dadi, Hannah, and Underdog. Dr. G.J.S. holds ownership in Sandstone Diagnostics Inc., developers of the Trak Male Fertility Testing System. In addition, Dr. G.J.S. has a patent pending related to Trak Male Fertility Testing System issued.

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Key words: cellular telephones / fecundability / semen quality / fertility / prospective cohort study

Introduction

Infertility, defined as the inability to conceive after 12 months of unprotected intercourse, affects 10–15% of couples in North America and Denmark (Schmidt et al., 1995; Thoma et al., 2013). Male-related factors contribute up to 50% of couple infertility (Irvine, 1998; Thoma et al., 2013), yet there are few confirmed risk factors for male infertility (Gabrielsen and Tanrikut, 2016). A meta-regression of 185 studies worldwide examining semen quality estimated a 50–60% decline in sperm concentration and total sperm count between 1973 and 2011 (Levine et al., 2017); however, causes of the decline have not been identified. Most research on male infertility has been conducted in selected populations, such as couples treated in infertility clinics (Messerlian et al., 2018) or in populations with limited geographic diversity (Buck Louis et al., 2014). In addition, research has focused on semen quality rather than demonstrated fecundity. Factors thought to adversely affect male fertility include high testicular heat exposure (Thonneau et al., 1998; Hjollund et al., 2000), obesity (Sermondade et al., 2013; Eisenberg et al., 2014), infections (Agarwal et al., 2018), occupational exposures (Jensen et al., 2006), dietary factors (Chiu et al., 2014; Hatch et al., 2018; Falsig et al., 2019), short sleep duration (Wise et al., 2018), and use of anti-depressant medications (Norr et al., 2016).

Cellular telephone use is a nearly ubiquitous exposure that has increased dramatically during the past few decades (Pew Research Center, 2019). Cell phones operate at frequencies of approximately 800–2600 megahertz, emitting low levels of radiofrequency radiation. Exposure to radiofrequency radiation from cell phones is measured by the specific absorption rate, which is legally required to be <2.0 watts/kg. Due to strict regulatory standards for the specific absorption rate and the power levels of phone operation, the increase in heat generated by cell phones in nearby tissues is small and unlikely to influence semen quality (Hamada, 2011). However, nonthermal effects of radiofrequency radiation have been described, including increases in reactive oxygen species that can lead to oxidative stress and sperm DNA damage (Agarwal et al., 2009; De Iuliis et al., 2009). Animal studies have found lower Leydig cell proliferation and testosterone secretion in mice (Lin et al., 2018), lower sperm counts and motility in rabbits (Salama et al., 2010), and lower sperm motility in rats following prolonged radiofrequency radiation exposure at levels comparable to those from typical cell phone use (Yan et al., 2007). Several human studies, including two meta-analyses of 10 and 11 studies, respectively (7 overlapping) (Adams et al., 2014; Liu et al., 2014), found that radiofrequency radiation from cell phone use may be associated with lower sperm motility, although recent studies suggest little association (Yan et al., 2007; Zhang et al., 2016; Lewis et al., 2017). To our knowledge, no study has examined the association between male cell phone exposure and fecundability.

We examined the association between hours of carrying a cell phone in different locations on the male body, with a focus on the front pants pocket as the main source of exposure, and fecundability in two parallel preconception cohort studies in North America and Denmark. In a subset of men, we also evaluated cell phone exposure in relation to selected semen parameters.

Materials and methods

Snart Foraeldre (SF) and Pregnancy Study Online (PRESTO) are ongoing internet-based preconception cohort studies with virtually identical designs; study methods have been described in detail elsewhere (Mikkelsen et al., 2009; Wise et al., 2015). Eligible women are aged 18–45 years (SF) and 21–45 years (PRESTO) and are trying to conceive without fertility treatments. Women complete a baseline questionnaire and shorter follow-up questionnaires every 8 weeks for up to 12 months. After baseline, women may invite their male partner to complete a baseline questionnaire.

Study population

Between January 2012 and October 2019, 7428 women enrolled in SF. Of the 1136 men who enrolled, 989 (87%) were linked to their female partner. We excluded 32 couples because the date of the last menstrual period (LMP) was implausible or more than 6 months before enrollment. We excluded another 206 couples because they had been attempting conception for more than 6 cycles at study entry, leaving 751 couples in the analytic dataset.

Between June 2013 and June 2020, 12 226 women enrolled in PRESTO. We excluded 202 women whose date of LMP was implausible or more than 6 months before the date of enrollment and 2500 women who had been attempting to conceive for more than six cycles at study entry. Of the remaining 9524 women, 5073 women invited their male partner to participate, and 2349 male partners enrolled.

Semen quality substudy

We examined semen quality in a subset of participants from both cohorts using the Trak® home-based semen testing kit, an FDA-approved device that enables men to measure sperm concentration, semen volume, and motility at home (Sommer et al., 2020). Measurements of sperm concentration and semen volume have been validated against traditional in-clinic collection methods (Schaff et al., 2017). Starting in April 2018, we added a Trak motility assay that was calibrated against gold standard measurements of highly motile samples (Fredriksen, 2018).

Between September 2015 and June 2020, we invited 871 PRESTO men to participate in this substudy. Of these, 463 (53%) completed an online consent form and were mailed a Trak test kit. Men were instructed to test two semen samples, 7–10 days apart, during their partner's luteal phase, and to be abstinent for 2–7 days before each test. A total of 341 (74%) men submitted their first test results and 248 (73%) submitted their second test results, for a total of 589 semen samples.

We conducted a pilot study of semen quality in SF from May 2019 to September 2019, using the same procedures as in PRESTO. In total, 52 (38%) of 136 invited males provided the first sample, and 49 (94%) provided the second sample.

Ethics approval

The studies were approved by the Boston University Medical Campus Institutional Review Board. SF is registered at Aarhus University to comply with Danish law on data protection and the Danish substudy on semen parameters was approved by The Committee on Health Research Ethics in Central Denmark Region. All participants provided informed consent.

Assessment of cell phone exposure

We asked men how often they carried their phone in various body locations: 'What is the average number of hours per day that you carry a cellular phone in the following places? (only count hours when the phone is on)'. The locations were front pants, back pants, side pants or shirt pocket, as well as belt carrier. We evaluated exposure in two ways: (i) any versus no time that the phone was carried in each location, and (ii) number of hours the cell phone was carried in each location (categorized as 0, <1–2, 3–7 and ≥8 h/day). For descriptive purposes, we defined the primary location where men usually carried their phone as the location with the most hours reported. Our a priori exposure of interest was front pants pocket exposure, which was assumed to have the greatest biologic plausibility for potential effects of radiofrequency radiation on testicular function, due to proximity.

Assessment of fecundability

Fecundability, defined as the average per-cycle probability of conception, is an integrated couple-based measure of fecundity (Weinberg *et al.*, 1989) that is considered more sensitive for identifying environmental effects on reproduction than studies measuring infertility dichotomously (Baird *et al.*, 1986). We used time-to-pregnancy (TTP), in discrete menstrual cycles, as the underlying measure for average computing fecundability during follow-up.

We measured TTP using information collected on the female questionnaires. At baseline, women reported their LMP date and the number of menstrual cycles during which they had been attempting pregnancy. On each follow-up questionnaire, women reported their LMP date, whether or not they had conceived since the last questionnaire, changes in pregnancy intention, initiation of fertility treatment, and changes in selected exposures and covariates. For women with irregular cycles, we estimated typical menstrual cycle length using the average number of cycles per year and LMP dates collected during follow-up. We calculated TTP in discrete menstrual cycles using the following formula: (cycles trying to conceive at study entry) + [(LMP date from most recent follow-up questionnaire − date of baseline questionnaire)/cycle length] + 1.

Assessment of covariates

We collected covariate data from male and female baseline questionnaires. Covariates of interest included male and female age, race/ethnicity (PRESTO only), education, income, body mass index (BMI), physical activity, smoking, sleep duration, medical history and reproductive factors such as frequency of intercourse, timing of intercourse during the fertile period, history of sexually transmitted infections (STIs) and whether the male had previously impregnated a female partner.

Statistical analysis

We conducted parallel analyses in SF and PRESTO since characteristics of cell phones, such as brand, use of protective covers and headphones, and other factors contributing to radiofrequency exposure (e.g. power level and average distance from base stations) may differ across the two cohorts. In addition, Danish cell phones operate over a narrower radiofrequency band (800–900 megahertz) than North American phones (800–2600 megahertz, depending on the generation of the phone and the carrier). We also conducted a fixed-effects meta-analysis to allow for variation in the exposure and covariates (Blettner *et al.*, 1999; Lin and Zeng, 2010).

Couples contributed cycles at risk until a reported pregnancy or a censoring event (initiation of fertility treatment, cessation of pregnancy attempts, 12 cycles of attempt without conception or loss to follow-up). We used proportional probabilities regression models (Weinberg *et al.*, 1989) to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs), adjusting for confounding variables (described below). A FR <1 reflects lower average fecundability in the exposed group compared with the referent group. We used the Andersen-Gill data structure to account for left truncation due to delayed entry into the risk set (Howards *et al.*, 2006; Schisterman *et al.*, 2013) and included binary indicator variables for cycle at risk in the model to account for the decline in average fecundability over time. We used the weighted copy method to aid in model convergence (Deddens and Petersen, 2008).

Potential confounders were chosen based on the literature and a directed acyclic graph. Final models were adjusted for the following male variables: age (<25, 25–29, 30–34, ≥35 years), race/ethnicity (non-Hispanic White vs. all other; PRESTO only), education (<16 vs. ≥16 years), household income (<50 000 vs. ≥50 000 US dollars/year or the equivalent in Denmark), BMI (<18.5, 18.5–24.9, 25–29.9, ≥30.0 kg/m^2), physical activity (metabolic equivalent tasks [METs] h/week), sugar-sweetened softdrink intake (drinks/week), current smoking, history of STI, sleep duration (<7, 7–8, >8 h), and work hours (≤20, 20–50, >50 h/week). We also adjusted for female age (<25, 25–29, 30–34, ≥35 years) and BMI (<18.5, 18.5–24.9, 25–29.9, 30–34.9, ≥35.0 kg/m^2), and frequency of intercourse reported by the female partner (≤3 vs. >3 times/week).

We collected data on cell phone exposure only once, on the baseline questionnaire. Because men may have altered where they carried their phones over the course of follow-up, we conducted sensitivity analyses restricting follow-up to the first three observed cycles. We also performed sensitivity analyses that excluded 125 men in PRESTO and 20 men in SF who completed their baseline questionnaire more than 3 months after their female partner completed her questionnaire, in an effort to reduce potential for differential exposure misclassification (e.g. recall bias). We conducted stratified analyses by pregnancy attempt time at study entry (<3 vs. 3–6 menstrual cycles) to evaluate potential for reverse causation, which could occur if men altered their cell phone habits with increasing duration of attempt time. We also stratified by whether the male had ever impregnated a partner, to assess whether radiofrequency exposure might be more harmful in men without proven fertility. Finally, we stratified by BMI (<25 vs. ≥25 kg/m^2), since excess adiposity may lower radiofrequency radiation exposure to the testes among men who carry their phone in their front pants pocket.

We used multiple imputation with five imputation data sets to impute missing data on exposure, outcome, and covariates (Sterne et al., 2009). We assigned one cycle of follow-up to women who completed only the baseline questionnaire (n = 164 (7%) (PRESTO) and n = 54 (7%) (SF)) and imputed their outcome (pregnant vs. not). Covariate missingness in PRESTO ranged from <0.1% (sugar-sweetened soda intake and educational level) to 5% (male job hours per week), and in SF from <1% (height) to 21% (male job hours per week).

Analysis of semen quality

We began collecting motility data in April 2018; therefore, in PRESTO, among the 589 semen samples in the analysis, 464 (79%) had motility data; we imputed values of motile sperm concentration for the remainder. We conducted a parallel analysis of semen quality among 95 samples from SF. We calculated total sperm count as sperm concentration (million/ml) × semen volume (ml); total sperm motility as motile concentration/total concentration; and total motile sperm count as volume × motile sperm concentration. We analyzed the percent difference in mean log-transformed semen quality parameters using generalized estimating equation (GEE) linear regression models to account for multiple semen samples per participant (up to two). We adjusted for abstinence time (days), age (years), current smoking (yes vs no), BMI (kg/m^2), work (hours/week), alcohol intake (drinks/week), sugar-sweetened soda intake (drinks/week) and sleep duration (<6 vs. ≥6 h/night).

Results

In SF, 751 couples contributed 2687 cycles to the analysis; 66% reported a pregnancy, 8% were lost to follow-up, 8% started infertility treatment, 4% stopped trying to conceive, 8% completed 12 cycles without becoming pregnant and 6% were still actively participating in the study. In PRESTO, 2349 couples contributed 9574 cycles to the analysis; 63% reported a pregnancy, 8% were lost to follow-up; 8% started infertility treatment, 3% stopped trying to conceive, 15% completed 12 cycles without becoming pregnant and 2% were still actively participating in the study.

Most men carried their phone in their front pants pocket (70% of SF and 62% of PRESTO participants reported this pocket as their primary location). They also reported more hours in the front pants pocket than in other body locations (Table I). Men in SF were on average 30 years old (SD: 4), with ages ranging from 20 to 54 years. Those who never carried their phone in their front pants pocket were older, reported greater educational attainment and physical activity, and were less likely to have a history of STIs, to have frequent sexual intercourse or to have ever impregnated a partner (Table II). Men in PRESTO were on average 32 years old (SD: 5), with ages ranging from 20 to 65 years. Those who never carried their phone in their front pants pocket had lower educational attainment and household income, higher BMI, were less physically active, and were more likely to be

Table I Characteristics of male cell phone use by amount of exposure in each pocket.

	Snart Foraeldre (n = 751 men)		PRESTO (n = 2349 men)	
	Number of men (%)[a]	Median (IQR) hours/day	Number of men (%)[a]	Median (IQR) h/day
Any location[a]				
Front pants pocket	662 (88)	6 (3–10)	1974 (84)	5 (3–6)
Shirt pocket	271 (36)	3 (2–7)	811 (35)	3 (2–4)
Back pants pocket	46 (6)	1 (1–2)	567 (24)	3 (2–5)
Side pocket	155 (21)	5 (1–8)	465 (20)	3 (2–5)
Belt carrier	<5 (<1)	2 (1–3)	92 (4)	5 (4–6)
Primary location[b]				
Front pants pocket	529 (70)	8 (4–10)	1458 (62)	5 (4–6)
Shirt pocket	69 (9)	4 (2–7)	170 (7)	5 (4–6)
Back pants pocket	8 (1)	6 (3.5–7)	190 (8)	5 (4–6)
Side pocket	75 (10)	8 (6–10)	151 (6)	5 (4–6)
Belt carrier	0 (0)	—	47 (2)	6 (5–6)

IQR, interquartile range.
[a]Percentages do not add to 100 as men could be in multiple categories.
[b]Excludes men with no primary location.

Table II Baseline characteristics[a] of males based on primary location and hours of exposure in front pants pocket.

	Snart Foraeldre (n = 751)[b]						PRESTO (n = 2349)[c]					
	Primary location				Hours in front pants pocket		Primary location				Hours in front pants pocket	
Characteristic	Back pants N = 8	Front pants N = 529	Side pants N = 75	Shirt N = 69	0 h N = 89	≥8 h N = 278	Back pants N = 190	Front pants N = 1458	Side pants N = 151	Shirt N = 170	0 h N = 375	≥8 h N = 707
Age at baseline (years, mean)	34.5	30.2	31.2	32.4	32.1	30.1	32.4	31.1	31.5	32.9	32.9	30.8
White, non-Hispanic (%)	100.0	100.0	100.0	100.0	100.0	100.0	81.4	86.4	82.4	86.8	83.8	85.9
Education ≥college degree (%)	79.0	77.5	47.4	67.6	71.7	77.6	56.1	71.7	56.2	66.7	54.6	67.4
BMI (kg/m^2, mean)	22.9	25.5	26.0	24.7	26.1	25.4	28.0	27.7	30.2	28.9	29.0	27.6
MET hours/week of physical activity (mean)	120.1	61.8	111.5	57.3	76.9	70.7	31.7	32.9	33.5	32.1	30.0	31.8
Alcohol (drinks/week, mean)	4.4	4.7	4.3	4.6	4.5	5.1	6.3	6.2	5.6	6.6	5.7	6.2
Sugar-sweetened soda (drinks/week, mean)	0.9	1.6	2.2	1.4	1.3	1.7	4.5	2.1	3.4	2.9	4.3	2.4
Daily multivitamin use (%)	20.4	28.3	31.3	30.9	23.4	27.5	32.3	35.6	34.4	38.0	34.4	33.0
Average sleep duration ≤6 h/night (%)	NA	NA	NA	NA	NA	NA	45.2	31.5	44.6	32.6	43.6	36.2
Work ≥50 h/week (%)	20.4	28.3	31.3	30.9	7.8	3.2	27.6	24.0	25.5	38.3	28.4	26.1
Perceived stress scale (mean)	NA	NA	NA	NA	NA	NA	16.0	14.5	15.3	15.2	15.6	14.8
Ever impregnated someone (%)	62.2	37.5	40.1	41.7	38.4	39.8	45.3	41.8	48.6	41.3	48.9	44.5
History of sexually transmitted infections (%)	5.4	23.7	19.6	22.3	15.3	23.6	4.9	5.1	5.9	5.7	7.1	5.5
Intercourse frequency <1 times per week (%)	18.2	21.1	17.3	22.2	21.2	18.8	23.7	27.6	26.5	27.6	25.0	27.8
Intercourse frequency ≥4 times per week (%)	0.0	14.6	18.5	8.6	12.8	15.5	14.9	11.7	14.5	12.8	16.1	12.4
Current smoker (%)	5.4	6.9	12.5	5.4	9.0	8.2	15.0	4.5	7.5	7.4	12.2	7.0
Doing anything to improve chances of conception (%)	64.4	76.7	73.0	59.3	70.2	74.0	75.3	79.1	73.4	74.4	74.7	76.9
Hormonal last method of contraception (%)	31.3	55.9	58.3	58.6	56.2	52.0	34.8	35.2	37.7	34.6	36.2	35.7
Household income >$50,000/year (%)	82.6	70.0	63.1	64.6	63.7	71.8	76.4	86.2	78.9	82.0	75.5	85.2
Female age at baseline (years, mean)	27.6	28.7	29.1	27.6	29.2	28.7	29.2	29.8	29.7	29.8	29.0	29.5
Female BMI (kg/m^2, mean)	22.5	24.0	23.7	23.5	24.4	23.7	28.5	27.2	30.3	28.1	29.0	27.2
Female education (≥college degree)	84.4	87.1	81.4	72.6	89.6	88.7	65.8	84.1	80.3	81.1	69.8	81.7

BMI, body mass index.
[a]All characteristics, except male age, were age standardized to the cohort at baseline.
[b]Snart Foraeldre had 0 individuals with a belt carrier as the primary location of exposure and 70 individuals with no primary location of exposure.
[c]PRESTO had 44 individuals with a belt carrier as the primary location of exposure and 302 individuals with no primary location.

smokers, have a history of STIs, have impregnated a partner and to report shorter sleep duration (Table II).

Overall, there was little association between carrying the phone in the front pants pocket at least some of time with fecundability when pooling across cohorts (Table III, FR = 0.94, 95% CI: 0.83–1.05). These results were similar in parallel analyses of the two cohorts (SF: FR = 0.96, 95% CI: 0.72–1.28; PRESTO: 0.93, 95% CI: 0.82–1.06). There was also little evidence for a dose–response relation between the number of hours that men carried their phones in the front pants pocket. Based on fixed-effects meta-analysis, FRs for carrying the cell phone in the front pants pocket for <1–2, 3–7, and ≥8 h were 0.89 (95% CI: 0.78–1.02), 1.00 (95% CI: 0.88–1.14), and 0.92 (95% CI: 0.80–1.06, Table IV). The results did not vary appreciably across the two cohorts. Results were also similar after excluding men who filled out their baseline questionnaire more than 3 months after their partner (Supplementary Table SI).

When we restricted the analysis to the first three cycles of follow-up, the results combining the two cohorts were also comparable

Table III Fecundability ratios for cell phone placement (any time vs. no time exposed in that location).*

	Snart Foraeldre				PRESTO				Pooled**	
	No. of pregnancies	No. of cycles	Adjusted[a]		No. of pregnancies	No. of cycles	Adjusted[a]		Adjusted[a]	
			FR	95% CI			FR	95% CI	FR	95% CI
Front pants pocket	442	2385	0.96	0.72–1.28	1,259	8059	0.93	0.82–1.06	0.94	0.83–1.05
Back pants pocket	25	142	1.29	0.82–2.03	360	2250	1.05	0.94–1.18	1.06	0.95–1.19
Side pants pocket	89	547	0.97	0.77–1.22	272	2012	0.93	0.82–1.05	0.94	0.84–1.05
Belt carrier	Sparse data				58	390	1.11	0.87–1.42	—	—
Shirt pocket	187	930	1.14	0.96–1.36	506	3489	0.93	0.84–1.02	0.97	0.90–1.05

CI, confidence interval; FR, fecundability ratio.
*Reference group for each category was 0 h exposed in a given pocket.
**Pooled across cohorts using fixed-effects meta-analysis.
[a]Adjusted for race/ethnicity, education, male BMI, household income, frequency of intercourse, female BMI, male history of STI, male current smoker, male sleep, male work, male age, female age, male MET-hours per week, and male sugar-sweetened soda intake.

Table IV Association between front pants pocket exposure and fecundability.

	Snart Foraeldre						PRESTO						Pooled*	
	No. of pregnancies	No. of cycles	Unadjusted		Adjusted[a]		No. of pregnancies	No. of cycles	Unadjusted		Adjusted[a]		Adjusted[a]	
			FR	95% CI	FR	95% CI			FR	95% CI	FR	95% CI	FR	95% CI
Hours per day														
0	52	302	1.00	Ref	1.00	Ref	227	1515	1.00	Ref	1.00	Ref	1.00	Ref
<1–2	97	578	0.92	0.67–1.26	0.90	0.64–1.26	370	2621	0.93	0.80–1.08	0.89	0.76–1.03	0.89	0.78–1.02
3–7	147	831	0.95	0.70–1.27	0.91	0.66–1.24	443	2535	1.11	0.96–1.29	1.02	0.88–1.18	1.00	0.88–1.14
≥8	198	976	1.08	0.81–1.45	1.01	0.75–1.38	446	2903	0.99	0.85–1.15	0.90	0.78–1.05	0.92	0.80–1.06
Restricted to first three cycles of follow-up														
Hours per day														
0	42	181	1.00	Ref	1.00	Ref	163	844	1.00	Ref	1.00	Ref	1.00	Ref
<1–2	67	346	0.77	0.53–1.10	0.77	0.53–1.13	251	1372	0.92	0.77–1.10	0.89	0.74–1.06	0.87	0.74–1.02
3–7	112	501	0.87	0.63–1.21	0.83	0.59–1.17	327	1437	1.15	0.97–1.36	1.06	0.90–1.26	1.01	0.87–1.18
≥8	151	601	0.99	0.72–1.37	0.94	0.68–1.30	326	1576	1.03	0.87–1.23	0.96	0.80–1.14	0.96	0.82–1.11

CI, confidence interval; FR, fecundability ratio.
*Pooled across cohorts using fixed-effects meta-analysis.
[a]Adjusted for race/ethnicity, education, male BMI, household income, frequency of intercourse, female BMI, male history of STI, male parity, male current smoker, male hours of sleep per night, male work hours per week, male age, female age, male MET-hours per week, and male sugar-sweetened soda intake.

(Table IV). In SF, results for front pants pocket exposure were slightly stronger (FRs were 0.77 (95% CI: 0.53–1.13), 0.83 (95% CI: 0.59–1.17), and 0.94 (95% CI: 0.68–1.30) for <1–2, 3–7, and ≥8 vs. 0 h/day, respectively). In contrast, the results were slightly attenuated in PRESTO, with FRs of 0.89 (95% CI: 0.76–1.03), 1.06 (95% CI: 0.90–1.26), and 0.96 (95% CI: 0.80–1.14), for <1–2, 3–7, and ≥8 h/day, respectively (Table IV).

Results for stratified analyses are shown in Supplementary Table SII. Overall, the inverse association between hours of front pants pocket exposure and fecundability was slightly stronger among couples who had been trying to conceive for <3 cycles at study entry, whereas among those who had been trying to conceive for 3–6 cycles at study entry, there appeared to be slightly increased fecundability for 3–7 and ≥8 h of front pocket exposure but results varied between the two cohorts. There was a slightly stronger reduction in fecundability among men who had never impregnated a partner, but no consistent monotonic trend with increasing hours in the front pants pocket. In both cohorts combined, an association between any exposure in the front pants pocket and reduced fecundability was evident among men with BMI <25 kg/m^2 (FR = 0.72, 95% CI: 0.59–0.88) but not among men whose BMI was ≥25 kg/m^2 (FR = 1.05, 95% CI: 0.90–1.22). These results were consistent across the two cohorts (SF: FR = 0.69, 95% CI 0.46–1.03, and FR = 1.02, 95% CI 0.69–1.51 for men with BMI <25 and ≥25 kg/m^2, respectively; corresponding FRs in PRESTO were 0.73, 95% CI: 0.59–0.92 and 1.05, 95% CI: 0.89–1.24). Similar patterns were seen when we examined hours/day in the front pants

Table V Percent differences for association between hours per day of cell phone use in the front pocket and semen quality, pooled analysis.[a]

	Total # of samples	Semen volume (ml)		Sperm concentration (million/ml)		Total sperm count (million)		Motility (%)		Total motile sperm count (million)	
		Median value (IQR)	Adjusted percent difference (95% CI)	Median (IQR)	Adjusted percent difference (95% CI)	Median (IQR)	Adjusted percent difference (95% CI)	Median (IQR)	Adjusted percent difference (95% CI)	Median (IQR)	Adjusted percent difference (95% CI)
Hours in front pants pocket											
0–2	264	4.0 (2.0)	0 (Ref)	47.6 (63.0)	0 (Ref)	170.0 (224.8)	0 (Ref)	0.53 (0.39)	0 (Ref)	91.4 (126.9)	0 (Ref)
3–7	209	4.0 (2.0)	1.0 (−8.2, 11.0)	44.0 (64.0)	9.6 (−13.7, 39.2)	190.5 (215.2)	10.6 (−13.7, 41.8)	0.51 (0.42)	−3.6 (−14.6, 8.8)	96.0 (139.8)	6.7 (−20.1, 42.5)
≥8	211	3.8 (2.2)	−4.5 (−12.4, 4.2)	48.0 (54.0)	13.8 (−7.4, 39.7)	165.0 (202.6)	8.7 (−12.2, 34.7)	0.52 (0.44)	−0.3 (−11.9, 12.9)	81.1 (120.4)	8.4 (−16.4, 40.6)

CI, confidence interval; IQR, Interquartile range; SD, standard deviation.
[a]Adjusted for abstinence time, age, current or occasional smoker, BMI (kg/m^2), hours of work per week, alcohol intake, sugar-sweetened soda, average hours of sleep per night, cohort.

pocket (Supplementary Table SII), although the trend was not monotonic. When we restricted further to those with <3 cycles of attempt time at study entry, and to men whose BMI was <25 kg/m^2, the inverse association was slightly stronger, although non-monotonic, in both cohorts (combined FRs were 0.68 (95% CI: 0.53–0.87), 0.70 (95% CI: 0.54–0.89), and 0.71 (95% CI: 0.56–0.90) for <1–2, 3–7, and 8 h/day compared with none, respectively).

Men in PRESTO tended to have better semen quality than those in SF, although mean semen volume was higher in SF (4.2 vs. 3.9 ml in SF vs. PRESTO). In SF versus PRESTO, mean sperm concentration (± SD) was 44.5 (±36.9) versus 62.5 (±48.3) million/ml; sperm count was 183 (±163) versus 232 (±197) million; % motile was 47 (±22) versus 57 (±25); and total motile count was 85.1 (±80.3) versus 136.3 (±141.1) million. Overall, in the pooled analysis, there was little association between cell phone exposure and any of semen quality parameters (Table V). Results were inconsistent across the two cohorts (Supplementary Table SIII). In SF, there were small reductions in semen quality associated with ≥8 h/day of front pants pocket exposure compared with 0–2 h. In contrast, in PRESTO, semen quality tended to be higher among men who reported ≥8 h/day of front pants pocket exposure compared with 0–2 h.

Discussion

In two preconception cohort studies from North America and Denmark, there was little dose–response relation between the number of hours carrying a cell phone in the front pants pocket and male fecundability overall. In both cohorts, however, we observed an inverse association between front pants pocket exposure and fecundability among men with BMI <25 kg/m^2 but no association among men with BMI ≥25 kg/m^2. Semen volume, sperm concentration, total sperm count, motility, and total motile count were not appreciably associated with semen parameters in PRESTO. In SF, there were small inverse associations with semen parameters comparing the highest and lowest categories of exposure, although the estimates were imprecise.

To our knowledge, no previous study has evaluated couple fecundability in relation to male cell phone use. Several experimental studies have randomly assigned fresh human semen samples to direct cell phone exposure (Erogul *et al.*, 2006; Agarwal *et al.*, 2009) or to radiofrequency radiation levels comparable with those from typical use of cell phones (Falzone *et al.*, 2008; De Iuliis *et al.*, 2009) and most (Erogul *et al.*, 2006; Agarwal *et al.*, 2009; De Iuliis *et al.*, 2009), but not all (Falzone *et al.*, 2008), have reported some adverse effects on semen quality, including two studies that reported slight increases in the percentage of sperm with DNA fragmentation (Gorpinchenko *et al.*, 2014; Zalata *et al.*, 2015). However, the *in-vitro* exposures in these experimental studies are unlikely to be comparable with *in-vivo* exposures from typical cell phone use, because they are shorter-term exposures that occur directly to semen after ejaculation. Several observational studies have evaluated self-reported cell phone use (current use, hours of use, daily talk time) in relation to semen quality, including sperm concentration, count, motility, viability, and DNA fragmentation (Fejes *et al.*, 2005; Agarwal *et al.*, 2008; Gutschi *et al.*, 2011; Rago *et al.*, 2013). Proximity to the testes was evaluated in some (Fejes *et al.*, 2005; Rago *et al.*, 2013), but not all observational studies (Agarwal *et al.*, 2008; Gutschi *et al.*, 2011). Two meta-analyses (Adams *et al.*, 2014; Liu *et al.*, 2014) of cell phone exposure and semen quality found small differences in the percent motile sperm in both experimental and observational studies, but little consistent relation with other semen parameters. One study found slight increases in DNA fragmentation among men who used the phone for more than 4 h/day and among those who reported carrying the phone in the front pants pocket (Rago *et al.*, 2013).

Two recent studies, not included in either meta-analysis, reported mixed findings (Zhang et al., 2016; Lewis *et al.*, 2017). Among 153 US men (350 semen samples) in an infertility clinic population (Lewis *et al.*, 2017), cell phone exposure (hours/day of use, pants pocket vs. other location, and use of a headset/earpiece) was not consistently associated with any semen parameters. The study lacked detail on hours of exposure in the front pants pocket and included only a small number of men, among whom a large proportion (31%) reported no cell phone use. A cross-sectional study of 794 college-aged men in China reported slight reductions in mean semen volume, sperm concentration and total sperm count with increasing duration of time/day spent talking on a cell phone. However, there was little association with sperm motility, and few consistent associations between any of the semen quality parameters and front pants pocket exposure compared with other locations (Zhang *et al.*, 2016).

We found a stronger reduction in fecundability among normal weight men compared with overweight men. It is possible that the distance between the testes and a cell phone carried in the front pants pocket is larger in overweight men, either due to different pants styles or to increased adipose tissue in the abdominal area, leading to lower radiofrequency exposures. It is also possible that adipose tissue serves as a physical barrier, thereby intercepting radiofrequency waves and reducing the exposure of the testes (Vale *et al.*, 2018).

A major challenge in studying cell phone use is exposure misclassification, partly due to the difficulty in measuring the amount of time cell phones are carried in different body locations. Such misclassification, presuming it is non-differential, would tend to attenuate our estimates for dichotomous exposures and extreme exposure categories (e.g. ≥8 vs. 0 h in the front pants pocket). In addition to inaccuracies in reporting hours/day carrying a cell phone in each location, exposure to radiofrequency radiation varies by characteristics that we did not collect information on, including type, brand and generation of phone, distance from the base station, use of earpieces and protective covers, proximity of the phone to the testes during use, and indoor versus outdoor use (Kelsh *et al.*, 2011). The extent to which exposures are greater during actual phone use (as opposed to when the phone is turned on but not in use) likely further contributes to exposure misclassification. Distance between a phone carried in the front pants pocket and the testes may also vary based on pants style. In addition, we were not able to account for other sources of radiofrequency radiation in the environment (Chiaramello *et al.*, 2019). In addition, we collected exposure information from male participants at baseline only. If men changed their cell phone habits (e.g. switched to back pants pocket or decreased total hours of use) as pregnancy attempt time increased, the results would have been attenuated because subfertile men would have been misclassified into lower exposure categories. However, results among men with <3 cycles of attempt time at study entry, in whom this possibility is less likely, were not largely or consistently different from the main results in either cohort.

We adjusted for many covariates in the fecundability analyses, but due to smaller numbers, we could adjust only for a few variables in the semen analyses. In both analyses, covariate adjustment had little effect on the estimates. Nevertheless, residual confounding remains possible. For example, location and use of cell phones may vary by type of occupation, and it is possible that men with occupational exposures affecting semen quality are less likely to carry their phone in their front pants pocket.

In summary, we found little consistent evidence of an overall association between male cell phone use and either fecundability or semen quality. In both cohorts, carrying the phone in the front pants pocket was associated with lower fecundability among leaner men (BMI <25), although the association did not increase with longer exposures.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

The data underlying this article cannot be shared publicly due to the privacy of individuals who participated in the study. The data will be shared on reasonable request to the corresponding author.

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Authors' roles

LAW, EEH, KJR, AKW, EMM, and HTS were responsible for study design, development and implementation of the study cohorts. EEH drafted the manuscript. SKW performed statistical analyses. All authors were responsible for critical interpretation of the results and revision of the manuscript. All authors approved the final version of the manuscript.

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Conflict of interest

In the last three years, PRESTO has received in-kind donations from Sandstone Diagnostics (for semen kits), Swiss Precision Diagnostics (home pregnancy tests), Kindara.com (fertility app), and FertilityFriend.com (fertility app). Dr. L.A.W. is a fibroid consultant for Abbvie Inc. Dr. H.T.S. reports that the Department of Clinical Epidemiology is involved in studies with funding from various companies as research grants to and administered by Aarhus University. None of these studies are related to the current study. Dr. M.L.E. is an advisor to Sandstone Diagnostics, Ro, Dadi, Hannah, and Underdog. Dr. G.J.S. holds ownership in Sandstone Diagnostics Inc., developers of the Trak Male Fertility Testing System. In addition, Dr. G.J.S. has a patent pending related to Trak Male Fertility Testing System issued.

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