Socioeconomic Variability in Human Fecundity

Jenna Nobles[1], Amar Hamoudi[1], Robert Nowak[2], Erin Landau, Alex Baron
Jane Brittingham[1], Blake Mason[2]

[1] Center for Demography and Ecology, University of Wisconsin, Madison
[2] Department of Engineering, University of Wisconsin, Madison

Fecundity is a fundamental but poorly understood driver of human population dynamics. Even the most basic fecundity-related outcomes are difficult to measure in real-world populations because of cost, ethics, and disciplinary mores. As a result, most of what we think we know about these outcomes at the population level is based (a) on self-reported assessments of fertility and/or duration attempting pregnancy, (b) on creative inferential designs applied to small sample prospective studies with pre-conception enrollment, or (c) on animal models (Chandra et al. 2013; Hardy & Hardy 2014; Keiding 2012). These measurement approaches have proved most useful in identifying extreme outcomes—for example, levels and trends in the fraction of a population that is infertile or subfecund (Chandra & Stephen 1998; Gurunath 2011; Scheike et al. 2008; Thoma et al. 2013).

There are significant gaps in our knowledge. We have almost no measurement at the population level that sheds light on distinct drivers of fecundity levels—e.g., germ cell quality, probabilities of fertilization, embryo implantation, and pregnancy loss. Biomedical research on recruited samples or couples using assisted reproductive technology fills important components of this gap (see for example, Hardy and Hardy 2014; Norwitz et al. 2001; Rolland et al. 2012; Snijder et al. 2011; Wang et al. 2003; Wilcox et al. 1988; Velez et al. 2015), though the estimates from this research are rarely able to capture early pregnancy for more than a few hundred cases and/or rarely come from population samples.

We also have minimal measurement on variability in fecundity levels across socioeconomic subgroups in real-world populations. The National Survey of Family Growth, and similar surveys collected in populations outside of the U.S., include questions on self-assessed subfecundity (for example, "As far as you know, would you, yourself, have any difficulty getting pregnant (again) or carrying (a/another) baby (after this pregnancy)?"). Researchers can compare distributions of responses to these questions across subgroups, but interpreting any differences is complicated in part because interpretation relies heavily on implicit or explicit assumptions about women's ability to assess outcomes that can be very difficult to observe (for example, the failure of an implanted embryo to develop). Current duration methods, which rely less heavily on subjective assessments (Keiding et al. 2012; Slama et al. 2006; Thoma et al. 2013), still require respondents to report on durations without clinical pregnancy, which masks many of the early drivers of fecundity.

Comparing self-assessed fecundity across subgroups can reveal some counterintuitive patterns. For example, patterns in some rounds of the NSFG indicate flat educational or poverty gradients in subfecundity (Chandra and Stephen 2008; Chandra et al. 2013; Wilcox & Mosher 1994), even though biological processes like inflammation are centrally involved in fertilization, implantation, and healthy development (Mor et al. 2011; Olsen et al. 2013) and themselves demonstrate educational gradients (e.g., Gruenewald et al. 2009; Seeman et al. 2008).

We innovate toward scaling the study of fecundity to the population level by leveraging administrative population data against data recorded by one million users of a commercial health tracking software application. Our analysis relies on techniques from formal demography and modern data science. Our results constitute some of the first estimates of subpopulation variability in fecundity in a large-scale human population.

We ask: Do either or both of time-to-pregnancy implantation and the probability of pregnancy loss vary by individual-level and place-based socioeconomic indicators? Combining these, what are the implications for social gradients in time to live birth?

DATA AND METHODS

To study variability in the probabilities of pregnancy implantation and pregnancy loss, we draw on a highly unusual longitudinal data asset: repeated observations of approximately one million users of a suite of commercial health journaling software applications between 2014-2016.

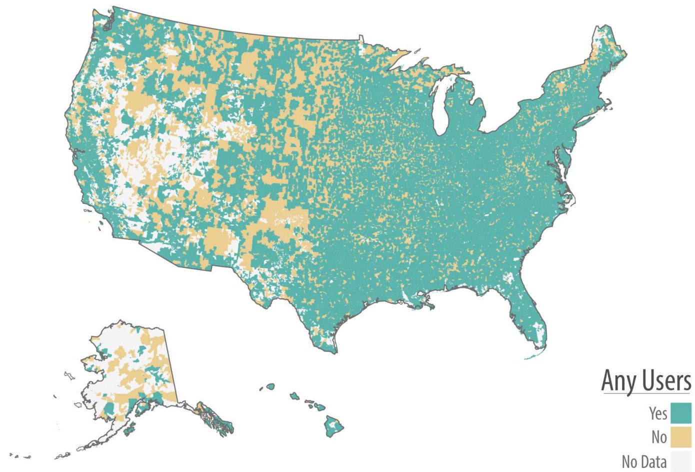
The application suite is designed to be used on mobile devices like smartphones and tablets, but they can also be used on laptop or desktop computers. The suite includes one application that allows women to track periods, ovulation (via reported over-the-counter ovulation tests, reported physical symptoms of ovulation, and basal body temperature), intercourse, contraceptive medications, and clinical pregnancies (via reported outcomes of over-the-counter HCG tests). Users can also track mood, physical symptoms, diet, exercise, weight, and sleep and report their date of birth and access to health insurance. All users are asked at sign-up whether they are trying to conceive and if so, for how long. Most importantly, users can generally be geolocated through a combination of direct self-reports and passively observed session characteristics. Users provide informed consent for their data to be used for the advancement of scientific research on fertility.

A second application in the suite allows women to track pregnancy development and is designed as a complement to the fertility application. When women using the fertility application report a pregnancy, they are offered an opportunity to transition seamlessly onto the pregnancy application. The pregnancy application provides users with daily updates about their ongoing pregnancies including fetal size and development and women's potential symptoms. Users can also journal health outcomes and behaviors including sleep, weight, exercise, prenatal vitamin use, and access to prenatal care. It also allows women to report special conditions in pregnancy, including the use of assisted reproduction and the occurrence of pregnancy termination. Women who deliver live births are asked basic information about the infant.

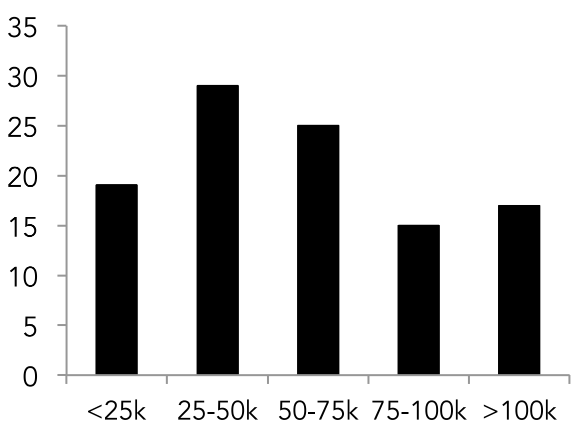
The data describe a large and diverse user population. Panel A of Figure 1 represents the spatial distribution of users across zip codes in the U.S. Panel B displays the proportion of users by income category. Though the sample over-represents high-income women relative to the U.S. population (discussed below), the sample contains nearly 200,000 users living on less than $25,000 USD a year. Similarly, 20% of users have a high school degree or less and 18% of users lack health insurance.

Figure 1.

A. Spatial distribution of users across U.S. zipcodes



B. Income distribution among users



The software is designed to minimize missing data on key pieces of information. Respondent burden is kept low through careful design; for example, users receive daily emails containing questions that can often be answered by touching a single box in the email. ("Did you have sex today? Touch yes or no below.")

The applications also collect data from subsets of users about numerous domains of their lives: race and ethnic identification, health, partner health, schooling, employment, stress, personality traits, preferences, partner relationship quality, birth history, sibship size, parental health histories among many others. They also answer questions about fecundity diagnoses (7% of users report trying unsuccessfully to get pregnant for more than 12 months), period regularity, fertility intentions (11% of users are trying to avoid pregnancy), contraceptive use, and STDs (14% of users report exposure to an STD). These questions arrive in a user's email inbox, one or two at a time from time to time. She can also scroll through a list of them within the application and answer as many as she likes. We use overlaps among the sets of users who answer each question to test approaches to impute missing data (described below).

Contextual data

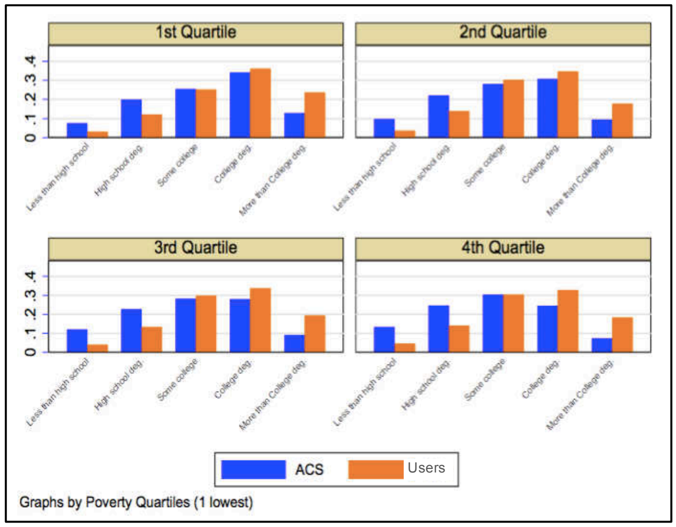
We build on the user data described above by linking a set of contextual indicators at the zip code and county level. To do so, we have built zip-code and county-level data files that draw from numerous data sources: the Bureau of Labor Statistics (annual unemployment), the Unified

Crime Reports (rates of violent and non-violent crime), the National Center for Health Statistics (infant and child mortality), the Census and ACS data (poverty, race/ethnic composition, proportion insured), state department lead monitoring systems (child blood lead levels), as well as GIS data that allow us to measure elevation, population density, and distance to highways.

APPROACH

Our analysis proceeds in several steps. (1) We begin by analyzing in detail whether and how the sample is distinct from the U.S. population. We draw on data from geocoded 2010 Census data and geocoded 2010-2015 ACS data. Initial estimates indicate that, although the sample is clearly selected, it is selected in similar ways across socioeconomic strata of interest (Figure 2). This analysis will allow us to generate a set of post-stratification weights that we will test with the data. That is, under assumptions about the distribution of unobserved traits within cells, we will assess whether it is possible to generate weights that make the data plausibly representative of the U.S. population.

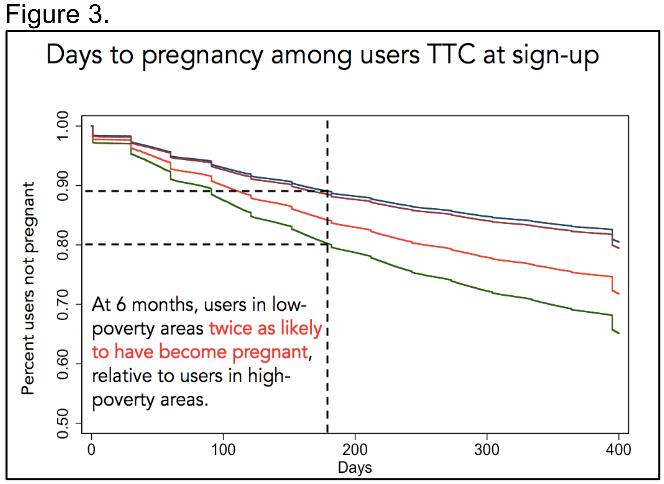
Figure 2. Distribution of women across education categories within poverty quartiles, in the ACS and among application users.



(2) We use a set of event-history models that describe time to pregnancy and time to pregnancy loss among users. Outcomes are recorded in real-time by users, and are also detected using a machine learning algorithm.

This algorithm assigns probabilities of sub-clinical pregnancy to a woman/month, based on outlier values in individual period cycle length with respect to a person's cycle timing. (If a menstrual period is subsequently reported, it is assigned an equivalent probability of being a sub-clinical pregnancy loss). These estimates use both individual-level and zip-code level information to capture socioeconomic and associated forms of variability. Figure 3 describes initial age-adjusted estimates of time-to-pregnancy in the sample, stratified by county-level poverty rates.

Figure 3.



(3) We then use a set of increment-decrement life-tables to combine the probabilities generated in step 2 into estimates of variability in the time to live birth. We will compare these predictions with pregnancy interval information observed in two national data sets: the NLSY-97 and the most recent cycle of the NSFG.

REFERENCES

Arck, P. C., Rücke, M., Rose, M., Szekeres-Bartho, J., Douglas, A. J., Pritsch, M., ... & Nakamura, K. (2008). Early risk factors for miscarriage: a prospective cohort study in pregnant women. *Reproductive biomedicine online*, *17*(1), 101-113.

Barut, M. U., Agacayak, E., Bozkurt, M., Aksu, T., & Gul, T. (2016). There is a Positive Correlation Between Socioeconomic Status and Ovarian Reserve in Women of Reproductive Age. *Medical Science Monitor*, *22*, 4386-4392.

Chandra, A., & Stephen, E. H. (1998). Impaired fecundity in the United States: 1982-1995. *Family planning perspectives*, *30*(1), 34-42.

Chandra, A., Copen, C. E., & Stephen, E. H. (2013). *Infertility and impaired fecundity in the United States, 1982-2010: data from the National Survey of Family Growth*. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics.

Gruenewald, T. L., Cohen, S., Matthews, K. A., Tracy, R., & Seeman, T. E. (2009). Association of socioeconomic status with inflammation markers in black and white men and women in the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Social science & medicine*, *69*(3), 451-459.

Gurunath, S., Pandian, Z., Anderson, R. A., & Bhattacharya, S. (2011). Defining infertility—a systematic review of prevalence studies. *Human reproduction update*, *17*(5), 575-588.

Hardy, K., & Hardy, P. J. (2015). 1st trimester miscarriage: four decades of study. *Translational pediatrics*, *4*(2), 189.

Joffe, M. (2009). What has happened to human fertility?. *Human Reproduction*, *25*(2), 295-307.

Keiding, N., Hansen H, O. K., Sørensen, D. N., & Slama, R. (2012). The current duration approach to estimating time to pregnancy. *Scandinavian Journal of Statistics*, *39*(2), 185-204.

Larsen, E. C., Christiansen, O. B., Kolte, A. M., & Macklon, N. (2013). New insights into mechanisms behind miscarriage. *BMC medicine*, *11*(1), 154.

Louis, G. M. B., Sundaram, R., Schisterman, E. F., Sweeney, A., Lynch, C. D., Kim, S., ... & Chen, Z. (2014). Semen quality and time to pregnancy: the Longitudinal Investigation of Fertility and the Environment Study. *Fertility and sterility*, *101*(2), 453-462.

Macklon, N. S., Geraedts, J. P., & Fauser, B. C. (2002). Conception to ongoing pregnancy: the 'black box'of early pregnancy loss. *Human reproduction update*, *8*(4), 333-343.

Mor, G., Cardenas, I., Abrahams, V., & Guller, S. (2011). Inflammation and pregnancy: the role of the immune system at the implantation site. *Annals of the New York Academy of Sciences*, *1221*(1), 80-87.

Nepomnaschy, P. A., Welch, K. B., McConnell, D. S., Low, B. S., Strassmann, B. I., & England, B. G. (2006). Cortisol levels and very early pregnancy loss in humans. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(10), 3938-3942.

Olive, D. L., & Pritts, E. A. (2006). Estimating infertility: the devil is in the details. *Fertility and sterility*, *86*(3), 529-530.

Rolland, M., Le Moal, J., Wagner, V., Royère, D., & De Mouzon, J. (2012). Decline in semen concentration and morphology in a sample of 26 609 men close to general population between 1989 and 2005 in France. *Human Reproduction*, *28*(2), 462-470.

Seeman, T., Merkin, S. S., Crimmins, E., Koretz, B., Charette, S., & Karlamangla, A. (2008). Education, income and ethnic differences in cumulative biological risk profiles in a national sample of US adults: NHANES III (1988–1994). *Social science & medicine*, *66*(1), 72-87.

Scheike, T. H., Rylander, L., Carstensen, L., Keiding, N., Jensen, T. K., Stromberg, and colleagues. (2008). Time trends in human fecundability in Sweden. *Epidemiology*, *19*(2), 191-196.

Slama, R., Ducot, B., Carstensen, L., Lorente, C., de La Rochebrochard, E., Leridon, H., ... & Bouyer, J. (2006). Feasibility of the current-duration approach to studying human fecundity. *Epidemiology*, *17*(4), 440-449.

Thoma, M. E., McLain, A. C., Louis, J. F., King, R. B., Trumble, A. C., Sundaram, R., & Louis, G. M. B. (2013). Prevalence of infertility in the United States as estimated by the current duration approach and a traditional constructed approach. *Fertility and sterility*, *99*(5), 1324-1331.

Wang, X., Chen, C., Wang, L., Chen, D., Guang, W., French, J., & Reproductive Health Study Group. (2003). Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. *Fertility and sterility*, *79*(3), 577-584.

Wilcox, A. J., Weinberg, C. R., O'connor, J. F., Baird, D. D., Schlatterer, J. P., Canfield, R. E., ... & Nisula, B. C. (1988). Incidence of early loss of pregnancy. *New England Journal of Medicine*, *319*(4), 189-194.

Wilcox, L. S., & Mosher, W. D. (1994). Characteristics associated with impaired fecundity in the United States. *Family Planning Perspectives*, 218-221.