

**Saving Lives:
The promise of Point of Care testing**
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The past few years have heralded much excitement around the uses of Point of Care Testing (PoCT). With advancements in electronics, the miniaturization and digitization of technology has spilled over into the realm of medical diagnostics. Through portable, transportable and handheld instruments, PoCT is the ability to bring the diagnostic capabilities of a laboratory to the patients' bedsides. It is effectively a potential solution to some of the health problems that India faces, especially in the context of the heavy burden of infectious diseases that plagues it and its large rural population with limited or no access to testing facilities.

But with all the applause it has received, PoCT still has its critics. The two most commonly stated reasons are often stated: the concern over the inaccuracy of the tests performed and the high cost of these tests. We believe, however, that such a view is the result of "narrow-lensing" the issue; a conclusion arrived at by comparing the PoCT with the existing "Gold Standard" tests performed at central laboratories and by plainly comparing the price to consumer of a traditional test to that incurred by PoCT.

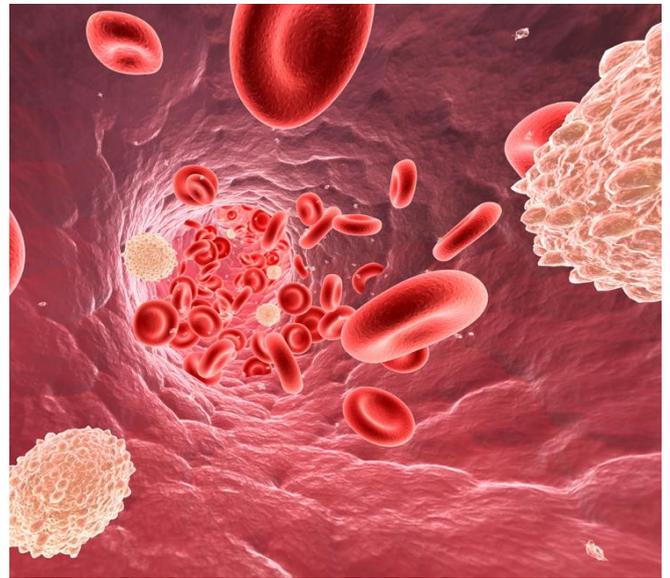
In this article, we hope to "broad-lens" the debate around PoCT. We believe that a country like India, with a population of 1.1 billion, with nearly 70% of the country residing in rural areas and almost 20% of its population living below the poverty line on less than \$1 per day, needs to examine this technology for the benefits it provides. Allowing for the early diagnosis and treatment of infectious diseases, particularly in rural settings, PoCT could have a potential positive impact on the nation's Gross Domestic Product (GDP) by reducing DALYS (Disability adjusted life years) and limiting the impact of the inter-generational spillover of diseases. Currently, deaths on account of TB, Cervical Cancer, HIV AIDS and Malaria together result in a loss of US\$ 10 bn per year, which cannot be ignored.

PoCT: The story so far

Encompassing many medical disciplines, covering both the non-communicable diseases segment (such as Diabetes and Heart diseases) as well as infectious communicable diseases segments, PoCT increasingly employs a variety of molecular diagnostic platforms, such as Polymerase Chain Reactions (PCR)^[i], Multiplex Immunoassays and Proteomics^[ii], to analyze minute quantities of sample fluid, (often only a pin prick of blood required) to diagnose a disease in a patient (Please refer to Exhibit 1).

Providing patients with the ability to self-monitor their disease (blood glucometers for daily at home blood sugar levels for Diabetes management) or doctors and nurses with the capability to make disease diagnosis faster (hand held blood gases analysers located at the patient bedside in an Intensive Care Unit), PoCT allows for faster and better management of diseases.

Traditionally biomedical technology has often been developed to cater to the needs of the developed world's medical community, with diagnostics technology not receiving the same support and resources as drug development and vaccine



discovery. But the past few years has seen a seismic shift in that regard, as POCT has now become economically viable and thus more emphasis has been given lately to develop these innovative technologies at low costs.

The past few years has witnessed significant interest in PoCT, at least in the developed world. In 2007 the POCT global market was estimated to be worth US\$ 11.32 billion. Growing at 11% per year, it is forecasted to reach US\$18.85 billion by 2012^[iv].

Exhibit - 1: Technologies employed in PoCT

Most of these platforms combine lateral flow^[iii] Rapid Diagnostic Test (RDT) technology with protein agglutination producing a simple colorimetric output (analogous to the pregnancy testing kit displaying a series of colored lines if positive). With great miniaturization of these technologies, these diagnostic platforms are encased in hand held sized devices built to be hard wearing, user friendly and require minimum resources at the testing site.

Another intrinsic property which PoCT uses also has its disadvantages. PoCT are often 'Multiplex' platforms, which refers to the simultaneous detection of more than one pathogen in a sample. Because there is a similarity in the way different infectious diseases present themselves to doctors, Multiplex Diagnostic platforms have been developed to rule out a differential diagnostic list. This also allows a cost reduction as it saves on the reagent costs which are placed within one detection kit. The technology works on the basis of having multiple antibodies/antigens (the detection protein which binds itself to the pathogen of interest) and then detecting the results of these simultaneous processes within the same reaction. These 'detectors' have to be selected with careful consideration to choose the relevant combinations of pathogens which are dependent not only on the local disease epidemiology but also vary from season to season. If one of the 'detectors' within the chemical mix is more efficient at binding its target protein than the others, overall amplification of that target increases and reduces the amplification of the other proteins within the sample. Called preferential amplification, it could result in a pathogen not being detected at all reducing individual pathogen sensitivity and specificity and increasing assay complexity.

Source: Point-of-Care Diagnostics for Global Health, Yager et al, 2008 ^[v]

Demystifying the debate

PoCT provides India with the ability to change the management of a disease like HIV/ AIDS, which commonly goes undetected for years as it lies dormant in the host and fails to display any significant symptoms whatsoever. PoCT allows the passage of these testing equipments to the areas which are currently under resourced, to parts of India with poorly established healthcare facilities and to populations isolated by long distances and geographies, thus reaching individuals who would have previously gone undiagnosed due to the lack of resources.

The major disadvantage of PoCT, critics say, is that these tests do not match up to the current gold standards and hence pose potential health hazards to the patients through inaccurate results. Many individuals question the reliability of the data as well as the reproducibility of these results. It is true that in some instances the quality can be questionable especially given the low levels of education and experience of the paramedical staff that perform these tests. There is the risk that the local paramedical team might get caught up in the 'simplicity' of the tests, inappropriately use a test outside of its licensed use and therefore generate inaccurate results^[vi]. There is also the issue which arises around the technology which is employed to detect the pathogen of interest, as the detection system used in PoCT is often different from those used in a central laboratory. This sometimes creates conflicts when comparing these field results to those generated from a lab. Additionally, because the result is often displayed as a binary 'yes' or 'no' to the presence of a particular pathogen or protein, PoCT tends to be more useful for screening and diagnosis of a disease rather than for follow up in positive individuals.

A lot of the initial inaccuracies were mainly caused by the low sample volume used in these



platforms. For example, the sensitivity of an RDT for detecting malaria depends upon the concentration of circulating antigens in the patient's blood, and also the ability of the labelled antibody on the RDT to bind the antigen and accumulate to form a visible line. In good conditions, some products can achieve sensitivities similar to that commonly achieved by microscopy. These sensitivities do however vary between products. Most products currently available have sensitivity^[vi] values of between 75%-90%, with specificities^[vii] of around 80-95%^[viii]. Recent work being done by the National Health Service has shown that the values tend to be lower than the published literature which sometimes quotes higher values^[ix].

Whilst the number of false negatives (individuals, who show a negative result but actually have the disease, i.e.: patients missed) when using this technology might be higher than those from the reference laboratory tests, one must not forget the purpose of this technology and the advantages that it brings in terms of patient convenience and rural outreach. Additionally, syndrome based treatment (i.e., treating a person

	Malaria		TB		HIV/ AIDS		Cervical Cancer	
	PoCT	G.S	PoCT	G.S	PoCT	G.S	PoCT	G.S
Test	HRP2 RDT	Malarial Antigen	Xpert MTB/ RIF	Liquid Culture	HIV ½ stat	HIV antibody	careHPV	PAP smear
Price	\$4.50	\$9	\$15	\$28	\$1.50	\$19	n/a currently	\$6
TAT	20 mins	4 hrs	2 hrs	1-2 wks	15 mins	24-48 hrs	3 hrs	24-48 hrs
Sensitivity	87%	99%	72-98%	90%	95%	99%	90%	80%
Specificity	96%	100%	99%	95%	99%	n/a	84%	70%

Diagram 1: Table highlighting differences between PoCT versus the Gold Standard for infectious diseases

on symptoms alone) can only reach sensitivities of 88% and specificities of 66%^[x], highlighting that PoCT (and its accuracy) is better than no testing at all. The number of false positives (individuals who show positive for a disease that they do not have) remains low and thus for use as a screening tool, PoCT is ideal for developing countries.

Measuring up to the gold standard

In our view, the debate surrounding PoCT versus the gold standard misses the key issue on how it fares against the current Gold Standard. While the PoCT does not match upto the gold standards available, it certainly works for screening a population at risk of infectious diseases, which accounts for c. 25% mortality in India^[xi]. The potential benefits for a country like India are:

1. Making it possible to reach out to people living in rural settings, (who have no diagnostic facilities in close proximity)
2. Making screening of populations at risk possible, (who would otherwise go undetected?)
3. Fighting the battle against drug resistant strains of pathogens, (which is increasingly becoming a global menace)

PoCT increases patient convenience and reduces the turnaround time to receive the results; thereby ensuring patients receive tests in a more effective manner to aid in the management of their condition. The biggest advantage PoCT has for a country like India is the role it has to play when applied to field settings, through rural programmes. These settings have a number of drawbacks associated within them, either due to poor infrastructure, untrained staff or limited resources. The single biggest advantage that PoCT provides is the ability to take diagnostic services to populations that would otherwise not be tested. India has more than 800 million people living in a rural setting and around 200 million living on less than US\$1 per day^[xii].

What chance do these people have of being tested for a disease which they may suffer from, especially if this requires them to travel vast distances to access such diagnostics, for symptoms they might not even be displaying yet,



and incur considerable cost in doing so?

Lifestyle related diseases are increasingly being cited as the major problem facing India. But whilst it is true that these disorders such as Obesity, Diabetes and Heart disease are growing in prevalence in India, infectious diseases still represent a major health challenge facing India with close to 25%^[xiii] of all deaths attributed to infectious disorders. Diseases such as Tuberculosis (TB), HIV, Malaria, Sexually Transmitted Diseases (STD's) and Gastroenteritis continue to plague Indians. Poor awareness, poor affordability and lack of diagnostic availability are three of the main reasons why the vast majority of these patients are still going untested and are poorly treated. Also, most of these infectious disorders present themselves in economically poor settings.

The burden of HIV on India presents a strong case for mass screening of the population at risk. The prevalence of HIV in India according to various studies has been pegged at 2.31 million, with adult prevalence i.e. between the ages of 15-49 at 0.34%^[xiii]. According to WHO estimates published in 2009, in the year 2004, 126,000 deaths were registered due to HIV/AIDS. Many observers believe that these number under-represents deaths due to AIDS as many deaths go unreported due to the attached social stigma attached. One of the main reasons, however, is that in many situations the victim is never diagnosed and death is attributed to opportunistic infections like TB.

Similarly, given the strong association of the HPV with Cervical Cancer, PoCT could be used to detect HPV^[xiv], and those tested positive could be diagnosed further using visual inspection

techniques or a pap smear as appropriate. Allowing the passage of these tests into rural areas of the country would allow an increased number of women to be tested for this virus.

Cervical cancer presents a formidable challenge for India. An estimated 360 mn women are at risk with an incidence rate of 26.2/100000 (against a world incidence of 16/100000)^[xiii]. With a lifetime risk of developing the cancer pegged at 2.5% (twice the world's average), currently only 2.5% of the women at risk are being screened in India^[xiv]. The disease is largely a lower socio-economic phenomenon, either in rural India or urban slums. It is not just sexual activity that contributes to this disease, but also poor living conditions, lack of awareness and poor hygiene.

PoCT also allows for timely, appropriate and judicious use of antibiotics in those who truly require them. This has two key advantages, the first is in the global battle against multi-drug resistant (MDR) pathogens and the second is in the cost savings that appropriate anti-biotic usage translates into. As the example of Africa illustrates (Exhibit 2), widespread syndrome based treatment of Malaria using Chloroquine has made the drug practically useless as the pathogens have developed Chloroquine resistance.

The cost merely reflects the lens one uses

Costs are still a concern and a limiting factor in the widespread deployment of these technologies.

Healthcare facilities have extremely low budgets in low income countries, particularly in the rural regions, and those are the regions that require it the most. Per test costs for PoCT are often significantly higher than the equivalent cost at central laboratories. Taking the test for the Malarial P. Falciparum parasite as an example, the fixed costs such as the microscope, staff training, and laboratory supervision remain the same regardless of the laboratory's throughput. As caseload increases, these costs are distributed across the patient population thus reducing the per individual cost. A WHO report suggested that in a low income country like India, assuming a typical case load of over 1,200 tests per centre each year, the cost per test is estimated to range between US\$0.32 and US\$1.27 depending on throughput, with a best estimate of US\$0.53. The per unit cost of a Rapid Diagnostic Test (RDT's) for Malaria on the other hand costs the same per patient, regardless of the caseload. Then there are the costs of maintaining the personnel and operators, the costs of their required training and the costs of managing the testing areas which are often medical camps in dozens of different sites. Adding to these costs are the costs of quality assurance and transportation of the testing equipment to the sites. Keeping all this in mind, the cost per RDT can range anywhere between US\$1.20 to US\$13.50, ten times as much as conventional blood film smears^[xvi].

But a growing mountain of data is becoming available illustrating exactly how at a population level these tests have become economically viable due to a number of reasons:

1. These tests are "lean processes", in the sense

Exhibit 2: The Case of Malaria Treatment in sub-Saharan Africa

Traditional interventional measures employed a technique of syndromic antibiotic for all febrile patients using Chloroquine. As we have seen however, syndromic measures are only accurate in two thirds of all cases. This resulted in vast numbers of individuals being treated for a pathogen they did not have, simply because they had a fever. Not only was this an expensive exercise, but over the years Chloroquine resistant genes have spread amongst the parasite rendering this drug practically useless against the pathogen now. With the next line of therapy being Artesunate, a much costlier drug the lessons of the past decade must be learnt. By employing these RDT for Malaria, it will allow only the diseases affected individuals to receive the drug, thus minimizing drug expenditures to developing nations and also extending the lifetime of Artesunate by slowing the progression of drug resistant strains.

Source: Cost-effectiveness study of three antimalarial drug combinations in Tanzania. Wiseman V, et al, 2006. PLoS Med. 3:e373^[xv].

that they remove wasteful, non-value added activities

2. Sample handling is more efficient, thereby limiting the impact of the contamination of the sample on the result of the test and thus saving on the cost of repeat tests

3. From a macro-economic perspective, the extra costs of screening and therapy pale in comparison to the impact on national GDP on account of DALYs [xvii]

4. The reduced cost of inter-generational spillover of a disease

The first and foremost benefit is that these tests are lean processes. The patient sample obtained is tested with the patient present and the results are immediately made available to them. There are fewer steps involved in this than in having to transport the patient specimen intact to a centralized laboratory, processing the sample and then communicating the results back the patient's local care provider. Viewing this through the eyes of the patient, one needs to factor in the cost of travel and days of income lost. Patients are very sensitive to loss of income: in the course of one of our consulting assignments in the area of infectious diseases, we discovered that patients chose to pay for a TB diagnostic at a private setting, as opposed to availing of free diagnostics in a public facility. The reason: long queues at the public setting did not guarantee patients being

tested the same day, often requiring them to visit the facility again resulting in additional days of loss in income.

PoCT technologies have also become more compact such that a very small sample volume is required and an equally small volume of reagent is required contributing to lower costs than previously quoted. The additional advantage of this miniaturization is that multiple tests can be carried out at the same time, in a variety of locations, with the flexibility to meet the local healthcare needs.

Most importantly, these samples do not have to be transported. Our experience in the diagnostic sector in India, suggests that transportation and manual handling of samples results is a big challenge. Temperature control is not maintained and often samples are contaminated when transported over very long distances. Only the large diagnostic chains use express logistics services with temperature control to maintain the patient specimen intact. Sample contamination results in tests often having to be repeated, the cost of which is borne by the patient. In addition to the threat of contamination, one also has to factor in the use of "home-brewed" reagents by laboratories, which impacts consistency of results, resulting in repeat tests being required, the costs of which are again borne by the patient.

From a macro-economic perspective, lives saved result in saving years of lost productivity as well

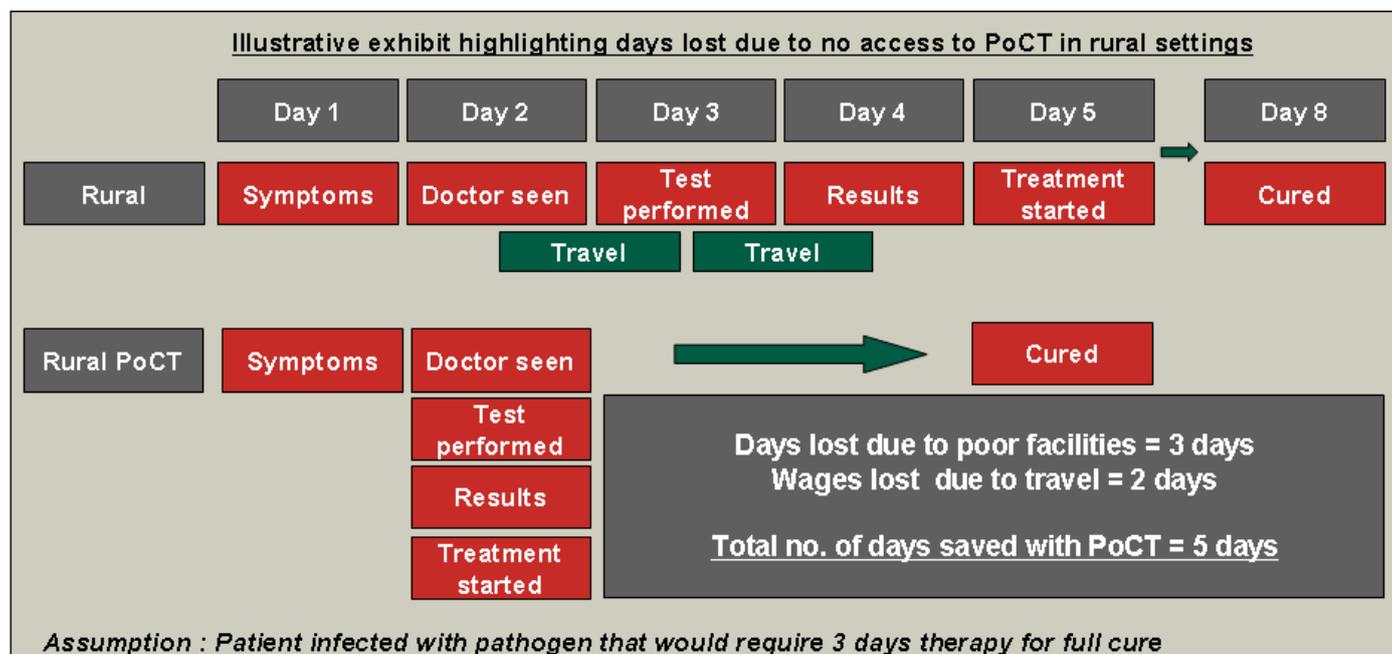


Diagram 2: Highlighting days lost due to no access to PoCT in rural settings

Exhibit 3: The Economic Impact of Diseases

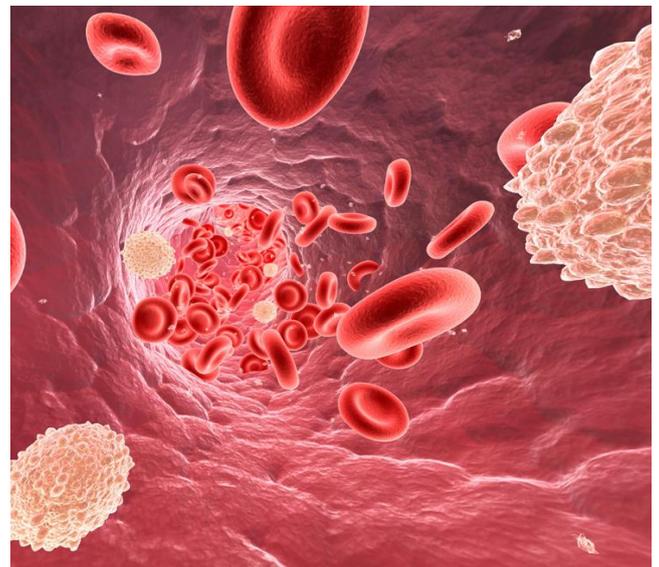
Infection	Deaths ('000)	DALYs ('000) ^[xxii]	DALY per Death	Loss per Death (US\$) ^[xxi]	Income Loss (US\$ mn)
Tuberculosis	309	7286	24	18863	5829
HIV /AIDS	126	3852	31	24457	3082
Cervical Cancer	72.6	987	14	10876	790
Malaria	15.9	603	38	30340	482
Diarrheas	515.5	17445	34	27073	13956

Source: WHO Estimates for 2004, published 2009

as leading to better quality of life. Health Economists talk of disability adjusted life years, or DALYs, which adds up increased years of life and reduced years of living with disabilities. For instance, according to WHO estimates for 2004 (Exhibit 3), 309,000 people died due to TB^[xix]. The DALYs was estimated to be 7,286,000^[xix] which translate into a DALY per death of 24. The loss in terms of per capita income, assuming a per capita income of US\$ 800 per year^[xx], amounts to US\$ 18860 (or rather 24 years of lost per capita income per death) and an overall economic impact of US\$ 5.8 billion. Similarly, the economic impact in terms of lost per capita income due to HIV/AIDS deaths is estimated to be US\$ 3 billion. The economic impact for India is clearly visible.

In a paper, "Tackling Tuberculosis: The Business Response", prepared by the Harvard School of Public Health in co-operation with the World Economic Forum^[xviii], the total budget per patient, including all other costs, was estimated below US\$ 100 in India, less than 10% of per capita

income. The paper also quotes from another study, which estimated that the cost of treating TB per DALY was anywhere between US\$ 5 to US\$ 50 i.e. ~6% of per capita income, in all regions except Central Asia and Europe where patients underwent extensive periods of hospitalization. Taken in this context, as the case of Syphilis in Kenya illustrates (Exhibit 4), PoCT is now shown to be cost effective

**Exhibit 4: The Case of PoCT in Screening of Syphilis in Kenya**

PoCT has now shown to be cost effective when looked at by the health economic impact that the application of this technology has on a population level for a developing country. A recent World bank report estimated that in a country like Kenya, with a good screening procedure for Syphilis in place, costing US\$1 per female tested, the health economic benefit for this screening was US\$19 per Disability-adjusted life year (DALY, which is a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death). PoCT gives us the ability to detect patients early, even if asymptomatic and is therefore crucial in reducing the morbidity and mortality that these disease cause in developing countries. Reducing patient's suffering and in the long run, allowing them to contribute positively to their local community and to the growth of the country.

Source: Sexually Transmitted Infections in Developing Countries, World Bank report, 2010 ^[xxv]

In the context of a low income country, these economics play an important role. Econometrics studies indicate that an economy in which a population is at zero-risk of malaria grows 1%^[xxiii] faster than an economy with high malaria risk, all other factors being equal. Since such a growth compounds over time, “malarious” economies tend to end up with a per-capita income which is much less than that of a “non-malarious” economy.

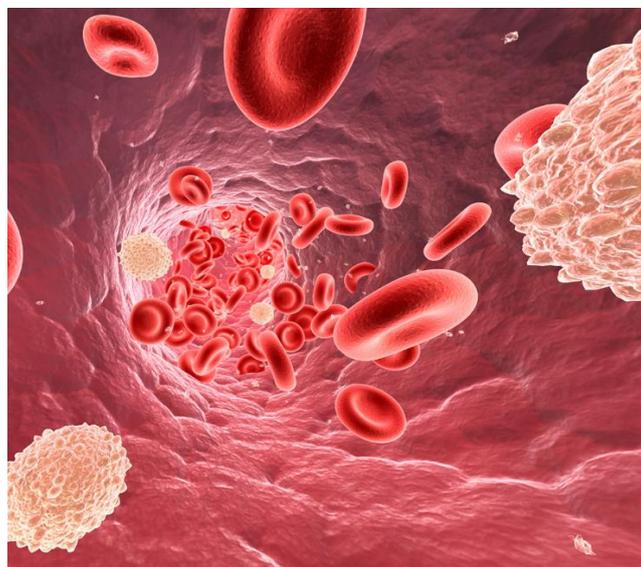
In addition to the above, one would have to factor the intergenerational and life cycle consequences of the diseases. In a low income setting like India, cost of dealing with diseases often results in depletion of assets of the household and debt. Impoverished households will lack the ability to make short term investments (e.g. farm implements), or invest in the education of their children. A study in India revealed that 11%^[xxiv] of children dropped out of school when a parent fell sick with TB. Given the communicable nature of the disease, children are often removed from school. Weak education is closely co-related with reduced productivity in adulthood and attendant reduced incomes.

Driving the adoption of PoCT

In driving the adoption of PoCT, stakeholders need to appropriately position this technology. As opposed to fighting the battle against the prevalent Gold Standards, it may be useful for diagnostic players to position the PoCT for what it really does: effective screening, faster turnaround and the enablement of early and appropriate treatment. At the very least, even with the false positives, this technology readily identifies a population at risk for monitoring and those requiring therapeutic intervention should further tests suggest the same. The challenge, we believe, lies in ensuring that local populations are convinced of the need of screening. Our experience leads us to believe that current awareness levels, as indicated by the amount of literature surrounding PoCT in India and the general opinions of microbiologists and prescribing physicians is below desired levels.

Framework for Action:

The first phase to achieve greater penetration of this technology would be for partnerships to be forged between the diagnostic manufacturers and those organisations that have the capabilities to



reach out into rural populations. These could either include Private- Public Partnerships (PPP's) between these manufacturers and government organisations and public bodies or between the diagnostic players and pharmaceutical companies (many of whom already have rural healthcare programmes) to create a closed loop system from diagnosis to the treatment of these infectious diseases. The role of these consortiums would be to create a national framework of action to combat the selected diseases, define the parameters in which the programme will be measured against and the tools which would be used to assess the economic impacts of such an initiative.

Following this, the next step would be to identify the target geographies to implement these programmes. Identifying populous areas with high incidences and prevalence of the target diseases is important to try and maximise the effect of a rural screening programme. Once decided upon, the consortium should partner with local NGO's, many of whom have the knowledge and infrastructure in the field to carry out the action plan. Local healthcare personnel and existing training programmes can be used as conduits to increase the impact of the PoCT technologies on a ground level. Our work done in the diagnosis of cervical cancer highlighted this. Large public hospitals in the state of Tamil Nadu (where the prevalence of the disease is amongst the highest in the country) have training programmes in place where by paramedical staff trained by consultant gynaecologists in these centres are then sent out into the interior of the state to conduct medical camps to screen for cervical lesions. Currently these healthcare workers are trained using the Pap smear or Visual

Inspection technique, but if the same programme were to be supplemented with more sophisticated and accurate PoCT tools, the effectiveness of these efforts would be increased.

Following the above steps, a vehicle for implementation should be chosen. The above example used local NGO's as a means to distribute these tests. An alternate vehicle that could be employed would be to use mobile diagnostic clinics to transport these tests to areas which require them most. The Health Management and Research Institute currently have such a programme in place to serve the health needs in the state of Andhra Pradesh. Through project '104 Mobile', it currently serves a population of approximately 1.6 million people through close to 300 Primary Health centres (PHC's) with the use of 475 mobile health clinics. It services 56 villages once a month for about 4 hours each providing medical provisions, basic diagnostic tests, treatment and medical advice for rural areas located more than 3 hours away from any form of health centre. With a similar model estimated to cost approximately \$0.75 per person

per year in most African countries [xxvi], it would seem most appropriate to integrate such innovative healthcare solutions with PoCT to allow for more detailed screening and diagnosis in rural areas.

These pilot schemes need to be rigorously monitored to measure its successes in order to assess the feasibility of a more wide spread implementation programme. And whilst the provision of the tests will be an initial step forward, the challenge does not end there. One must then be in a position to be able to deal with the outcome of the test, to provide the necessary treatment and the appropriate follow up there after.

Although faced with a large problem in front of it, India has made a commitment to reduce the public burden of preventable infectious diseases that befalls so many of its population. Through innovation, medical technology has developed a solution to this in the form of Point of Care diagnostics. What we have tried to do through this article is to highlight some of the promises that PoCT brings to the clinicians tool kit. Traditional diagnostics are reactive; they often have long turnaround times and are a many stage process from obtaining the sample from the patient to finally delivering their result. Companies, governments and clinicians alike should now look to PoCT through the lenses of time, portability and the early initiation of the appropriate treatment. PoCT is definitely better than syndromic treatment, which is the current best alternative to no diagnosis at all.

The real test now lies in the ability to harness this capability in the correct fashion, to create the correct environment for this technology to be deployed in its most effective manner and help alleviate some of the problems and challenges that afflict rural India. And whilst it may not be the most accurate or the cheapest, they help save time and save lives.

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Notes and References:

- i. PCR is technology that is used to amplify DNA by several orders of magnitudes and is used extensively in medical biological research, especially diagnostics
- ii. Proteomics refers to the large scale study of proteins, especially its structure and functions and extensively applied in the field of diagnostics
- iii. Lateral flow tests are simply called strip tests. Lateral flow tests are used for the specific qualitative or semi-quantitative detection of many analytes including antigens, antibodies, and even the products of nucleic acid amplification tests. One or several tests can be performed simultaneously on the same strip
- iv. Epsicom Business Intelligence. The Global Market for Point of Care Diagnostics: Major Players and Key Issues 2007, Volume 1. Publication No. ISBN: 978 1 85822 306 3. Epsicom Business Intelligence. Epsicom Business Intelligence, 2007.
- v. Point-of-Care Diagnostics for Global Health, Paul Yager, Gonzalo J. Domingo, and John Gerdes, *Annu. Rev. Biomed. Eng.* 2008.10:107-144.
- vi. Sensitivity also called recall rate in some fields) measures the proportion of actual positives which are correctly identified as such (e.g. the percentage of sick people who are correctly identified as having the condition)
- vii. Specificity measures the proportion of negatives which are correctly identified (e.g. the percentage of healthy people who are correctly identified as not having the condition)
- viii. Moody A. 2002. Rapid diagnostic tests for malaria parasites. *Clin. Microbiol. Rev.* 15:66–78
- ix. Delivering the NHS Health Check: A practical guide to point of care testing, NHS Improvement, 2010
- x. Bojang KA, Obaro S, Morison LA, Greenwood BM. 2000. A prospective evaluation of a clinical algorithm for the diagnosis of malaria in Gambian children. *Trop. Med. Int. Health* 5:231–36
- xi. World Health Organisation, India Mortality data factsheet 2006
- xii. IndiaStat, <http://www.indiastat.com>
- xiii. World Health Organisation, Country specific, India data
- xiv. HPV refers to Human Papilloma Virus, several types of which is high risk and can lead to Cervical Cancer. The presence of HPV does not necessarily mean that the patient suffers from Cervical Cancer, but is indication that the patient may be at high risk
- xv. Wiseman V, Kim M, Mutabingwa TK, Whitty CJM. 2006. Cost-effectiveness study of three antimalarial drug combinations in Tanzania. *PLoS Med.* 3:e373
- xvi. Determining Cost Effectiveness of Malaria Rapid Diagnostic Tests in Rural Areas with High Prevalence, Western Pacific Region, WHO, 2009
- xvii. DALYs or Disability Adjusted Life Years, adds together the increased years of life and the reduced years of living with disabilities
- xviii. Tuberculosis: The Business Response, Harvard School of Public Health in co-operation with the World Economic Forum, Feb 2008
- xix. World Health Organisation, Estimates for 2004, published 2009

- xx. We have assumed a per capita income of US\$ 800 and that each DALY is valued at 1 x per capita income. There are a number of reasons to value DALY at multiples of per capita income as they do not take into account the impact of better health on faster economic growth
- xxi. When an individual dies, the death is associated with many years of life lost. Also, disease can cause disability for years before eventual death. For these reasons, the DALYs per year are a multiple of deaths per year
- xxii. When an individual dies, the death is associated with many years of life lost. Also, disease can cause disability for years before eventual death. For these reasons, the DALYs per year are a multiple of deaths per year
- xxiii. Macro Economics an Health: Investing in Health for Economic Development – Report of the Commission on Macro Economics an Health presented by Jeffrey Sachs, 20, Dec 2001
- xxiv. Tuberculosis: The Business Response, Harvard School of Public Health in co-operation with the World Economic Forum, Feb 2008
- xxv. Sexually Transmitted Infections in Developing Countries, World Bank report, 2010
- xxvi. Three practical steps to better health for Africans, McKinsey Quarterly, 2010

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