JOSHA`s Critical Review of: “Systematic reanalysis of clinical exome data yields additional diagnoses: implications for providers”: IS THERE A NEED FOR “RECALL” IN CLINICAL MEDICINE?

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Abstract: In this study, the importance of new information generated after the initial diagnostic genome analysis was performed is strikingly demonstrated by the fact that new information was of relevance in 10% of the patients in this analysis. While this study focusses on clinical exome analysis, the implications go far beyond this study and potentially apply to all diagnostic and therapeutic procedures performed.

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"Systematic reanalysis of clinical exome data yields additional diagnoses: implications for providers": IS THERE A NEED FOR "RECALL" IN CLINICAL MEDICINE?

By Aaron M. Wenger, PhD[1], Harendra Guturu, PhD[1], Jonathan A. Bernstein, MD, PhD[1] and Gill Bejerano, PhD[1,2,3]

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JOSHA`s Comments

In this study, the importance of new information generated after the initial diagnostic genome analysis was performed is strikingly demonstrated by the fact that new information was of relevance in 10% of the patients in this analysis. While this study focusses on clinical exome analysis, the implications go far beyond this study and potentially apply to all diagnostic and therapeutic procedures performed.

The principal of "product recall", e.g. to inform car owners, purchasers of consumer products etc. of defects detected after their purchase is a legal obligation. In medicine, new information regarding drugs or medical devices is distributed by the regulatory agencies to care givers and frequently also to the general public. The need to "recall" patients is well recognized in this and other studies. However, it is argued that this is an unsurmountable challenge in clinical reality. We feel, that this argument is valid, but should not lead to resignation but should be considered a challenge in order to optimize patient care.

While IT-based approaches will most likely be the answer in the future, a more practical approach to be immediately implemented, are regular visits of such patients, like the “annual physical examination”. In a recent discussion in the New England Journal of Medicine (Goroll 2015, Mehrotra 2015) of the value of the “Annual Physical” this aspect has been overlooked, not addressing the difference between patients without a history of diagnostic or therapeutic interventions and those with interventions in the past. This aspect is the focus of the paper by Mastroleo et al. (JOSHA, in press), while the ethical aspects of the information process have been convincingly detailed by Holzer and Mastroleo (Holzer et al. 2014, Holzer 2015).

JOSHA`s Conclusion:

“Recall” of patients, when new and relevant information regarding diagnostic and therapeutic interventions performed in the past becomes available, is an ethical, medical, and most likely a legal obligation. While no easy solutions are available to solve this organizational challenge, regular doctor visits by such patients might be a practical approach to begin to address this deficit in clinical medicine.

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Original Article

Systematic reanalysis of clinical exome data yields additional diagnoses: implications for providers

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Original Abstract

Purpose: Clinical exome sequencing is non-diagnostic for about 75% of patients evaluated for a possible Mendelian disorder. We examined the ability of systematic reevaluation of exome data to establish additional diagnoses.

Methods: The exome and phenotypic data of 40 individuals with previously non-diagnostic clinical exomes were reanalyzed with current software and literature.

Results: A definitive diagnosis was identified for 4 of 40 participants (10%). In these cases, the causative variant is de novo and in a relevant autosomal-dominant disease gene. The literature to tie the causative genes to the participants' phenotypes was weak, nonexistent, or not readily located at the time of the initial clinical exome reports. At the time of diagnosis by reanalysis, the supporting literature was 1 to 3 years old.

Conclusion: Approximately 250 gene–disease and 9,200 variant–disease associations are reported annually. This increase in information necessitates regular reevaluation of non-diagnostic exomes. To be practical, systematic reanalysis requires further automation and more up-to-date variant databases. To maximize the diagnostic yield of exome sequencing, providers should periodically request reanalysis of non-diagnostic exomes. Accordingly, policies regarding reanalysis should be weighed in combination with factors such as cost and turn- around time when selecting a clinical exome laboratory.

Key Words: diagnostic yield; exome; reanalysis

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