Research Conducted Using Data Obtained through Online Communities: Ethical Implications of Methodological Limitations

Anna Janssens, Emory University
Peter Kraft, Harvard School of Public Health

Journal Title: PLoS Medicine
Volume: Volume 9, Number 10
Publisher: Public Library of Science | 2012-10-23, Pages e1001328-e1001328
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1371/journal.pmed.1001328
Permanent URL: https://pid.emory.edu/ark:/25593/s5bq2

Final published version: http://dx.doi.org/10.1371/journal.pmed.1001328

Copyright information:
© Janssens, Kraft.
This is an Open Access work distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

Accessed April 23, 2020 4:56 AM EDT
Research Conducted Using Data Obtained through Online Communities: Ethical Implications of Methodological Limitations

A. Cecile J. W. Janssens¹,², Peter Kraft³

¹ Department of Epidemiology, Erasmus University Medical Center Rotterdam, The Netherlands, ² Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States of America, ³ Program in Molecular and Genetic Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America

Introduction

An increasing number of public and commercial initiatives invite individuals to participate in scientific research via the internet (Table 1). People are asked to provide information about personal medical history, medications, physical traits and measurements, ethnicity/ancestry, lifestyle and environmental exposures, and to donate biological material, generally saliva or blood, for DNA analysis. Some initiatives, such as the Personal Genome Project, have been launched with the specific goal of conducting scientific research, whereas others perform scientific analyses using data that were at least partly collected for other purposes. For example, PatientsLikeMe is an online community where patients can share information on symptoms, health state, and treatments to learn from each other's experiences, and the company 23andMe sells personal genome tests to individuals who want to learn their genetic risks of common diseases, carrier status of rare diseases, response to drug treatment, and ancestry. Data are collected predominantly through self-report online questionnaires and some initiatives offer the opportunity to make data accessible for the public. For example, the Personal Genome Project publishes anonymized data online and participants of PatientsLikeMe can choose to publish all data publicly available on the web or make data accessible only to registered users.

Strong claims regarding the benefits of research using these resources are often made in order to encourage individuals to provide personal (health) information. For example, 23andWe, the research arm of 23andMe “gives customers the opportunity to leverage their data by contributing it to studies of genetics. With enough data, we believe 23andWe can produce revolutionary findings that will benefit us all” [1]. PatientsLikeMe tells patients that sharing personal stories and health data does not only enable individuals to “put your disease experiences in context and find answers to the questions you have” but also gives “the opportunity to help uncover great ideas and new knowledge” [2]. But how valid are these claims? Can online data collection lead to major breakthroughs in health research? We worry that overstating the conclusions that can be drawn from these resources may impinge on individual autonomy and informed consent. Just as researchers must take care to accurately convey direct benefits to study participants (which, we argue, in these situations are often small), they should also describe the likely outcomes and known limitations of observational studies conducted using volunteers. Clarity regarding the benefits of research using solicited personal data is particularly important when the data collected are also used for other purposes (e.g., PatientsLikeMe may sell members’ information to pharmaceutical and insurance companies [2]), lest the allure of participation in a scientific study be used as a Trojan horse to entice individuals to part with information they might not otherwise volunteer.

“Revolutionary” Findings?

As early examples of such initiatives, 23andMe and PatientsLikeMe have already published their first scientific results. Using self-reported phenotypic data provided by their customers, 23andMe reported that they replicated over 100 genetic associations from the catalogue of genome-wide association studies (GWAS) of the National Human Genome Research Institute’s Office of Population Genomics [3], identified genetic associations for miscellaneous traits long suspected of having a genetic basis [4], and identified two novel loci and a substantial genetic component for Parkinson disease [5]. And in a study of 447 patients, PatientsLikeMe showed that lithium carbonate did not affect the rate of progression in amyotrophic lateral sclerosis (ALS) [6].

But how valid and new are these findings? One of the loci for Parkinson disease that 23andme discovered was confirmed in collaboration with the International Parkinson Disease Genomics Consortium [7], but the other loci need further replication [8,9], and

Citation: Janssens ACJW, Kraft P (2012) Research Conducted Using Data Obtained through Online Communities: Ethical Implications of Methodological Limitations. PLoS Med 9(10): e1001328. doi:10.1371/journal.pmed.1001328

Published: October 23, 2012

Copyright: © 2012 Janssens, Kraft. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: This study was supported by the Centre for Medical Systems Biology (CMSB) in the framework of the Netherlands Genomics Initiative (NGI). ACJW Janssens was sponsored by the VIDI grant of the Netherlands Organization for Scientific Research (NWO). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: a.janssens@erasmusmc.nl

Provenance: Commissioned; externally peer reviewed.
also the newly identified associations for various traits still need to be replicated in independent samples [4]. The replication of 180 associations concerned 144 out of 392 attempted associations in case-control and quantitative phenotypes from the GWAS catalogue and 39 out of 106 attempted associations with phenotypes that were in weak correspondence with those in the catalogue. In both instances, the observed percentage of replications was less than expected based on the statistical power for each of the phenotypes tested [3]. And finally, as acknowledged by the authors, the absence of an association between lithium carbonate and ALS progression reported by Patients-LikeMe was in line with earlier observations and two prematurely stopped randomized clinical trials [10,11]. Still, it is not clear that the absence of a statistically significant finding of this particular study can be interpreted as the absence of a treatment effect, given the methodological limitations in online data collection. Using self-reported data from self-selected individuals is subject to several known biases in the presence of which reported frequencies, prevalences, and associations can be over- or underestimated. Table 2 lists the sources of bias in observational studies that are commonly observed but particularly relevant for studies using self-reported data from self-selected individuals [12]: selection bias, information bias, and confounding.

**Sources and Implications of Bias**

The first source of bias, selection bias, occurs when the study population does not represent the target or sampling population, for example when customers of personal genome tests are healthier, higher educated than the general population [13], or when participating patients are more motivated, literate, and empowered [14,15]. Selection bias is also observed when participation in a study by cases is related to a certain risk factor and participation amongst control individuals is unrelated to that factor, e.g., when depressed people are less likely to join online communities. In that example, the validity of studies in psychiatric, neurological, and geriatric diseases might be reduced, because the frequency of the risk factor in cases and its impact on disease risk are likely underestimated. Statistical techniques, such as inverse-probability sample weighting, can correct the effects of selection bias, but these require that the sampling population is known. The fact that the sampled population is unknown is a major shortcoming in studies that recruit online through participant self-selection.

The second source of bias, information bias, concerns any systematic error in the collection of data. Errors in exposure reporting that are unrelated to the phenotype being studied (“non-differential misclassification”) cannot create an association when none truly exists, although they can attenuate the estimated size of a true association. Of greater concern, errors that are related to the phenotype being studied (“differential misclassification”) can create spurious associations where none exist, or over- or underestimate the size of true associations. For example, individuals with a disease may recall their exposure history differently than those without (reporting and recall biases), especially if the exposure is widely suspected to be linked to the disease. Misclassification of outcome typically occurs for outcomes that apparently follow from certain exposures (detection bias). In studies with continuous online data collection, outcome misclassification may be particularly troublesome because participants may report their phenotype status after learning about their risk factors and

### Table 1. Examples of online research initiatives.

<table>
<thead>
<tr>
<th>Initiative</th>
<th>Aims and Claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>PatientsLikeMe.org</td>
<td>“To provide a better, more effective way for you to share your real-world health experiences in order to help yourself, other patients like you and organizations that focus on your conditions.”</td>
</tr>
<tr>
<td>23andMe.com</td>
<td>“Our research arm, 23andWe, gives customers the opportunity to leverage their data by contributing it to studies of genetics. With enough data, we believe 23andWe can produce revolutionary findings that will benefit us all.”</td>
</tr>
<tr>
<td>Personal Genome Project</td>
<td>“The mission of the Personal Genome Project is to encourage the development of personal genomics technology and practices that are effective, informative, and responsible; yield identifiable and improvable benefits at manageable levels of risk; are broadly available for the good of the general public.”</td>
</tr>
<tr>
<td>personalgenomes.org</td>
<td></td>
</tr>
<tr>
<td>DIYgenomics.com</td>
<td>“A non-profit research organization founded in March 2010 to realize personalized medicine through crowdsourced health studies and apps.”</td>
</tr>
<tr>
<td>Genomera.com*</td>
<td>“We’re crowd-sourcing health discovery by helping anyone create group health studies.”</td>
</tr>
<tr>
<td>CureTogether.com**</td>
<td>“Bringing patients into research as active partners is one of our big missions at CureTogether.” [21]</td>
</tr>
</tbody>
</table>

Quoted information was downloaded from the organizations’ websites on July 1, 2012.

*Beta version.

**Acquired by 23andMe.

doi:10.1371/journal.pmed.1001328.t001
The new initiatives of public participation in science (citizen science) by online and continuous data collection have changed our views on how to most efficiently and effectively conduct scientific studies [17], and their greatest value may be in that area. These initiatives can speed up scientific research by facilitating the recruitment of participants in a relatively easy way, which is particularly relevant for rare diseases such as ALS and Parkinson disease. PatientsLikeMe has a trial search tool, linked to clinicaltrials.gov, through which patients can see which trials are still recruiting [2]. And with their rich data collections and online opportunities for fast data updates, they can quickly put new topics on the scientific agenda and question published observational studies and trials. An excellent example was provided by 23andMe. Within a week of the high-profile publication of a putative genetic predictor of longevity, 23andMe showed that the predictor did not replicate in their data. After re-examination of their study protocol and data analysis, the authors of the longevity study retracted their initial publication [18,19]. Nevertheless, the biases in the design and data collection of the citizen science organizations warrant that most conclusions from their studies need further replication.

Initiators of online data collections are strong advocates of openness and trans-
progression, will patients discontinue treatment? Will they still trust their doctors when they were prescribed a drug that apparently does not work? Researchers should clearly explain the limitations of their approach and their findings and stress that participants should not change their medical regimens without consultation of their doctor (Table 3).

We have focused on the ethical implications of methodological limitations of research involving self-reported data from self-selected participants. Research using data obtained through online communities faces new dilemmas in relation to old issues, which require further ethical analysis and public debate, including the provision of adequate consent, the safeguard of public trust, disclosure of commercial development of research results, and the sale of participants’ data to third parties [17]. Only a responsible approach with realistic expectations about what can be done with and concluded from the data will benefit science in the long run.

**Author Contributions**

Wrote the first draft of the manuscript: ACJWJ PK. Contributed to the writing of the manuscript: ACJWJ PK. ICMJE criteria for authorship read and met: ACJWJ PK. Agree with manuscript results and conclusions: ACJWJ PK.

**References**


---

**Table 3. Recommendations for communicating opportunities and limitations of research conducted using data obtained through online communities.**

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Recommendations and/or Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before data collection</td>
<td>Information about what can and cannot be done with the data collected</td>
</tr>
<tr>
<td></td>
<td>Clear discussion of immediate benefits that study participants may or may not receive</td>
</tr>
<tr>
<td></td>
<td>Presentation of realistic and fair claims about scientific knowledge that is likely to be gained</td>
</tr>
<tr>
<td></td>
<td>Disclosure about potential for sharing participants’ data with third parties as well as the commercial uses of research findings</td>
</tr>
<tr>
<td>After data analyses</td>
<td>Comprehensive and balanced presentation of research results</td>
</tr>
<tr>
<td></td>
<td>Clear interpretation of results, especially in light of other studies and need for replication</td>
</tr>
<tr>
<td></td>
<td>Discussion of implications for health behavior or medical decisions, if any</td>
</tr>
</tbody>
</table>

**doi**:10.1371/journal.pmed.1001328.t003