G-FINDER | 2022

A NEED FOR NOVEL DIAGNOSTICS: **MEETING THE MOMENT**

DECEMBER 2022

POLICY CURES RESEARCH.

FIND
Diagnosis for all

The need for novel diagnostics

Appropriate patient care, disease surveillance and effective public health responses all hinge on accurate and timely diagnosis. As a major driver of health and economic outcomes, diagnostics represent a core pillar of global health security and universal health coverage, as a fundamental component of functioning health systems.

Despite this, the importance of access to timely diagnosis remains underappreciated, and diagnostics research and development (R&D) systematically underfunded, with nearly half of the world's population having little or no access to critical diagnostics. This 'diagnostics gap' is most strongly felt in low- and middle-income countries (LMICs), especially in primary healthcare settings where only 19% of the population has access to essential diagnostics for conditions other than HIV and malaria.[1] This has major implications for the health and wellbeing of billions of people both now and in the future. Without intervention, lack of affordable and effective diagnostics will continue to remain a life-threatening crisis worldwide, stunting efforts to address global public health priorities.

In this report – prepared collaboratively by Policy Cures Research and FIND, the global alliance for diagnostics – we look into historical funding for diagnostics R&D, including areas of progress, where funding still lags behind, and what the global response to COVID-19 can tell us about the level of R&D funding we really need. We shed light on potential key drivers in the ongoing shortfall in diagnostics R&D investment for neglected diseases, emerging infectious diseases and sexual & reproductive health (SRH) issues. We then outline the case for expanded diagnostics R&D funding and how investments in diagnostics can strengthen health systems to drive progress in universal health coverage and global health security.

The content draws on more than a decade of diagnostics R&D funding data captured by Policy Cures Research's G-FINDER project, and FIND's expertise in the policy- and field-level challenges that have limited access to the range of reliable diagnostics needed, suitable and available for use in low-resource settings.

KEY FINDINGS

1. **Diagnostics receive only a small share of global health R&D funding**. Over the last decade, the share of global funding going to diagnostics R&D has ranged from a low of 4.7% ($142m) in 2013 to a high of 7.0% ($272m) in 2017, before peaking – in absolute terms – in 2020, when more than $200m was allocated to COVID-19 diagnostics R&D alongside much larger investments in COVID-19 vaccines and therapeutics. Although differences in development costs mean we would not necessarily expect equal funding across different product areas, the size of the gap in diagnostic funding appears too large to be explained solely by more expensive trials for vaccines and therapeutics.
2. **The biggest funders of diagnostics R&D are also among the largest funders of global health R&D overall.** The US National Institutes of Health, the Bill & Melinda Gates Foundation, the US Department of Defense, the US Biomedical Advanced Research and Development Authority, the European Commission, and industry together account for 69% of funding for diagnostics and diagnostic platforms over the last decade.
3. **The small share of investment in diagnostics R&D persists across all three global health areas tracked by G-FINDER, and for COVID-19.** Diagnostics receive less than a tenth of R&D funding for neglected diseases, emerging infectious diseases, sexual & reproductive health issues, as well as COVID-19.
4. **Benefits of improved diagnostics extend beyond the patient, but can be hard to measure formally.** Metrics for measuring impact need to evolve to capture the vital role of diagnostics in management of population health, pandemic preparedness and public health response at the national and global levels.
5. **A coordinated global approach is needed to provide the funding required to address the diagnostics R&D gap**. The global responses to COVID-19 and – eventually – to Ebola show that the rapid development of crucial diagnostics is possible, cost effective and comparatively cheap. We need better mechanisms for funding product development in the absence of an obvious crisis.

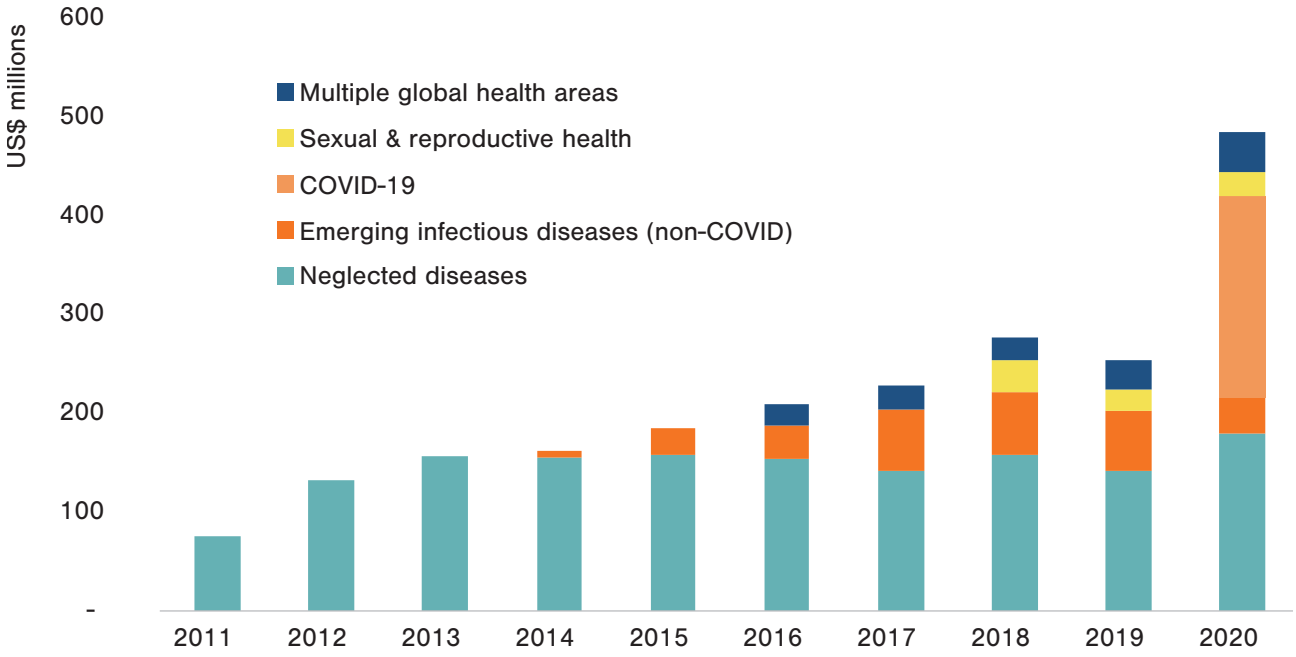
1 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00673-5/fulltext

Diagnostics R&D: a small share of all global health R&D funding

The G-FINDER survey captures R&D investment data across a range of global health areas (39 neglected diseases, 10 emerging infectious diseases, and six SRH issues or areas), spanning a number of biomedical products (drugs, vaccines, biologics, devices, vector control products, diagnostics and microbicides), as well as investment in basic research and products that have the potential to address more than one disease or health area (such as platform technologies).[2] The funding included for neglected diseases excludes areas primarily intended to meet the needs of high-income countries or for which there is a robust commercial market, instead focusing exclusively on R&D which is aimed at LMICs. Funding for SRH issues recognises a dual market across some health areas, and therefore only excludes R&D for products that are not suitable for use in LMICs. All R&D funding for emerging infectious diseases is included.

Across all global health areas and all biomedical products covered by the G-FINDER project, the share of total global R&D funding directed towards diagnostics R&D has ranged over the last decade from a low of 4.7% (US$142m) in 2013 to a high of 7.0% ($272m) in 2017.[3] In absolute terms, however, diagnostics R&D peaked in 2020 when more than $200m was invested in COVID-19 diagnostics. Even still, this figure was swamped by COVID-driven increases in R&D for vaccines ($2.1bn) and therapeutics ($1.14bn) in the same year. In other words, for every one dollar invested in COVID-19 diagnostics, $5.20 was spent on developing therapeutics, and $11 on vaccine R&D.

Figure 1: Funding for diagnostics R&D by global health area, 2011-2020



The overall upward trend in investment in diagnostics R&D since the start of the decade partly reflects the gradual rise in overall R&D funding over time, as well as the broadening scope of the G-FINDER survey over that period: we began including data on R&D for emerging infectious diseases in 2014, technologies targeting multiple global health areas in 2016, and SRH issues in 2018.

While the share of neglected disease funding over the last decade has remained relatively consistent – averaging just 5.4% – diagnostics' share of non-COVID emerging infectious disease R&D has been a little higher, making up 6.1% of total R&D funding since this health area's 2014 inclusion. This peaked in 2017 at 7.9%, thanks to a focus on Zika diagnostics and emerging infectious disease-specific diagnostic platforms. Funding for diagnostics R&D for key SRH issues, though lower in absolute terms than all other thematic

2 A list of pathogens, product types and issues covered by the survey is available at https://www.policycuresresearch.org/rd-needs-for-global-health/.

3 All figures are in 2020 US dollars and exclude funding which was not directed to a specific research area. 'Product development' funding shares also exclude funding for basic research.

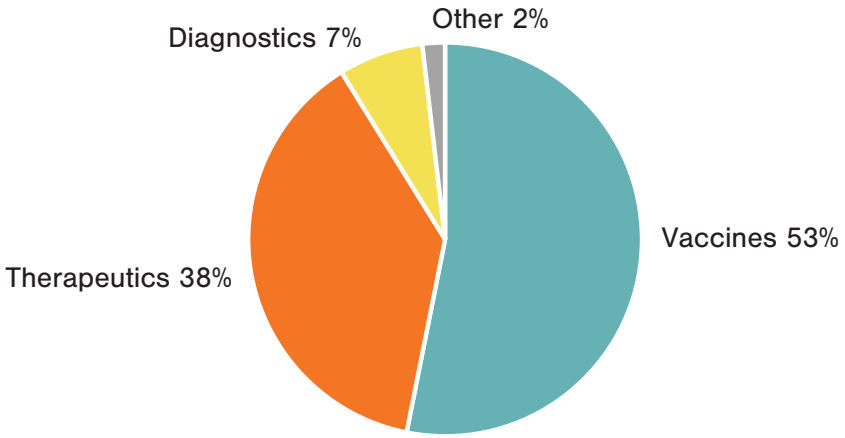
health areas under G-FINDER, received a larger share of the overall R&D budget for SRH, averaging 8.3% since 2018 when data collection commenced. Similarly, for R&D investment in products that are identified as targeting more than one global health area, a substantially larger share – over a quarter – went to diagnostics R&D, though the absolute amounts remain comparatively small. This funding was exclusively via investments in general diagnostic platforms and multi-disease diagnostics.

A broadly similar pattern of limited proportional spend of overall R&D funding invested in diagnostics is reflected in funding to combat antimicrobial resistance (AMR). While G-FINDER does not track AMR funding beyond inclusion of AMR-related pathogens in its scope, data from the Global AMR R&D Hub suggests that around 7.5% of global AMR R&D funding goes to diagnostics, compared with around 23% for therapeutics R&D.[4]

Overall, investment in diagnostics R&D is clearly lacking. The limited share of R&D funding going to diagnostics can partly be explained by lower costs of developing a diagnostic product relative to the development of novel vaccines or therapeutic products. However, it may also be representative of the persistent difficulty in demonstrating impact and return-on-investment of diagnostic products.

Diagnostics R&D for neglected disease: consistently deprioritised

Figure 2: R&D funding for neglected disease products, 2007-2020



In 2020, 4.9% of overall neglected disease funding – and 7.1% of actual product development funding (i.e., excluding basic research) – was invested in diagnostics R&D, broadly in line with the preceding ten-year average. Levels of funding to diagnostics R&D for neglected diseases have in fact fallen by $23m (-12%) over the last two years, albeit alongside slight decreases in overall investment in global health R&D during the same period. This drop in diagnostics interest was mostly due to decreases in funding for HIV diagnostics (down $7.7m in 2019 and a further $9.2m in 2020), as well as an $11m drop in funding for malaria diagnostics in 2020, the latter a result of more than halving of malaria diagnostics funding from the UK Department of Health and Social Care and the Gates Foundation. As highlighted in the spotlight on early infant HIV diagnostics below, these changes may partly reflect successes in the product development pipeline – and perhaps the effects of COVID-19 on funders' priorities – but there remain significant unmet needs for improved diagnostics for HIV and especially in malaria, where parasites are evolving to escape detection with existing tests.[5]

The picture is similar for the other neglected diseases included in our survey, with relatively limited progress in the pipeline alongside persistent unmet need for diagnostics across a range of use-cases. Despite tuberculosis (TB) receiving the most diagnostics funding amongst neglected diseases over the last ten years, there are still unmet diagnostic needs for this disease, including LMIC-appropriate point-of-care tests, paediatric diagnostic tools, and tests for drug resistance and susceptibility. Of the total $632m invested in TB diagnostics over the last ten years, at least $50m was for R&D which explicitly targeted development for

4 https://dashboard.globalamrhub.org/reports/investments/overview

5 https://www.nature.com/articles/s41564-021-00962-4

paediatric use, and another $31m for R&D explicitly intended to help detect drug resistance and susceptibility – both of which remain key areas of need to ensure proper application of the next generation of pipeline drugs.

Neglected tropical diseases (NTDs) have historically received very little diagnostics funding. In fact, mycetoma reported its first and only diagnostics funding in 2019 ($0.3m). Likewise, trachoma has seen decreasing funding almost every year since 2011, and none at all in 2020. Funding for leprosy diagnostics has also trended downwards in the years following its peak in 2012, falling to $0.2m in 2020 and leaving an ongoing unmet need for the reliable detection of asymptomatic cases.

Funding for Buruli ulcer diagnostics is currently the lone bright spot, which after four years of stable but low levels of investment ($0.6m per year in the four years prior to 2020) grew five-fold in 2020, bringing it to $3.2m. This boost was thanks to new investment by Japan's Global Health Innovative Technology Fund (GHIT) in a new rapid diagnostic test (RDT) which detects mycolactone, the nerve-damaging cytotoxin the ulcers produce.

SPOTLIGHT: POINT-OF-CARE TECHNOLOGIES FOR EARLY INFANT DIAGNOSIS OF HIV

With the goal of accelerating access to improved diagnostic tools for early HIV diagnosis among exposed infants, Unitaid partnered with the Elizabeth Glaser Pediatric AIDS Foundation, the Clinton Health Access Initiative and UNICEF in 2015 for the development, implementation and scale-up of point-of-care HIV testing technologies in nine African countries. The novel tests were designed to be portable, robust, battery-powered, and suitable for use in primary health centres. In field evaluation, the tests were able to deliver results to patients at a significantly faster rate with 99.5% of tested infants receiving results within 60 days.

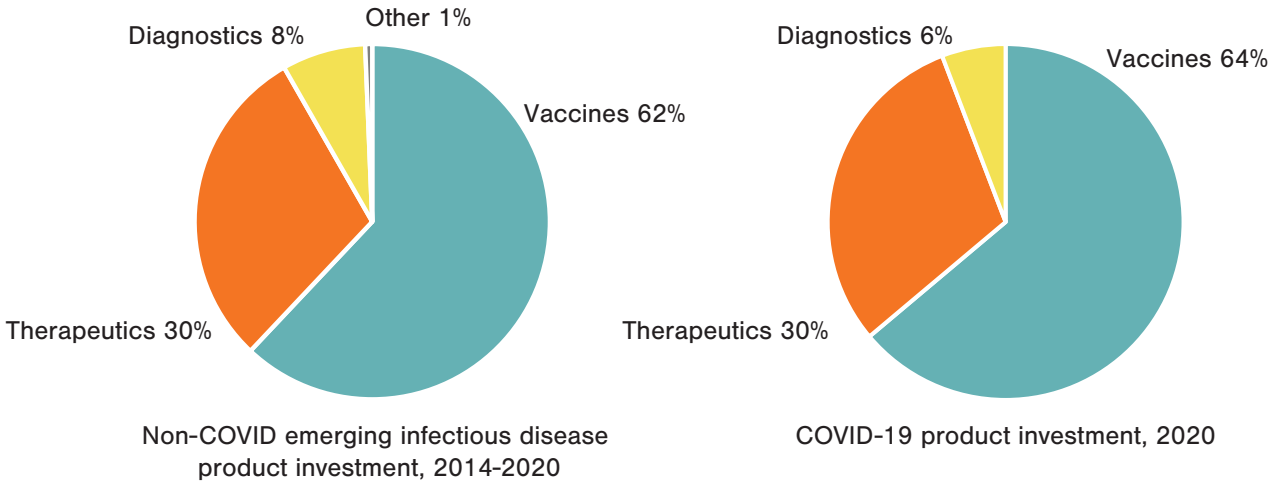
From 2015 to 2018, approximately 250,000 tests were used in the nine project countries, incorporating point-of-care early infant diagnosis into national diagnostic networks. This allowed for more than 5,000 HIV-positive infants to be identified for first-line antiretroviral treatment. By 2020, more than 20,000 HIV-positive children aged under 14 years had been identified and 66% were receiving first-line antiretrovirals. The new diagnostic, in combination with improved antiretroviral formulations, is projected to result in 2,057 disability-adjusted life years (DALYs) averted by 2025.

This initiative demonstrates that access to innovative point-of-care technologies can greatly accelerate access to HIV testing in exposed infants, enabling more HIV-positive infants to be linked to life-saving antiretroviral treatment faster than if the diagnosis were through centralised lab-based testing.

Mothers wait to get their children tested for HIV at a clinic in Kakamega, Kenya, as part of a programme to prevent mother-to-child transmission of the virus (Image: John Rae/ The Global Fund)

Diagnostics R&D for emerging infectious diseases: follow the outbreak

Figure 3: R&D funding for non-COVID emerging infectious disease products and COVID-19 products



While neglected diseases tend to receive small, ongoing flows of diagnostics funding based on the priorities of specific funders, diagnostics R&D for the priority pathogens with greatest outbreak potential identified in the World Health Organization's R&D Blueprint follows a different pattern: spiking in response to an outbreak, before dropping again sharply once the situation is under control. This was the case with Ebola, which saw diagnostics funding trend downwards from a peak of $21m in 2015 – early in the West African outbreak – before falling to just $2.9m in 2020. The decline can be linked to both the near-disappearance of new infections from Ebola's Zaire strain – as opposed to the Sudan strain active in Uganda in 2022 – and the registration of the first RDT for Ebola. While Zika experienced a similar rise and fall in diagnostics R&D funding to match disease outbreaks – maxing out at $24m in 2017 before dropping to $7.3m in 2020 – this was however not matched with the production of a viable diagnostic.

In contrast, COVID-19 diagnostics R&D funding totaled a huge $203m in 2020, far more than all Ebola diagnostics R&D funding since 2014 ($52m), and in fact all individual non-COVID emerging infectious disease diagnostics funding combined ($152m between 2014 and 2020). Moreover, COVID-19 diagnostics funding to date, together with preliminary figures suggesting an even greater investment in 2021, has resulted in the creation of dozens of novel, easy to use, rapid and accurate diagnostics, including numerous portable molecular tests. Clearly, sufficient political will and investment can facilitate development and delivery of critical diagnostics quickly.

The US Biomedical Advanced Research and Development Authority (BARDA) is the largest single funder of COVID-19 diagnostics R&D. Their committed funding totaled $265m directed to the 25 diagnostic products (including different versions of 14 individual technologies) which ultimately received Emergency Use Authorization. This suggests that BARDA's cost for developing a COVID-19 diagnostic was in the order of $11m, or $19m for each distinct technology. As a comparison, this is broadly in line with the $10m total BARDA reported investing in OraSure Technologies towards the successful development of OraQuick – the sole registered RDT for Ebola (though its development may have benefited from funding provided prior to 2014 or by funders not captured in the G-FINDER survey). Together, this implies that the price tag for developing a successful diagnostic during an active emerging infectious disease outbreak may be a little over $10m. However, a significantly larger financial commitment is required to compensate for the possibility of failed attempts at product development. This would leave the NTDs discussed above – each with at most a few million in diagnostics R&D funding over the last decade – even optimistically decades away from successful product registrations.

Beyond COVID-19, Ebola and the post-outbreak decline in Zika funding, emerging infectious disease diagnostics funding experienced a big jump in bunyaviral disease R&D, which increased by $1.5m in 2020 – more than the total over the previous three years. This increase was entirely due to new projects funded by the US National Institutes of Health (NIH) and contributed to the development of diagnostics for both Crimean Congo haemorrhagic fever and Rift Valley fever (RVF). In addition to gradual progress against RVF and the developments in Lassa fever diagnostics highlighted below, India's Molbio Diagnostics received approval in 2021 for a molecular test based on its Truenat platform – also spotlighted below – to detect Nipah virus. Though funding for emerging infectious disease diagnostics R&D is, reasonably enough, still concentrated on the most immediate threats, steady progress is being made in a number of other emerging diseases, potentially reflecting the opportunity presented by (and relative ease of) trialing diagnostics during an active outbreak in a population with high local rates of infection.

SPOTLIGHT: THE IMPACT OF A PAN-LASSA RAPID DIAGNOSTIC TEST

The viral haemorrhagic Lassa fever ('LASV') is endemic to parts of West Africa. With over two million cases and 5,000–10,000 deaths every year, Lassa is one of the region's most lethal emerging infectious diseases. Due to its non-specific presentation, mimicking other common diseases, early diagnosis is difficult, resulting in a higher case-fatality ratio than if early diagnosis was routinely possible.

The phylogenetic diversity of the Lassa virus, which is comprised of five unique genomic lineages, further contributes to diagnostic challenges. Until recently, laboratory diagnosis relied on viral isolation protocols, ELISA detection of viral proteins or Lassa-specific antibodies, and real-time polymerase chain reaction (RT-PCR) amplification of viral nucleic acid. All of this is of limited use during large outbreaks, due to the need for high-level biocontainment facilities and highly trained personnel.

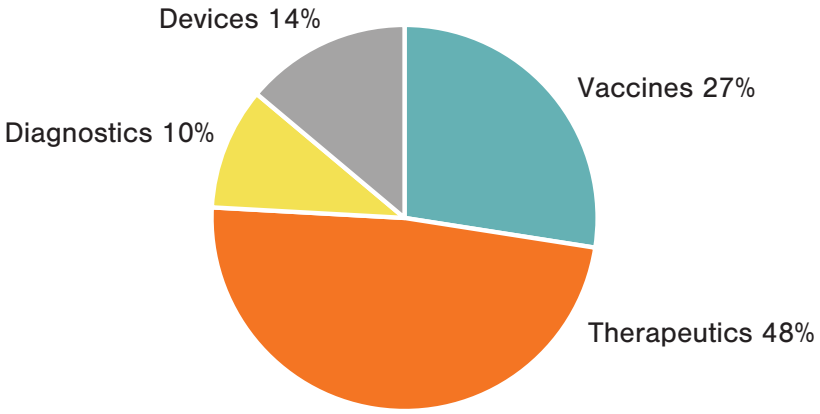
The need for a pan-LASV point-of-care RDT deployable during ongoing outbreaks, across geographic regions, with satisfactory levels of efficacy was clearly needed. In response, Zalgen Labs developed the ReLASV Pan-Lassa Antigen Rapid Test, a dipstick lateral flow immunoassay that can be used to make a diagnosis within 15 to 25 minutes utilising blood or serum samples. With broad-based applicability against Lassa clades II and III found in Nigeria, as well as the Josiah strain IV found in Guinea, Liberia, and Sierra Leone, Zalgen's candidate offers the broad applicability missing in existing diagnostic alternatives.

At the onset of one of Nigeria's deadliest LASV outbreaks on record in 2018, the ReLASV candidate was deployed alongside gold-standard laboratory-based PCR testing to facilitate early diagnosis of suspected cases. Compared with the PCR benchmark, ReLASV was found to correctly identify positive cases ('sensitivity') 93% of the time and correctly exclude negatives ('specificity') 83% of the time. Similarly, it demonstrated 91% sensitivity and 86% specificity against the Josiah strain of Lassa in another field evaluation study in Sierra Leone, eclipsing even the best available laboratory-based tests.

In 2021, Zalgen and the Coalition for Epidemic Preparedness Innovation (CEPI) announced a collaboration for Zalgen to supply ReLASV Pan-Lassa ELISA to CEPI's *Enable* study partners in the four Lassa-endemic West African countries. The partnership will test over 7,000 participants for antibodies to facilitate the development of the world's first Lassa fever vaccine, helping to provide better epidemiological data on the spread of differing Lassa strains in the region.

Diagnostics R&D for SRH issues: diversity of interest

Figure 4: R&D funding for SRH products, 2018-2020



SRH is a broad field encompassing a spectrum of diseases and health issues. This includes infectious diseases (sexually transmitted infections (STIs)), gynaecological conditions, multisystem pregnancy disorders, and issues not directly related to ill-health at all, such as contraception. The focus of SRH diagnostics R&D is exclusively on the subset of diseases and health issues with diagnosable features – whether pathogen or biomarker-related – which for G-FINDER includes STIs, human papillomavirus (HPV) and HPV-related cervical cancer, and the pregnancy-specific condition pre-eclampsia/eclampsia. Given this distinction between diagnosable and non-diagnosable conditions, interpreting the share of SRH funding focused on diagnostics is a little less straightforward than for emerging infectious diseases and neglected diseases, where most pathogens have some form of unmet need for novel diagnostics. To maintain a comparable macro view across the landscape, our headline figures show the percentage of *overall* SRH R&D funding spent on diagnostics R&D, acknowledging that some of this funding goes to areas with no scope for diagnosis. However, where appropriate, we have also indicated the share of diagnostics funding to diagnosable conditions.

As with neglected diseases and emerging infectious diseases, funding for diagnostics R&D for SRH issues is lower than all other biomedical product R&D. Between 2018 and 2020, just 10% of product development funding for SRH issues was invested in diagnostics R&D, compared with 48% for therapeutics, 27% for vaccines and 14% for devices. If we look only at funding for diagnosable conditions, the share of funding for diagnostics R&D jumps to 17%, but remains substantially below the 36% for therapeutics and 46% for vaccines. While the pattern of lower investment in diagnostics R&D is similar across G-FINDER health areas, the actual values are significantly smaller for SRH than for neglected diseases and emerging infectious diseases – an average of just $26m a year for SRH diagnostics R&D, compared with $71m a year for emerging infectious diseases and $155m for neglected diseases. This is partly due to the latter two health areas including a larger number of diseases, but likely also reflects the general under-investment in SRH more broadly.[6]

Half of SRH diagnostics funding between 2018 and 2020 went towards diagnostics for STIs (not including HPV), the majority of which was for multi-STI diagnostics (44%), followed by gonorrhoea (40%), much of the latter focused on combating AMR. Funding for HPV diagnostics R&D represents 40% of the diagnostics R&D total, although it has also declined sharply since 2018, falling from $15m to $7.9m in 2020. In contrast, while the small amount of pre-eclampsia diagnostics R&D funding has been relatively stable over the last three years, it has also remained pitifully small in comparison, averaging $2.7m. While STIs, and in particular AMR-related 'super gonorrhoea' and HPV-related cervical cancer are flagship global public health issues with significant attention and focus geared towards R&D, pregnancy-related conditions such as pre-eclampsia remain relatively 'niche', despite being major causes of maternal morbidity and mortality.[7]

6 https://www.thelancet.com/commissions/sexual-and-reproductive-health-and-rights

7 https://www.conceptfoundation.org/wp-content/uploads/2021/11/AIM-Market-analysis-report.pdf

On top of these, funding since 2018 to hepatitis B diagnostics was $2.5m and HIV diagnostics was a further $88m. While HIV and hepatitis B are considered both SRH issues and neglected diseases, funding for these two diseases is included under the neglected disease section above, and excluded here as a proportion of SRH diagnostics funding to avoid double counting. Nonetheless, significant achievements in diagnostics related to these two diseases applies also to achievements in STI diagnostics in general. As such, we highlight below the impact of improved hepatitis B diagnostics as a win in SRH-related diagnostics R&D.

SPOTLIGHT: FASTER AND MORE SENSITIVE DIAGNOSTICS FOR HEPATITIS B

Hepatitis B virus infection is one of the world's leading causes of chronic liver disease, nearly 40% of cases being sexually transmitted. Globally, hepatitis B is estimated to affect 292 million people, 90% of whom remain undiagnosed. For a disease known to be 50 to 100 times more infectious than HIV, the diagnosis gap is staggering. In a bid to reduce the global burden of hepatitis B, WHO, in its 2017 Global Hepatitis Report, set a baseline target to diagnose 30% of cases by 2020 and 90% by 2030.

To achieve these targets, there is a need for highly sensitive and specific point-of-care RDTs that meet the WHO-ratified limit of detection or analytical sensitivity (0.130 IU/mL). Until recently, no hepatitis B RDT met this criterion.

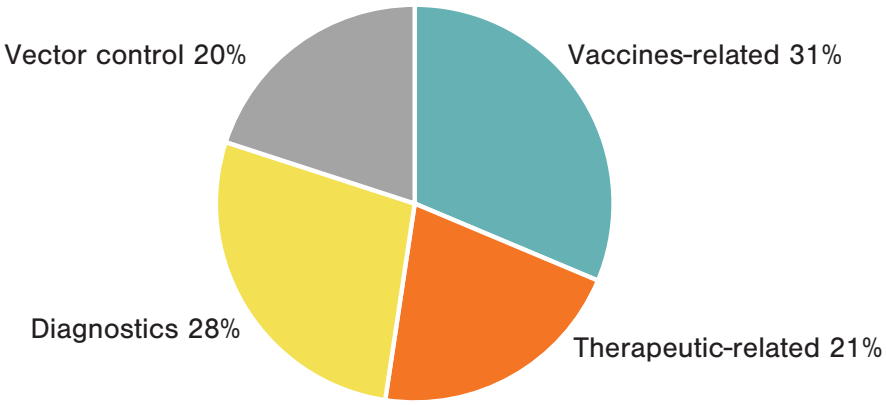
In 2019 however, Alere Medical Co launched Determine HBsAg 2, the world's most sensitive RDT for detection of hepatitis B surface antigen (HBsAg). An *in vitro*, visually read, qualitative lateral flow immunoassay for detecting HBsAg, Determine is the first hepatitis B RDT candidate to meet the 0.13 IU/mL threshold. It utilises whole blood, serum or plasma and detects the hepatitis B virus within 15 minutes, with a sensitivity rate of 97.9% and specificity rates ranging from 99% to 100% depending on choice of test sample. It received WHO pre-qualification in early 2020, and is currently commercially available across Europe, Africa, Asia and Latin America. In 2022, it was recommended for use in Africa for large-scale hepatitis B screening programmes, due to its low-cost, diagnostic performance, and clinical utility. Preliminary results indicate that screening using Determine is cost-effective in a variety of settings, and can result in net reductions in healthcare spending when early detection averts costly end-stage liver diseases.[8]

FIND/George Muiruri

8 https://www.thelancet.com/pdfs/journals/langlo/PIIS2214-109X(21)00517-9.pdf; https://onlinelibrary.wiley.com/doi/pdf/10.1111/tmi.13528

‘Crossover’ funding for more than one global health area: plug-and-play platforms

Figure 5: R&D funding for products that address multiple global health areas, 2016-2020



G-FINDER ‘diagnostic platform’ funding data includes both general diagnostic platforms – plug-and-play platforms which can be used with disease-specific assays – and multi-disease diagnostics, which are multiplex diagnostic technologies capable of detecting multiple pathogens or biomarkers simultaneously. Based on the intentions of the funder, G-FINDER treats some platform investments as specific to an individual global health area, but in practice, even notionally disease-specific platforms can end up being applied in unexpected ways once their development is complete.

In fact, much of the growth in overall diagnostics R&D funding prior to 2020 came from investment in diagnostic platforms and multi-disease diagnostics, which grew from less than $13m in 2015 to $77m in 2019. In 2020 however this started to decline slightly (to $73m), as funders pivoted to the development of COVID-19 diagnostics – in many cases building on the exact platforms created by this pre-COVID-19 funding. Platform-based product development can help equip health systems with the tools to respond rapidly to outbreaks of new or forgotten diseases, and can allow much of the initial cost of product development to be spread across multiple pathogens. Particularly for the rarer neglected diseases, product development is increasingly reliant on plug-and-play implementation of specific tests using proven general-purpose platforms.

The big jump in funding for these types of platforms started in 2016, a reflection at first of the addition of emerging infectious disease platforms to the G-FINDER scope. Since then, funding for emerging infectious disease-specific diagnostic platforms increased each year until 2019, where it peaked at $41m, before dropping to $24m in 2020. Diagnostic platforms which target both neglected diseases and emerging infectious diseases received almost half (47%) of all funding for diagnostic platforms in 2020. This is a big increase relative to the three years prior when emerging infectious disease-specific platforms dominated the funding profile. In contrast, platform funding which covers all global health areas was first captured in 2018 with the inclusion of SRH funding, and has remained relatively low since, though it grew twelvefold to $6.2m in 2020 from just $0.5m in 2018.

FIND & MYRADA/Adithya Shankar

SPOTLIGHT: THE TRUENAT "LAB-ON-A-CHIP" PLATFORM

Molbio Diagnostics developed Truenat – an RT-PCR microchip point-of-care technology that relies on nucleic acid amplification for accurate diagnoses. The technology involves the use of a portable, battery-operated RT-PCR platform that can be deployed in resource-constrained settings, with a turnaround time of one hour. Truenat's development commenced in 2014, with the goal of developing a mini-PCR platform for rapid diagnosis of drug-resistant TB.

By 2018, following extensive clinical validation studies by the Indian Council of Medical Research (ICMR), FIND, and WHO, the platform was adopted for use by the Indian National TB Elimination Programme, and subsequently deployed across India. It also received WHO pre-qualification in 2020, and was recommended by WHO as a first-line diagnostic test for drug-resistant TB.

Recognising a unique opportunity at the onset of the COVID-19 pandemic, Molbio successfully developed SARS-CoV-2 diagnostic assays running on the Truenat platform. This assay was one of the first COVID-19 diagnostic tests approved by the ICMR, underlining the Truenat platform's versatility. Since then, Molbio has developed assays for up to 30 different neglected disease and emerging infectious disease pathogens for use on the Truenat platform, including *Shigella*, HIV, malaria's *P. falciparum* and *P. vivax*, and Nipah, making it the world's first truly point-of-care, multi-disease RT-PCR diagnostic platform.

Funders of diagnostics R&D: who are the biggest players?

The US NIH is by far the biggest funder of diagnostics R&D, having provided a third of all funding – a total of $712m – to diagnostics across neglected diseases, emerging infectious diseases, and SRH issues over the last ten years. This is followed by investment from the Gates Foundation, which saw a big ($35m) increase in 2020, due entirely however to its contribution to the then-novel field of COVID-19 diagnostics.

For the most part, the top funders of diagnostics look similar to the top overall funders across other biomedical product areas, with the US NIH, the Gates Foundation, the US BARDA, the EC and the combined contributions from industry regularly occupying the top spots. A small number of funders devote an unusually large share of their contributions to diagnostics R&D, including Unitaid – the third largest funder of diagnostics R&D across the last decade – who have directed 44% of all their global health R&D funding towards novel diagnostics. Over half of this funding was for HIV diagnostics R&D (56% of their diagnostics total), alongside a strong focus on diagnostics R&D for hepatitis C (14%), and HPV (12%). Meanwhile, despite only reporting funding in two years, Gates Ventures – a Bill Gates-founded initiative separate from the Gates Foundation – also ranks among the top ten diagnostics funders, with large investments in TB and malaria diagnostics R&D in both 2017 and 2018.

FIND/Ben Phillips

Meeting the need for diagnostics R&D: demonstrating impact

While the global health R&D funding landscape appears to have less focus on diagnostics over other biomedical products, this is potentially short-sighted. Diagnostics serve as a kind of force multiplier for vaccines and therapeutics, by identifying patients most likely to benefit from treatment as well as priority areas for the deployment of ring vaccination and pre-exposure prophylaxis. Moreover, by preventing the transmission of infectious disease and combatting the rise of AMR, the benefits of diagnostics can extend far beyond the individual patient.

The WHO roadmap for NTDs highlights the need for more suitable and accessible diagnostic tools for the majority of these diseases. Six of the NTDs (Buruli ulcer, echinococcosis, foodborne trematodiases, mycetoma, onchocerciasis, taenia/cysticercosis) still have no diagnostic tests available at all, while the remainder are in urgent need of adaptation, modification, or improved access.

That said, while it is easy to talk about the value of diagnostics in general terms, it can be much more difficult to design trials which can properly measure the full health and economic impact of improved diagnostics. To attempt this, from a researcher's perspective we need to be able to correctly model the health system's response to improved diagnoses and accurately replicate the real-world standard-of-care for undiagnosed patients in a study's non-intervention arm, without treating participants unethically. As such, it is often hard to present decision-makers with clear evidence of the benefits delivered by improved diagnostics, given the number of moving pieces involved in studying their cost-effectiveness. While some of the investment gap between vaccines, therapeutics and diagnostics reflects genuine differences in cost, some of the shortfall likely relates to these difficulties in measuring and demonstrating the real-world impact of novel diagnostics.

SPOTLIGHT: CAPTURING THE TRUE VALUE OF IMPROVED DIAGNOSTICS

Carolyn Gomes and Fifa Rahman are ACT-Accelerator Civil Society Platform representatives and provided the following reflections on how the absence of timely, practical access to diagnostics can impact patients and communities.

How does one measure the economic impact of poor testing policies? What are the economic costs of a workplace shut down because an absence of testing allowed a single worker to infect the entire workforce? An entire school closed, an entire locality or country shut down, family members dead because the index case couldn't afford or wasn't able to access timely testing?

How does one measure the impact from long COVID-19 – a condition described as 'going beyond health to quality of life, employment, schooling and the ability to look after yourself'? This study, of almost 100,000 persons who had COVID-19, found that only 20% of the cohort had received a positive test and 42% stating that they had only partially recovered, raising questions about how accessible tests could have averted long COVID-19 and resulting disruptions to life and careers.[9]

And how does one measure the impact of inequity and the resulting trust deficit in government authorities where early routine testing was not available, either due to affordability of tests, government policies, or PCR fundamentalism? What metrics apply to those who weren't able to access self-tests because their government insisted they travel to a lab for PCR?

We will be trying to count this cost for a very long time. These questions cannot remain unanswered for the remainder of this COVID-19 pandemic, or the next.

9 https://doi.org/10.1038/s41467-022-33415-5

Looking to the future of diagnostics R&D: coordination is key

In theory, the global health community recognises diagnostics as one of the three pillars of the global health system. In practice – as this paper demonstrates – this pillar receives less than a tenth of R&D funding across each of the different global health areas tracked by the G-FINDER survey. Although significant progress in diagnostics is evident in the areas highlighted above – HIV in infants, Lassa fever, Ebola, hepatitis B, multi-disease diagnostic platforms, and of course COVID-19 – for far too many other diseases this is not the case. Negligible investment in diagnostics R&D means that patients' needs will continue to go unmet, while health systems will consistently lack the information needed to properly target novel vaccines, therapeutics and other public health interventions. The knock-on effect of the neglect of diagnostics R&D investment is thus potentially huge, with far-reaching health and economic implications in the short, medium and long-term.

In addition, while the global R&D response to COVID-19 shows that, with sufficient resources, dozens of novel diagnostics can be developed in a matter of months, it also shows that in the absence of ongoing coordination – such as is provided, for example, by CEPI for vaccine R&D – product developers may end up engaged in duplicative research, and wasting limited investment that could otherwise have been spent in collaborative and mutually reinforcing efforts.

Now is the time to capitalise on the lessons and successes provided by COVID-19 to accelerate progress across diagnostics R&D more broadly. To achieve this, a coordinated global approach to diagnostics R&D and access is needed, and soon. Moreover, this will need to be accompanied by better, less resource-intensive means of estimating the true impact of diagnostics on global health, in order to garner the necessary support and attention to drive interest and investment in this space.

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