

0-Sep-2016

Dear Prof. Jena

Manuscript ID BMJ.2016.034760 entitled "Do celebrity endorsements matter? An analysis of BRCA gene testing and mastectomy rates following Angelina Jolie's New York Times editorial"

Thank you for sending us this Christmas paper, which we discussed at a recent manuscript meeting

We found it a clear read on an important topic, but identified some issues that need clarification before we make a final decision about publication.

Would you be willing to revise and let us take another look?

You will find reviewers' reports at the end of this letter, along with a report from our manuscript meeting, and some further information about resubmitting. Please address all comments in full. We hope you find them constructive.

I'm afraid we can't promise to publish the revision, but we should be in a position to make a quick decision.

Please be aware that if we accept your revision, we can't guarantee publication in the print issue of the Christmas BMJ (which goes only to UK doctors). Definitive publication is on line at thebmj.com.

DEADLINE:

If you are happy to proceed with the BMJ, please let us have the revised paper back by the end of October. Or earlier if you can manage it. Late submission could jeopardise your chances of consideration for Christmas this year.

IMPORTANT: CHRISTMAS PAPERS HAVE A STRICT WORD LIMIT. Please make sure your revision is no longer than 1500 words excluding abstract, tables, figures, references, and "what this paper adds" box. Do not cut detail from the methods. Please prune the introduction and discussion instead. Readers need enough detail in the methods to replicate your findings.

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And finally, we also require a copy of the manuscript with changes highlighted. Please upload this file with file designation 'Revised Manuscript Marked copy'.

Many thanks again. We look forward to seeing your revised paper

With best wishes

Alison Tonks
Clinical editor BMJ
atonks@bmj.com

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****Report from The BMJ's manuscript committee meeting****

These comments are an attempt to summarise the discussions at the manuscript meeting. They are not an exact transcript.

Members of the committee were: Wim Weber [Chair], Elizabeth Loder, Georg Roeggla, Tiago Villanueva, Raphael Perera, Alison Tonks, Daoxin Yin

Decision: Put points

Detailed comments from the meeting:

*As reviewers say, the 15 day window for evaluating BRCA testing is short. An explanation of why this window was

chosen would be useful.

*We were more concerned about the mastectomy window. 60 days is likely too short a time in which to get tested, get opinions, and arrange for an elective operation. This makes it difficult to be certain why this finding is negative -- is it real or a function of too short an interval?

*If possible, a series of sensitivity analysis changing this 60 day window would make the paper stronger (if the results are robust to these analyses).

*Perhaps mention that population screening for BRCA is still not well researched. A recent guideline mentions:

"Additional research on interventions is needed. Practice standards for screening have preceded supporting evidence despite known harms of overscreening."

Ann Intern Med. 2014 Feb 18;160(4):255-66.

Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: a systematic review to update the U.S. Preventive Services Task Force recommendation.

Nelson HD, Pappas M, Zakher B, Mitchell JP, Okinaka-Hu L, Fu R.

*In terms of interpretation, could it also be that some BRCA positives did not want further intervention therefore identifying relevant population that did not act? This, although less likely, could be an alternative explanation for the lack of impact.

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g. Footnotes and statements

REVIEWERS' COMMENTS

Reviewer: 1

Recommendation:

Comments:

Thank you for the invitation to review this interesting paper. This study examines the consequences of highly salient celebrity endorsements on health care seeking behavior, in this case uptake of BRCA gene testing and downstream preventive mastectomy rates. The authors use event-study and differences-in-differences approaches, along with a large, unique claims-based data source, to demonstrate an a sharp increase in the BRCA gene testing and decrease in mastectomy rates conditional on testing. These changes are exactly timed with the celebrity endorsement.

I really enjoyed this paper and believe that it makes an important contribution to our understanding of the various factors that influence the demand for health care. For me, the key contribution is the insight that celebrity endorsements – which are more and more ubiquitous in the digital age – do influence demand, but not necessarily in a manner that follows underlying population disease risks.

Overall, the paper is very well done. I do have a few comments that might improve the paper, though several are minor:

1. The +/- 15 day analysis is very interesting and helps establish a jump in BRCA tests the very day after the editorial was written. This is compelling. It would be useful to know the rationale behind the choice of the window. It may have to do with data limitations (around identified BRCA gene tests) in the 2012 data and/or the a priori design feature of limiting seasonal influences (in the same way bandwidth is chosen for a regression discontinuity study). Both are good reasons for the author to make this choice.

2. I would be interested to see how uptake varied by age and level of education over time. The latter can be proxied by MSA or three digit zip code-level mean schooling for women in the age range covered by the study (these geographic levels may be identifiable in the data source the authors use, though it seems to depend on the exact data product they are using – e.g., Hansen and Chang, 2011). Typically, uptake of health interventions and technology are highest among higher educated individuals, with lower socioeconomic status individuals following suit. This has real implications for the widening of health disparities. Examining age and (more so) educational differences in uptake would be interesting for two reasons. First, are celebrities uniquely positioned to “equalize” take up of new technologies by virtue of their fame. The particular example the authors take on is ideal to test out this hypothesis given the massive profile of the editorial in question and its author. Second, a pattern of spreading diffusion to different population groups may explain the persistence of the editorial’s impact (Fig 2 and 4). While persistence cannot be inferred for sure, since data from other years to facilitate a differences-in-differences comparison is not available, the duration of the potential effect is striking and is worth trying to understand. (The study examining the effect of Katie Couric’s endorsement of colonoscopies also finds a similar long-duration effect.

3. Pg 7 – The authors state that they use an “individual-level differences-in-differences model.” I understand that they mean they are using de-identified individual level data to estimate their model. However, some readers may take this as pre-post comparisons of the same individual. I think it is worth rewriting this.

4. Figures 2, 3, and 4 – the hashed vertical line denoting the month should be lined up with the publication of the Jolie editorial, not the month before.

Once again, I enjoyed reading this paper and thank you for the opportunity to review it.

Additional Questions:

Please enter your name: Atheendar Venkataramani

Job Title: Assistant Professor of Medicine

Institution: Massachusetts General Hospital, Harvard Medical School

If you have any competing interests (please see BMJ policy) please declare them here:

Reviewer: 2

Recommendation:

Comments:

The authors describe an analysis of insured healthcare usage in relation to mastectomy rates and usage of BRCA testing following the Angelina Jolie revelation in the New York Times in May 2013. They showed an immediate 64% increase in BRCA testing in the 15 working days post revelation and an overall 31% increase for the rest of 2013. However mastectomy rates did not rise. the 7% of BRCA tests associated with mastectomy is based on a 31% increase equivalent to the 10% rates prior to the revelation. The main limitation of this data is that the authors do not have data specific to preventive surgery but rather ALL mastectomies. As such many mastectomies could have been in women with breast cancers.

Specific comments:

1. The use of the term 'pervasive' which has an English Oxford Dictionary meaning of: '(especially of an unwelcome influence or physical effect) spreading widely throughout an area or a group of people.' Appears to be subjective and not backed up by evidence. I suggest using a less subjective term. Can the authors really say that these endorsements are unwelcome?
2. The authors state there is limited evidence on the effects of the AJ article. However there are a host of publications on this that are not referred to. These include reference to effects in Australia and elsewhere. Also Risk reducing mastectomy rates did go up in the UK which the authors cannot state categorically did not happen in the US (<http://www.ncbi.nlm.nih.gov/pubmed/26603733>; <http://www.ncbi.nlm.nih.gov/pubmed/26546111>).
3. The authors state that they do not believe that BRCA testing after the AJ article could have brought forward a group of women less likely to undergo preventive surgery. In fact this may have brought forward women who were reluctant previously. Indeed the mastectomy rates in the UK which rose were mainly in the non BRC subset
4. The authors use a very tight time window after the article of only 15 days. Is it really possible that the effect would have been so quick? Can an appointment and testing be done without previous counselling in such a short time window? What was the effect in the following month?
5. In the UK there are strict guidelines on risk reducing mastectomy that require a number of appointments including psychological assessments. This usually takes at least 6-8 months taking a potential rise in mastectomy rates as a result of BRCA testing outside the study envelope. Can the authors be certain that this is not the case in the USA?
6. The authors state 'Angelina Jolie, who in a May 14, 2013 New York Times editorial titled "My Medical Choice" urged women to undergo BRCA1/2 genetic testing and announced her decision to undergo preventive mastectomy.' This is somewhat different to the actual statement in the article- 'For any woman reading this, I hope it helps you to know you have options. I want to encourage every woman, especially if you have a family history of breast or ovarian cancer, to seek out the information and medical experts who can help you through this aspect of your life, and to make your own informed choices' In fact she also revealed in the article that her risk reducing mastectomy process was complete not in the future as implied by the 'decision to undergo' wording.

DGR Evans

Additional Questions:

Please enter your name: Prof D Gareth Evans

Job Title: Professor of Medical Genetics and cancer Epidemiology

Institution: University of Manchester

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Fee from AstraZeneca for webinar involvement May 2015

Reviewer: 3

Recommendation:

Comments:

This submission to the BMJ Christmas Edition analyzes the impact on BRCA gene testing of a popular NYT editorial by

the Hollywood actress Angelia Jolie, in which she stated that she was BRCA positive and would undergo prophylactic bilateral mastectomy. The authors are correct to state that the editorial penned by Mrs. Jolie attracted much attention. The authors find large and nearly immediate increases in rates of BRCA testing in a large sample of privately insured American women, with an estimated national cost of \$13 million (which is tremendous and driven in part by the test's high cost). Those rates persist throughout the year. A similar spike was not observed during the same period in the prior year, which serves as a control. To assess whether the additional testing was effective in identifying new BRCA cases that might lead to mastectomy, the authors look at overall mastectomy rates over the period, which they find to be constant, and rates of mastectomy among women who had a BRCA test, which they find to decline after the spike in testing. Both of these point to the additional testing being potentially inappropriate in the sense that the patients induced to be tested after the editorial were likely women at relatively lower pre-test probability of having a BRCA positive mutation.

This is an innovative paper that fits into the mold of the BMJ Christmas edition. I suspect that it will generate a lot of attention for obvious reasons. The methods are appropriate, the writing is clear, and the topic is of general interest.

I have a few suggestions for improvement, space allowing.

1. If possible, I would briefly describe a bit more (in the discussion) other work that is related to this, e.g., the prior study of the Katie Couric effect (what population was studied, how large were the effects) and the related papers on Angelina Jolie's article that the authors cite. This paper makes, in my opinion, substantive and creative additions to prior studies but it a brief discussion would be useful.
2. Implicitly, the authors' findings suggest that the marginal women induced to be screened by Mrs. Jolie's editorial was at lower pre-test risk of having a BRCA mutation, otherwise we would have expected that rates of mastectomy in the overall study population would have gone up (if even slightly) and that rates of mastectomy conditional on a BRCA test would have been unchanged. It may be worth it to take a slightly stronger 'stance' on whether the editorial induced 'wasteful' additional testing. The dollar magnitude of the additional testing is large, approximately \$13 million in those two weeks alone. Although the efforts of Mrs. Jolie were no doubt well intended, the consequences as the authors describe them were unintended byproducts with arguably net negative benefit.

Respectfully submitted,

Eric C Sun

Additional Questions:

Please enter your name: Eric Sun

Job Title: Instructor

Institution: Stanford University

If you have any competing interests (please see BMJ policy) please declare them here:

Reviewer: 4

Recommendation:

Comments:

Thank you for the opportunity to review this study. In this paper, the authors examine the impact of Angelina Jolie's editorial in the New York Times on BRCA testing and mastectomy rates in the United States. The authors do a wonderful job of presenting this study as an interesting and clever policy evaluation. They find that BRCA testing rates increased in a discontinuous fashion after the intervention and remained elevated, while mastectomy rates did not change. The decline in mastectomy rates among women who received BRCA testing suggested that more tests were done on lower-risk women. A primary take-away from the study is that celebrity endorsements can shift utilization but may not target the most ideal group. I would note the following issues.

1. One concern with the mastectomy analysis is that preventive mastectomies may not be covered by private employer-sponsored insurance plans, and people in the Truven data may move or change employers before they obtain (or in order to obtain) a mastectomy. For women near age 65, they could conceivably wait to age into Medicare before obtaining a mastectomy, as Medicare has a likely lower coinsurance than a private HMO (or even PPO) plan, if it is even covered by private insurance. Such movements may not be captured by the data, as the Truven data is a sample of large employers. It is also possible that there may be a response in mastectomy rates in the young Medicare population (65-75 year olds), who were not a part of this analysis. As one suggestion, the authors could analyze Medicare beneficiaries in the Truven data (they are only Medicare beneficiaries with Medicare Supplemental coverage through their employer, however).

2. Another concern is that the impact of the announcement on mastectomy rates may have been delayed. For example, a busy working woman (by definition the data is of employer-sponsored health insurance recipients) who hears the announcement in May will need time to think about the announcement, make an appointment with her primary care physician, make an appointment with a breast surgeon, see the breast surgeon, potentially receive a second opinion, potentially need a pre-operative medical risk assessment visit, and take more time to discuss the decision with family or friends before proceeding. For women who are working and busy, this process could take time,

especially women who are less intensely motivated by the announcement. Therefore, for the mastectomy to take place, it may well take over 6 months (into 2014, which is not in the data). Figure 3 seems to show that mastectomy counts did gradually increase in the second half of 2013, which is not inconsistent with a delayed effect.

3. Similarly, for the 60-day monthly mastectomy rates (Figure 4), one reason for the lower 60-day rates after BRCA testing may be that 60 days is too little to accomplish the sequence of events above. Another reason is that lower-risk women who were swayed by the announcement needed more time to weigh their decision before undergoing this major procedure. Compared to higher-risk women whose decisions can be, in some ways, more clinically indicated and easier to make, lower-risk women for whom the benefits of surgery vs. costs/risks are less clear may need more time to get second opinions and think about it. If they take more than 60 days to receive the surgery, that would not be reflected in Figure 4 if I am interpreting the figure correctly.

4. It would be preferable to control for cost-sharing (% cost-sharing). The limitation of controlling for insurance plan type (HMO, PPO, etc) is that these distinctions mean different things for different employers and different insurers. One insurer's HMO plan may be as generous as another insurer's PPO plan. Similarly, one employer's negotiated coverage in its HMO plan may differ from another's. Thus, I would recommend taking a set of sentinel services and calculating the % cost-sharing at the patient level. That would better reflect the plan's generosity, which is the demand side parameter of interest.

Thank you again for the privilege of reviewing this manuscript. I hope these comments can be helpful to the authors. Overall, this is an incredibly interesting study that is a great fit for the Christmas issue of BMJ. The policy relevance of the impact of celebrity endorsements is poorly understood and likely underappreciated. This study would add an important piece of evidence to the literature that is relevant beyond the present scenario. I congratulate the authors on this wonderful and creative study.

Additional Questions:

Please enter your name: Zirui Song

Job Title: Resident

Institution: Massachusetts General Hospital

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END

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