Reviewer’s report

Title: Value-based genomic screening: Exploring genomic screening for chronic diseases using triple value principles

Version: 0 Date: 14 Aug 2019

Reviewer: June C. Carroll

Reviewer's report:
General comments

The interesting aspect of this article is the use of triple value principles and how they apply to genomic medicine. Many articles have been written on the evaluation of genetic/genomic tests. This adds a somewhat different lens through which to look at it. The article appears to be written for a broad audience of what they call "healthcare professionals" including policy makers, payers and providers although some sections apply more to some than others. It might be helpful to be more specific in the conclusions regarding how each group might use the triple value principles in their work.

Specific comments

- I have some concerns about the term "genomic screening" - I think the authors should define this term. It seems to me that they use it to mean different things in their examples. Screening often implies "population screening" yet I don't think they mean this most of the time. They do however talk about implementing genomic screening "on a wide scale" which does somewhat imply that. Sometimes they are referring to family history screening, sometimes cascade screening - really unclear

- The authors use the term "waste" - I think that should be defined in this context of genomic medicine

- Line 71 - the authors say the paper is focusing on genomic screening of chronic diseases and that "the evidence base around using genomic screening for chronic conditions is relatively more established than its use for other conditions" - I'm not convinced that the paper is addressing genomic screening for chronic diseases - rather for relatively rare hereditary breast and ovarian cancer and colorectal cancer, and for more common familial hypercholesterolemia. Using family history as a screen might meet the criteria of screening for chronic diseases but I'm not sure the authors are always meaning that. These could be used as case examples for future implementation of genomic medicine but are not common chronic diseases. This relates to the definition of "genomic screening" and whether the authors mean population screening or not.
- Line 88 - now they are talking about "screening of first degree family members" - ? of those with a known mutation - again more detail re definitions of what they are referring to would be helpful

- Line 92 - "recommends screening all newly diagnosed cases for LS" - are the authors referring to testing first degree relatives of those newly diagnosed with LS - should be more specific - if so - agree this is cascade screening - not regular screening

- Re LS - many countries are implementing routine/reflex testing of colorectal cancers for tumor markers suggestive of LS, then offering LS genetic testing to those individuals who test positive - sometimes I thought the authors were referring to this - but not clear

- Line 97 - I would suggest that women with positive screening results should "be offered" genetic counseling and if indicated - "offered" genetic testing

- Line 99,100 - A "similar" program - is not clear - on reading reference 16 - both Georgia and Italy introduced a systematic collection of family history to indicate those who would be eligible to go on to genetic counselling - the author implies BRCA testing as a routine. Many countries use family history as a triage to identify those at increased risk of hereditary cancer - perhaps this is the "genomic screening" they are referring to (e.g. Eisen et al Genetic assessment wait time indicators in the High risk Ontario Breast screening program Molecular Genetics and Genomic Medicine 2017)

- Line 102 - Familial hypercholesterolemia - this is an example of cascade screening - seems to be mixing up family history identifying those at increased risk and cascade screening - they are quite different

- Line 103 - I don't understand the point of this Dutch example - needs better explanation

- Line 133-135 - this concept of opportunity cost is true in all of medicine - might consider citing McGuire and Burke. An unwelcome side of direct-to-consumer personal genome testing: raiding the medical commons - JAMA 2008 - as they describe it eloquently

- Line 140 on - Resource allocation - this concept of disease areas having their own budget is complex and requires more discussion and justification - ref 29 could be elaborated on

- Line 161 - Lynch syndrome associated with increased incidence of these cancers - at a younger age of onset generally

- Lines 165-170 - yes - increased detection possibly earlier - this isn't a full cost/benefit analysis - more tests earlier vs sicker people later and death
- Lines 181 on - there are many reviews of these frameworks to evaluate genetic tests - one example is found at https://www.ncbi.nlm.nih.gov/books/NBK425803/ as there are more than cited here

- Lines 218-223 - this is a good section on patient experience

- Line 232 - some reference on shared decision making would be good here

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If not, please specify what is required in your comments to the authors.

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