Opinion Paper

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Theranos phenomenon – part 2

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Abstract: Theranos' Chief Executive Officer recently published a paper in *The Wall Street Journal* committing to submit all of their tests for FDA approval and renewing her promise that self-testing by the general public will empower people to detect asymptomatic disease early, which will lead to life-saving therapeutic or preventive measures. This opinion paper provides additional information on the benefits and harms of self-testing and self-interpretation of laboratory tests by asymptomatic individuals. We conclude that the health benefit claims of Theranos are hypothetical and they are not supported by evidence. Until such evidence is provided, self-testing of the healthy population should be discouraged.

Keywords: overdiagnosis; overtesting; overtreatment; self-interpretation; self-testing; Theranos.

A few months ago, one of us authored a manuscript [1] which analyzed the Theranos phenomenon and outlined its promises and fallacies. In the previous contribution we commented on the novelty of the Theranos technology, their promise of speedy and cheap results, the advantages and disadvantages of venipuncture vs fingerprick blood sampling, etc. The report was welcomed by many readers, who provided their own input on the issues raised.

We take this opportunity to continue analyzing this company, and others with similar goals, after *The Wall Street Journal* article from the CEO of Theranos, Elizabeth Holmes on July 29, 2015 (http://www.wsj.com/articles/how-to-usher-in-a-new-era-of-preventive-healthcare-1438125343). This article deals with some issues that have already been commented upon, as well as some new issues. One is Ms. Holmes' commitment to submit all of her tests for review by the Food and Drug Administration (FDA) and Theranos has already at least 1 FDA-approved test in the market. This is certainly a positive step forward. We should mention here a few caveats on FDA approvals, which are probably not well known to the public. FDA approval means that the new test is equivalent to other approved tests of similar kind. In this respect, FDA approval does not mean that the new test is superior to already existing ones, and FDA does not examine on how the tests were performed; i.e. with more or less sophisticated technology. Another issue is that FDA approval does not guarantee the long-term performance of the test. As mentioned earlier [1], it will take time to verify if the Theranos results are of high-quality long-term, with different lots of reagents, etc. These data will become available through external quality assurance programs to which Theranos is obliged to participate.

Another major point raised in Ms. Holmes' article relates to her promise that by empowering patients to get any lab test on their own, they may get a health advantage, as they could discover early asymptomatic disease, before it is too late. This implies that early, life-saving therapeutic or preventative measures could be taken. The promise and the gains are purely hypothetical, and based on what we know today about laboratory testing, the suggestions are not likely to succeed. Additionally, the self-testing, and the self-interpretation, have hidden risks which are not mentioned in Ms. Holmes letter.

At the 2015 American Association for Clinical Chemistry annual meeting in Atlanta, Georgia (July 26–30, 2015), we presented a symposium, entitled "The Side Effects of Translational Omics: Overtesting, Overdiagnosis and Overtreatment". Among the over 200 participants, we asked questions and recorded the responses, related to the practices of Theranos and other similar companies [e.g. the newly created wellness company Arivale, which promises to provide individuals a scientific path to optimize wellness and avoid disease by using preventive diagnostic testing (https://www.arivale.com/)].

We asked the audience (clinical chemists, pathologists, and laboratory technologists who are familiar with

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laboratory testing) if they will choose to undergo "proactive" laboratory testing if they feel good and they do not suspect any health problems; over 90% chose to not subject themselves to such testing, unless they had a specific symptom. Ms. Holmes did not comment on the fact that even sophisticated laboratory scientists and clinicians, would have difficulty in selecting among the available 100–200 tests, one, or a few, for wellness testing. The likely approach would be to "do all just in case to cover all bases", if cost would not be an issue. When we asked participants which disease they would want to diagnosis early, only diabetes was mentioned. So, it was clear that the suggested wellness testing was a shot in the dark and not a logical and thoughtful decision.

We also draw attention that with the possible exception of detection of exposure to infectious agents (such as detecting antibodies to viruses and bacteria), most laboratory tests are not pathognomonic of any disease. Assessment of laboratory results (numbers) without considering patient history and clinical findings could be dangerous, especially if the interpreters (in this case the general public) are not familiar with human physiology. For example, the most powerful test we have to test kidney function is serum creatinine, which is among the top 5 most frequently ordered tests. With a reference range of 50–115 μmol/L, a lay person would interpret a creatinine of 110 μmol/L to be within the normal (reference) range but a physician would know that almost 50% of kidney function could have been lost, if a previously measured serum creatinine was 80 μmol/L. Examples of this sort pinpoint to one significant problem of self-testing and self-interpretation. Results may falsely reassure patients that nothing is wrong, while there is an underlying disease and vice versa. A results of total protein of 82 g/L will be considered abnormal by a lay person (upper limit is 80 g/L), and possibly trigger anxiety, visits to doctors and hospitals and additional and probably invasive and expensive investigations, while it is known that 5%–10% of the population without any disease, could present with this value. Many laboratory tests are also temporally affected; for example, testing for cardiac troponin to detect a myocardial infraction 2–3 days after the onset of symptoms, will likely produce a false negative result and false reassurance. Additional examples of tests with important caveats in interpretation have been provided earlier [1].

Physicians and laboratory scientists are well-aware that no laboratory test is perfect and that each testing (especially panels) will produce false positive and false negative results which could lead to additional and costly interventions; these weaknesses have not been mentioned by Ms. Holmes. As also mentioned earlier [1], testing asymptomatic individuals to detect low prevalence diseases is usually ineffective, because the positive predictive value of the test (i.e. your chances of having the disease if the test is positive) will be very low, in the order of 5% or lower, due to the anticipated many false positives. These caveats are not familiar to the people that Theranos and other similar companies are targeting. False positives would likely cause their costumers stress and trigger unnecessary visits to family doctors and hospitals, with little or no benefit to their overall health.

When we asked participants of the AACC conference if they want to take their health into their own hands (as proclaimed by Theranos and other similar companies) or instead have their family doctor be the guardian of their health, the majority chose the second. Regarding Arivale, which suggests that their customers will have their own coaches to monitor their health, and advise them on what to do, the audience commented that the cost of such an approach would be prohibitive to the general public, and only wealthy individuals may take advantage of such an initiative.

We conclude that the article of Ms. Holmes in *The Wall Street Journal* disseminates simplistic information about diagnosis, prevention and treatment of human diseases by using self-directed laboratory testing. These practices will not only fail to diagnose early and asymptomatic disease, but will likely drive large numbers of anxious customers to their family doctors and hospitals, to perform supplementary, costly, and probably invasive investigations with very low yields. We predict that such testing will produce very few good stories and very many bad stories, in years to come. Unfortunately, the bias of public media to promote more good than bad stories, may skew the public opinion on the subject. We suggest that at least some pilot studies by independent groups should the conducted, so that the actual facts on benefits and risks of such practices are more rationally presented.

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References

1. Diamandis EP. Theranos phenomenon: promises and fallacies. Clin Chem Lab Med 2015;53:989–93.