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Impact of men's dairy intake on assisted reproductive technology outcomes among couples attending a fertility clinic

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SUMMARY

Intake of full-fat dairy has been linked to lower semen quality but whether this leads to decreased fertility is unknown. To address this question, we prospectively evaluated the association of men's dairy intake with treatment outcomes of subfertile couples undergoing assisted reproductive technology (ART). We followed 142 men from couples undergoing infertility treatment with ART

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AUTHOR CONTRIBUTIONS
RH and JEC designed the research study; WX and YHC analyzed data; JBF, RH, and JEC contributed to the acquisition of data; JEC and WX wrote the manuscript; WX, YHC, MA, PLW, JBF, CT, IS, JEC and RH were involved in the critical revision of the manuscript and approval of the submitted and final versions.

DISCLOSURES
Myriam C. Afeiche is an employee of the Nestlé Research Center. The authors declare that there is no conflict of interest.

at an academic fertility center between 2007 and 2014. Couples completed dietary assessments prior to treatment, and the female partners underwent a total of 248 ART cycles. Multivariable generalized linear mixed models were used to examine the association of dairy intake with fertilization, implantation, clinical pregnancy and live birth rates adjusting for age, body mass index (BMI), smoking status, total exercise time, dietary patterns, alcohol, caffeine, total energy intake, and female dairy intake. Intake of dairy foods, regardless of their fat content, was not associated with fertilization, implantation, clinical pregnancy, or live birth rates. The adjusted live birth rates (95% Confidence Interval) for couples in increasing quartiles of men's dairy intake were 0.42 (0.25, 0.60), 0.25 (0.13, 0.42), 0.26 (0.15, 0.41), and 0.44 (0.27, 0.63) (p, linear trend = 0.73). Results remained similar after adjustment for female partner intake of dairy foods. Overall, men's dairy intake was not associated with treatment outcomes of couples undergoing ART.

Keywords

Cohort studies; men; dairy intake; infertility; assisted reproductive technology

INTRODUCTION

In the United States, infertility is a common problem, and approximately 15 percent of couples have difficulty becoming pregnant (Thoma et al., 2013). Male factors contribute to nearly half of the infertility cases (Thonneau et al., 1991). However, whether potential modifiable risk factors play a role in male infertility is still unclear. Increasing evidence indicates that diet may affect male reproductive function as evidenced by reports of associations between dietary factors and semen quality parameters (Chavarro et al., 2008; Jensen et al., 2010; Attaman et al., 2012; Mínguez-Alarcón et al., 2012). In addition, the results of a recent systematic review and meta-analysis of randomized trials suggests a positive effect on semen quality and infertility treatment outcomes in subfertile men treated with antioxidant supplementation (Showell et al., 2014).

Intake of dairy foods has garnered interest as a potential risk factor for male factor infertility (Davaasambuu et al., 2001). Dairy products contain measurable amounts of naturally occurring estrogens, accounting for 60%-80% of exposure to environmental estrogens in Western countries (Hartmann et al., 1998), and other pregnancy hormones (Pape-Zambito et al., 2010) that may be related to lower semen quality (Rozati et al., 2002). In addition, dairy foods contain environmental contaminants such as pesticides and chlorinated pollutants (Schaum et al., 2003), that have been previously associated with lower semen quality (Meeker & Hauser, 2010). Furthermore, full-fat dairy foods are an important source of saturated fat, which has been previously related to lower sperm counts among young, healthy men as well as among men from subfertile couples (Attaman et al., 2012; Jensen et al., 2013). We previously reported that full-fat dairy intake was associated with a lower percentage of morphologically normal sperm and lower progressive motility among healthy young men (Afeiche et al., 2013), and low-fat dairy intake was related to higher sperm concentrations and progressive motility among subfertile men (Afeiche et al., 2014). Moreover, other researchers have noted associations between greater intake of dairy with oligoasthenoteratospermia and asthenospemia (Mendiola et al., 2009; Eslamian et al., 2012).

It is well known, however, that conventional semen parameters do not adequately predict fertility in natural or assisted conception (Jedrzejczak et al., 2008; Buck et al., 2014). As a result, it remains unclear whether the recently described variations in semen quality seen in relation to dairy food intake translate into differences in fertility potential. To address this issue, we examined the association of men's dairy intake with infertility treatment outcomes of subfertile couples undergoing assisted reproductive technology (ART).

MATERIALS AND METHODS

Study Population

Subfertile couples presenting for evaluation and treatment to the Massachusetts General Hospital (MGH) Fertility Center were invited to participate in the Environment and Reproductive Health (EARTH) Study, an ongoing study of environmental factors and fertility (Mok-Lin et al., 2010). Men (18-55 years) and women (18-45 years) using their own gametes for ART during infertility treatment were eligible. Between 2007 and 2014, 390 men were recruited for this study, of which 241 (62%) men completed a validated food frequency questionnaire (FFQ). Of these 241 men, 46 had female partners who did not join the study; 44 had female partners who had not undergone any ART cycles by July 2014, and 9 had female partners who had started an ART cycle before men's diet was assessed. After these exclusions, there were 142 men whose female partners underwent a total of 248 ART cycles (in vitro fertilization [IVF] with either conventional insemination or intracytoplasmic sperm injection [ICSI]). Of these, 130 men also had dietary information available on their female partner, with a total of 219 corresponding ART cycles. At enrollment, trained study staff measured height and weight of each participant who completed a general health questionnaire including demographics, lifestyle, and reproductive history. This study was approved by the Human Subject Committees at the Harvard T.H. Chan School of Public Health and MGH. Informed consent was obtained from all participants.

Dietary Assessment

Participants completed a previously validated 131-item FFQ (Rimm et al., 1992). They were asked to report how often, on average, they had consumed specific food during the past year. In a separately published validation study, the de-attenuated correlation coefficient comparing FFQ-reported intakes with intakes obtained from the 1-year average of prospectively collected diet ranged from 0.52 for cottage cheese to 0.88 for skim milk (Feskanich et al., 1993). The FFQ had nine categories for intake frequency, from never to two or more servings/day. In the FFQ, there were 15 questions that addressed dairy food intake. The nutrient content of each food and the specified portion size was obtained from a database at the United States Department of Agriculture (USDA, 2012). Full-fat dairy intake was defined as the sum of whole milk, cream, ice cream, and cheese. Low-fat dairy was defined as the sum of low-fat milk, yogurt, and cottage cheese. Total dairy food intake was defined as the sum of full-fat and low-fat dairy (Afeiche et al., 2014). Two dietary patterns were identified using principal component analysis: the Prudent pattern and the Western pattern, as previously described (Gaskins et al., 2012). For each pattern, a summary score was calculated to reflect how closely each participant adhered to the patterns, with higher scores indicating higher adherence to the respective dietary pattern.

Clinical Procedures and Assessment of Outcomes

Women underwent one of three ovarian stimulation treatment protocols for IVF: (1) luteal phase GnRH-agonist protocol; (2) GnRH-antagonist protocol; or (3) follicular phase GnRH-agonist/flare protocol. Briefly, on day three of induced menses, treatment with gonadotropins was initiated, and the GnRH agonist or antagonist was continued or started according to the usual ovarian stimulation protocols (Colaci et al., 2012). Oocyte retrieval was completed when transvaginal ultrasound showed at least three dominant follicles (≥16mm), and serum estradiol reached at least 800pg/ml. Oocytes were classified by embryologists as germinal vesicle, metaphase I(MI), metaphase II(MII), or degenerated. Oocytes underwent either conventional IVF or ICSI as clinically specified. At our center, ICSI is typically recommended in cases of severe teratospermia (≤2% normal morphology), low total motile count (<1 M) after swim up or gradient separation, or prior failed fertilization with conventional insemination. Fertilized oocytes were classified as normally fertilized if they had two pronuclei. After an embryo was transferred, clinical outcomes were measured. Successful implantation was defined as an elevation in plasma β-hCG levels above 6 IU/L measured two weeks after embryo transfer. The confirmation of an intrauterine pregnancy by ultrasound at 6 weeks was considered clinical pregnancy. Live birth was defined as the birth of a neonate on or after 24 weeks gestation.

Statistical Analysis

Men were categorized into quartiles according to total dairy intake. To test for differences in demographic, reproductive, and dietary characteristics across quartiles, we used a Kruskal-Wallis test for continuous variables and an extended Fisher's exact test for categorical variables. Multivariable generalized linear mixed models with a random intercept, binominal distribution, and logit link function were used to examine the association of dairy intake with fertilization and clinical outcomes, while accounting for multiple treatment cycles per couple and adjusting for other covariates. Tests for linear trend were performed by modeling intake as a continuous variable where each man was assigned the median intake of the quartile category he was assigned. All results were presented as population marginal means, adjusted for the covariates in the model (Searle et al., 1980). Confounding was evaluated using previous knowledge on biological relevance. Covariates considered in this way in all models included: age (continuous), body mass index (BMI, continuous), total exercise time (continuous), two dietary patterns (continuous), alcohol (continuous), caffeine (continuous), total energy intake (continuous), female age (continuous), female dairy intake (continuous), and smoking status (never smoker, past smoker, current smoker). We first ran models adjusted for all of the above-mentioned covariates (except female dairy intake), then ran a second model taking into account female dairy intake. To evaluate whether the relations between dairy intake and ART outcomes differed by mode of insemination (conventional vs. ICSI), we introduced a multiplicative interaction term to the fully adjusted multivariable model. Similarly, we assessed effect modification of dietary associations with fertilization rate and live birth rate by men's median age (<38 vs.≥38 years), smoking status (ever vs. never smokers) and BMI (<25 kg/m^2 vs. ≥25 kg/m^2). Statistical analyses were performed using Statistical Analysis Software (SAS) version 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

The study population consisted of 142 men whose female partners underwent a total of 248 ART cycles. The men's mean (SD) age and BMI were 37.2 (4.6) years and 27.0 (3.8) kg/m^2; most men were Caucasian (92%) and the majority had never smoked (65%). Thirty five percent (35%) of the couples received a primary diagnosis of male factor infertility. The participant's female partners had a mean (SD) age of 35.5 (3.9) years and BMI of 23.7 (4.0) kg/m^2.

Intake of cheese (38%) and low-fat milk (24%) accounted for more than half of the total dairy food intake. Only one man reported not consuming any dairy food. Men who consumed more dairy foods had higher intake of total calories, dairy protein, dairy fat, saturated fat, and lower intake of monounsaturated fats. Dairy intake was positively related to greater adherence scores for the Prudent dietary pattern. The men with a higher intake of dairy food were also likely to spend more time exercising (Table 1). The correlation between men's total dairy food intake with that of their female partner's was relatively weak ($r_{spearman}$=0.19). Other baseline characteristics were not associated with men's total dairy intake.

Total dairy food intake was not associated with fertilization rates. Results were similar when conventional insemination and ICSI cycles were examined separately, when low-fat and full-fat dairy foods were considered separately and when results were further adjusted for female partner intake of dairy foods (Table 2).

We then examined the relation of men's dairy intake with implantation, clinical pregnancy, and live birth rates. Men's total dairy intake, as well as intake of full-fat and low-fat dairy, was not associated with implantation, clinical pregnancy or live birth rates per initiated ART cycle (Table 3) or per embryo transfer (Table 4). Results were similar when ICSI and conventional IVF cycles were examined separately (Supplemental tables 1 and 2). In addition, there was no evidence of effect modification by men's age, smoking or BMI (P, heterogeneity >0.10 in all cases).

DISCUSSION

In this prospective cohort study of male partners of couples undergoing infertility treatment, we found no evidence that intake of total dairy foods was related to ART outcomes. These null findings stand in contrast to a growing literature finding consistent associations between dairy food intake and semen quality parameters as proxy measures of male fertility (Mendiola et al., 2009; Eslamian et al., 2012; Afeiche et al., 2013; Afeiche et al., 2014). This dichotomy further highlights the fact that semen quality is a poor predictor of fertility (Jedrzejczak et al., 2008; Christina et al., 2014) and that risk factors for poor semen quality are not necessarily risk factors for poor reproductive male performance (Gaskins et al., 2014; Mínguez-Alarcón et al., 2015).

The literature on the relation between men's dairy intake with direct measures of fertility is scarce. In agreement with our findings, Braga et al. found that in couples undergoing ICSI, the consumption of men's dairy foods was not associated with fertilization, implantation, and clinical pregnancy rates (Braga et al., 2012). Nevertheless, several studies have reported on the relation between dairy intake and semen quality parameters (Mendiola et al., 2009; Eslamian et al., 2012; Afeiche et al., 2013; Afeiche et al., 2014). We previously found in this same cohort that low-fat dairy intake was related to higher sperm concentrations and progressive motility (Afeiche et al., 2014), and full-fat dairy intake was associated with lower sperm morphology and lower progressive motility among healthy young men (Afeiche et al., 2013). In addition, Eslamian et al. found that increased intake of dairy products was associated with a significantly higher risk of asthenozoospermia (Eslamian et al., 2012), and Mendiola et al. reported that there was significantly higher intake of dairy products among oligoasthenoteratospermic patients (Mendiola et al., 2009). Because of the general scarcity of data regarding the relation of diet, in general, and of dairy food intake, in particular, with markers of male reproductive capacity, it is important that these relations are further evaluated in large prospective studies of couples planning pregnancy with or without medical intervention.

There are multiple possible explanations to describe the discordance between findings related to semen quality versus outcomes of ART. First, it is possible that the modest effects of dairy foods on semen quality are inconsequential in contrast to the large positive effects of ART itself. Additional studies addressing the effect of men's dairy food intake on couple's fertility among those trying to conceive naturally could shed light on this possibility. It is also possible that this discordance simply reflects the poor performance of semen quality parameters as predictors of fertility (Jedrzejczak et al., 2008; Christina & Ronald, 2014). In fact, similar dichotomies have been identified for the effect of male physical activity (Gaskins et al., 2014; Gaskins et al., 2015) and soy intake (Chavarro et al., 2008; Xia et al., 2013; Mumford et al., 2014; Mínguez-Alarcón et al., 2015) on ART outcomes. This second possibility has important implications for practice and research in reproductive medicine and may signal a need to abandon crude markers of men's contribution to couples' fertility and instead move towards the identification, validation and incorporation of more functional markers with greater diagnostic and prognostic power.

Our study has some limitations. First, because only dietary assessment was performed, diet during the relevant etiologic window may have been misclassified over time with misclassification being highest for couples with the least successful treatment outcomes. If error is indeed highest for couples with the lowest success, a spurious inverse relation would have been expected. On the other hand, if misclassification is independent of treatment outcome, attenuation of the results towards the null would be expected. Second, it may not be possible to extrapolate the findings to a general population that conceives without medical intervention. Nevertheless, couples in our study are comparable to other couples undergoing fertility treatment with ART in the United States (Chandra et al., 2014), and the findings may thus be generalizable to couples undergoing infertility treatment. The fact that the range of total dairy intake observed in this study is comparable to that of adult men in the USA (Beydoun et al., 2008) further supports the generalizability of our data to this subgroup of men. Low statistical power may have played a role in some of the null findings. Our study was sufficiently powered to detect differences of 27% in live birth rates between the top and bottom quartiles of dairy food intake. However the observed differences in live birth rates between top and bottom quartiles of total dairy intake (2%) suggest that a true lack of association rather than lack of statistical power accounted for the null findings. Of all the associations evaluated, only the associations between intake of full-fat dairy and live births (adjusted difference 16%) may have been affected by low statistical power. Strengths of our study include the prospective design and the use of a previously validated FFQ. Furthermore, using more direct and objective measures of male fertility potential, including fertilization, implantation, clinical pregnancy, and live birth rates, is a novel approach that improves on the traditional semen quality parameters as a proxy for male fertility.

In summary, men's intake of dairy food was not associated with ART fertilization, implantation, clinical pregnancy or live birth rates in a prospective cohort study. Our study expands the understanding of the relationship between diet and markers of male fertility. However, as data on the relationship between dairy food and male reproductive potential remains limited, further research is needed to expand its role in human reproduction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

Afeiche MC, Williams PL, Mendiola J, Gaskins AJ, Jorgensen N, Swan SH, Chavarro JE. Dairy food intake in relation to semen quality and reproductive hormone levels among physically active young men. Hum Reprod. 2013; 28:2265–75. [PubMed: 23670169]

Afeiche MC, Bridges ND, Williams PL, Gaskins AJ, Tanrikut C, Petrozza JC, Hauser R, Chavarro JE. Dairy intake and semen quality among men attending a fertility clinic. Fertil Steril. 2014; 101:1280–7. [PubMed: 24636397]

Attaman JA, Toth TL, Furtado J, Campos H, Hauser R, Chavarro JE. Dietary fat and semen quality among men attending a fertility clinic. Hum Reprod. 2012; 27:1466–74. [PubMed: 22416013]

Beydoun MA, Gary TL, Caballero BH, Lawrence RS, Cheskin LJ, Wang Y. Ethnic differences in dairy and related nutrient consumption among US adults and their association with obesity, central obesity, and the metabolic syndrome. The American Journal of Clinical Nutrition. 2008; 87:1914–1925. [PubMed: 18541585]

Braga DP, Halpern G, Figueira RC, Setti AS, Laconelli AJ, Borges EJ. Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection outcomes. Fertil Steril. 2012; 97:53–9. [PubMed: 22078783]

Buck Louis GM, Sundaram R, Schisterman EF, Sweeney A, Lynch CD, Kim S, Maisog JM, Gore-Langton R, Eisenberg ML, Chen Z. Semen quality and time to pregnancy: the Longitudinal Investigation of Fertility and the Environment Study. Fertil Steril. 2014; 101:453–62. [PubMed: 24239161]

Chandra A, Copen CE, Stephen EH. Infertility service use in the United States: data from the National Survey of Family Growth, 1982-2010. Natl Health Stat Report. 2014; 73:1–21. [PubMed: 24467919]

Chavarro JE, Toth TL, Sadio SM, Hauser R. Soy food and isoflavone intake in relation to semen quality indicators among men from an infertility clinic. Hum Reprod. 2008; 23:2584–90. [PubMed: 18650557]

Christina W, Ronald SS. Limitations of semen analysis as a test of male fertility and anticipated needs from newer tests. Fertil Steril. 2014; 102:1502–1507. [PubMed: 25458617]

Colaci DS, Afeiche MC, Gaskins AJ, Wright DL, Toth TL, Tanrikut C, Hauser R, Chavarro JE. Men's body mass index in relation to embryo quality and clinical outcomes in couples undergoing in vitro fertilization. Fertil Steril. 2012; 98:1193–9 e1. [PubMed: 22884013]

Davaasambuu G, Wang PY, Qin LQ, Hoshi K, Sato A. Is milk responsible for male reproductive disorders? Med Hypotheses. 2001; 57:510–4. [PubMed: 11601881]

Eslamian G, Amirjannati N, Rashidkhani B, Sadeghi MR, Hekmatdoost A. Intake of food groups and idiopathic asthenozoospermia: a case-control study. Hum Reprod. 2012; 27:3328–36. [PubMed: 22940769]

Feskanich D, Rimm EB, Giovannucci EL, Colditz GA, Stampfer MJ, Litin LB, Willett WC. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Dietetic Assoc. 1993; 93:790–6.

Gaskins AJ, Colaci DS, Mendiola J, Swan SH, Chavarro JE. Dietary patterns and semen quality in young men. Hum Reprod. 2012; 27:2899–907. [PubMed: 22888168]

Gaskins AJ, Afeiche MC, Hauser R, Williams PL, Gillman MW, Tanrikut C, Petrozza JC, Chavarro JE. Paternal physical and sedentary activities in relation to semen quality and reproductive outcomes among couples from a fertility center. Hum Reprod. 2014; 29:2575–82. [PubMed: 25164027]

Gaskins AJ, Mendiola J, Afeiche M, Jørgensen N, Swan SH, Chavarro JE. Physical activity and television watching in relation to semen quality in young men. Br J Sports Med. 2015; 49:265–70. [PubMed: 23380634]

Hartmann S, Lacorn M, Steinhart H. Natural occurrence of steroid hormones in food. Food Chem. 1998; 62:7–20.

Jedrzejczak P, Taszarek-Hauke G, Hauke J, Pawelczyk L, Duleba AJ. Prediction of spontaneous conception based on semen quality indicators. Int J Androl. 2008; 31:499–507. [PubMed: 17651398]

Jensen TK, Swan SH, Skakkebaek NE, Rasmussen S, Jorgensen N. Caffeine intake and semen quality in a population of 2,554 young Danish men. Am J Epidemiol. 2010; 171:883–91. [PubMed: 20338976]

Jensen TK, Heitmann BL, Jensen MB, Halldorsson TI, Andersson AM, Skakkebaek NE, et al. High dietary intake of saturated fat is associated with reduced semen quality among 701 young Danish men from the general population. Am J Clin Nutr. 2013; 97:411–8. [PubMed: 23269819]

Meeker JD, Hauser R. Exposure to polychlorinated biphenyls (PCBs) and male reproduction. Syst Biol Reprod Med. 2010; 56:122–131. [PubMed: 20377311]

Mendiola J, Torres-Cantero AM, Moreno-Grau JM, Ten J, Roca M, Moreno-Grau S, Bernabeu R. Food intake and its relationship with semen quality: a case-control study. Fertil Steril. 2009; 91:812–8. [PubMed: 18314116]

Mínguez-Alarcón L, Mendiola J, Lopez EJ, Sarabia CL, Vivero SG, Vioque J, Navarrete EM, Torres AC. Dietary intake of antioxidant nutrients is associated with semen quality in young university students. Hum Reprod. 2012; 27:2807–14. [PubMed: 22752607]

Mínguez-Alarcón L, Afeiche MC, Chiu YH, Vanegas JC, Williams PL, Tanrikut C, Toth TL, Hauser R, Chavarro JE. Male soy food intake was not associated with in vitro fertilization outcomes among couples attending a fertility center. Andrology. Jun 20.2015 doi:10.1111/andr.12046.

Mok-Lin E, Ehrlich S, Williams PL, Petrozza J, Wright DL, Calafat AM, Ye X, Hauser R. Urinary bisphenol A concentrations and ovarian response among women undergoing IVF. Int J Androl. 2010; 33:385–93. [PubMed: 20002217]

Mumford SL, Sundaram R, Schisterman EF, Sweenev AM, Barr DB, Rybak ME, Maisog JM, Parker DL, Pfeiffer CM, Louis GM. Higher urinary lignan concentrations in women but not men are positively associated with shorter time to pregnancy. J Nutr. 2014; 144:352–8. [PubMed: 24401816]

Pape-Zambito DA, Roberts RF, Kensinger RS. Estrone and 17b-estradiol concentrations in pasteurized-homogenized milk and commercial dairy products. J Dairy Sci. 2010; 93:2533–40. [PubMed: 20494161]

Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, Willett WC. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol. 1992; 135:1114–26. [PubMed: 1632423]

Rozati R, Reddy PP, Reddanna P, Mujtaba R. Role of environmental estrogens in the deterioration of male factor fertility. Fertil Steril. 2002; 78:1187–1194. [PubMed: 12477510]

Schaum J, Schuda L, Wu C, Sears R, Ferrario J, Andrews K. A national survey of persistent, bioaccumulative, and toxic (PBT) pollutants in the United States milk supply. J Expo Anal Environ Epidemiol. 2003; 13:177. [PubMed: 12743612]

Searle SR, Speed FM, Milliken GA. Population marginal means in the linear model: an alternative to least square means. Am Stat. 1980; 4:216–221.

Showell MG, Mackenzie PR, Brown J, Yazdani A, Stankiewicz MT, Hart RJ. Antioxidants for male subfertility. Cochrane Database Syst Rev. 2014; 12:CD007411. [PubMed: 25504418]

Thoma ME, McLain AC, Louis JF, King RB, Trumble AC, Sundaram R, Buck Louis GM. Prevalence of infertility in the United States as estimated by the current duration approach and a traditional constructed approach. Fertil Steril. 2013; 99:1324–31. [PubMed: 23290741]

Thonneau P, Marchand S, Tallec A, Ferial ML, Ducot B, Lansac J, Lopes P, Tabaste JM, Spira A. Incidence and main causes of infertility in a resident population (1,850,000) of three French regions (1988–1989). Hum Reprod. 1991; 6:811–6. [PubMed: 1757519]

USDA/Agricultural Research Service. USDA National Nutrient Database for Standard Reference, Release 25. 2012. Nutrient data laboratory home page. Available from: http://www.ars.usda.gov/ba/bhnrc/ndl

Xia Y, Chen M, Zhu P, Lu C, Fu G, Zhou X, Chen D, Wang H, Hang B, Wang S, Zhou Z, Sha J, Wang X. Urinary phytoestrogen levels related to idiopathic male infertility in Chinese men. Environ Int. 2013; 59:161–7. [PubMed: 23820060]

Table 1

Baseline demographic, nutritional, and reproductive characteristics of study participants by quartile of total dairy intake from the EARTH study

	Q1	Q2	Q3	Q4	P
N	35	36	36	35	
Median, serving/day	0.97	1.67	2.19	3.32	
Range(min, max)	0, 1.31	1.39, 1.86 Median (IQR) or n (%)	1.87, 2.73	2.75, 5.77	
Men's demographics					
Age, years	37.9 (34.3, 40.8)	37.3 (33.3, 39.1)	38.0 (35.6, 41.4)	35.1 (31.7, 40.9)	0.22
BMI, kg/m^2	25.4 (22.7, 28.9)	27.7 (24.7, 29.4)	27.1 (24.6, 29.0)	26.9 (23.8, 28.6)	0.17
White, n (%)	29 (82.9)	35 (97.2)	33 (91.7)	33 (94.3)	0.18
Smoking status, *n* (%)					0.02
Never smokers	26 (74.3)	19 (52.8)	22 (61.1)	26 (74.3)	
Past smokers	8 (22.9)	17 (47.2)	10 (27.8)	5 (14.3)	
Current smokers	1 (2.8)	0 (0.0)	4 (11.1)	4 (11.4)	
Moderate or vigorous exercise, h/w	2.5 (0.2, 7.0)	2.9 (1.7, 5.7)	4.6 (0.9, 6.7)	5.3 (1.9, 7.5)	0.36
Total exercise, h/w	3.4 (1.5 , 10.4)	4.4 (2.5, 9.6)	7.0 (1.9, 11.0)	7.5 (5.0, 11.5)	0.07
Diet					
Prudent pattern score	−0.53 (−1.02, −0.02)	−0.35 (−0.75, 0.50)	−0.04 (−0.51, 0.70)	0.13 (−0.49, 0.79)	0.03
Western pattern score	−0.53 (−0.95, 0.30)	−0.05 (−0.57, 0.55)	−0.16 (−0.40, 0.53)	0.44 (−0.73, 1.26)	0.07
Folic acid, μg/d	343.0 (163.0, 531.0)	356.0 (150.5, 631.0)	446.5 (230.5, 512.0)	255.0 (152.0, 484.0)	0.71
B12, μg	8.36 (4.16, 11.79)	10.79 (6.12, 15.65)	10.53 (7.20, 13.91)	8.20 (6.16, 11.71)	0.14
Vitamin D, IU	398.6 (116.3, 612.7)	370.7 (205.0, 611.5)	426.0 (271.9, 580.8)	332.3 (245.8, 459.9)	0.76
Total carbohydrate, % energy	48.6 (41.1, 57.2)	46.9 (42.4, 51.8)	46.0 (42.1, 51.9)	47.6 (41.8, 53.5)	0.82
Total protein, % energy	15.6 (14.2, 17.6)	16.6 (14.7, 18.1)	16.4 (15.5, 18.8)	15.4 (14.2, 17.5)	0.10
Dairy protein, % energy	2.36 (1.52, 2.73)	3.05 (2.43, 3.55)	3.37 (2.91, 3.83)	4.62 (3.59, 5.81)	<0.0001
Total fat, % energy	32.6 (28.3, 36.8)	32.3 (28.4, 35.3)	32.4 (27.6, 35.8)	31.9 (26.2, 35.4)	0.95
Alcohol, g/d	6.67 (2.01, 16.51)	14.38 (8.39, 20.31)	12.34 (4.22, 18.28)	14.27 (2.95, 35.66)	0.07
Caffeine, g/d	138.5 (74.6, 246.0)	243.1 (85.4, 273.3)	239.6 (99.7, 268.0)	163.4 (111.3, 294.6)	0.59
Total energy intake, kcal/d	1571 (1210, 2052)	2013 (1629, 2244)	2039 (1754, 2362)	2367 (1977, 2864)	<0.0001
Dairy fat, % energy	5.12 (3.33, 6.60)	6.64 (5.11, 8.31)	7.10 (5.11, 9.89)	9.21 (6.90, 11.46)	<0.0001
Saturated fat, % energy	9.88 (8.22, 10.92)	10.52 (8.67, 11.58)	11.05 (8.81, 12.44)	11.52 (9.32, 13.10)	0.02

	Q1	Q2	Q3	Q4	P
Monounsaturated fat, % energy	13.18 (10.33, 14.69)	12.53 (11.64, 14.78)	12.27 (10.59, 13.93)	11.98 (9.54, 13.50)	0.47
Polyunsaturated fat, % energy	6.41 (5.51, 8.14)	5.96 (5.04, 7,14)	5.80 (5.19, 6.24)	5.36 (4.35, 6.22)	0.002
Total *trans* fat, % energy	1.04 (0.75, 1.17)	0.97 (0.76, 1.22)	0.94 (0.78, 1.19)	1.00 (0.85, 1.21)	0.96
Reproductive History					
History of varicocele, n (%)	3 (8.6)	6 (16.7)	2 (5.6)	4 (11.4)	0.48
History of cryptorchidism, n (%)	1 (2.9)	0 (0.0)	3 (8.3)	4 (11.4)	0.11
Primary infertility diagnosis					0.23
Male factor	17 (48.6)	12 (33.3)	6 (16.7)	13 (37.1)	
Female factor	7 (20.0)	11 (30.6)	14 (38.9)	10 (28.6)	
Diminished ovarian reserve	4 (11.4)	2 (5.7)	2 (5.6)	4 (11.4)	
Tubal disease	1 (2.9)	2 (5.7)	3 (8.3)	3 (8.6)	
Ovulatory dysfunction	0 (0.0)	4 (11.4)	7 (19.4)	2 (5.7)	
Other disease	2 (5.7)	3 (8.6)	2 (5.6)	1 (2.9)	
Unexplained	11 (31.4)	13 (36.1)	16 (44.4)	12 (34.3)	
ICSI cycles, n (%)	17 (51.5)	17 (50.0)	12 (35.3)	15 (53.6)	0.44
Day 3 FSH Levels, IU/L	7.2 (6.1, 8.8)	6.7 (5.8, 8.9)	6.7 (5.6, 8.3)	7.3 (5.7, 8.6)	0.78
Initial stimulation protocol, n (%)					0.51
Luteal phase agonist	25 (71.5)	29 (80.6)	31 (86.1)	29 (82.8)	
Antagonist	6 (17.1)	3 (8.3)	2 (5.6)	5 (14.3)	
Flare	4 (11.4)	4 (11.1)	3 (8.3)	1 (2.9)	
No. of embryos transferred, n (%)					0.34
None	1 (2.9)	3 (8.3)	2 (5.6)	0 (0.0)	
1	7 (20.0)	5 (13.9)	5 (13.9)	5 (14.3)	
2	20 (57.1)	20 (55.6)	21 (58.3)	20 (57.1)	
≥3	6 (17.1)	7 (19.4)	7 (19.4)	3 (8.6)	
Egg donor or cryo cycle	1 (2.9)	1 (2.8)	1 (2.8)	7 (20.0)	
Embryo transfer day, n (%)					0.33
No embryos transferred	1 (2.9)	3 (8.3)	2 (5.6)	0 (0.0)	
Day2	1 (2.9)	2 (5.6)	2 (5.6)	1 (2.9)	
Day3	21 (60.0)	17 (47.2)	15 (41.6)	16 (45.7)	
Day5	11 (31.4)	13 (36.1)	16 (44.4)	11 (31.4)	

	Q1	Q2	Q3	Q4	P
Egg donor or cryo cycle	1 (2.8)	1 (2.8)	1 (2.8)	7 (20.0)	
Previous infertility exam, n (%)	27 (79.4)	31 (86.1)	31 (86.1)	24 (68.6)	0.24
Female Partner (N=130)					
Age, years	35.0 (33.0, 38.0)	35.0 (32.5, 39.0)	36.0 (33.0, 38.0)	34.0 (32.0, 39.0)	0.92
BMI, kg/m^2	22.0 (20.4, 25.8)	23.2 (21.0, 25.0)	23.8 (21.2, 26.6)	22.3 (20.9, 24.5)	0.33
Total dairy intake, sv/day	1.61 (0.93, 3.09)	1.92 (1.34, 2.48)	1.99 (1.43, 3.53)	2.14 (1.58, 3.10)	0.21
Prudent pattern score	−0.14 (−0.89, 0.23)	−0.11 (−0.71, 0.50)	−0.23 (−0.77, 0.00)	−0.23 (−0.74, 0.56)	0.60
Western pattern score	−0.25 (−0.88, 0.41)	−0.14 (−0.63, 0.42)	−0.09 (−0.68, 0.35)	−0.01 (−0.52, 0.23)	0.72

P values from Kruskal-Wallis test for continuous variables and Fisher's exact test for categorical variables. IQR=interquartile range, BMI=body mass index, sv=servings, h/w=hours/week. All variables use the measure for the first cycle.

Table 2

Association between men's dairy intake and fertilization rates in couples from the EARTH Study

	Adjusted mean fertilization rate (95% Confidence Interval)								
	Total cycles			Conventional IVF			ICSI		
	N	Model 1	Model 2	N	Model 1	Model 2	N	Model 1	Model 2
Number of cycles		**207 cycles**	**184 cycles**		**101 cycles**	**85 cycles**		**106 cycles**	**99 cycles**
Quartile intake of total dairy									
Q1 [0.00-1.31]	52	0.72 (0.63, 0.80)	0.74 (0.64, 0.82)	23	0.65 (0.47, 0.79)	0.66 (0.45, 0.83)	29	0.81 (0.71, 0.89)	0.82 (0.71, 0.89)
Q2 [1.39-1.86]	43	0.72 (0.64, 0.80)	0.71 (0.61, 0.79)	19	0.63 (0.48, 0.76)	0.60 (0.42, 0.76)	24	0.82 (0.71, 0.89)	0.81 (0.70, 0.88)
Q3 [1.86-2.73]	68	0.71 (0.64, 0.78)	0.70 (0.61, 0.78)	41	0.65 (0.53, 0.75)	0.60 (0.43, 0.75)	27	0.81 (0.72, 0.88)	0.80 (0.70, 0.87)
Q4 [2.75-5.77]	44	0.75 (0.66, 0.82)	0.74 (0.64, 0.82)	18	0.75 (0.60, 0.86)	0.73 (0.54, 0.86)	26	0.72 (0.58, 0.82)	0.72 (0.59, 0.82)
P trend		0.67	0.95		0.29	0.42		0.18	0.15
Quartile intake of full-fat dairy									
Q1 [0.00-0.59]	51	0.73 (0.64, 0.81)	0.74 (0.63, 0.82)	25	0.67 (0.50, 0.80)	0.65 (0.46, 0.81)	26	0.80 (0.69, 0.88)	0.80 (0.69, 0.88)
Q2 [0.61-1.04]	49	0.74 (0.66, 0.81)	0.74 (0.65, 0.81)	24	0.70 (0.55, 0.81)	0.68 (0.50, 0.83)	25	0.82 (0.72, 0.89)	0.81 (0.71, 0.88)
Q3 [1.06-1.71]	61	0.72 (0.64, 0.79)	0.71 (0.62, 0.79)	34	0.60 (0.48, 0.71)	0.53 (0.37, 0.69)	27	0.87 (0.79, 0.92)	0.86 (0.77, 0.92)
Q4 [1.73-5.45]	46	0.71 (0.62, 0.78)	0.71 (0.61, 0.79)	18	0.76 (0.61, 0.86)	0.77 (0.58, 0.89)	28	0.70 (0.58, 0.80)	0.70 (0.58, 0.80)
P trend		0.56	0.58		0.65	0.72		0.19	0.24
Quartile intake of low-fat dairy									
Q1 [0.00-0.24]	45	0.70 (0.61, 0.78)	0.71 (0.61, 0.80)	18	0.62 (0.44, 0.77)	0.63 (0.38, 0.82)	27	0.78 (0.67, 0.86)	0.78 (0.67, 0.86)
Q2 [0.26-0.63]	53	0.73 (0.64, 0.80)	0.72 (0.63, 0.80)	26	0.65 (0.49, 0.78)	0.63 (0.45, 0.79)	27	0.81 (0.70, 0.89)	0.80 (0.68, 0.88)
Q3 [0.65-1.10]	66	0.72 (0.64, 0.78)	0.70 (0.62, 0.78)	31	0.66 (0.53, 0.77)	0.62 (0.45, 0.77)	35	0.82 (0.72, 0.88)	0.79 (0.69, 0.87)
Q4 [1.12-3.54]	43	0.75 (0.66, 0.82)	0.76 (0.66, 0.84)	26	0.73 (0.58, 0.84)	0.73 (0.54, 0.87)	17	0.75 (0.61, 0.85)	0.77 (0.64, 0.86)
P trend		0.45	0.55		0.25	0.40		0.59	0.79

Abbreviations: ICSI, intra-cytoplasmic sperm injection; IVF, in vitro fertilization. BMI=body mass index

Model 1: adjusted for total energy intake, age, BMI, alcohol, caffeine, smoking status, total exercise time, Prudent dietary pattern, Western dietary pattern and female age; Model 2: adjusted for total energy intake, age, BMI, alcohol, caffeine, smoking status, total exercise time, Prudent dietary pattern, Western dietary pattern and female dairy intake.

Test for trend were performed using the median level of dairy in each quartile as a continuous variable in the model.

Table 3

Men's dairy intake in relation to adjusted rates of clinical outcomes per initiated ART cycle from the EARTH Study

		Implantation rate		Clinical pregnancy rate		Live birth rate	
		Model 1	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Number of cycles	**N**	**248 cycles**	**219 cycles**	**248 cycles**	**219 cycles**	**248 cycles**	**219 cycles**
Quartile intake of total dairy							
Q1 [0.00-1.31]	59	0.67 (0.48, 0.81)	0.69 (0.48, 0.84)	0.63 (0.45, 0.79)	0.65 (0.45, 0.81)	0.41 (0.25, 0.60)	0.45 (0.27, 0.65)
Q2 [1.39-1.86]	53	0.36 (0.21, 0.54)	0.37 (0.21, 0.57)	0.37 (0.22, 0.55)	0.37 (0.21, 0.57)	0.25 (0.13, 0.43)	0.24 (0.12, 0.42)
Q3 [1.86-2.73]	77	0.51 (0.36, 0.66)	0.54 (0.36, 0.71)	0.44 (0.30, 0.58)	0.49 (0.32, 0.66)	0.25 (0.14, 0.40)	0.29 (0.16, 0.47)
Q4 [2.75-5.77]	59	0.58 (0.40, 0.74)	0.61 (0.41, 0.78)	0.51 (0.34, 0.68)	0.56 (0.36, 0.73)	0.46 (0.28, 0.65)	0.45 (0.27, 0.65)
P trend		0.87	0.99	0.54	0.80	0.65	0.76
Quartile intake of full-fat dairy							
Q1 [0.00-0.59]	61	0.52 (0.33, 0.70)	0.52 (0.32, 0.72)	0.49 (0.31, 0.67)	0.49 (0.29, 0.69)	0.28 (0.15, 0.46)	0.28 (0.14, 0.47)
Q2 [0.61-1.04]	60	0.54 (0.36, 0.71)	0.54 (0.34, 0.73)	0.51 (0.34, 0.68)	0.52 (0.32, 0.70)	0.38 (0.22, 0.56)	0.39 (0.23, 0.59)
Q3 [1.06-1.71]	68	0.50 (0.35, 0.66)	0.52 (0.33, 0.70)	0.46 (0.31, 0.61)	0.50 (0.32, 0.68)	0.28 (0.17, 0.43)	0.30 (0.17, 0.47)
Q4 [1.73-5.45]	59	0.60 (0.42, 0.75)	0.66 (0.46, 0.81)	0.52 (0.36, 0.69)	0.59 (0.39, 0.76)	0.43 (0.27, 0.61)	0.48 (0.30, 0.67)
P trend		0.57	0.35	0.85	0.50	0.31	0.20
Quartile intake of low-fat dairy							
Q1 [0.00-0.24]	52	0.64 (0.45, 0.79)	0.71 (0.50, 0.85)	0.61 (0.43, 0.76)	0.68 (0.47, 0.83)	0.42 (0.26, 0.60)	0.49 (0.30, 0.69)
Q2 [0.26-0.61]	63	0.42 (0.26, 0.60)	0.44 (0.26, 0.64)	0.40 (0.25, 0.57)	0.42 (0.25, 0.61)	0.30 (0.17, 0.47)	0.31 (0.17, 0.49)
Q3 [0.63-1.10]	75	0.47 (0.31, 0.63)	0.50 (0.32, 0.68)	0.40 (0.26, 0.56)	0.43 (0.26, 0.61)	0.26 (0.15, 0.41)	0.28 (0.16, 0.45)
Q4 [1.12-3.54]	58	0.61 (0.42, 0.78)	0.62 (0.39, 0.80)	0.54 (0.36, 0.72)	0.58 (0.37, 0.77)	0.39 (0.23, 0.58)	0.38 (0.21, 0.59)
P trend		0.72	0.91	0.92	0.95	0.91	0.67

Model 1: included 248 cycles in 142 female partners of men studied, adjusted for total energy intake, age, BMI, alcohol, caffeine, smoking status, total exercise time, Prudent dietary pattern, Western dietary pattern and female age; Model 2: included 219 cycles in 130 female partners of men studied, adjusted for total energy intake, age, BMI, alcohol, caffeine, smoking status, total exercise time, Prudent dietary pattern, Western dietary pattern and female dairy intake.

Tests for trend were performed using the median level of dairy in each quartile as a continuous variable in the model.

Table 4

Men's dairy intake in relation to adjusted rates of clinical outcomes per embryo transfer from the EARTH Study

		Implantation rate		Clinical pregnancy rate		Live birth rate	
		Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Number of cycles	**N**	**232 cycles**	**205 cycles**	**232 cycles**	**205 cycles**	**232 cycles**	**205 cycles**
Quartile intake of total dairy							
Q1 [0.00-1.31]	59	0.69 (0.51, 0.83)	0.72 (0.52, 0.86)	0.66 (0.47, 0.80)	0.68 (0.48, 0.83)	0.43 (0.26, 0.61)	0.47 (0.29, 0.67)
Q2 [1.39-1.86]	53	0.42 (0.25, 0.60)	0.43 (0.25, 0.64)	0.42 (0.26, 0.60)	0.43 (0.25, 0.63)	0.29 (0.16, 0.48)	0.29 (0.15, 0.48)
Q3 [1.86-2.73]	77	0.55 (0.40, 0.69)	0.57 (0.39, 0.74)	0.47 (0.33, 0.62)	0.51 (0.34, 0.68)	0.27 (0.16, 0.43)	0.31 (0.17, 0.49)
Q4 [2.75-5.77]	59	0.59 (0.41, 0.75)	0.62 (0.42, 0.79)	0.52 (0.35, 0.69)	0.56 (0.37, 0.74)	0.47 (0.30, 0.65)	0.46 (0.28, 0.65)
P trend		0.76	0.79	0.44	0.62	0.71	0.90
Quartile intake of full-fat dairy							
Q1 [0.00-0.59]	61	0.54 (0.35, 0.72)	0.56 (0.35, 0.75)	0.50 (0.32, 0.68)	0.52 (0.32, 0.71)	0.29 (0.16, 0.47)	0.30 (0.16, 0.49)
Q2 [0.61-1.04]	60	0.60 (0.41, 0.76)	0.62 (0.41, 0.80)	0.57 (0.39, 0.73)	0.60 (0.39, 0.77)	0.43 (0.26, 0.62)	0.46 (0.27, 0.65)
Q3 [1.06-1.71]	68	0.52 (0.36, 0.68)	0.54 (0.35, 0.71)	0.47 (0.32, 0.62)	0.52 (0.34, 0.69)	0.29 (0.17, 0.44)	0.31 (0.18, 0.48)
Q4 [1.73-5.45]	59	0.64 (0.47, 0.79)	0.68 (0.48, 0.83)	0.56 (0.39, 0.72)	0.60 (0.41, 0.77)	0.47 (0.31, 0.64)	0.50 (0.32, 0.68)
P trend		0.52	0.49	0.83	0.67	0.28	0.28
Quartile intake of low-fat dairy							
Q1 [0.00-0.24]	52	0.66 (0.47, 0.81)	0.71 (0.50, 0.86)	0.63 (0.45, 0.78)	0.68 (0.47, 0.83)	0.44 (0.27, 0.61)	0.49 (0.30, 0.68)
Q2 [0.26-0.61]	63	0.45 (0.28, 0.63)	0.48 (0.29, 0.68)	0.43 (0.27, 0.60)	0.46 (0.28, 0.65)	0.32 (0.18, 0.50)	0.34 (0.19, 0.52)
Q3 [0.63-1.10]	75	0.53 (0.37, 0.69)	0.57 (0.37, 0.74)	0.45 (0.30, 0.61)	0.48 (0.31, 0.66)	0.30 (0.18, 0.46)	0.33 (0.19, 0.51)
Q4 [1.12-3.54]	58	0.62 (0.42, 0.79)	0.64 (0.41, 0.82)	0.55 (0.36, 0.72)	0.60 (0.38, 0.78)	0.39 (0.23, 0.58)	0.39 (0.21, 0.60)
P trend		0.77	0.87	0.83	0.98	0.85	0.68

Model 1: included 232 cycles in 140 female partners of men studied, adjusted for total energy intake, age, BMI, alcohol, caffeine, smoking status, total exercise time, Prudent dietary pattern, Western dietary pattern and female age; Model 2: included 205 cycles in 128 female partners of men studied, adjusted for total energy intake, age, BMI, alcohol, caffeine, smoking status, total exercise time, Prudent dietary pattern, Western dietary pattern and female dairy intake.

Tests for trend were performed using the median level of dairy in each quartile as a continuous variable in the model.