# Outcome report for Rapid Health Technology Assessment of Gazelle for Sickle Cell Disease/Trait diagnosis among high-risk population in India


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## LIST OF ABBREVIATIONS

| | |
|---|---|
| CHSI | Costing of Health System in India |
| CI | Confidence Interval |
| DBS | Dried Blood Spot |
| Hb | Hemoglobin |
| HPLC | High Performance Liquid Chromatography |
| HTA | Health Technology Assessment |
| ICER | Incremental Cost-Effectiveness Ratio |
| MoHFW | Ministry of Health and Family Welfare |
| NFHS | National Family Health Survey |
| PICOT | Population, Intervention, Comparison, Outcomes and Time Horizon |
| POC | Point of Care |
| PSA | Probabilistic Sensitivity Analysis |
| SCD | Sickle Cell Disease |
| SCT | Sickle Cell Trait |
| SOC | Standard of Care |

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# CHAPTER 1: INTRODUCTION

Sickle cell disease, an autosomal recessive disorder of red blood cell, is the most common monogenic disease with more than 300000 affected births annually, worldwide. The condition is mostly prevalent in the low-middle-income countries. An estimated 7% of the population carry an abnormal hemoglobin gene, while about 300000-500000 are born annually with significant hemoglobin disorders. They consist of two different groups: thalassemia and sickle cell syndromes. Sickle cell syndromes are more frequent and constitute 70% of affected births worldwide, the rest are due to thalassemia. Sickle cell syndromes include Sickle cell disease (SCD, HbSS) also called sickle cell anemia, as well as disorders due to sickle cell gene combined with another hemoglobinopathy such as Hb C, E or beta thalassemia.

Persons carrying only one of these genes are called carriers. They do not suffer from the disease, but carry the gene and can genetically transmit it to the next generation. Carriers cannot be recognized clinically. Only specific blood tests can identify them. If the father and mother are carriers, there is a chance that their children could be carriers themselves, remain healthy, or become severely affected by sickle cell and/ or thalassemia syndromes.

Screening prior to conception or during pregnancy can help controlling hemoglobinopathies by preventing birth of affected children by – avoiding marriage between two carriers or by prenatal diagnosis in pregnancies of couples where both partners are carriers, with the option of termination of pregnancy in case of an affected fetus. Newborn screening can detect abnormal hemoglobin variants like HbS, both carriers as well as those with disease (HbSS) states. SCD requires lifelong management and contributes to infant and childhood morbidity and mortality. Cost effective population screening programs are possible for detection of diseased or carriers, as low-cost screening tests with high negative predictive value are available. Genetic counseling, community education and awareness play a very important role in successful implementation of prevention programs.

The National Sickle cell elimination mission was introduced by the National Health Mission in 2023. The mission aims to eliminate SCD as a public health problem in India before 2047. The prevention strategy of universal screening and early detection is a part of the objectives of this mission. Therefore, cost-effectiveness analysis of the available POC tests for detection of SCD was carried out.

Several POC tests have been introduced in India. Hemotype Sc is one such POC test that is manufactured by Silverlake Corporation USA. Sickle Scan is another POC test, manufactured by Biomedomics Inc. Sickle CERT was developed in India, by Indian Institute of Science. All these rapid diagnostic tests could be used for the detection of HbA, HbS and HbC, but it cannot detect haemoglobin variants like HbD, HbE and HbF. It also cannot differentiate between HbSS and sickle- β0-thalassemia.

The previous evaluations on cost-effectiveness of Hemotype Sc and Sickle Scan showed that the kits would be cost-effective in an Indian economy only if the kits are procured at a cost below INR 100 for HemotypeSc and INR 110 for Sickle Scan. Sickle CERT was a cost-

effective intervention. The National Health Mission has guided the SCD endemic states in India to consider procuring these POC tests at the recommended rates, based on the HTA evaluations. Even though conducting the cost-effectiveness analysis of Gazelle was considered earlier we did not pursue it along with the other POC tests because, from discussion with experts we identified that Gazelle cannot be used as a community level POC test like the other tests in the research question (Hemotype Sc, Sickle Scan and Sickle CERT). However, there was a consensus that it could be recommended as a primary health facility-based test and hence this HTA was conducted.

## CHAPTER 2: OBJECTIVES

**Research Question:**

To conduct an HTA on Gazelle for screening for Sickle cell disease/ traits.

**Objectives:**

1. To collate evidence on clinical-effectiveness of Gazelle vs solubility test and HPLC to diagnose sickle cell trait/disease
2. To estimate cost of test per case screened and detected using Gazelle
3. To access the health system costs of using Gazelle for facility-based screening

## CHAPTER 3: METHODOLOGY

This analysis is part of an HTA which was structured to answer the policy question put forward by the Ministry about "To conduct HTA of rapid diagnostic tests and current standard of care in population level screening for sickle cell disease/trait".

### 3.1 PICOT:

| | |
|---|---|
| Population | A hypothetical cohort of tribal population between 6 weeks to 40 years of age from six high prevalence states [Madhya Pradesh, Maharashtra, Gujarat, Chhattisgarh, Tamil Nadu, Odisha] in India |
| Intervention | ➢ Gazelle with confirmation of positives with HPLC at all level of care. |
| Comparator | ➢ **Primary level**: Solubility test with confirmation of positives with HPLC<br>➢ **Secondary level**: Solubility test with confirmation of positives with HPLC<br>➢ **Tertiary level**: HPLC test for screening all cases |
| Outcomes | ➢ **Cost per case detected** using intervention and comparator<br>➢ **Cost per case screened** using intervention and comparator<br>➢ **Additional number of cases detected** by intervention vs comparator |
| Perspective | Health system perspective |

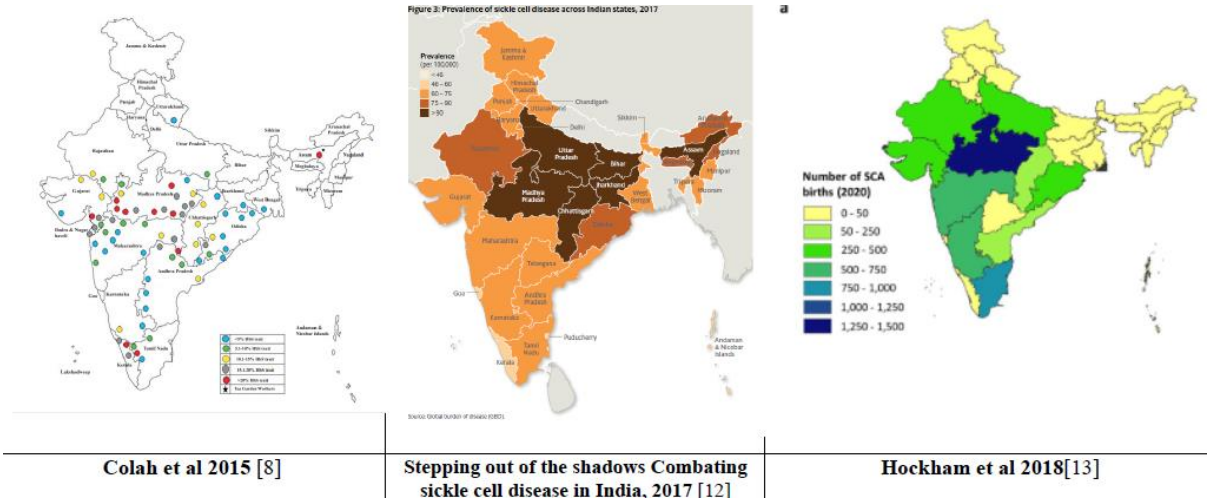
### 3.2. **Review of Literature:**

3.2.1 **Burden of diseases in India:** A review of literature was conducted to understand the burden of the disease in India

More than 300,000 babies are thought to be born each year with sickle cell disease (SCD) globally, and it is predicted that this number would rise from 305,800 in 2010 to 404,200 in 2050. SCD, a common genetic disorder prevalent in Sub-Saharan Africa, the Mediterranean, the Middle East, and the Indian subcontinent. Three nations, including India, bear over half of the world's SCD burden. [1]. Majority of these infants are born in India and Sub-Saharan Africa [2-4], where SCD has a large impact on childhood morbidity and mortality [5-7]. While the death rate for children under five with SCD can reach as high as 90% in some low-income nations. In India, where 1.5 lakh children are affected, 20% of infants die before the age of two. [7]. The high SCD prevalence is also reflected in the high proportion of individuals who are carriers of the sickle cell gene, also known as sickle cell trait (SCT) (13–20%) [6].
The overall prevalence of SCD among tribal population of India varies from 1-34%. Madhya Pradesh, has the highest load of prevalence that varies from 10%-33% followed by Maharashtra with 0-35%, Kerala (18.2%-34.1%), Gujarat (6.3%-22.7%) and few other states as shown in figure below [8]. Kaur et al have summarized from individual states that there are still many

gaps in our knowledge about the distribution of the HbS gene in tribal communities in India [9].

With more than 5200 affected new-borns with SCD each year [10, 11], it is a serious public health issue in India. SCD is common across several ethnic groups in India, a huge country with various ethnic groups. India's central region has the highest frequency of the SCD, with Chhattisgarh, Bihar, Uttar Pradesh, Madhya Pradesh, Jharkhand, Assam, Meghalaya, Arunachal Pradesh, and Rajasthan among the states with the highest prevalence. SCD is most frequent among tribal cultures, but as more people are migrating into cities, it is becoming widespread [12].




**Colah et al 2015** [8] | **Stepping out of the shadows Combating sickle cell disease in India, 2017** [12] | **Hockham et al 2018**[13]

Figure 1: Prevalence of SCD in districts and states of India

Out of six studies, only one study was based on new-borns, rest all other five studies included all age groups. Only one study showed prevalence by male-female, while other represented the overall SCD ranges between 0.1 to 9.02 % while SCT ranges from 1.3-88.7% respectively. Four studies adapted HPLC as a screening test, while one with solubility test and one with sickling test followed by HPLC (see table 1 below).

**References**


1. Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN. Global Burden of Sickle Cell Anaemia in Children under Five, 2010‑2050: Modelling Based on Demographics, Excess Mortality, and Interventions. PLOS Medicine 2013;10:e1001484. https://doi.org/10.1371/journal.pmed.1001484.
2. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Dewi M, et al. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model based map and population estimates. The Lancet 2013;381:142‑151.
3. Serjeant G. World sickle cell day: lessons for India. The Indian Journal of Medical Research 2017;145:705.
4. Ware RE, de Montalembert M, Tshilolo L, Abboud MR. Sickle cell disease. The Lancet 2017;390:311‑323.
5. Grosse SD, Odame I, Atrash HK, Amendah DD, Piel FB, Williams TN. Sickle cell disease in Africa: a neglected cause of early childhood mortality. American Journal of Preventive Medicine 2011;41:S398‑S405.

6. Makani J, Cox SE, Soka D, Komba AN, Oruo J, Mwamtemi H, et al. Mortality in sickle cell anemia in Africa: a prospective cohort study in Tanzania. PloS One 2011;6:e14699.
7. Tewari S, Rees D. Morbidity pattern of sickle cell disease in India: a single centre perspective. The Indian Journal of Medical Research 2013;138:288.
8. Colah RB, Mukherjee MB, Martin S, Ghosh K. Sickle cell disease in tribal populations in India. The Indian Journal of Medical Research 2015;141:509.
9. Kaur M, Dangi CBS, Singh M, Singh H, Kapoor S. Burden of sickle cell diseases among tribes of India-a burning problem. International Research Journal of Pharmaceutical and Applied Sciences 2013;3:60‑80.
10. Verma IC. Burden of genetic disorders in India. The Indian Journal of Pediatrics 2000;67:893‑898.
11. Verma IC, Bijarnia S. The burden of genetic disorders in India and a framework for community control. Public Health Genomics 2002;5:192‑196.
12. Stepping out of the shadows Combating sickle cell disease in India. The Economist Intelligence Unit Limited; 2020.
13. Hockham C, Bhatt S, Colah R, Mukherjee MB, Penman BS, Gupta S, et al. The spatial epidemiology of sickle-cell anaemia in India. Scientific Reports 2018;8:1‑10.
14. Ahmad MM, Gupta HN, Shinde DS, Ruparel ND. The Prevalence and Severity of Sickle Cell Disease in Amravati District of Maharashtra. Indian Journal of Pharmacy Practice 2018;11.
15. Italia Y, Krishnamurti L, Mehta V, Raicha B, Italia K, Mehta P, et al. Feasibility of a newborn screening and follow-up programme for sickle cell disease among South Gujarat (India) tribal populations. Journal of Medical Screening 2015;22:1‑7.
16. Patel AP, Naik MR, Shah NM, Sharma NP, Parmar PH. Prevalence of common hemoglobinopathies in Gujarat: an analysis of a large population screening program. National Journal of Community Medicine 2012;3:112‑116.
17. Patel AG, Shah AP, Sorathiya SM, Gupte SC. Hemoglobinopathies in South Gujarat population and incidence of anemia in them. Indian Journal of Human Genetics 2012;18:294.
18. Balgir RS. The spectrum of haemoglobin variants in two scheduled tribes of Sundargarh district in north-western Orissa, India. Annals of Human Biology 2005;32:560‑573.
19. Mistry S, Shah K, Patel J. Prevalence of sickle cell disease in tribal peoples of Valsad district region in Gujarat, India. Tropical Journal of Pathology and Microbiology 2018.

Table 1: Sickle Cell Disease prevalence studies from India

| S no. | Title | Time period | Age | Place | Sample size | Population | Prevalence | screen test adapted |
|---|---|---|---|---|---|---|---|---|
| **1** | Ahmed et al 2018 [14] | 2 years | 0-10<br>11-15<br>16-20 | Amravati, Maharashtra | 2,50,424 | (SC & ST) tribal | Over all =0.1%,<br>SC= 0.0015%,<br>ST=0.0013%, | Solubility test |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Above 20 | | | | Male=0.176%,female=0.106% | |
| **2** | Italia et al 2015 [15] | 2 years period | newborns were screened | Community (newborn screening) (South Gujarat) | 5467 (samples collected from 13 different centres) | tribal populations | SCD - 0.60%, SCT - 12.5 | HPLC |
| **3** | Patel et al 2012 [16] | 4 Years (Sept. 2004 to Nov.2008) | <17 17-35 35+ | Community based (Gujarat) | 168495 persons from tribal areas,149044 from non-tribal areas | tribal and non-tribal population | SCT - 6.54% SCT (tribal) - 11.38% SCT (nontribal) - 1.1%, male-11.6%, female- 11.13% | HPLC |
| **4** | Patel et al 2012 [17] | - | <18 18+ | Gujarat | 35857,<18 n >18 | tribal | SCD - 0.03%, SCT - 1.3% | HPLC |
| **5** | Balgir et al 2005 [18] | - | 0-61+ | Odisha | 836 (primary data collection) | tribal village | SCT=5.3%, SCD=0.3 | HPLC |
| **6** | Mistry et al 2018 [19] | January 2015 to December 2016 | All age group | Valshad, Gujarat | 1186 were tested positive with Sickling test (DTT test) | Tribal | SCD= (107/1186)= 9.02%, SCT= (1052/1186)=88 .7% | sickling test+ HPLC (either SCD or SCT) |

3.2.2. **<u>Evidences on cost-effectiveness analysis for SCD screening in other countries:</u>**

We found four cost-effectiveness studies that examined screening versus no screening strategy [1- 4]. We did not find any cost-effectiveness study that looked at POC tests. In the base-case scenario, three studies [1-3] used the healthcare system perspective, while one [4] did not. All

the four studies were model-based, while one used a discrete-event simulation model [3]. The lifetime horizon was used in two of the model-based studies, while one used 10 years as a time horizon for new-borns. The screening studies have different effectiveness measure. In Spain during a 10-year period (fiscal year 2013), Sub-Saharan Africa (fiscal year 2014) and Angola (fiscal year 2012–2014), the ICER for new-born screening vs no screening was €34,169 ($US45,445) per LYG, $US213 every DALY averted, and $US2214–2824 each HLY gained over a lifetime horizon (fiscal year not available) [2-4]. In comparison to a midwife care strategy (sequential testing at the first midwife consultation) over a 10-week period in the UK, the primary care parallel strategy (testing mother and father at the same time in primary care) and primary care sequential strategy (testing mother in primary care and then the father if the mother is a carrier) resulted in an ICER of £25 ($US39) and £13 ($US20) per woman screened, respectively (fiscal year 2010) [1]. SCD complications were examined in two studies [2,3]. Stroke (two studies) [2-3], vasoocclusive crisis or pain crisis (one study) [2], and acute chest syndrome (one study) [2] were the most frequent problems in those studies. Healthy life-years (HLYs; one study) [2], life years gained (LYG; one study) [3], Disability adjusted life-years (DALYs; one study) [4] and were three effectiveness measures that captured both quality and length of life. One antenatal screening study measured the number of women screened [1].

Table 2: Description of studies with cost-effectiveness analysis for SCD screening in other countries

| | Study | Study design | Region | Perspective | Intervention type | Study Population | Time Horizon | Intervention/Comparator | Effectiveness Measure |
|---|---|---|---|---|---|---|---|---|---|
| **1** | Castilla-Rodríguez et al 2016 | Model-based study | Spain | Healthcare system | Screening | New-borns | 10 years | Intervention: Newborn screening program<br>Comparator: No screening | LY<br>The ICER for newborn screening versus no screening<br>was €34,169 ($US45,445) per LYG in Spain over 10 years |
| **2** | Kuznik et al. 2016 | Model-based study | Sub-Saharan Africa | Healthcare system | Screening | New-borns | Lifetime | Intervention: Newborn screening and prophylactic intervention Comparator: No screening | DALY<br>$US213 per DALY averted in SubSaharan Africa (fscal year 2014 |
| **3** | McGann et al. 2015 | Model-based study | Angola | NA | Screening | New-borns | Lifetime | Intervention: Newborn screening and treatment program for sickle cell anemia Comparator: No screening | HLY<br>$US2214–2824<br>per HLY gained in Angola over a lifetime horizon |
| **4** | Bryan et al. 2011 | Model-based study | UK | Healthcare system | Screening | Pregnant women (biological moth- ers); their partners (biological fathers) | Pregnancy to conclusion | Intervention: Primary care sequential<br>Comparator: Midwife care<br>Intervention: Primary care parallel<br>Comparator: Midwife care<br>Intervention: Primary care parallel<br>Comparator: Primary care sequential | woman screened<br>£13 ($US20) per woman screened<br>£25 ($US39) per woman screened<br>More costly, less effective |

## References


1. Bryan S, Dormandy E, Roberts T, Ades A, Barton P, Juarez-Garcia A, et al. Screening for sickle cell and thalassaemia in primary care: a cost-effectiveness study. British Journal of General Practice 2011;61:e620‑e627.
2. McGann PT, Grosse SD, Santos B, de Oliveira V, Bernardino L, Kassebaum NJ, et al. A cost-effectiveness analysis of a pilot neonatal screening program for sickle cell anemia in the Republic of Angola. The Journal of Pediatrics 2015;167:1314‑1319.
3. Castilla-Rodriguez I, Cela E, Vallejo-Torres L, Valcarcel-Nazco C, Dulin E, Espada M, et al. Cost-effectiveness analysis of newborn screening for sickle-cell disease in Spain. Expert Opinion on Orphan Drugs 2016;4:567‑575.
4. Kuznik A, Habib AG, Munube D, Lamorde M. Newborn screening and prophylactic interventions for sickle cell disease in 47 countries in sub-Saharan Africa: a cost effectiveness analysis. BMC Health Services Research 2016;16:1‑12.

3.2.3 **Description of standard of care:**

As per the National guidelines on hemoglobiopathies, screening of SCD has been recommended using solubility test followed by confirmation by either Iso electric Focussing or HPLC. For new born screening solubility test is not useful due to the presence of high levels of HbF. In new-borns DBS with HPLC is the recommended test. However, the positive ones need to be re-confirmed of their diagnosis at the age of 9 months to 1 year.

**Solubility test** is a very cheap test that uses phosphate buffer a haemolysing agent and sodium Dithionate. Due to insolubility of HbS in presence of these solutions, the HbS crystallises resulting in precipitation of the cells causing turbidity.

**Sensitivity and Specificity of Solubility test:**

Three studies from literature were reviewed to extract the diagnostic effectiveness of **Solubility test**, two of which were Indian studies and one from Uganda [1, 2, 3]. The comparators were either HPLC or Hb Electrophoresis. While the Indian study conducted in Gadchiroli had a high sensitivity and specificity of 93.8% and 100% respectively, the one conducted in Gujarat had a very low specificity of 29.6% and a high specificity of 96.8%. However, the study conducted in Uganda had a low sensitivity of 45% in comparison to the specificity of 90%. [Table 3]

Table 3: Studies discussing the diagnostic effectiveness of Solubility Test

| Sl.No | STUDY | REFERENCE TEST | LOCATION | POPULATION | SAMPLE SIZE | SENSITIVITY | SPECIFICITY | PPV | NPV |
|---|---|---|---|---|---|---|---|---|---|
| 1. | Surve et al, 2000 [1] | HPLC, Hb electrophoresis | Dhule, Gadchiroli | Adults | 3246 | 93.8 | 100 | | |
| 2. | Okwi Andrew et al. 2010 [2] | Hb electrophoresis | Uganda | 6 months – 5 years | 200 | 45% | 90% | | |
| 3. | Richa Jain et al 2020 [3] | HPLC | Gujarat | | 1890 | 96.8% | 29.6% | 87.9 % | 64 % |

**References**


1. Surve R, Mukherjee M, Kate S, et al. Detection of the βs gene: An evaluation of the solubility test against automated chromatography and haemoglobin electrophoresis. *British journal of biomedical science*. 2000;57:292-294.

2. Andrew O, Byarugaba W, Parkes A, Ocaido M. The Reliability of Sickling and Solubility Tests and Peripheral Blood Film Method for Sickle Cell Disease Screening at District Health Centers in Uganda. *Clinics in Mother and Child Health*. 2010;7:1-5. doi:10.4303/cmch/C101947

3. Jain R, Saxena S. The efficacy and reliability of Solubility test followed by High-Performance Liquid Chromatography (HPLC) for sickle cell disorders in Gujarat- An original research article. *Tropical Journal of Pathology and Microbiology*. 2020;6(2):199-204. doi:10.17511/jopm.2020.i02.13

3.2.4 **Description of Gazelle [intervention]**

**Gazelle,** manufactured by Hemex Health India (in Rajasthan) is a make in India product using a USA based technology. This HemeChip cellulose acetate paper-based microchip electrophoresis system consists of Gazelle reader and Cartridge. The reader is a touch-screen tablet computer with an integrated imaging system and has a rechargeable battery. The cartridge consists of a single strip of cellulose acetate paper, a pair of blotting pads and integrated stainless-steel electrodes. Apart from HbA, HbS and HbC detected by other POCs it also detects HbA, HbF, HbA2, and HbE, thereby making it capable of differentiating between HbSS and sickle- β0-thalassemia. The time required for completion of one test by Gazelle is reported to be 13 mins and the blood volume utilized per test is approx. 0.2 microliter. It is however expected to require a skilled interpretation and web-based image processing application for automated results.

There is no literature evidence for conducting this test in newborns. However, the test can be done at 6 weeks onwards and repeated for confirmation of positives with HPLC at 3 months of age [1] [2].


Figure 2: Representation of the Gazelle test

**Sensitivity and Specificity of Gazelle:**

There are limited studies in literature validating Gazelle for diagnosing Sickle Cell Disease. Of the two studies available in the literature, one was conducted exclusively in India and the other included both Indian and Nigerian cohort. Both the studies reported a sensitivity and specificity above 98%.

Table 4: Studies discussing the diagnostic effectiveness of Gazelle

| Sl. No | STUDY | REFERENCE TEST | LOCATION | POPULATION | SAMPLE SIZE | SENSITIVITY | | SPECIFICITY | | PPV | NPV |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Sickle Trait | Sickle Disease | Sickle Trait | Sickle Disease | | |
| 1. | Srivas et al, 2021 [20] | Hb electrophoresis & HPLC | Chattisgarh & Madhya Pradesh | 6 months to 65 years | 1050 | 98.2 | 100 | 99.6 | 99.3 | SCD :91.8 Trait : 98.9 | SCD: 100 Trait: 99.3 |
| 2. | Hasan et al, 2020 [21] | Lab electrophoresis, HPLC | India & Nigeria | 6 weeks to 5 years | 566 | 100 | 100 | 100 | 98.7 | SCD :78.6 Trait :100 | SCD: 100 Trait: 100 |

**References:**


1. Shrivas S, Patel M, Kumar R, et al. Evaluation of Microchip-Based Point-Of-Care Device "Gazelle" for Diagnosis of Sickle Cell Disease in India. *Front Med (Lausanne)*. 2021;8:639208. doi:10.3389/fmed.2021.639208
2. Hasan MN, Fraiwan A, An R, et al. Paper-based microchip electrophoresis for point-of-care hemoglobin testing. *Analyst*. 2020;145(7):2525-2542. doi:10.1039/c9an02250c


Table 5: Technical comparison between various tests

| Features | POC techniques for sickle cell disease | | | |
|---|---|---|---|---|
| | **Sickle Scan** | **Hemotype SC** | **Gazelle** | **HPOS** |
| Country of origin | USA | USA | USA but manufactured in India | IISC Bengaluru, India |
| Technique used | Lateral flow immunoassays, utilizes polyclonal antibodies | Lateral flow immunoassays, utilizes monoclonal antibodies | Automated Microchip electrophoresis | Optical Absorbance Spectrometry based + Deoxygenating the Blood sample |

| | | | | |
|---|---|---|---|---|
| Feasibility at the POC | Feasible | Feasible | Moderately feasible; More confirmatory | Feasible |
| Cost per test | <100 INR | <100 INR | <200 INR | Rs. 55 /- (@Volumes) Rs. 125/- (@Retail) |
| Amount of blood required | 5 µl | 15 µl | 20 µl | 5 µl |
| Sensitivity | 97.8 | 97.3 | 100 | 96.9 |
| Specificity | 99.2 | 99.9 | 99 | 98.6 |
| Can be used for Hb estimation | No | No | No | Yes |
| Requirement of extra device apart from kit | No | No | Yes (Gazelle Reader) | Yes (HPOS Device) |

3.3 **Input parameters:**

3.3.1 **Estimation of costs:**

The health system costs for screening in the public health facilities were obtained from a previous study [Table 6]. Cost of screening included the economic cost of sample collection, supplies, personnel and additionally transport and laboratory processing cost for HPLC confirmation. Other costing heads included human resources, area cost, drugs and consumables, medical and non-medical equipment and overhead costs. The sources to obtain this data was secondary sources of available data.

The cost of the Gazelle machine and kit per patient was obtained from the current quotes from the manufacturer. The costs at each levels of healthcare were calculated separately based on the current service utilization [70% in primary level, 10% in secondary level and 20% in tertiary level]. The cost of the machine was apportioned based on the number of health facilities [2] at each level of healthcare and the population availing the services. Threshold analysis, and PSA was performed as part of the cost analysis. The cost parameters are enlisted in Table 6.

Table 6: Input parameters specific to cost estimation

| Input parameter | Value in INR | Source |
|---|---|---|
| **Primary Level_ Gazelle** | | |
| Cost of capital and shared resources per person | 38.172 | [1] |
| Cost of kit per person | 180 | Obtained from Manufacturer |
| Cost of Gazelle machine | 2,50,000 | Obtained from Manufacturer |
| **Secondary Level_ Gazelle** | | |

| | | |
|---|---|---|
| Cost of capital and shared resources per person | 91.08 | [1] |
| Cost of kit per person | 180 | Obtained from Manufacturer |
| **Tertiary Level_ Gazelle** | | |
| Cost of capital and shared resources per person | 59 | [1] |
| Cost of kit per person | 180 | Obtained from Manufacturer |
| **Primary Level_ Solubility test** | | |
| Cost of capital and shared resources per person | 28.172 | [1] |
| Cost of kit Consumables | 17.32 | CHSI Data and Procurement prices of MoHFW |
| **Secondary Level_ Solubility test** | | |
| Cost of capital and shared resources per person | 52.98 | [1] |
| Cost of kit per person | 17.32 | CHSI Data and Procurement prices of MoHFW |
| **Tertiary Level_ Solubility test** | | |
| Cost of capital and shared resources per person | 34.16 | [1] |
| Cost of kit per person | 17.32 | CHSI Data and Procurement prices of MoHFW |
| HPLC test cost for SCD (Including capital and recurrent cost) | 393 | Primary Source |

**References:**


1. Muniyandi M, Karikalan N, Ravi K, Sengodan S, Krishnan R, Tyagi K, Rajsekar K, Raju S, Selvavinayagam TS. An economic evaluation of implementing a decentralized dengue screening intervention under the National Vector Borne Disease Control Programme in Tamil Nadu, South India. Int Health. 2022 May 2;14(3):295-308. doi: 10.1093/inthealth/ihab045.
2. Press Information Bureau, Government of India. Available from: https://pib.gov.in/newsite/PrintRelease.aspx?relid=180948


3.3.2 **Estimation of effects:**

The number of individuals living with SCD among the eligible population was estimated using the prevalence of the condition. Sensitivity and specificity of the tests were used to estimate the number of true positives, true negatives, false positives and false negatives. This was used to identify the number of cases detected and undetected using Gazelle and solubility test followed by confirmation with HPLC. The input parameters are enlisted in Table 7.

**Table 7: Input parameters specific to effects estimation**

| Input parameters | Values | Source |
|---|---|---|
| Eligible population | 39954483 | Census 2011 |
| Prevalence of SCD | 0.0167 | Colah et al. 2018 |
| Sensitivity of solubility test | 0.938 | Surve et al. 2000. 2001 |
| Specificity of solubility test | 0.999 | |

| | | |
|---|---|---|
| Sensitivity of HPLC | 0.968 | Jain et al. 2020, 2021 |
| Specificity of HPLC | 1 | |
| Sensitivity of Gazelle | 1 | Srinivas 2021 |
| Specificity of Gazelle | 0.99 | Hasan et al. 2020 |
| Coverage of solubility, Gazelle | 1 | Author assumption |
| Coverage of HPLC | 1 | |

### 3.3.3 **Expert Opinion**

Several clinicians and researchers were consulted to get a perspective of their experiences in screening diagnosis and management of sickle cell patients using various POC tests as well as standard modalities. Disease progression and most common clinical presentations were agreed upon and algorithms to manage the same were discussed. In the discussion it was identified that Gazelle has several advantages over the other POCs under consideration. It could be used for diagnosis of other hemoglobinopathies at a faster rate. The rates of the machinery and kit, feasibility of replacing HPLC with Gazelle was discussed. Existing literature shows that Gazelle can be used as a confirmatory test [Sensitivity 100%; Specificity 99%] but more research is warranted to make an informed inference.

## 3.4 Analysis

The input parameters were used to estimate the cost per test screened, cost per test detected, number of cases detected, and number of cases undetected using Gazelle and Solubility test at primary and secondary level followed by confirmation with HPLC and HPLC at tertiary level. PSA was done to ascertain the upper and lower limits of the outcomes.

The health system cost for rolling out the screening program using Gazelle and Solubility test with HPLC was determined. The marginal cost (additional cost) of establishing Gazelle and Solubility test with HPLC within the current health system, for screening of SCD was also determined. The costs of Gazelle machine and kit was varied to identify the cost per case detected where it is cost saving as compared to Solubility with HPLC. Varied marginal costs corresponding to these costs of Gazelle machine and kit was also calculated providing reference for negotiation during procurement.

# CHAPTER 4: RESULTS

The cohort was selected from six high prevalence states of the country [Gujarat, Madhya Pradesh, Tamil Nadu, Maharashtra, Odisha, and Chhattisgarh]. The cohort size was 3.9 crores as obtained from the Census data 2011. The cohort included tribal population of 6 weeks to 40 years of age.

## 4.1 **Effect of Gazelle and Solubility test**

Based on the prevalence of SCD, among the cohort, 667239.866 people could be SCD patients. When screened using Gazelle, all cases would be detected as the sensitivity of the test is 100%. Meanwhile, 392872.4 false positives were identified. All diagnosed positive disease cases by Gazelle were further confirmed by HPLC to identify true positives. This strategy helps identify only true positives and excludes all false positives diagnosed by Gazelle as it has slightly low specificity.

When screened using Solubility test at primary and secondary level followed by HPLC at tertiary level, 37,365 cases went undetected and 3928.7 cases were false positives based on sensitivity and specificity of solubility test. The false positives get eliminated by confirmation with HPLC, however 37,365 still remain undetected as senisitivity of solubility is poor. Therefore, gazelle has definitely an advantage over solubility as an estimate of 37,365 more cases get detected using Gazelle.

## 4.2 **Costs of screening with Gazelle and Solubility test**

Based on the current levels of service utilization at primary, secondary and tertiary levels of healthcare, 27968138 eligible population obtained services from a primary facility, 3995448 from a secondary facility, and 7990897 from a tertiary facility. The total cost for the screening program, cost per case screened and the cost per cases detected are then estimated and is presented in Table 8.

Although the cost of screening and detecting cases were higher for Gazelle, it may be noted that the number of cases undetected using Solubility test followed by HPLC is much higher than Gazelle. This makes Solubility test followed by HPLC less reliable compared to Gazelle [Table 8].

## 4.4 **Probabilistic sensitivity analysis**

The PSA was performed. Using Monte Carlo simulation method, we ran 1000 simulations for various parameters. The lower and upper limits of 95% CI intervals were ascertained corresponding to 2.6 percentile and 97.5 percentile values. The results are presented in Table 8.

**Table 8: Outcomes for conducting the facility-based screening program using Gazelle and Solubility test at all levels of healthcare.**

| Parameters (Previous analysis) | Values (All costs presented in INR) |
|---|---|
| **Total costs of screening using Intervention at various levels of care *** | |
| At primary level | 8565614626 |
| At secondary level | 1805586125 |
| At tertiary level | 2348152955 |
| **Total costs of screening using Comparator at various levels of care *** | |
| At primary level | 1272326538 |
| At secondary level | 280880016 |
| At tertiary level | 3336063818 |
| **Cost per case screened using Intervention at various levels of care** | |
| At primary level | 306.26 (148.59, 469.48) |
| At secondary level | 451.91 (336.64, 562.14) |
| At tertiary level | 293.85 (138.79, 409.15) |
| **Cost per case screened using Comparator at various levels of care** | |
| At primary level | 45.49 (34.15, 57) |
| At secondary level | 70.30 (52.67, 88.50) |
| At tertiary level | 417.48 (212.93, 629.72) |
| **Cost per case screened** | |
| Intervention | **318.35** (158.86, 474.62) |
| Comparator | **122.37** (60.00, 181.90) |
| **Cost per case detected** | |
| Intervention | **19062.64** (9565.08, 28229.49) |
| Comparator | **7762.29** (3691.15, 11839) |
| **Additional number of cases detected by intervention vs comparator** | **37365.43** (18809.05, 56400.91) |

*****Sum total of capital costs, recurrent costs, kit cost and machine cost

### 4.3 **Health system costs and marginal costs of using Gazelle vs Solubility in the program**

The health system costs were determined to assess the screening program with Gazelle and with solubility tests. The costs are presented in Table 9.

The additional cost that needs to be spent to towardsscreening program in the public healthcare facilities using the existing resources is presented as the marginal costs for rolling out the screening program. The figures are presented in Table 9.

**Table 9: The health system costs and marginal costs for rolling out the screening program with Gazelle and Solubility tests at identified 6 endemic states of India (all costs are presented in INR)**

| Parameters | Values |
|---|---|
| **Health system cost** of rolling out the screening program with **Intervention** (capital, recurrent and consumable cost including Gazelle machine and kit for 6 states) | 12719353706 [1271.93 crores] |
| **Health system cost** of rolling out the screening program with **Comparator** (capital, recurrent and consumable cost including HPLC machine and Solubility kit for 6 states) | 4889270372 [488.92 crores] |
| **Marginal cost** for rolling out the screening program with **Intervention** [After considering only the cost of Gazelle machine and kit.] | 10400056940 [1040.00 crores] |
| **Marginal cost** for rolling out the screening program with **Comparator** [After considering only the cost of the Solubility kit and HPLC machine] | 3220341629 [322.03 crores] |

### 4.4 Willing to pay at differential cost of Gazelle machine and kit:

This analysis was performed to identify the cost for procurement of the Gazelle machine and kit. As mentioned in Table 8, the cost per case detected as per standard of care ie Solubility followed by HPLC is 7762 INR.

Treating this as a reference, the price of Gazelle machine and kit was varied to calculate the cost per case detected for Gazelle to assess at what cost the intervention could become cost saving. The corresponding differential marginal cost based on the varied Gazelle kit and machine cost was calculated and presented in the Table 10 below.

Depending on the health systems' willingness to pay, these costs can be utilised to negotiate the cost of procurement of kit and machine. The procurement of kit at <40 INR and a Gazelle machine <90000 INR would be cost saving as compared to Solubility followed by HPLC with marginal cost of 275.31 crores INR for the health system.

Considering the current marginal health system cost of solubility followed by HPLC as benchmark (322.03 crores INR), the ideal cost of procurement of kit is determined to be <50 INR and a Gazelle machine <95000 INR for screening using Gazelle.

**Table 10: Differential Cost per case detected and Marginal health system cost for varied Gazelle machine and kit cost (all costs are presented in INR)**

| Gazelle Machine cost | Kit cost | Cost per case detected | Marginal Cost of rolling out Gazelle |
|---|---|---|---|
| 250000 | 180 | 19062.64 | 10400056940 |
| 245000 | 170 | 18367.67 | 9936347110 |
| 240000 | 160 | 17672.71 | 9472637280 |
| 230000 | 140 | 16282.77 | 8545217620 |
| 220000 | 120 | 14892.84 | 7617797960 |
| 210000 | 100 | 13502.90 | 6690378300 |
| 200000 | 90 | 12711.77 | 6162503470 |
| 180000 | 80 | 11728.31 | 5506298640 |
| 150000 | 70 | 10552.52 | 4721763810 |
| 100000 | 60 | 8992.07 | 3680568980 |
| 95000 | 50 | 8297.10 | 3216859150 |
| 90000 | 40 | 7602.13 | 2753149320 |

## REANALYSIS BASED ON RECOMMENDATION OF TAC

### 4.5 Background:

As per the requirement from the TAC the following analysis evaluates the cost-effectiveness of Gazelle with HPLC. As Gazelle (Heme-Chip cellulose acetate paper-based microchip electrophoresis system) is a facility based screening method with 100% sensitivity it has been suggested to be compare it with HPLC for diagnosis of Sickle Cell Disease/Trait without need for additional confirmation with HPLC due to its high sensitivity . The comparator HPLC test is available only at tertiary level of care. Hence, the comparator for the evaluation at primary and secondary level was Solubility test with confirmation of positives by HPLC and at tertiary level all test will be through HPLC test. The details of the intervention and comparator are presented in the PICOT table below.

### 4.6 Research Question:

- To conduct an HTA on Gazelle for screening for Sickle cell disease/ traits.

### 4.7 Objectives:

1. To collate evidence on clinical-effectiveness of Gazelle vs solubility test and HPLC to diagnose sickle cell trait/disease
2. To estimate cost of test per case screened and detected using Gazelle
3. To access the health system costs of using Gazelle for facility-based screening

**4.8 PICOT:**

| | |
|---|---|
| **Population** | A hypothetical cohort of tribal population between 6 weeks to 40 years of age from six high prevalence states [Madhya Pradesh, Maharashtra, Gujarat, Chhattisgarh, Tamil Nadu, Odisha] in India |
| **Intervention** | ➢ Gazelle at all level of care. |
| **Comparator** | ➢ **Primary level**: Solubility test with confirmation of positives with HPLC<br>➢ **Secondary level**: Solubility test with confirmation of positives with HPLC<br>➢ **Tertiary level**: HPLC test for screening all cases |
| **Outcomes** | ➢ **Cost per case detected** using intervention and comparator<br>➢ **Cost per case screened** using intervention and comparator<br>➢ **Additional number of cases detected** by intervention vs comparator |
| **Perspective** | Health system perspective |

**4.9 Result:**

The cohort was selected from six high prevalence states of the country [Gujarat, Madhya Pradesh, Tamil Nadu, Maharashtra, Odisha, and Chhattisgarh]. The cohort size was 3.9 crores as obtained from the Census data 2011. The cohort included tribal population of 6 weeks to 40 years of age.

**4.10 Estimations of screening by Gazelle and HPLC:**

Based on the prevalence of SCD, among the cohort approximately 667240 individuals could be SCD patients. As the sensitivity of the screening device Gazelle (HemeChip cellulose acetate paper-based microchip electrophoresis system) is 100% all the prevalent true positives 667239 were detected. However, it detected approximately 392872 false positives cases as diseased individuals.

The screening using the comparator HPLC at tertiary and Solubility test at primary and secondary levels with confirmation of positives with HPLC, detected 629874 cases of SCD among all screened cases. As HPLC has 100% specificity no false positives were reported at tertiary level, however, at primary and secondary level the solubility test reported 3143 cases as false positives.

Thus, using the intervention Gazelle for screening of SCD could incrementally detect 37,365 more cases than the comparator HPLC and Solubility test. However, Gazelle also detected approximately 392872 false positives who would be subjected to unnecessary treatment.

### 4.11 Estimation of Cost of Screening with Gazelle and HPLC:

The total cost for the screening program, costs per case screened and the cost per case detected are estimated and presented in Table 11. Although the cost of screening and detecting cases were higher for Gazelle, it may be noted that the number of cases detected using Gazelle were much higher than HPLC .

### 4.12 Probabilistic sensitivity analysis:

The PSA was performed. Using the Monte Carlo simulation method, we ran 1000 simulations for various parameters. The lower and upper limits of 95% CI intervals were ascertained corresponding to 2.6 percentile and 97.5 percentile values. The results are presented in Table 11.

**Table 11: Outcome summary for conducting a facility-based screening program for SCD using Gazelle and HPLC**

| Parameters | Values (All costs presented in INR) |
|---|---|
| **Total costs of screening using Intervention at various levels of care *** | |
| At primary level | 8565614626 |
| At secondary level | 1805586125 |
| At tertiary level | 1931824287 |
| **Total costs of screening using Comparator at various levels of care *** | |
| At primary level | 1272326538 |
| At secondary level | 280880016 |
| At tertiary level | 3336063818 |
| **Cost per case screened using Intervention at various levels of care** | |
| At primary level | 306.26 (206.08, 346.93) |
| At secondary level | 451.91 (336.64, 562.14) |
| At tertiary level | 241.75 (179.11, 305.69) |
| **Cost per case screened using Comparator at various levels of care** | |
| At primary level | 45.49 (34.15, 57) |
| At secondary level | 70.30 (52.67, 88.50) |
| At tertiary level | 417.48 (212.93, 629.72) |
| **Cost per case screened** | |
| Intervention | **307.93** (231.57, 385.21 ) |
| Comparator | **122.37** (60.00, 181.90) |
| **Cost per case detected** | |
| Intervention | **18438.68** (13666.92, 23057.88) |
| Comparator | **7762.29** (3691.15, 11839) |
| **Additional number of cases detected by intervention vs comparator** | **37365.43** (18809.05, 56400.91) |

***Sum total of capital costs, recurrent costs, kit cost and machine cost

### 4.13 Health system costs and marginal costs of rolling out the program:

The health system costs and marginal costs (additional cost for screening with existing resources) were determined for screening program with intervention and comparator at identified 6 endemic states of India. The costs are presented in Table 12.

**Table 12: Health system cost and marginal cost for rolling out screening program for SCD**

| Parameters | Values (All costs presented in INR) |
|---|---|
| **Health system cost** of rolling out the screening program with **Intervention** (capital, recurrent and consumable cost including Gazelle machine and kit for 6 states) | 12303025038 [1271.93 crores] |
| **Health system cost** of rolling out the screening program with **Comparator** (capital, recurrent and consumable cost including HPLC machine and Solubility kit for 6 states) | 4889270372 [488.92 crores] |
| **Marginal cost** for rolling out the screening program with **Intervention** [After considering only the cost of Gazelle machine and kit.] | 10400056940 [1040.00 crores] |
| **Marginal cost** for rolling out the screening program with **Comparator** [After considering only the cost of the Solubility kit and HPLC machine] | 3220341629 [322.03 crores] |

### 4.14Willingness to pay at differential cost of Gazelle machine and kit:

This analysis was performed to identify the cost for procurement of the Gazelle machine and kit. The cost per case detected for the Solubility followed by HPLC was 7762 INR which is considered as a benchmark to identify the cost at which the Gazelle would become cost saving.

The price of Gazelle machine and kit was varied to calculate the cost per case detected for Gazelle. The corresponding differential marginal cost based on the varied Gazelle kit and machine costs were calculated and presented in the Table 13 below. Depending on the health systems' willingness to pay, these costs can be utilised to negotiate the cost of procurement of kit and machine.

The procurement of kit at <50 INR and a Gazelle machine <95000 INR would be cost saving as compared to Solubility followed by HPLC with marginal cost of 321.68 crores INR for the health system.

Keeping the current marginal health system cost of solubility followed by HPLC as benchmark (322.03 crores INR) the ideal cost of procurement of kit is determined to be <50 INR and a Gazelle machine <95000 INR for screening using Gazelle.

**Table 13: Differential Cost per case detected and Marginal health system cost for varied Gazelle machine and kit cost (all costs are presented in INR)**

| Gazelle Machine cost | Kit cost | Cost per case detected | Marginal Cost of rolling out Gazelle |
|---|---|---|---|
| 250000 | 180 | 18438.68399 | 10400056940 |
| 245000 | 170 | 17743.71678 | 9936347110 |
| 240000 | 160 | 17048.74957 | 9472637280 |
| 230000 | 140 | 15658.81514 | 8545217620 |
| 220000 | 120 | 14268.88072 | 7617797960 |
| 210000 | 100 | 12878.95 | 6690378300 |
| 200000 | 90 | 12087.81426 | 6162503470 |
| 180000 | 80 | 11104.35259 | 5506298640 |
| 150000 | 70 | 9928.561294 | 4721763810 |
| 100000 | 60 | 8368.110723 | 3680568980 |
| 95000 | 50 | 7673.14351 | 3216859150 |

## CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

1) HPLC is gold standard but access to using this strategy for mass screening is limited. Gazelle has performance efficiency similar to HPLC. In comparison with HPLC, Gazelle takes lesser time for obtaining the results. The costs for the machinery is also lesser than HPLC. Gazelle does not require the expertise for performing and interpreting the test as it is required for HPLC. Therefore, public health facility-screening of high risk population with Gazelle would improve access to screening using a highly sensitive test.

**2)** The expenses and machinery required for screening suggests that Gazelle could be used as a facility-based POC screening test. However, present analysis was considered from SCD point of view only.

**3)** Even though the cost of Gazelle is high, the 3% of true positive cases which are being missed by HPLC due to its sensitivity being 97% are captured by Gazelle which has 100% sensitivity indicating no cases will go undetected. **Gazelle detects 37365 more cases of SCD compared to HPLC.**

**4)** However, in our cohort, Gazelle has detected approximately 392872 false positives cases as diseased individuals. Thus 392872 false positives cases will be subjected to unnecessary treatment. **As the specificity of HPLC is 100% the confirmation of all positives disease cases by HPLC to rule out false positives will be a useful strategy to reduce additional financial burden and avoid unnecessary treatment of these cases.**

5) **Thus using Gazelle with confirmation of all disease positive cases is the recommendation for use in public health settings**.

6) The Cost per case detected for Gazelle followed by confirmation with HPLC is INR 19062.64 as compared to Comparator of solubility test with HPLC which is INR 7762.29.

**7)** The total health system cost of the screening program at public health facilities for Gazelle followed by confirmation with HPLC would be INR 1271.93 crores. The health system cost for the comparator solubility test with HPLC is INR 488.92 crores.

**8)** The marginal cost of implementing the screening program for Gazelle followed by confirmation with HPLC is estimated to be INR 1040.00 crores and for with solubility test with HPLC would be INR 322.03 crores.

9) There is only one literature evidence that recommends Gazelle for neonatal screening. More studies are recommended to evaluate this.

**10)** This test can also be used to diagnose thalassemia. It is essential to plan a multi-centric study for further evaluation on the application of Gazelle for screening and diagnosis of thalassemia.

# CHAPTER 6: STRENGTHS AND LIMITATIONS

## 6.1 Strengths:

1. The study results could be used to negotiate the costs of procurement of Gazelle machine and kit for use in public health system.
2. We have also analyzed and presented the marginal costs of implementing a facility based SCD screening program using Gazelle using the current health system resources.
3. We have used literature references from Indian study settings to ascertain the input parameters used for the analysis.
4. Expert opinions and suggestions were obtained and this assures the quality of the analysis
5. The 3% true positive cases missed out as undetected due to 97% sensitivity of HPLC were captured by Gazelle which has 100% sensitivity. An additional 37365 number of cases were detected due to SCD screening with Gazelle as compared to HPLC.

## 6.2 Limitations:

1. Gazelle could also detect thalassemia along with SCD. This additional benefit of the test is not considered in the present analysis due to unavailability of literature evidences to carry out the analysis. Therefore, the analysis would have underestimated the health benefits of the test.
2. There were only two studies that were conducted to understand the sensitivity and specificity of Gazelle in an Indian context. More studies are warranted to improve the certainty on the generated values of diagnostic accuracy.
3. Newborns were not considered due to lack of literature evidence.
4. The current analysis measures the effects in terms of cases detected by the test. There could be various other health benefits of screening SCD in a high prevalence population. These benefits will be reflected in terms of better health outcomes due to early management cost because of early detection. This was not considered in the current analysis and this could have underestimated its health benefits.

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