Potential Market for Novel Tuberculosis Diagnostics: Worth the Investment?

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Background. The potential available market (PAM) for new diagnostics for tuberculosis that meet the specifications of the high-priority target product profiles (TPPs) is currently unknown.

Methods. We estimated the PAM in 2020 in 4 high-burden countries (South Africa, Brazil, China, and India) for tests that meet the specifications outlined in the TPPs. The yearly PAM was estimated for the most likely application of each TPP.

Results. In 2020 the PAM for all 4 countries together was estimated to be (1) 12M tests/year with a value of 48M-71M USD for a sputum smear-replacement test; (2) 16M tests/year with a value of 65M–97M USD for a biomarker test; (3) 18M tests/year with a value of 18M–35M USD for a triage test; (4) 12M tests/year with a value of 59M–2238M USD for a tuberculosis detection plus drug susceptibility test (DST) all-in-one or 1.5M tests/year for a DST that follows a positive tuberculosis detection test with a corresponding value of 75M–121M for both tuberculosis detection and DST.

Conclusions. Although there is a considerable potential market for novel tuberculosis diagnostics that fit the specification of the TPPs in the 4 high-burden countries, the actual market for an individual product remains uncertain.

Keywords. tuberculosis; diagnostics; market analysis; market projection; cost; tests; target product profiles.

Recently the World Health Assembly adopted the post-2015 global tuberculosis strategy setting the target for a world free of tuberculosis [1].

Without the introduction of new tools that can cause a more rapid decline in tuberculosis incidence than the current global decline of 2% per year, it is obvious that the post-2015 targets will not be achieved. The development and implementation of new tools and interventions, such as a more effective tuberculosis vaccine, and tuberculosis treatment regimens or more accurate diagnostics that reach more patients are therefore urgently needed.

Recently the tuberculosis community identified the highest needs for new tuberculosis diagnostics [2, 3].

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Four of these detailed target product profiles (TPPs) were developed, and the tuberculosis community reached consensus on the most important specifications laid out in each of these TPPs [4, 5]. The 4 TPPs, described in detail elsewhere in this supplement [4] included (1) A point of care sputum-based test as a replacement for smear-microscopy ('smear replacement test'); (2) A point of care, non-sputum-based test capable of detecting all forms of tuberculosis via the identification of characteristic biomarkers or biosignatures, ideally suitable for use at levels below microscopy centers ("non-sputum based biomarker test"); (3) A simple, low cost, point of care triage test, for use by first-contact health care providers as a rule-out test, ideally suitable for use by community health workers ("triage test"); and (4) A rapid drug susceptibility test (DST) that either combines tuberculosis detection and DST into one step ("tuberculosis detection plus DST upfront") or performs tuberculosis detection first and is followed by DST as a second step whenever tuberculosis (or tuberculosis and rifampicin resistance) is detected ("DST after tuberculosis detection test").

Test developers have indicated that apart from clearly specified product requirements, key drivers for them to

start or continue product development are the time to return on investment, the global market size, the market size on a country level, and the market dynamics [6].

Thus far, several analyses of the tuberculosis diagnostic market have been done, either on a global level or on a country level [7–9]. The tuberculosis diagnostic market has been determined for South Africa and Brazil, and others are underway for China and India [7,9]. Those assessments focused on the current, served available market of existing tuberculosis diagnostics and did not make any inferences on the potential market of novel tests that target other (new) populations now or in the near future.

In this article, we estimate the potential available market (PAM) for the 4 novel high-priority tests, for which TPPs are in place. This market is described for 4 high-burden countries, being South Africa, Brazil, China, and India, which are part of the BRICS countries (including Russia). The BRICS countries amount to 60% of the total burden of tuberculosis in the 22 high-burden countries and therefore are of special interest for test developers and for tuberculosis control.

METHODS

The potential market in 2020 was estimated both in terms of volume and value for the following 4 selected countries; South Africa, Brazil, China, and India. These countries are emerging economies that are of interest for test manufacturers and have a high tuberculosis burden (they account for 46% of the 6 million tuberculosis cases detected in 2012). The potential market value was calculated by multiplying the projected volume for each of the tests by its lowest and highest price as indicated in the TPP. However, the prices indicated in the TPP are ex-works costs which include the manufacturers' price but do not include any costs related to shipping, import, tax, and distribution. Because there was no consensus reached on the price of the rapid DST TPP, we assumed that the price of the "tuberculosis detection plus DST upfront test" would lie in the range of US$5 to US$20 per test, similar to what was assumed by Pantoja et al [10]. When DST would only follow a positive tuberculosis detection (or rifampicin resistant) test, we assumed that the price of the tuberculosis detection test would be similar to that of a sputum smear-replacement test outlined in TPP 1 (US$5) and that the price of the DST would be between US$10 and US$40 (corresponding with a total of US$15–US$45 for tuberculosis detection and DST).

Using country-specific notification data and prevalence estimates [11], we first determined the potential market per country for each of the TPPs for the year 2012 as a base. For each country, the proportion of tuberculosis patients with pulmonary tuberculosis (PTB), extrapulmonary tuberculosis (EPTB), and children with tuberculosis (assumed to be unable to provide a sputum sample and therefore not included in the number of PTB patients), were estimated separately. Next, the number of prevalent tuberculosis patients in 2012 in each of these categories was determined, using the World Health Organization's (WHO) estimated prevalence data.

To calculate the number of individuals with signs and symptoms suggestive of tuberculosis that need to be tested to find all prevalent tuberculosis, we applied a country specific "suspect-to-case" ratio, defined as the number of individuals that is being tested in order to find 1 tuberculosis case. For each of the countries this ratio was calculated based on PTB cases and was then extrapolated to other non-PTB cases due to lack of information for the latter. This ratio was either determined based on country specific data on the number of individuals that were screened in 2012 with smear (and/or the Xpert MTB/RIF® assay "Xpert") as the initial test (South Africa and India) or number of smears done for the initials diagnosis (China and Brazil) and the number of notified PTB cases in 2012 dependent on the availability of data.

Because no novel tests that meets the specification outlined in the TPPs is on the market yet, but tests are anticipated to become available within the next 5 years, we estimated the potential market for each of the novel products for the year 2020. The number of prevalent tuberculosis cases in 2020 was estimated based on the 3-year average decline in the tuberculosis prevalence rate and multiplied by the expected population size in 2020 according to the World Bank [12].

For each TPP, the potential market of the base case scenario represented the most likely use of the test with regard to where in the health-care system it would be implemented and its purpose and intended target population (eg, adults and children suspected of PTB, EPTB). In addition, the potential market was determined for alternative scenarios where the test would, for instance:

1. be used on more or less individuals with presumptive tuberculosis than the current estimate by assuming a lower or higher "suspect-to-case" ratio (applicable for all tests but shown for the smear replacement test);

2. be deployed at a lower level of the health-care system and therefore reach a larger population (applicable for the biomarker and triage test); or

3. only be able to test a subset of the intended target population (applicable for the biomarker test or triage test if these would not detect EPTB but only test individuals with presumptive PTB and children with tuberculosis, such as for instance a breath test); or

4. for the DST detection test, would be done after a more sensitive tuberculosis detection test or be done in a staged approach only after rifampicin resistance is found (eg, after Xpert MTB/RIF testing up-front). The different scenarios of each TPP for which we determined the potential market size and value are explained in Table 1. The method we describe and applied for estimating and projecting the potential market size could be used to estimate the potential market in other countries.

Table 1. Base Case and Alternative Scenarios of the Target Product Profiles (TPPs) for Which the Potential Market is Determined

	Scenario	Description
TPP1: smear replacement test	Base case	Sputum-based smear replacement test, deployed at microscopy centers, used for the initial diagnosis in individuals with presumptive PTB
	Plus treatment monitoring	Sputum-based smear replacement test, deployed at microscopy centers, used for the initial diagnosis as well as for treatment monitoring in individuals with PTB. Two additional tests were assumed per diagnosed PTB case for treatment monitoring.
	Low suspect-to case ratio	Sputum-based smear replacement test, deployed at microscopy centers, used for the initial diagnosis in individuals with presumptive PTB. A 'suspect-to-case' ratio of 5 was used to estimate the number of individuals tested to find one PTB case instead of the country specific ratio.
	High suspect-to-case ratio	Sputum-based smear replacement test, deployed at microscopy centers, used for the initial diagnosis in individuals with presumptive PTB. A 'suspect-to-case' ratio of 15 was used to estimate the number of individuals tested to find one PTB case instead of the country specific ratio.
TPP2: biomarker test	Base case	Non-sputum-based biomarker test, deployed at microscopy centers and health-care clinics with a lab attached (equal to a 10% increase compared to deployment at microscopy centers only), used for the initial diagnosis in individuals with presumptive PTB, EPTB or children with tuberculosis.
	Deployment at health posts	Non-sputum-based biomarker test, deployed at health posts (without the necessity of a lab), used for the initial diagnosis in individuals with presumptive PTB, EPTB or children with tuberculosis. An increase of 20% in the number of individuals that get tested was assumed compared to when this test would only be deployed at microscopy centers.
	Deployment at microscopy centers, excluding EPTB testing	Non-sputum-based biomarker test, deployed at microscopy centers and health-care clinics with a lab attached (equal to a 10% increase compared to deployment at microscopy centers only), used for the initial diagnosis in individuals with presumptive PTB or children with tuberculosis.
TPP3: triage test	Base case	Non-sputum-based triage test, deployed at health posts (20% increase in number of individuals tested compared to use at a microscopy centre), used to rule out tuberculosis in individuals with presumptive PTB, EPTB or children with tuberculosis.
	Sputum based test, deployment at health posts	Sputum-based triage test, deployed at health posts (20% increase in number of individuals tested compared to use at a microscopy centre), used to rule out tuberculosis in individuals with presumptive PTB.
	Non-sputum based test, deployment at community	Non-sputum-based triage test, deployed at community care (30% increase in number of individuals tested compared to use at a microscopy centre), used to rule out tuberculosis in individuals with presumptive PTB, EPTB or children with tuberculosis.
TPP 4A: tuberculosis detection plus DST upfront	Scenarios are equal to those described for TPP1. This TPP is not shown separately.	Sputum-based tuberculosis detection and DST in one, deployed at microscopy centers, used for the initial diagnosis of PTB and drug susceptibility testing of at least 1 drug in individuals with presumptive PTB.
TPP4B: DST after tuberculosis detection test	Base case, DST after tuberculosis detection	Sputum-based DST, deployed at microscopy centers, used to test for drug susceptibility in individuals who are diagnosed with PTB. An 80% sensitivity was assumed for the diagnosis of PTB.
	Increased sensitivity of PTB detection (95%)	Sputum-based DST, deployed at microscopy centers, used to test for drug susceptibility in individuals who are diagnosed with PTB. An increased sensitivity of 95% was assumed for the diagnosis of PTB.
	DST detection after detection of RIF resistance	Sputum-based DST, deployed at microscopy centers, used to test for drug susceptibility in individuals who are diagnosed with RIF resistant PTB. A 80% sensitivity was assumed for the diagnosis of PTB. Country-specific prevalence of MDR tuberculosis was used as indicator for RIF resistance prevalence.

Abbreviations: DST, drug susceptibility test; EPTB, extrapulmonary tuberculosis; MDR, multidrug resistant; PTB, pulmonary tuberculosis; RIF, rifampicin.

RESULTS

In 2012 a total of 17 million individuals with presumptive PTB were evaluated for the initial diagnosis of active tuberculosis using the current tests for detection available (smear microscopy or Xpert) in the four countries (Table 2). We estimated that approximately 46% of the individual with presumptive PTB were not tested (range between 12% and 57% for the individual countries). Based on the country specific

Table 2. Key Variables and Assumptions per Country

Variable or Assumption	South Africa		Brazil		China		India		Total		Source
	2012	2020	2012	2020	2012	2020	2012	2020	2012	2020	
Prevalent tuberculosis cases	450 000	426 660	120 000	130 606	1 400 000	962 642	2 800 000	1 628 969	4 770 000	3 148 878	2012: WHO report 2013 2020: estimated based on population size in 2020 according to World Bank and estimated tuberculosis prevalence rate (using country specific 3-year average decline in tuberculosis prevalence rate)
Percentage of all prevalent tuberculosis patients that have PTB	76%	Same as 2012	78%	Same as 2012	98%	Same as 2012	72%	Same as 2012	80%	Same as 2012	WHO report 2013
Percentage of all prevalent tuberculosis patients that have EPTB	14%	Same as 2012	14%	Same as 2012	0.75%	Same as 2012	20%	Same as 2012	14%	Same as 2012	WHO report 2013: % of notified tuberculosis cases with EPTB
Percentage of all prevalent tuberculosis patients that are children with tuberculosis (unable to provide sputum)	10%	Same as 2012	8%	Same as 2012	1%	Same as 2012	8%	Same as 2012	6%	Same as 2012	Calculation: notified smear-positive tuberculosis cases among children assumed to represent 5% of all children with tuberculosis (personal communication A. Mandelakas and B. Kampmann) and 85% of children with tuberculosis assumed to be unable to produce sputum.
Number of individuals with presumptive tuberculosis needed to test to find one tuberculosis case ('suspect to case ratio')	7	Same as 2012	15	Same as 2012	7	Same as 2012	9	Same as 2012	8.3[a]	8.6[a]	Country specific ratio's obtained from NTPs or data from NTPs
Estimated number of individuals with presumptive PTB	2 393 650	2 986 623	1 400 100	1 523 843	9 596 671	6 598 687	18 177 579	10 575 255	31 568 000	21 684 408	Calculation: (number of prevalent PTB cases in 2012 multiplied by the suspect-to-case-ratio)

Table 2 continued.

Variable or Assumption	South Africa		Brazil		China		India		Total		Source
	2012	2020	2012	2020	2012	2020	2012	2020	2012	2020	Source
Number of individuals with presumptive PTB suspects tested in 2012 (in microscopy centers)	2 116 667 (88% of PTB suspects)	88% of PTB suspects	965 544 (69% of PTB suspects)	69% of PTB suspects	6 173 936 (64% of PTB suspects)	64% of PTB suspects	7 867 194 (43% of PTB suspects)	43% of PTB suspects	17 123 341 (54% of PTB suspects)	54% of PTB suspects	Number of individuals tested with smear and/or Xpert in each country (data provided by NTPs)
Number of individuals with presumptive PTB not tested in 2012	276 983	12% of PTB suspects	434 556	31% of PTB suspects	3 422 735	36% of PTB suspects	10 310 385	57% of PTB suspects	14 444 659	46% of PTB suspects	Calculation: (number of prevalent PTB cases in 2012 multiplied by suspect-to-case-ratio) − (tuberculosis suspects tested in the public and private sector in 2012)
Number of individuals with presumptive EPTB (assumed all not tested in 2012)	441 000	418 127	252 000	274 272	73 500	50 539	5 040 000	2 932 144	5 806 500	3 675 082	Calculation: number of EPTB cases in 2012 multiplied by suspect-to-case ratio
Number of children with presumptive tuberculosis (unable to provide sputum; therefore assumed not tested in 2012)	315 350	298 994	147 900	160 972	129 829	89 271	1 982 421	1 153 322	2 575 500	1 702 559	Calculation: number of children with tuberculosis, unable to provide sputum in 2012 multiplied by suspect-to-case ratio
Total number of individuals with presumptive tuberculosis (PTB, EPTB and children combined) in the country	3 150 000	2 986 623	1 800 000	1 959 087	9 800 000	6 738 496	25 200 000	14 660 721	39 950 000	26 344 927	Calculation: sum of number of individuals with presumptive PTB, EPTB and children with presumptive tuberculosis (unable to provide sputum)

Abbreviations: EPTB, extrapulmonary tuberculosis; NTP, national tuberculosis programmes; PTB, pulmonary tuberculosis; WHO, World Health Organization.
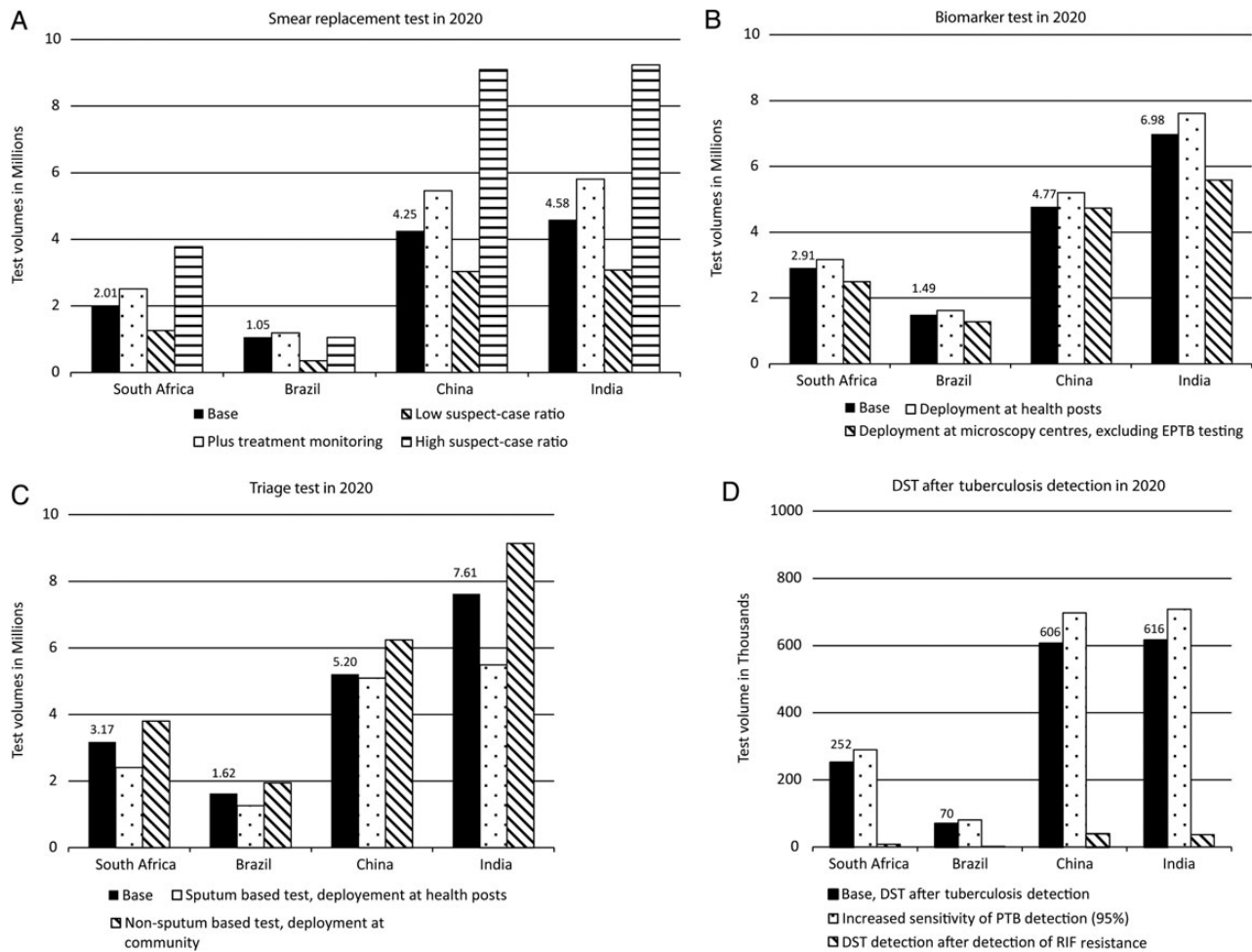
[a] Weighted averages.

Figure 1. Potential available market (volume) for novel tuberculosis diagnostics in 2020 in 4 example countries. *A*, Smear replacement test (TPP 1 and TPP 4A). *B*, Biomarker test (TPP 2). *C*, Triage test (TPP 3). *D*, drug susceptibility test (DST) after tuberculosis detection test (TPP 4B). Abbreviations: PTB, pulmonary tuberculosis; RIF, rifampicin; TPP, target product profile.

"suspect-to-case" ratio, which ranged between 7 in South Africa and China up to 15 in Brazil, we estimated that an additional 5.8 million individuals with presumptive EPTB and another 2.6 million children with presumptive sputum-scarce tuberculosis could have been evaluated in these countries in 2012.

The absolute number of prevalent tuberculosis cases is expected to decline in the coming years in all 4 countries because the population growth rate is smaller than the decline in the tuberculosis incidence rate. The total number of prevalent cases in these 4 countries in 2020 was estimated to be around 3.1 million.

Potential Available Market for a Smear Replacement Test in 2020

For a novel smear replacement test with increased sensitivity for the detection of PTB on sputum that can be deployed at microscopy centers with quick turnaround time, the potential market size in 2020 was estimated at 2.0 million in South Africa, 1.1 million in Brazil, 4.3 million in China, and 4.6 million in

India. This amounts to a total of 12 million tests in that year (Figure 1A). If the smear replacement test could also be used for treatment monitoring and on average 2 additional tests per diagnosed PTB case would be conducted during therapy, the potential market size would grow to 15 million tests per year in all four countries combined. Considering changes in the assumed number of individuals that is tested in order to find one tuberculosis case (eg, lower or higher "suspect-to-case-ratio") the potential market size would vary between 7.7 million (ratio of 5 in all countries) and 23 million tests (ratio of 15 in all countries). The potential market value for a smear replacement test under the base scenario will range between US$48 million for a US$4 test up to US$71 million for a US$6 test in all 4 countries together (Figure 2).

Potential Available Market for a Biomarker Test in 2020

According to its TPP, a novel biomarker test that uses a non-sputum based sample should ideally detect all forms of tuberculosis and be feasible to conduct at least in microscopy centers or
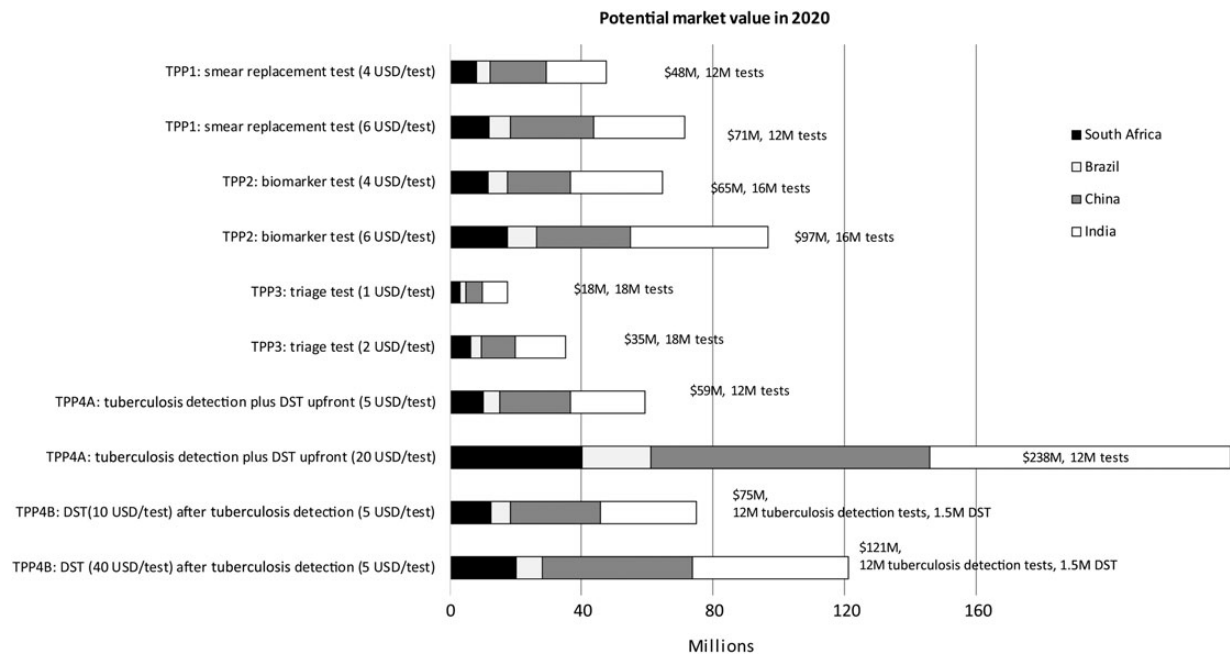
Figure 2. Potential available market (PAM) (value) for novel tuberculosis diagnostics in 2020 in 4 example countries. PAM in 2020 is presented for the base case TPPs at their 2 price points. TPP1 shows the potential market value in 2020 for a TPP for a smear replacement test, deployed at microscopy centers, used for the initial diagnosis of individuals with presumptive pulmonary tuberculosis, and at a price per test of US$4 and US$6. TPP2 shows the potential market value in 2020 for a TPP for a biomarker based test, deployed at microscopy centers and health-care clinics with a lab, used for the initial diagnosis of individuals with presumptive active tuberculosis (all forms), and at a price per test of US$4 and US$6. TPP3 shows the potential market value in 2020 for a TPP for a community triage test, deployed at health posts, used for the screening of individuals with presumptive active tuberculosis (all forms), and at a price per test of US$1 and US$2. TPP4A shows the potential market value in 2020 for a TPP of a tuberculosis detection and drug susceptibility test (DST) in one, deployed at microscopy centers, used for the detection of drug susceptibility in individuals with pulmonary tuberculosis, and at a price per test of US$5 and US$20 for tuberculosis detection and DST combined. TPP4B shows the potential market value in 2020 for a TPP where the DST is conducted after a positive tuberculosis detection. Both tests are deployed at microscopy centers, used for the detection of drug susceptibility in individuals with pulmonary tuberculosis, and at a price of US$5 per tuberculosis detection test and US$10 or US$40 for the DST is assumed. Abbreviation: TPP, target product profile.

health-care clinics with some form of a laboratory attached. Due to its wider applicability, both in terms of target population and in the number of facilities where the test can be conducted, the PAM size in 2020 was estimated at 16.1 million tests for all 4 countries (Figure 1B). Obviously, the market size would increase if the test could be deployed at lower levels of the health-care system such as health posts without a laboratory (total estimated at 17.6 million). On the other hand, if the biomarker test would not be able to diagnose EPTB but would detect only PTB and tuberculosis in children, its market size would be reduced by 13% compared to the base scenario (total market size 14 million tests).

The potential market value for a biomarker test, for the base case scenario, will range between US$65 million for a US$4 test and US$97 million for a US$6 test in total in all 4 countries.

Potential Available Market for a Triage Test

A non-sputum based triage test that is easy to conduct at health posts that do not have a laboratory attached and be used to rule out tuberculosis in individuals with presumptive tuberculosis could have a potential market size of 17.6 million tests in the 4 example countries combined (Figure 1C). In essence, the triage test is expected to have about 10% larger market size than the biomarker test because the test aims to reach difficult to reach populations that did not have access to tuberculosis testing before. Although the potential market size for the TPPs described here is largest for a triage test, its market value is lowest (range between US$18 and US$35 million in total for all 4 countries under the base scenario) because the optimal price range anticipated is US$1 to US$2 per test.

Potential Available Market for a DST in 2020

For a novel (sputum-based) rapid DST there are 2 possible options. First, the test can combine tuberculosis detection and DST into one step (as in the case of Xpert) and test both for the presence of *Mycobacterium tuberculosis* as for resistance against at least one anti-tuberculosis drug in the same sample and in the same test run. For such a test, the potential market

size is equal to that of the smear replacement test (Figure 1A), but because this test may cost slightly more, its potential market value in 2020 in all 4 countries is estimated between US$59 and US$238 million for a US$5 to US$20 test (Figure 2).

The second option is that DST only is done after a positive tuberculosis detection test. In this case, the potential market size for the DST would be much smaller with a total of 252 000 tests in South Africa, 70 000 in Brazil, 606 000 in China, and 616 000 in India (Figure 1D; a total of 1.5 million tests). Nevertheless, the potential market value for both tuberculosis detection at an average price of US$5 per test followed by DST (at least one drug but preferably more first-line drugs) at a price range between US$10 and US$40 for DST would amount between US$75 million and US$121 million (Figure 2).

DISCUSSION

In this study, we described the PAM in 2020 for 4 novel diagnostics that meet the specification outlined in the TPPs described elsewhere in this supplement [4, 5]. This PAM was determined both in size and in value for 4 countries (South Africa, Brazil, China, and India) that have a high tuberculosis burden but also are emerging economies that can invest in the implementation and rollout of new, modern technologies that have the potential to lead to increased testing and enhanced case detection and which are therefore of interest for test developers.

Product developers need data on issues such as potential global market size, the potential country specific market size, and return on investment, but such information is often lacking (D. Dolinger, FIND, personal communication) [6]. We showed a general approach for estimating the PAM for novel products when used in their intended target population and at their intended level of the health-care system, which can be adapted for other countries or for other assumptions.

Our results indicate that, of the 4 TPPs, the greatest PAM in terms of value would be for a (sputum-based) tuberculosis detection and DST upfront test although this is mainly a result of the high cost per test that we assumed (up to US$20). Such a test, essentially, would be a more sensitive "Xpert"-like test that not only tests for the presence of *M. tuberculosis* and rifampicin resistance but also resistance against additional drugs. Although the potential market looks promising, it is questionable if such a test would be affordable for all countries at this price point [10]. Cost-effectiveness studies on an individual country level are recommended which can take the local epidemiology (eg, prevalence of MDR-tuberculosis) and current testing algorithms in place into account to assess which test strategies are most effective and least costly. Tests that can be deployed at lower levels of the health-care system and which could be used for the detection (or rule-out) of all forms of tuberculosis, such as a biomarker test or a triage test would have the largest potential market volume. And a triage test algorithm might

even be cost-effective even at an even higher price point than what we have used here [13].

In this study, we determined the total PAM for novel tests under the assumption that these would be implemented throughout the whole country and cover 100% of the intended health-care facilities. When different products will reach the market that fit within the same TPP, obviously these products would compete for a share of the same potential available market. Products that meet more of the criteria listed under the "optimal" scenario of the TPPs might account for a larger market share.

In addition, there is interplay between the different TPPs. Although the tuberculosis community has expressed a need for each of the TPPs, and there will be a market for each of them, there is potential overlap in the target populations of some of the tests. Although a triage test and rapid DST are unlikely to compete, a biomarker test for instance will likely replace a smear-replacement test. As a result, there may not only be competition for products that fit the same TPP, but competition could also occur between products that meet different TPPs. The time that novel products will enter the market, the strength of evidence on the test, the recommended use by national and international guidelines of these products in global or local diagnostics algorithms, but also the local epidemiology and preferences will therefore greatly determine the actual market size and penetration.

Several limitations should be taken into consideration when interpreting our results. First, one of the main assumptions in our analysis was the country-specific "suspect-to-case" ratio. Upon changes in this ratio either to a higher or lower number the estimated market size and consequently its volume fluctuated considerably (−35% or +96% when all 4 countries were combined). Although we determined country specific ratios, these were based on the number of individuals with presumptive PTB tested in order to find one PTB case and were assumed to be equal for EPTB and children with tuberculosis (unable to provide sputum), which might not be true. Moreover, we assumed that this ratio would remain constant and not change when tests would be applied at lower levels of the health-care system, while in fact this ratio is likely to increase over time when the prevalence decreases.

In our estimates we used the prevalence estimates according to the WHO. Although these estimates are yearly updated and refined, there is uncertainty around the precise prevalence rates and therefore also the estimates that we presented here for the potential market size for novel test.

Another limitation is that we assumed that an additional 10%, 20%, and even 30% of individuals would get tested when a test would be conducted in health-care clinics with a lab attached, health posts, or in the community besides its use in microscopy centers. Although we did not have accurate data to underpin this assumption, a study conducted by Girosi and Olmsted et al in 2006 estimated that up to 25% of the

population in Africa had access to facilities with no infrastructure, 47% to infrastructure with minimal infrastructure, and 28% to facilities with moderate to advanced infrastructure [14, 15]. Finally, there is uncertainty around the prices of novel tests. The prices used in our calculations should be considered purely indicative as it is hard to predict real prices (which are based on donor investments, special pricing and access agreements, volume-based discounts, etc.).

By 2020, it is highly like that new tuberculosis drug regimens will be available. Because newer drug regimens are critically dependent on companion diagnostics for scale-up, there are ongoing efforts to achieve convergence between diagnostics and new drug regimens [16]. The introduction of newer regimens is not expected to affect the PAM estimates outlined here, unless these will affect current testing practices and for instance lead to an increase in testing during treatment.

In conclusion, we showed that there is a great PAM in the 4 example high-burden countries for novel diagnostics such as a smear replacement test, a biomarker test, a triage test, and DST when these would meet the specifications outlined in the TPPs.

Notes

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