Alstonia Impact

Landscaping Sickle Cell Disease in India to identify opportunities for system-level improvements

June 2024

Released on World Sickle Cell Day

Agenda

- **About Alstonia Impact**
- Executive Summary
- Summary report
- Detailed findings

Alstonia Impact is a global impact-focused consulting firm

About Alstonia Impact

- Set-up in 2018, headquartered in New Delhi by professionals with previous donor-side experience
- Multi-sectoral + global expertise: health, education, and climate
- Three verticals:
  1. **Strategy consulting and landscaping services** for philanthropic foundations and impact investors, and their portfolio organizations: Building investment/ organizational strategies, market expansion and sector building, identification of blended finance opportunities
     - Example clients: BMGF, Omidyar Network
  2. **Quantitative/Qualitative research:** Performing quantitative and qualitative research and market advisory services as well as creating and measuring impact pathways
     - Example clients: Prevail/One Acre Fund, BMGF, World Bank, Medicines Patent Pool, World Health Organization
  3. **Operational excellence**: Support on setting up and improving indigenous production and supply chain in LMICs through our network of partners
     - Example clients: Medicines Patent Pool, Sanofi
- Lean core team with a network of experts

Our network

Our clients …

Gates Foundation · The World Bank · UN · unicef · jhpiego · qure.ai · medicines patent pool · Wadhwani AI · Pfizer

… and where we come from

Gates Foundation · McKinsey & Company · Johns Hopkins Bloomberg School of Public Health · Oxford Policy Management · Siemens · sanofi · INSEAD The Business School for the World®

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- About Alstonia Impact
- **Executive Summary**
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- Detailed findings

Executive summary (1/2)

x Additional information on dedicated pages

1. Sickle Cell Disease is a hereditary condition characterized by an abnormality in the genetic code, leading to the creation of atypical haemoglobin. This anomaly causes red blood cells (RBCs) to lose their typical shape and take on a crescent or sickle-like form. This leads to **chronic anemia, immune system challenges, and persistent damage to the spleen**. These complications manifest as a range of health issues, including recurrent infections, pain, swelling, and damage to vital organs. Symptoms of SCD usually appear around 6 months of age and have a debilitating and chronic impact on the patient.

2. This report covers the findings of a **landscaping study on Sickle Cell Disease (SCD) in India**, with the aim of helping the funder community and government stakeholders understand the ongoing public and private initiatives to tackle SCD and identify the key gaps as well as associated opportunities to engage and strengthen the health system in this domain. For the preparation of this report, a mixed-method approach was used, based on secondary research **(~110 documents reviewed)** and Key Informant Interviews **(16 experts interviewed)**

3. **India** has the 2nd **highest sickle cell disease burden** around the globe. **Existing state-level SCD burden studies have limitations**. Therefore, new burden estimates were created to reflect additional considerations. We estimate that there are **~1 million SCD patients in India**. SCD patients are **concentrated in the "tribal belt"** of India, in the heart of the country. In absolute figures, the **states with the highest burden are Odisha, Jharkhand, Madhya Pradesh and Maharashtra**. In terms of prevalence rates, the 3 states with the highest SCD rates are Odisha, Madhya Pradesh and Jharkhand. Prevalence outside the tribal belt is non-negligible, and is likely driven by internal migration

4. The "**National Sickle Cell Anaemia Elimination Mission**" was launched in 2023 **by the Government of India** with the objective of eliminating SCD as a public health problem in India by 2047. While options for preventing and treating SCD are becoming more accessible to the Indian population, challenges persist. The current focus of the program is on mass screening.

5. From our research, several **major challenges** emerged, for both patients and the health system, across the whole care journey. The most significant ones:
   - **Lack of awareness / mistrust of institutions**: affected populations, esp. tribal populations tend to hold many incorrect beliefs about SCD and are hesitant to seek support because of the stigma associated with it, while healthcare workers might struggle to recognize the symptoms and to diagnose the disease. In the tribal belt, lower trust in public health facilities is well-documented
   - **Limited resources**: the number of testing centres, diagnostic tools, treatment centres and treatment resources are fewer than what is needed to comply with the guidelines
   - **Execution challenges and tools**: program implementation still has some areas of improvement, including lack of integration with local communities / pharmacists, stock-outs of key medicines and limited coverage of new-born screening, limited / no availability of new drugs and recommended vaccines
   - **Limited relevant evidence**: data gaps about burden, leakages in the care cascade and treatment adherence limit the ability to steer the program effectively

SOURCE: Team analysis

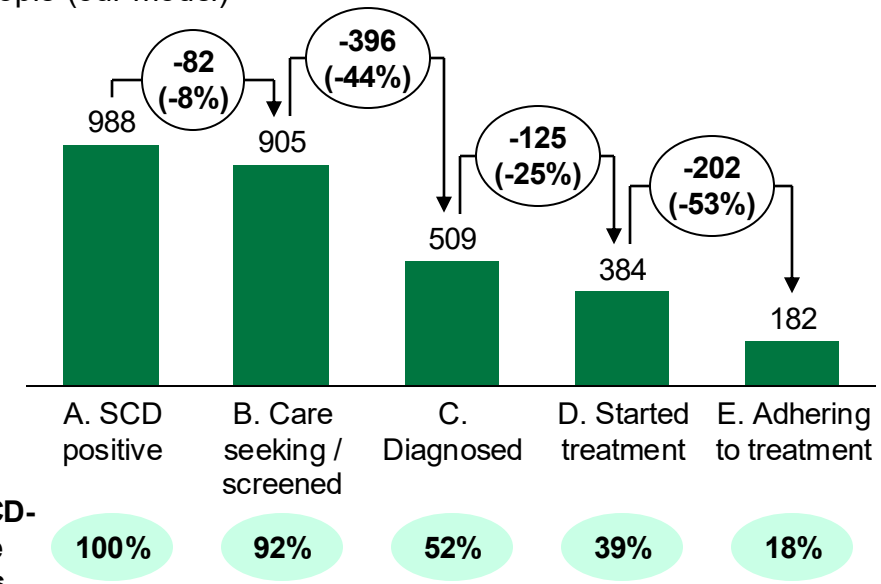
Executive summary (2/2)

x Additional information on dedicated pages

6 To prioritize challenges and find solutions to address them, **we built a care cascade for SCD to estimate the drops at each level**: care seeking, diagnosis, treatment initiation and treatment adherence. Our model estimates the **biggest drops** for the care cascade of SCD patients to be at **diagnosis and treatment adherence stages**, with lack of awareness playing a significant role across the whole journey

- Given finite resources, we recommend a higher priority on challenges related to **timely diagnosis** and **treatment adherence** of those identified.
  - **Within early diagnosis**, improving new-born screening offers a high-return strategy given an existing interaction with the health system at this stage (in comparison with mass screening or even pre-natal screening where there are practical challenges). Improving care-seeking behaviour, which drives patients to trained providers (vs. traditional healers) can also pay off dividends
  - **Within improved treatment adherence**, given that low adherence is a problem common to all chronic diseases in India, especially for tribal populations, a holistic approach to strengthen the health system for tribal populations could be the best approach

Patients through the steps of the care cascade,
'000 people (our model)



7 Based on these considerations, we identified several **key recommendations** for donors and key stakeholders to tackle the SCD challenges at system level. High priority interventions (based on impact and feasibility considerations) include:

- **Improve awareness / trust for institutions**: including mass media campaigns to fight social stigma and to build trust in the public system, and training campaigns focused on doctors and relevant healthcare workers in high prevalence areas
- **Provide more resources**: building and scaling Centres of Excellence for advanced treatment, and training lower-level facilities
- **Improve execution**: by focusing on new-born screening in public facilities and strengthening the health system for tribal populations as a whole
- **Build relevant evidence**: conducting interventional studies to discover the optimal operating model to serve the affected communities and understanding how beliefs and myths vary by region and tribes to be able to design better interventions

SOURCE: Team analysis

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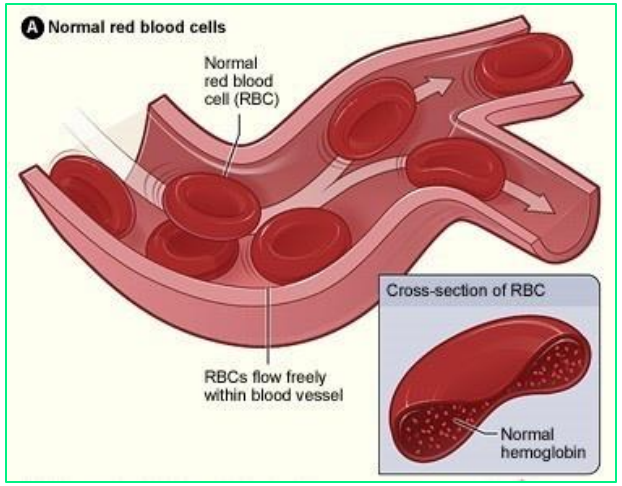
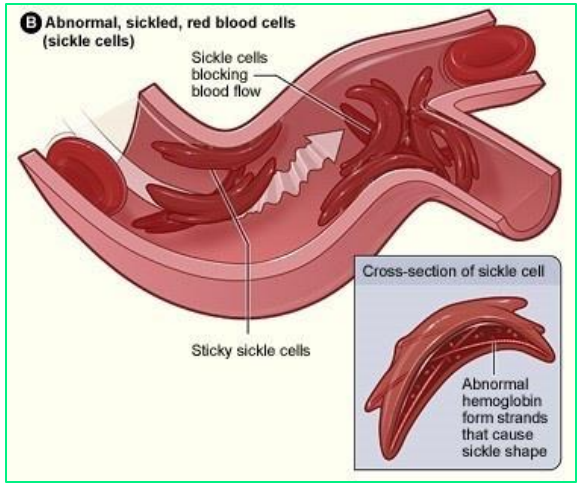
1 Sickle Cell Disease is a hereditary condition which can lead to chronic anemia and immune system challenges

Description of the disease

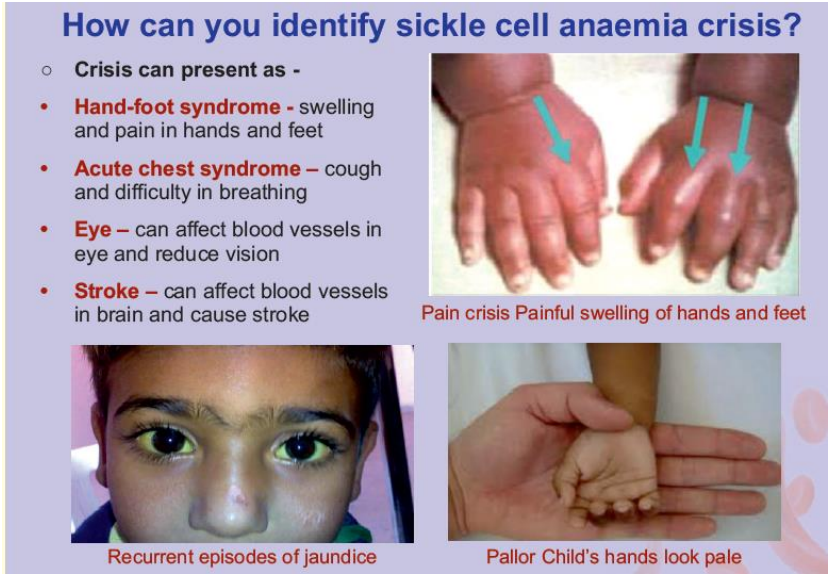
- Sickle Cell Disease is a hereditary condition characterized by an abnormality in the genetic code, leading to the creation of atypical hemoglobin. This anomaly causes red blood cells (RBCs) to lose their typical shape and take on a crescent or sickle-like form
- In contrast to the 120-day lifespan of healthy RBCs, sickle cells endure for only 10 to 20 days. This reduced lifespan, along with their altered shape, leads to **chronic anemia, immune system challenges, and persistent damage to the spleen**. These complications manifest as a range of health issues, including Sickle Cell Anemia, recurrent infections, pain, swelling, and damage to vital organs





Impact of the disease

- According to a study, in the United States, patients with sickle cell disease have lower life expectancy (54 vs 76 years), and lower projected lifetime income (~1.3 M$ vs 1.9 M$), reflecting lost income (~695 k$) owing to reduced life expectancy >>
- Symptoms of SCD usually appear around 6 months of age and have a significant impact on the patient
- People with SCD are at risk of severe infections, such as the flu, meningitis and pneumonia, therefore taking early vaccination becomes important to prevent infection and complications in later stages of life >> >>



SOURCE: NHM India – Operational Guidelines, NHLBI, NHM India – Awareness Module

2 For the preparation of this report, a mixed approach was used, based on secondary research and Key Informant Interviews (KIIs)

Objectives & Methodology

- The **objective** of this study is to help the funder community and government stakeholders understand the ongoing public and private initiatives to tackle SCD and to identify the key gaps as well as associated opportunities to engage and strengthen the health system
- The team performed **extensive secondary research**, identifying and processing more than 110 sources, including reports, regulations & guidelines, documents from the Indian central & states' governments, etc.
- In addition to those, **16 key informant interviews (KIIs)** were performed to collect additional insights and to validate hypotheses emerged during the secondary research *(see details on the right side of the page)*
- Leveraging all the limited available quantitative sources, a **care cascade model** was created, to estimate where the biggest challenges are in the patients' end-to-end care journey
- Based on those inputs, a **structured collection of the challenges** faced by the patients and by the health system was prepared (available in section "Key challenges faced by patients and health system"). Those challenges were scored qualitatively according to the impact they have on the patients
- Starting from the list of challenges and from the findings of the research, a **long list of possible recommendations** was prepared to improve the journey of SCD patients in India. All those recommendations were mapped in an impact / feasibility matrix
- Only those recommendations which scored "High" on both impact and feasibility dimensions were kept as **key recommendations for this report**; the other recommendations are also reported for completeness and shown in section "Recommendations for the broader ecosystem"

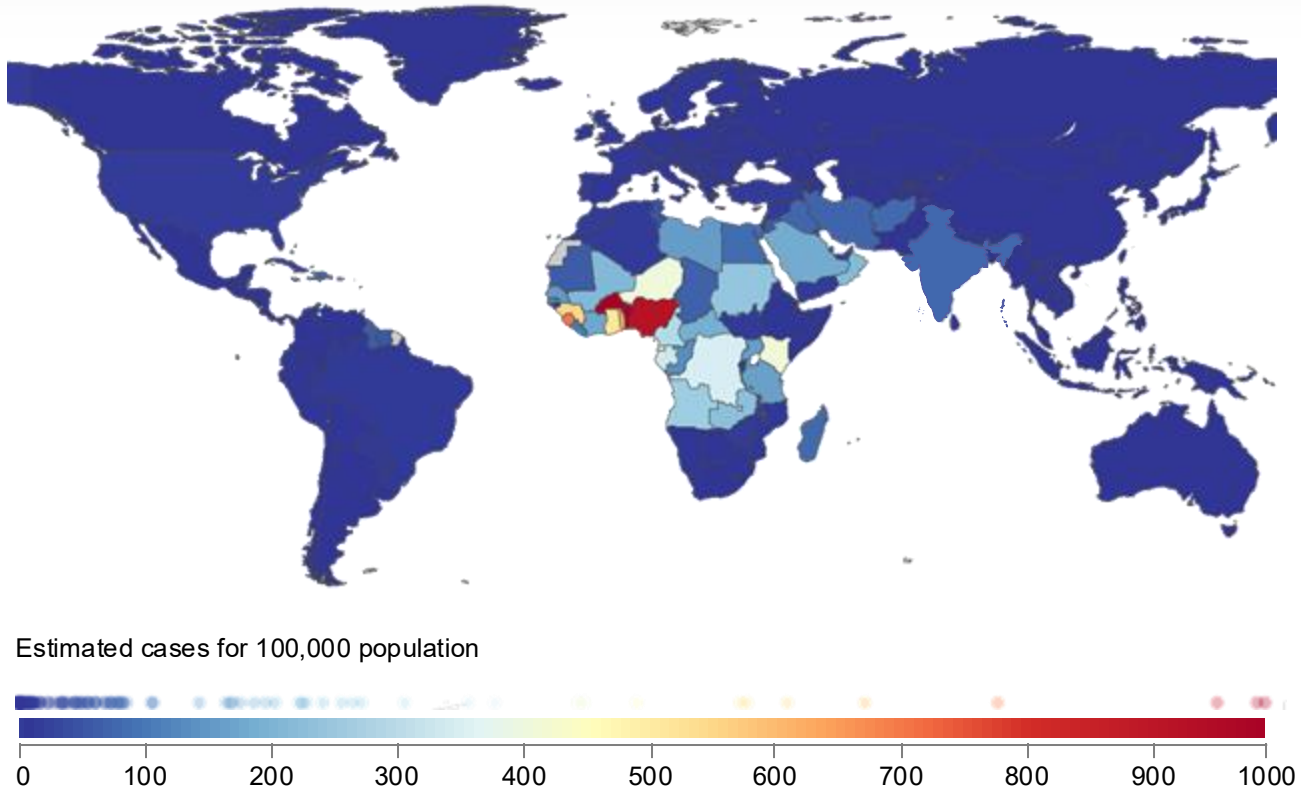
List of interviewed people, split by stakeholders' group

Government Stakeholders	1. Ministry of Tribal Affairs 2. Sickle Cell Disease Control Program, Madhya Pradesh 3. Sickle Cell Disease Control Program, Maharashtra 4. ICMR-NIRTH, Jabalpur 5. AIIMS, New Delhi (2 interviews) 6. Gandhi Medical College, Bhopal, Madhya Pradesh 7. Government Medical College, Nagpur, Maharashtra (former Professor)
Alliances, NGOs and others	8. Jan Swasthya Sahyog, Chhattisgarh 9. ADEETECH, Pune, Maharashtra 10. SEARCH, Gadchiroli, Maharashtra 11. Sickle Cell Awareness Foundation, Bharuch, Gujarat 12. Association for Health Welfare in the Nilgiris (ASHWINI), Tamil Nadu
Donors	13. Bill and Melinda Gates Foundation 14. Tribal Health Collaborative, Piramal Foundation
Patients' representative	15. National Alliance of Sickle Cell Organization (NASCO), Nagpur, Maharashtra

SOURCE: Team analysis

3 India has the one of the highest sickle cell disease burden around the globe

Sickle cell disease (SCD) prevalence around the globe, 2021

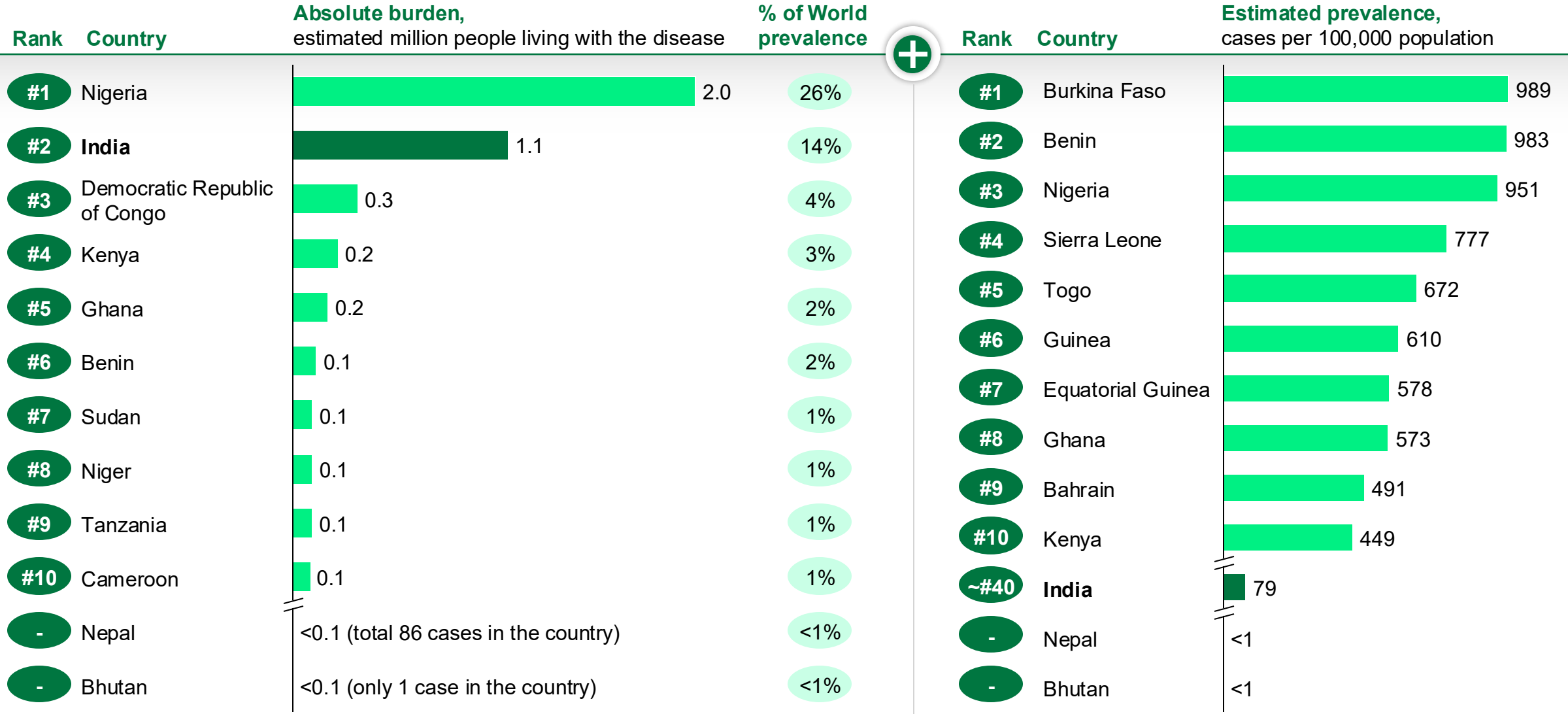


Findings from the GBD study

- WHO declared sickle cell disease (SCD) as a public health priority in 2006. Despite its life-threatening nature that affects millions of people worldwide, the disease has remained neglected in the global health agenda for decades >>
- According to Global Burden of Disease Study 2021, the burden of disease is concentrated in low-income and middle-income countries (LMICs), with the highest sickle cell disease disability burden concentrated in western and central sub-Saharan Africa and India
- As per the report, the number of people living with sickle cell disease globally in 2021 was 7.74 million, an increase of 41.4% from the figure of 5.46 million in 2000
  - The increase is driven by the population growth in the Caribbean and western and central sub-Saharan Africa
  - The national incidence rates of sickle cell disease have been relatively stable

SOURCE: Prevalence map and burden data sourced from The Lancet Hematology

3 India ranks 2nd in terms of absolute SCD burden, but it ranks only ~40th by prevalence rate



SOURCE: Data from Global Burden Disease

3 Existing India-wide SCD burden studies have limitations; in the context of this study, new burden estimates were created

Used for all quantitative considerations within the report

Limitations of current data sources

- Limited availability of primary sources, concentrated in specific small areas
- Lack of data regarding the prevalence of SCD in the non-tribal population of India
- Limited data availability on the prevalence of SCD in northeastern states
- Comprehensive state-wise surveys have been done only in 4 states, leading to skewed India-wide estimates
- Variability in the accessibility and accuracy of diagnostic tools for SCD can impact the reliability of prevalence data

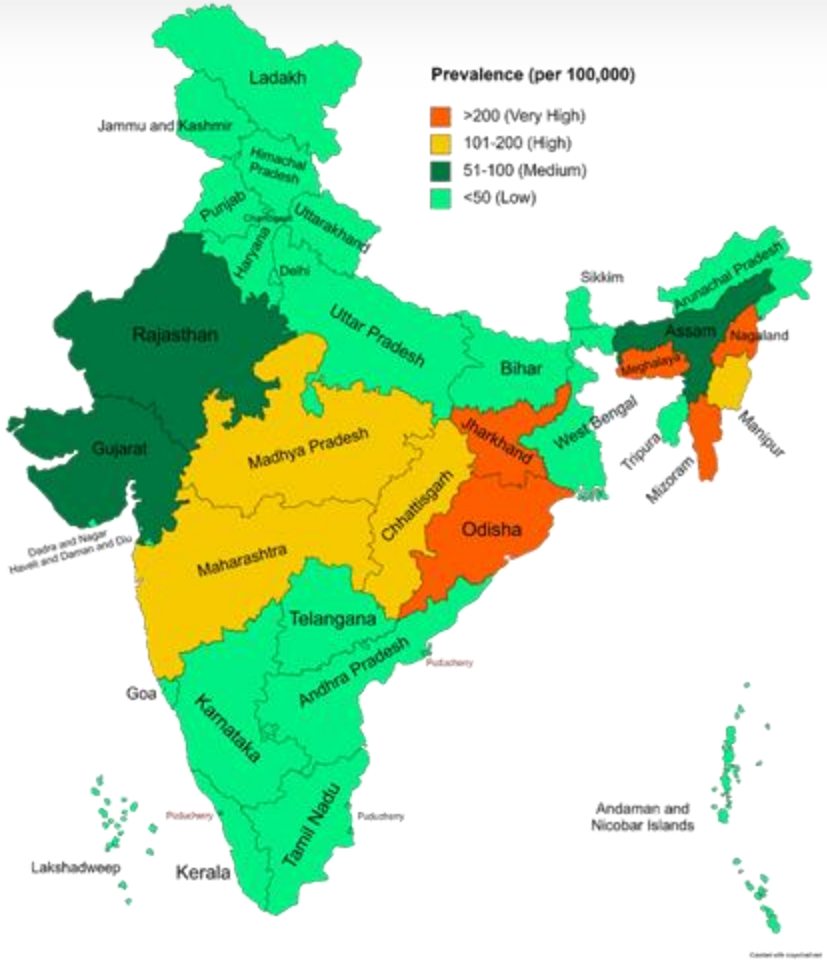
Relevant studies for SCD India prevalence

Studies	Limitations
1 Global Burden of Disease (GBD) Study	▪ Aggregated results not consistent with specific studies (e.g., UP and Maharashtra, Northern States) ▪ Based on hospitalization data, not publicly available
2 ICMR Study	▪ Consolidation of state-wide surveys where Gujarat and Maharashtra account for ~90% of the screening results
3 Gujarat NHM Estimates	▪ Burden of SCD in Gujarat, a high burden state, being used to project India-wide prevalence ▪ Estimates from 2012 and 2021 vary widely
4 Our estimate	▪ No additional primary data ▪ Non-tribal estimate based only on one data point ▪ Data extrapolation for multiple states

SOURCE: Team analysis

2 According to our analysis, the 3 Indian states with the highest SCD cases are Odisha, Maharashtra and Madhya Pradesh

Estimated prevalence, cases per 100,000



States	Estimated SCD cases, '000	Prevalence cases per 100,000
Odisha	240	541
Maharashtra	146	116
Madhya Pradesh	142	164
Jharkhand	100	253
Uttar Pradesh	49	21
Gujarat	49	68
Rajasthan	45	55
Chhattisgarh	36	119
West Bengal	35	36
Bihar	26	21
Assam	19	53
Tamil Nadu	16	21
Other states	85	26
Total India	988	71

1. Indicates the states that are not in the list of "17 high prevalence states" covered under National Sickle Program Guidelines, 2023 >>

SOURCE: Team analysis

4 The "National Sickle Cell Anaemia Elimination Mission" was launched in 2023 by the Government of India with the objective of eliminating SCD as a problem by 2047

The National Sickle Cell Anemia Elimination Mission

- Announced by Finance Minister Nirmala Sitharaman in the Union Budget 2023-2024 and officially launched by Prime Minister Narendra Modi in **July 2023**
- The program is led by Ministry of Health and Family Welfare (MoHFW), Government of India and implemented by National Health Mission (NHM) with the support of Ministry of Tribal Affairs in a mission mode
- The mission is being implemented in **278 districts of 17 states[1] in India**
- To date, the government has undertaken several initiatives under the mission such as:
  - Awareness modules have been launched to raise awareness about SCD among the population
  - Targets for screening have been established to increase the coverage of screening programs across the country
  - Software for data management has been developed to facilitate the monitoring of SCD screening program
  - Hydroxyurea availability has been increased, with the medication now included in the essential drug list, ensuring improved access for patients in need

Objectives of the mission

- Eliminate sickle cell disease as a public health problem in India before 2047
  - The focus is to eliminate sickle cell genetic transmission by the year 2047 >>
- Quantify current burden and implement a robust monitoring system
- Increase **awareness** about the disease in the community
  - Primary prevention by focusing on awareness generation, pre-marital and pre-conceptional counselling
  - Secondary prevention by focusing on screening new-born and providing early diagnosis and care
- Implement **mass screening** activities for early identification
- Strengthen existing **primary health care** mechanism to incorporate SCD related strategies
- Provide **comprehensive care** and support to SCD patients

1. The 17 target states are Andhra Pradesh, Assam, Bihar, Chhattisgarh, Gujarat, Jharkhand, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Odisha, Rajasthan, Tamil Nadu, Telangana, Uttar Pradesh, Uttarakhand, West Bengal

SOURCE: NHM India – Operational Guidelines

5 From our analysis, the following major challenges emerged (1/2)

Group	Sub-group	Description of major challenges
Lack of awareness / mistrust of institutions 	**Community and Patients**	▪ Affected populations have **limited awareness** about the disease and many hold incorrect beliefs, patients might be hesitant to seek support because of the **stigma associated with the disease** – *General population often lacks a proper understanding of the disease, leading to discrimination (interview with doctors, experts)* ▪ High **reliance on traditional healers in tribal areas across health areas** due to **low trust in public health system**
	Health care workers (including doctors, community health workers and local healers)	▪ **Doctors, nurses and other community health workers at primary health care centres** have **limited awareness and knowledge** of the disease, so less likely to diagnose it, refer and to provide proper treatment including monitoring and dosage – *Healthcare workers are often unaware about SCD (patients' representative)* ▪ **Traditional healers and pharmacists** have low awareness and **often misdiagnose** condition
Lack of resources 	**Limited funding for research**	▪ Limited funding for research and development of tools (diagnostics, therapies)
	Not enough testing centres / diagnostic tools	▪ Challenges in conducting **pre-natal screenings due to limited diagnostic tools at facilities close to populations**; the screening techniques are invasive and carry a 0.5-2.0% risk of foetal loss (ICMR guidelines)
	Not enough treatment centres or treatment resources	▪ **Centres of Excellence for advanced and inter-disciplinary treatment** not in place evenly

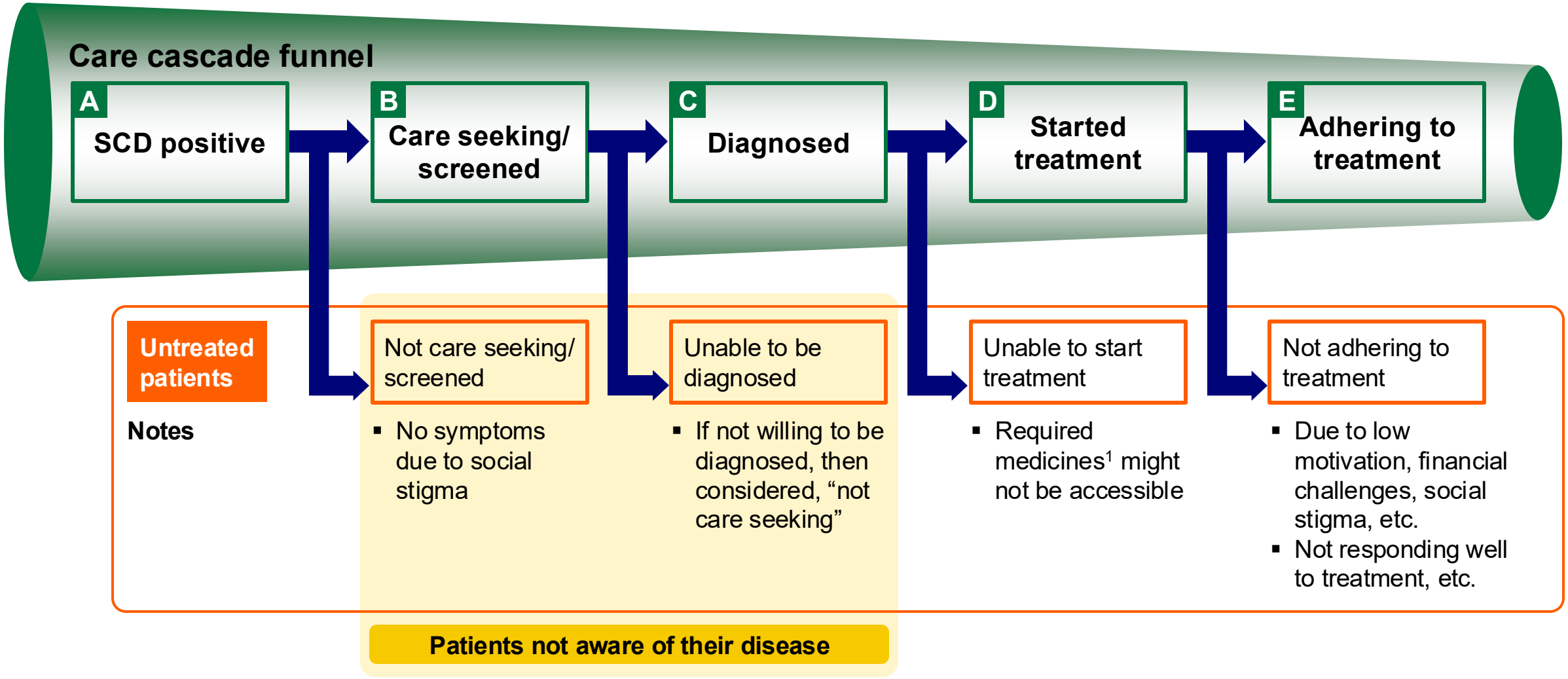
5 From our analysis, the following major challenges emerged (2/2)

Group	Sub-group	Description of major challenges
Execution-related	Governance	▪ Some **states may have limited capacity** to implement mission
	Program design	▪ Limited **access to quality care including medicines[1] close to patients;** limited support from community health workers leading to **adherence challenges** – *Lack of access to convenient quality care for managing the disease (interview with NGO)* ▪ **Lack of integration of local healers and pharmacists** into the system
	Program implementation	▪ **Stock-outs of key medicines** (hydroxyurea and vaccines) – *Vaccines and hydroxyurea are often not available (interview with patients' representative and NGO)* ▪ **Limited coverage of new-born screening** at health facilities
	Screening and diagnosis tools	▪ **Point of care diagnostics** have not scaled up yet; program may not be using the cheapest / best diagnostic solutions (e.g., Hemex Health's Gazelle, Mylab's PathoCatch, etc.) – *The solubility kits being used are of often of poor quality and result in a lot of false positives (interview with doctor)*
	Treatment tools	▪ **New drugs (Voxelotor and Crizanlizumab) are not available[2]** in India, but they **could benefit several patients** – *"Some patients do not respond to standard medication or do not tolerate side effects" (interview with doctor)* – *~10% patients can not use Hydroxyurea and would benefit from newer therapies (interview with doctor)* ▪ **Standard treatment might not be appropriate** for all patients – *"Due to the heterogenous nature of the disease, the severity and pattern of infections differ among patients. Therefore, a standard dose of any medicine does not work" (interview with doctor)* ▪ **Relevant vaccines** reach only a limited number of SCD patients (**catch up vaccines are not currently part of the program**) ▪ **Pediatric dosage** is not available – *500 mg dose of hydroxyurea is available in the market while a child requires 150 mg. Syrups are also yet not available for children (interview with NGO)*
Limited relevant evidence	-	▪ **Major gaps in evidence** to steer program: gaps in understanding burden, leakages in care cascade and impact of disease and treatment on Indian patients among others

1. As of January 2024, Hydroxyurea has been incorporated into the NHM Essential Drugs List and is being recommended for ensuring availability at PHCs and CHCs >>
2. With the exception of Novartis' Crizanlizumab in those Indian states: Andhra Pradesh, Madhya Pradesh, Chhattisgarh, Gujarat , West Bengal, Odisha, Karnataka, and Rajasthan

6 A detailed funnel was used to create the model for the care cascade

Structure for prevalence-based SCD care cascade



1. The majority of the patients will need Hydroxyurea, which is commonly available in India and its cost is meant to be covered by the government program. Nevertheless, in some cases, should the standard treatment not work, more advanced medicines could be needed, and they are not covered by the government program, and they might be inaccessible

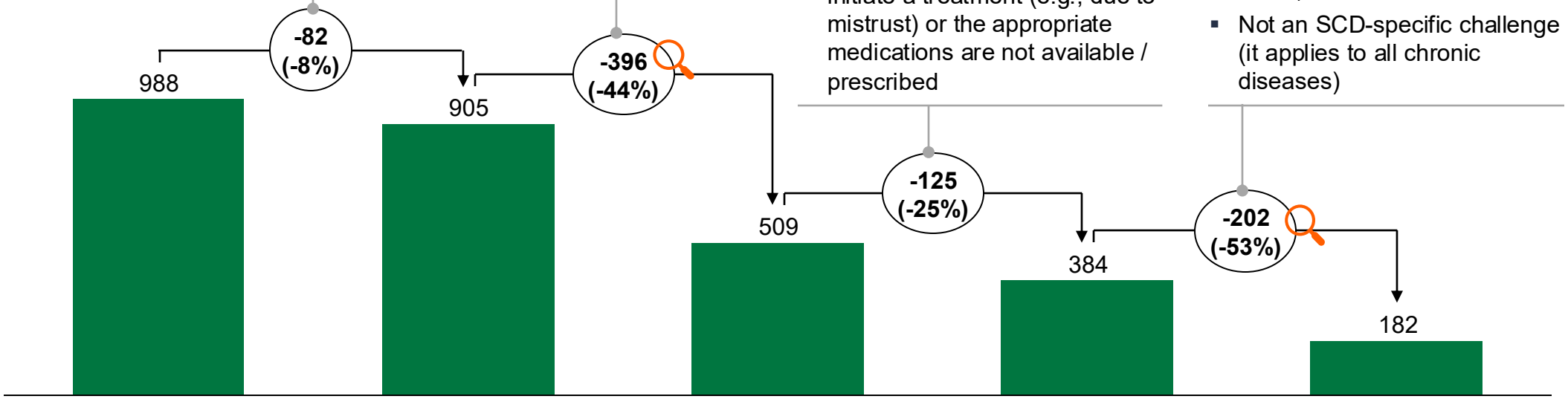
SOURCE: Team analysis

6 Our assumption-based model estimates the biggest drops to be at diagnosis and treatment adherence, with lack of awareness playing a significant role

Patients through the steps of the care cascade, '000 people

- SCD-positive patients with moderate/grave symptoms are likely to seek care
- SCD-positive patients with moderate/grave symptoms are likely to proceed with **diagnosis** (regardless of the screening result)
- Several doctors lack **awareness** of SCD or do not think about it
- Even when diagnosed positive, several patients decide not to initiate a treatment (e.g., due to mistrust) or the appropriate medications are not available / prescribed
- Low **treatment** adherence for all chronic diseases in India (especially for scheduled tribes)
- Not an SCD-specific challenge (it applies to all chronic diseases)

Large drops at this stage



% of SCD-positive patients	100%	92%	52%	39%	18%

1. "Treatment" includes SCD-specific medications. Symptomatic solutions (e.g., using pain killers) is not included

7 Based on our research, we identified several key recommendations for donors and key stakeholders to tackle the SCD challenges at systemic level

Group	Sub-group	Suggested recommendations (shortlisted)
Improve awareness / trust for institutions	**Community**	1 Run / Fund mass media campaigns for community to fight social stigma and build trust in the public system, learning from the TB and Polio programs
	Healthcare workers[1]	2 Run training campaigns focused on doctors and relevant healthcare workers in high prevalence areas, including when and how to provide vaccines, hydroxyurea and other treatments
Provide more resources	**Not enough treatment centres or treatment resources**	3 Support in building and scaling Centres of Excellence for advanced treatment and training lower-level facilities (e.g., using a phased approach, creating working role models to scale up, etc.)
Improve execution	**Program implementation**	4 Investigate opportunities to strengthen systems to improve coverage of new-born screening in public facilities 5 Provide holistic technical assistance to the government program (especially at state level) to manage human resources effectively, prevent stock-outs of key commodities (e.g., hydroxyurea), measure program progress and success (e.g., number of successful follow-ups, etc.) 6 Strengthen health system for tribal populations as a whole; investigate synergies with other programs *(not SCD-specific)*
	Treatment and disease management	7 Consider including catch-up vaccines and new therapies in the program
Build relevant evidence	**Evidence generation**	8 Conduct interventional studies to discover the definition of an optimal operating model for providing care close to the communities and scale up model 9 Understand how beliefs and myths vary by region and tribes to be able to design better SBCC (Social and Behaviour Change Communication) efforts

x Deep dive on dedicated pages

These recommendations are those which scored “High” / “High” in an impact vs feasibility analysis.
See additional details in section “Recommendations for the ecosystem ”
De-prioritized initiatives and additional details are available in the appendix

1. Including doctors, community health workers and local healers

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The authors of this report would like to give their sincere gratitude to the many people who contributed to the development of this report, through insightful conversations and document reviews. We would like to extend thanks to (in alphabetical order):

1. Dr. Vinita Srivastava, MoTA
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12. Ramya Rajagopalan, Senior VP, Strategic Partnerships, Piramal Foundation

The project team would also like to express their gratitude to those who contributed to the development of this report but preferred to remain anonymous. We appreciate your valuable contributions and respect your privacy

This work was made possible by the generous financial support of the Pfizer Medical Grants team

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- About Alstonia Impact
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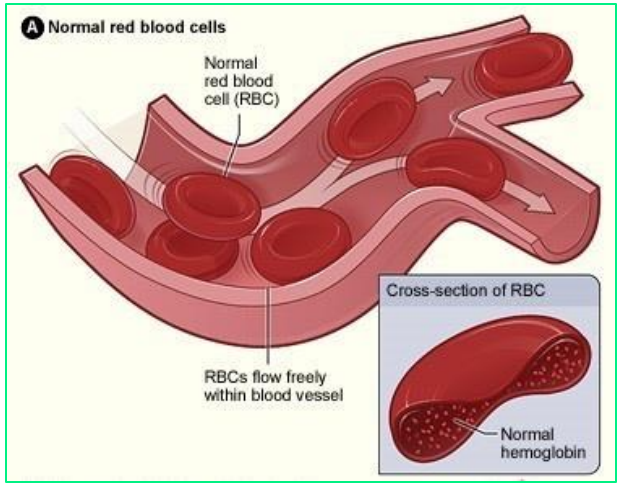
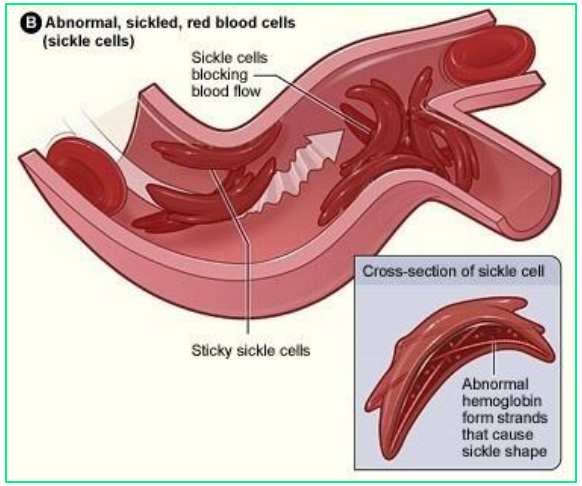
- **Detailed findings**
  - **Disease context**
  - Burden analysis
  - Current prevention and treatment approaches
  - Current health system response
  - Key challenges faced by patients and health system
  - Mapping of efforts from the non-profit and corporate foundation system
  - Recommendations for the ecosystem

Sickle Cell Disease is a hereditary condition which can lead to chronic anemia and immune system challenges

Description of the disease

- Sickle Cell Disease is a hereditary condition characterized by an abnormality in the genetic code, leading to the creation of atypical hemoglobin. This anomaly causes red blood cells (RBCs) to lose their typical shape and take on a crescent or sickle-like form
- In contrast to the 120-day lifespan of healthy RBCs, sickle cells endure for only 10 to 20 days. This reduced lifespan, along with their altered shape, leads to chronic anemia, immune system challenges, and persistent damage to the spleen. These complications manifest as a range of health issues, including Sickle Cell Anemia, recurrent infections, pain, swelling, and damage to vital organs





Types of the disease

- Replacement of normal hemoglobin (HbA) with faulty hemoglobin leads to either sickle cell trait or sickle cell disease. Presence of one affected beta globin sub-unit results in the trait, while both result in the disease.
- The various types of SCD are:
  - **Hemoglobin SS**: People inherit sickle cell genes (“S”), from both parents. This is commonly called sickle cell anemia and is usually the most severe form
  - **Hemoglobin SC:** People inherit one sickle cell gene (“S”) from one parent and another abnormal gene C, from the other parent. This is a mild to moderate form of SCD and is uncommon in India
  - **Hemoglobin beta thalassemia**: People inherit one sickle cell gene (“S”) from one parent and one gene for beta thalassemia, from the other parent. The subtype beta+ is a mild form of SCD while the subtype beta0 is more severe >>
  - **Others**: less common (especially in India) and milder form of the SCD are **Hemoglobin SD**, **Hemoglobin SE** and **Hemoglobin SO**, which occur when a person inherits one sickle cell gene (“S”) and one copy of another abnormal gene that affects the structure or function of hemoglobin >>
- People who inherit only one sickle cell genes (“S”) from one parent and a normal gene from the other parent are said to have **sickle cell trait**. They do not have SCD, but they can pass on the abnormal gene to their children

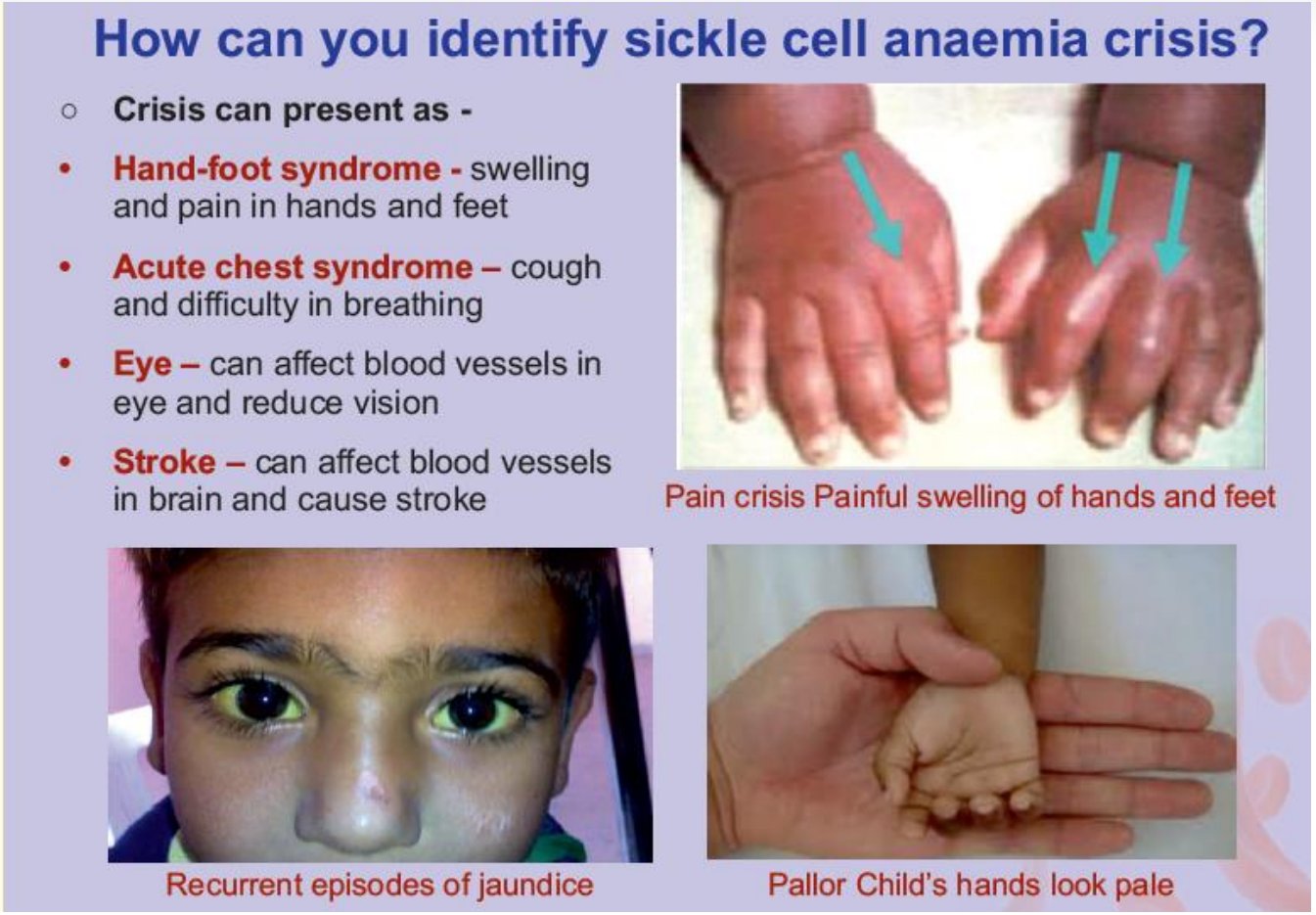
SOURCE: NHM India – Operational Guidelines, NHLBI

Sickle Cell Disease has a significant impact on life expectancy and quality of life of the patients

Impact of the disease

- According to a study, in the United States, patients with sickle cell disease have lower life expectancy (54 vs 76 years), and lower projected lifetime income (~1.3 M$ vs 1.9 M$), reflecting lost income (~695 k$) owing to reduced life expectancy >>
- Symptoms of SCD usually appear around 6 months of age and have a significant impact on the patient
- People with SCD are at risk of severe infections, such as the flu, meningitis and pneumonia, therefore taking early vaccination becomes important to prevent infection and complications in later stages of life >> >>

Symptoms of the disease

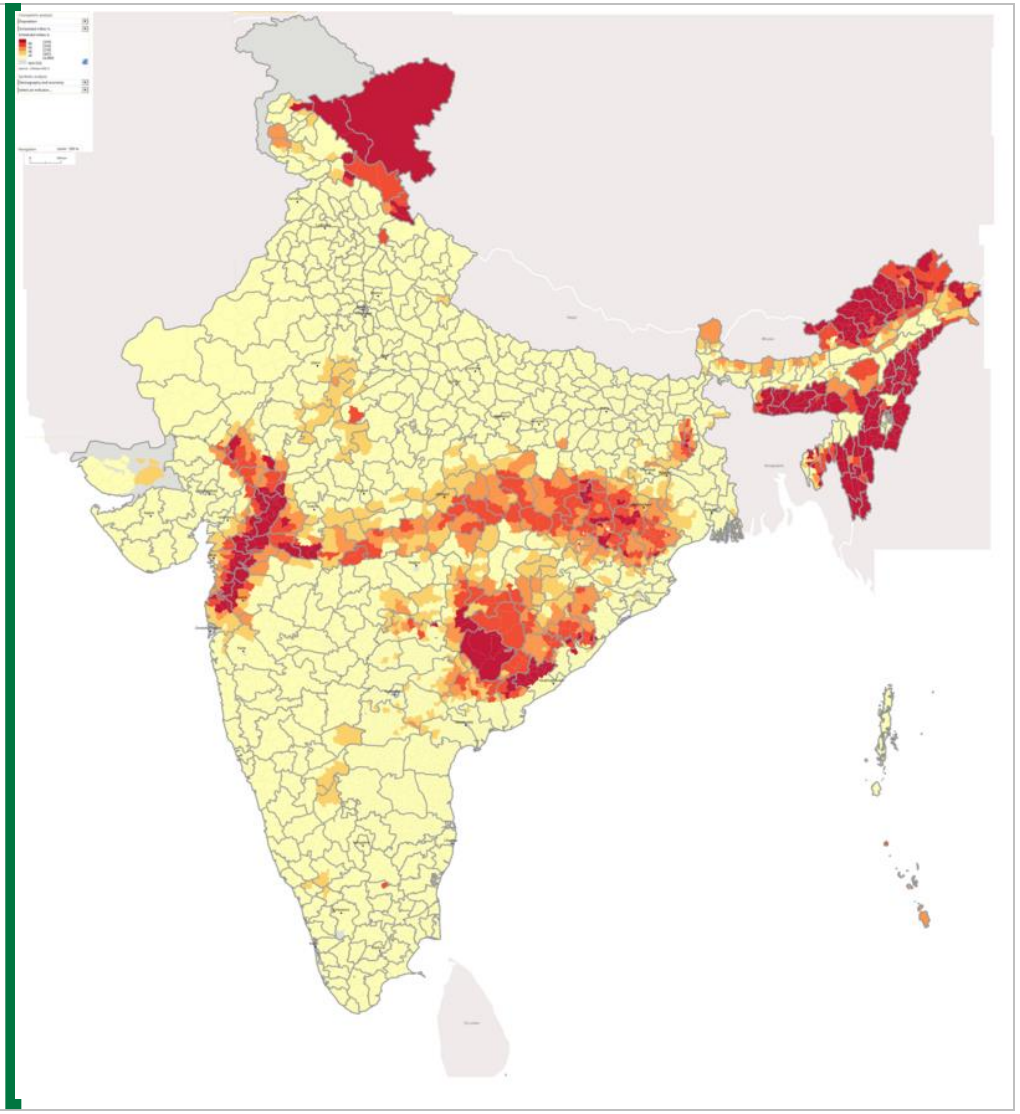


SOURCE: NHM India – Awareness Module

The risk of Sickle Cell Disease is higher in tribal populations

Considerations about risks of contracting SCD

- Tribal populations are at greater risk of SCD. Due to a historical prevalence of malaria, they developed sickle-shaped red blood cells as an evolutionary response. This adaptation increased their susceptibility to SCD. Over time, this protective mechanism became a hereditary condition >>
- Additionally, due to the practice of endogamy within tribal communities, there is an increased likelihood of both parents carrying the sickle cell trait and the disease persisting within the community >>
- According to the Global Burden of Disease Study 2021, disease patterns were comparable between females and males
  - Globally in 2021, the all-age prevalence of sickle cell disease among females was 3.90 million, similar to all-age prevalence among males at 3.84 million
  - This seems to stem from the fact that SCD is a genetic disorder and does not have any gender-specific occurrence, unless there is a peculiar sex ratio in the affected community
  - Few other sources also support the above finding of no difference in burden by gender >> >>



SOURCE: Map with density of tribal population in India as of 2011 >>, Team analysis

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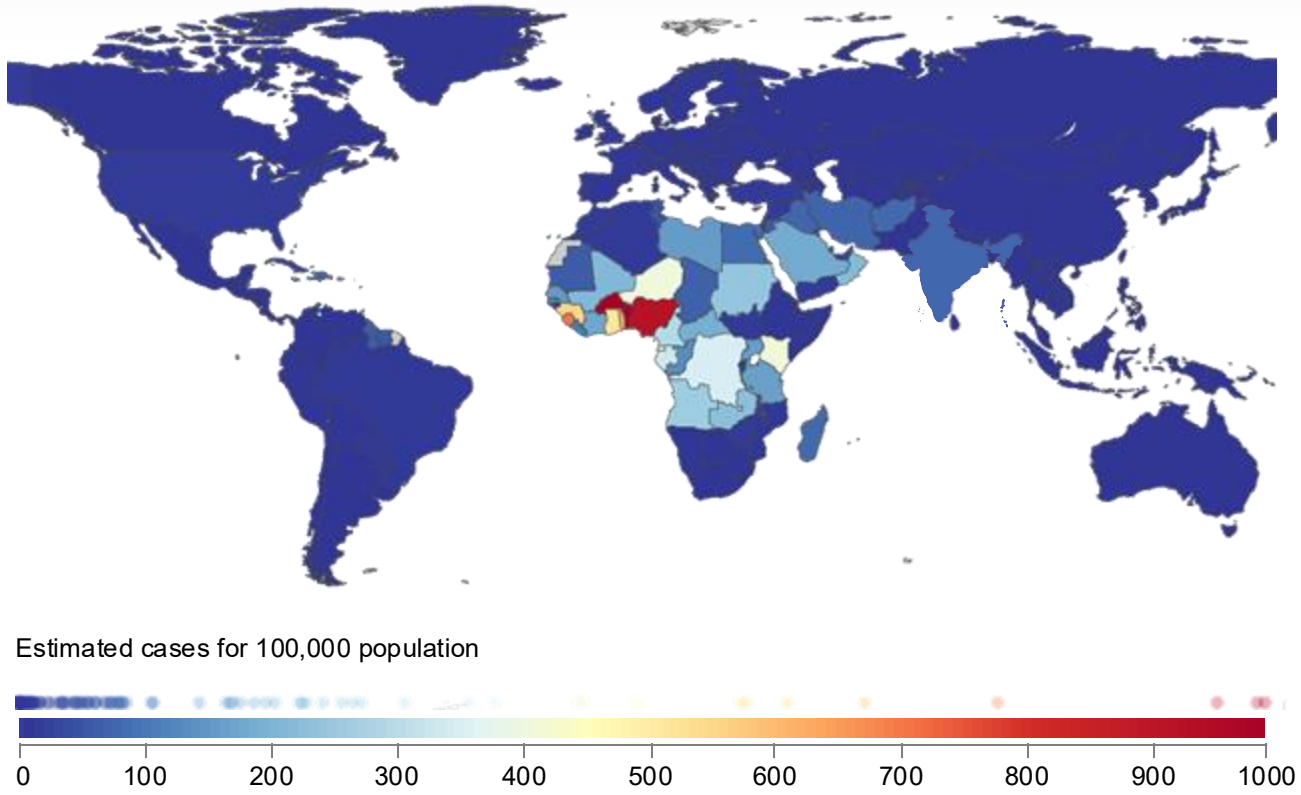
India has the one of the highest sickle cell disease burden around the globe

Sickle cell disease (SCD) prevalence around the globe, 2021

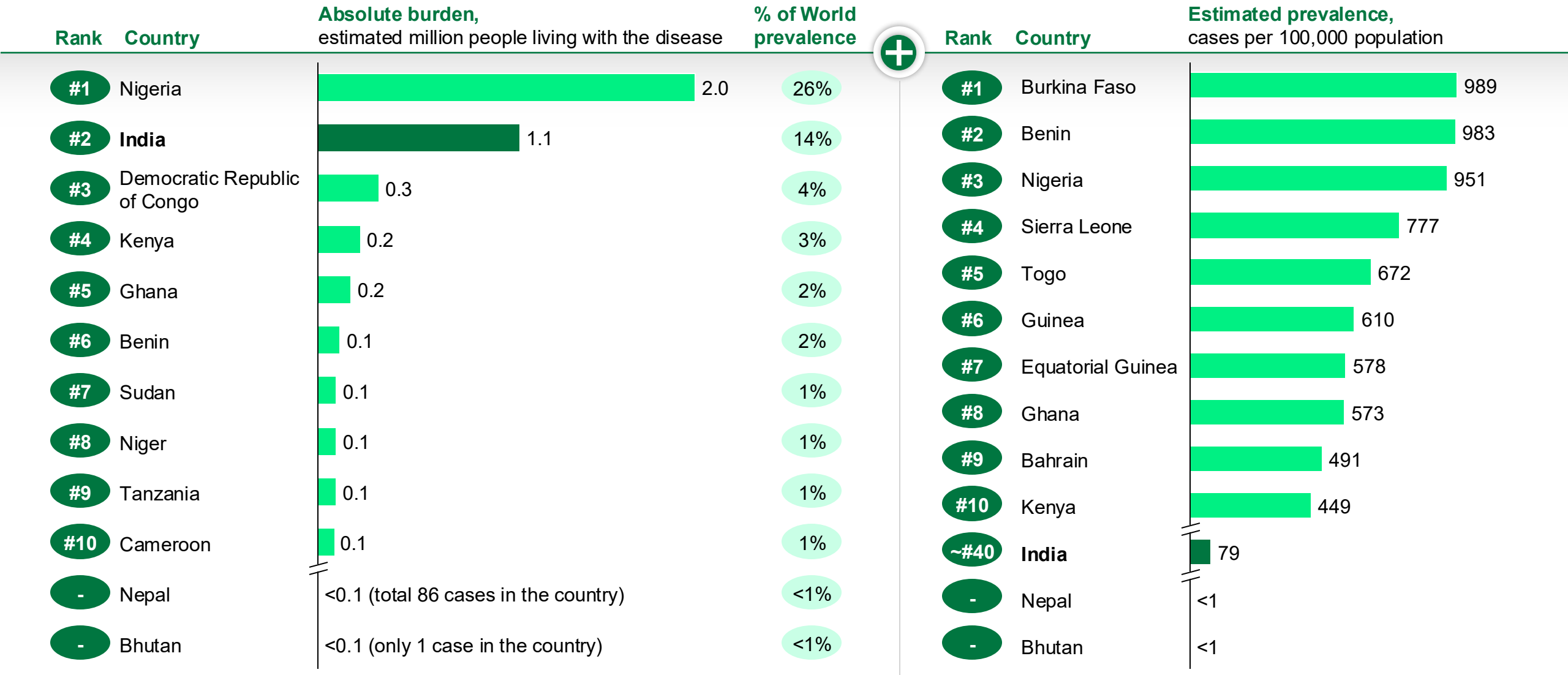


Findings from the GBD study

- WHO declared sickle cell disease (SCD) as a public health priority in 2006. Despite its life-threatening nature that affects millions of people worldwide, the disease has remained neglected in the global health agenda for decades >>
- According to Global Burden of Disease Study 2021, the burden of disease is concentrated in low-income and middle-income countries (LMICs), with the highest sickle cell disease disability burden concentrated in western and central sub-Saharan Africa and India
- As per the report, the number of people living with sickle cell disease globally in 2021 was 7.74 million, an increase of 41.4% from the figure of 5.46 million in 2000
  - The increase is driven by the population growth in the Caribbean and western and central sub-Saharan Africa
  - The national incidence rates of sickle cell disease have been relatively stable

SOURCE: Prevalence map and burden data sourced from The Lancet Hematology

India ranks 2nd in terms of absolute SCD burden, but it ranks only ~40th by prevalence rate



SOURCE: Data from Global Burden Disease

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Existing India-wide SCD burden studies have limitations; in the context of this study, new burden estimates were created

Used for all quantitative considerations within the report

Limitations of current data sources

- Limited availability of primary sources, concentrated in specific small areas
- Lack of data regarding the prevalence of SCD in the non-tribal population of India
- Limited data availability on the prevalence of SCD in northeastern states
- Comprehensive state-wise surveys have been done only in 4 states, leading to skewed India-wide estimates
- Variability in the accessibility and accuracy of diagnostic tools for SCD can impact the reliability of prevalence data

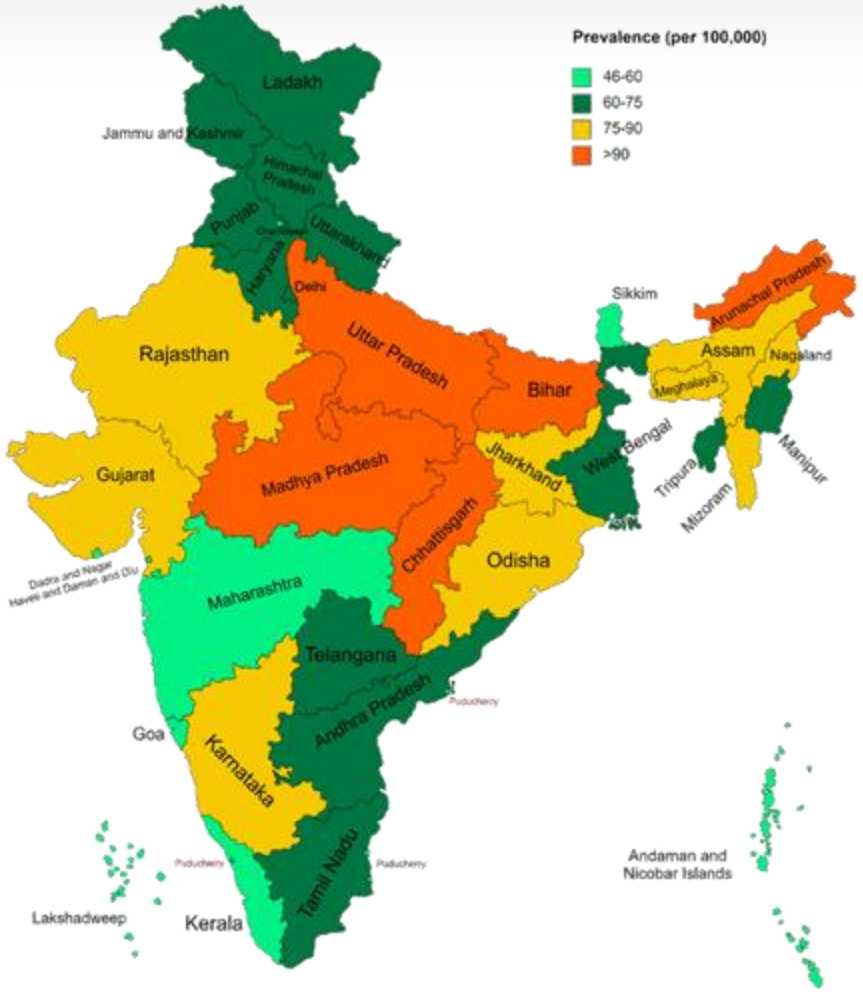
Relevant studies for SCD India prevalence

Studies	Limitations
A **Global Burden of Disease (GBD) Study**	▪ Aggregated results not consistent with specific studies (e.g., UP and Maharashtra, Northern States) ▪ Based on hospitalization data, not publicly available
B **ICMR Study**	▪ Consolidation of state-wide surveys where Gujarat and Maharashtra account for ~90% of the screening results
C **Gujarat NHM Estimates**	▪ Burden of SCD in Gujarat, a high burden state, being used to project India-wide prevalence ▪ Estimates from 2012 and 2021 vary widely
D **Own estimate**	▪ No additional primary data ▪ Non-tribal estimate based only on one data point ▪ Data extrapolation for multiple states

SOURCE: Team analysis

A Other credible sources were also evaluated to understand the prevalence of SCD in India – GBD (1/3)

Estimated SCD prevalence distribution in India (2019), Global Burden of Disease study



Methodology, limitations and key differences from the final output

- **Data sources and methodology**
  - High level approach across for all diseases
  - The major input for India is reported to be the "India Hospital Inpatient Data 2014-2017“ (not only for SCD, but for all the disease), which is used to estimate mortality rates, from which burden is extrapolated using a meta-regression approach

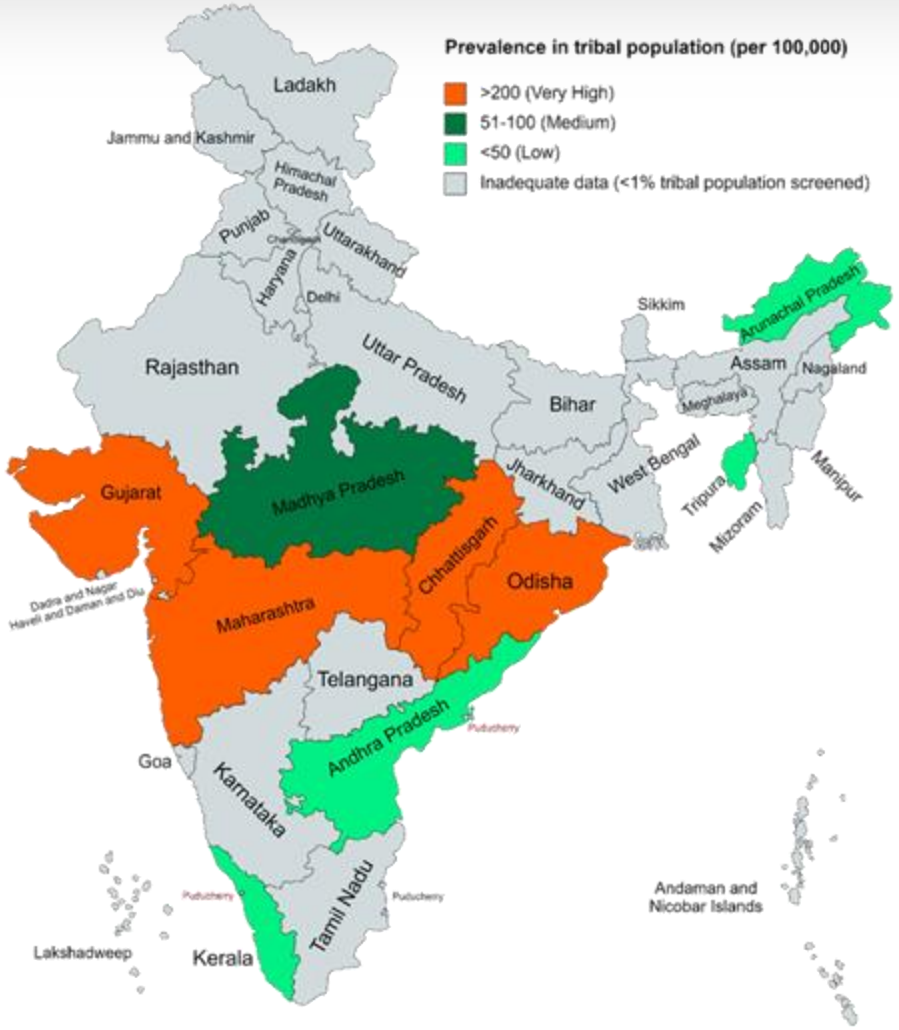
- **Limitations of the study**
  - Aggregated results for Uttar Pradesh, Maharashtra and Northern States are in contradiction with other studies, which are shown as evidence #1-#4 in the forthcoming slides
  - Prevalence is based on hospitalization data, but the data is not available or shared publicly, for further investigation

- **Key differences in terms of conclusion vs own estimate**
  - Maharashtra is one of the states with the highest burden based on our estimates as well as several qualitative studies >>, contrary to GBD findings
  - % tribal population is very low in the Northern states (Punjab, Haryana) which suggests that these states have very low SCD burden. This is reflected in our estimates but is contrary to GBD findings

SOURCE: Data in the map from Global Burden Disease

B Other credible sources were also evaluated to understand the prevalence of SCD in India – ICMR (2/3)

Estimated SCD prevalence in tribal population in India (2016-18), ICMR



Methodology, limitations and key differences from the final output

- **Data sources and methodology**
  - ICMR conducted a consolidation of state-wide surveys and not new screenings altogether. The surveys considered screenings done among the tribal population >>
- **Limitations of the study**
  - The data uses 76% of these screenings conducted in Gujarat and 12% in Maharashtra, so both these states account for ~90% of the screening results
  - The survey has been done only for the tribal population
- **Key differences in terms of conclusion vs own estimate**
  - Our estimates build off the surveys consolidated by ICMR and modifies the data where the numbers appear incorrect
  - Our estimates include non-tribal population as well and projects the disease burden among the tribal population where the data is not available
  - The survey does not provide total estimated figures for cases of SCD across states, while we have calculated such estimates for all the states

SOURCE: Data for the map from Ministry of Tribal Affairs

C Other credible sources were also evaluated to understand the prevalence of SCD in India – NHM Gujarat (3/3)

Estimated SCD prevalence distribution in India (2012, 2021), National Health Mission - Gujarat

Estimated Prevalence of Sickle Cell Anemia in Gujarat and India (Year 2011)

	Gujarat	India
Total Population	6,03,83,628	1,21,01,93,422
Tribal Districts	12	593
Tribal Population @ 14.76%	89,12,623	17,86,24,549
Estimated Person with Sickle Trait @ 10.0 %	8,91,262	1,78,62,455
Estimated Person with Sickle Cell Disease Patients @ 0.75 %	66,845	13,39,684

Estimated Total Population of India (2021)	Total Tribal Population of India @ 8.6%	Suspected Sickle Cell Trait -Carriers @ 7.46 %	Suspected Sickle Cell Disease Patients @ 0.30 %
139 Cr.	11.95 Cr.	**89.70 Lakhs**	**3.58 Lakhs**
Approx. New Births Every year in India @17.64 % decadal growth			
	New Tribal Births 21.08 Lakhs	**New Sickle Cell Trait Birth 1.57 Lakhs**	**New Sickle Cell Disease Births 6,324**

Estimated Prevalence of SCA in India considering Mass Sickle Cell Screening data of Gujarat

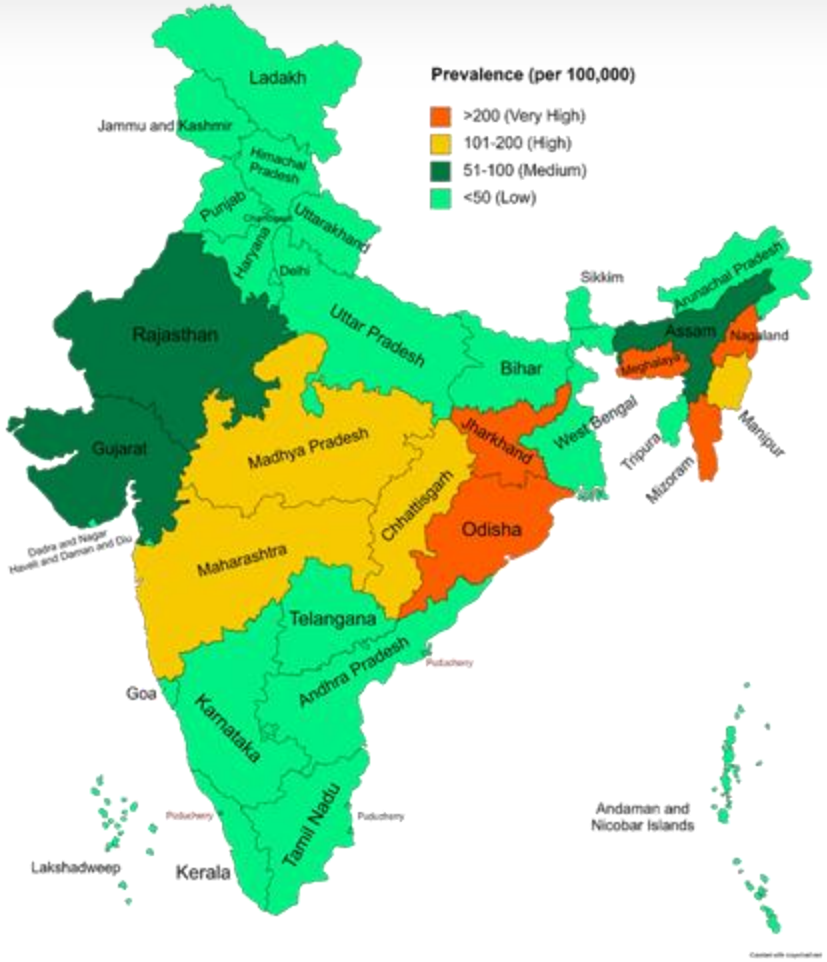
Methodology, limitations and key differences from the final output

- **Data sources and methodology**
  - The government of Gujarat has conducted state-wide mass sickle cell screening program for its 14 tribal districts since 2006 >>
- **Limitations of the study**
  - The data used is skewed with estimates from one state being used to generate country-wide estimates by taking a flat 0.75% disease prevalence in 2012 and 0.30% in 2021 for the entire country
  - There are two wide apart estimates for country wide SCD burden based on the mass sickle screening done among the tribal population in Gujarat in 2012 and in 2021 with the country-wide suspected sickle cell disease patients of 1.5 million in 2011 to 0.36 million in 2021
  - State-level estimates were provided using only very broad ranges
- **Key differences in terms of conclusion vs own estimate**
  - Our overall estimates of sickle cell disease burden among the tribal population (0.72 million) is in between the two estimates provided by the Gujarat screenings in 2012 (1.5 million) and 2021 (0.36 million)
  - Our estimates include non-tribal population as well

SOURCE: Images from National Health Mission, Gujarat (2012 and 2021)

D According to our analysis, the 3 Indian states with the highest SCD cases are Odisha, Maharashtra and Madhya Pradesh

Estimated prevalence, cases per 100,000



States	Estimated SCD cases, '000	Prevalence cases per 100,000
Odisha	240	541
Maharashtra	146	116
Madhya Pradesh	142	164
Jharkhand	100	253
Uttar Pradesh	49	21
Gujarat	49	68
Rajasthan	45	55
Chhattisgarh	36	119
West Bengal	35	36
Bihar	26	21
Assam	19	53
Tamil Nadu	16	21
Other states	85	26
Total India	628 240 35 85 988	71

1. Indicates the states that are not in the list of "17 high prevalence states" covered under National Sickle Program Guidelines, 2023 >>

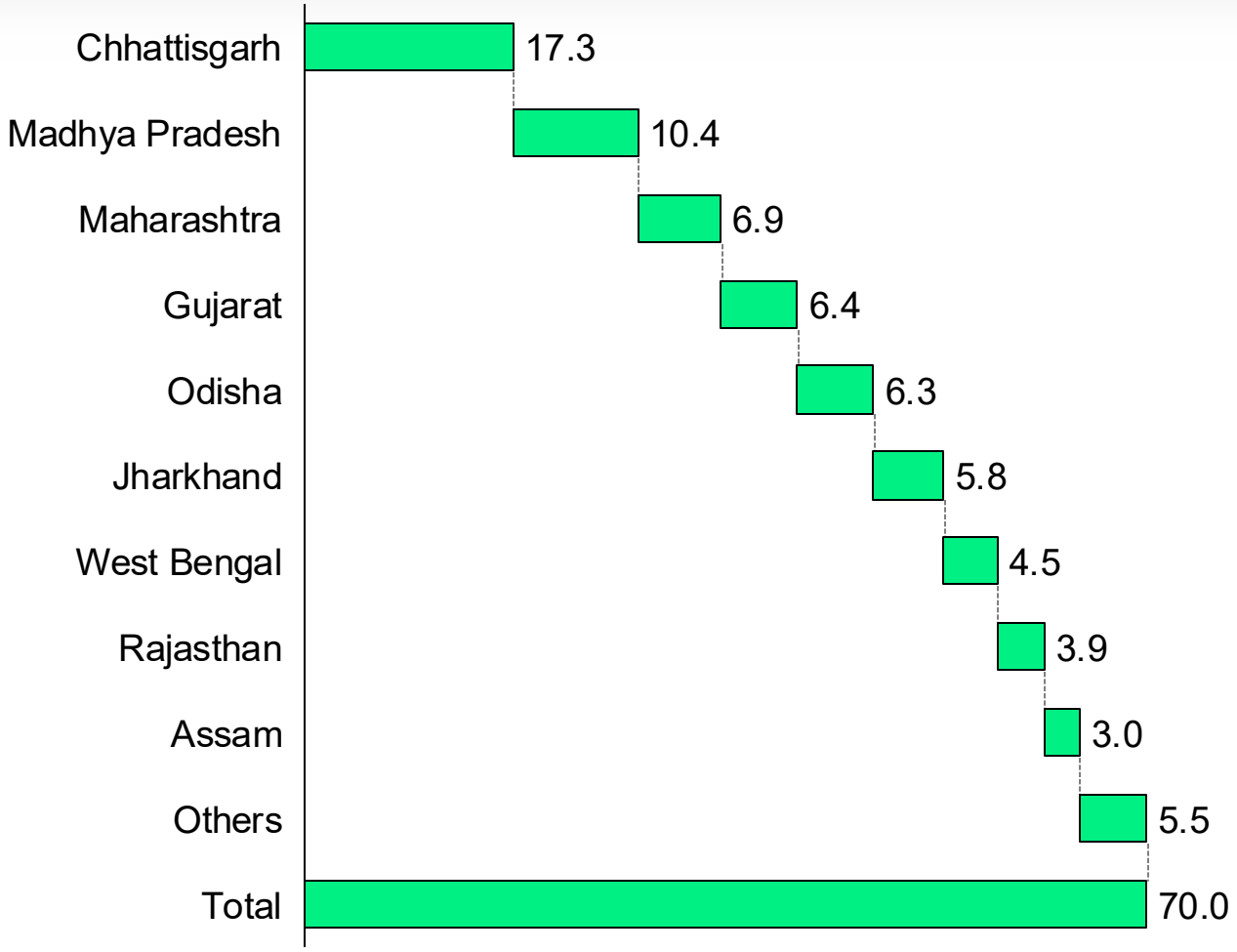
SOURCE: Team analysis

D Our analysis is consistent with government's state-wide allocation of 70 million screening target and ICMR survey

Analysis assumptions and government data

- According to the screening targets set by the National Sickle Mission for a three-year period, the states with the highest number of absolute tests targets are Chhattisgarh, Madhya Pradesh, Maharashtra, Gujarat, Odisha, and Jharkhand (figure on right)
- As per the screening survey conducted by ICMR-MoTA from 2016 to 2018, Odisha, Maharashtra, Jharkhand, and Madhya Pradesh are the states where the percentage of sickle cell patients among the total screened is the highest
- Both the above parameters align with our state-wide burden estimate, where the top 4 states in terms of absolute estimated burden are
  - Odisha, 240,000 cases
  - Maharashtra, 146,000 cases
  - Madhya Pradesh, 142,000 cases
  - Jharkhand, 100,000 cases

Government screening target for 3 Years, split by state, millions



SOURCE: Team analysis

To perform the burden analysis, the following methodology was used

Burden analysis methodology

- For **tribal population**
  - We gathered prevalence data from the 2016-2018 Ministry of Tribal Affairs and ICMR survey for states with sample sizes exceeding 20,000 >>
  - In the case of Madhya Pradesh, although the sample size exceeded 20,000, the percentage of individuals with the trait and disease did not match the estimates provided by the Madhya Pradesh government, therefore we relied on the numbers published by NHM Madhya Pradesh >>
  - We categorized all states from high to low prevalence rates by considering the following factors as proxies to predict the burden where data are not available: (1) percentage of tribal population, (2) historical malaria prevalence, and (3) qualitative research
  - We then assigned average prevalence values to the remaining states with no relevant data, based on their respective categories, extrapolating data from the states where data were available
- For **non-tribal population**, the finding that 27% cases belong to them was extrapolated, assuming the same prevalence for all people not belonging to tribes (~0.02%) >>

Key sources for prevalence rates

Sources	Corresponding states
Ministry of Tribal Affairs, ICMR and Department of Biotechnology	For tribal population: Chhattisgarh, Odisha, Telangana, Andhra Pradesh, Gujarat, Maharashtra, Kerala, Tripura, Arunachal Pradesh
National Health Mission	For tribal population: Madhya Pradesh
Calculations based on respective categories	For tribal population: Jharkhand, Uttar Pradesh, West Bengal, Rajasthan, Bihar, Tamil Nadu, Karnataka, Uttarakhand, Himachal Pradesh, Goa, Rest of NE States and Union Territories
Oxford Academic Research Paper, 2021	For non-tribal population: all states

SOURCE: Team analysis

D Other relevant analyses support our conclusions (1/2)

Evidence #1 – Sickle cell belt in India map from MP gov.

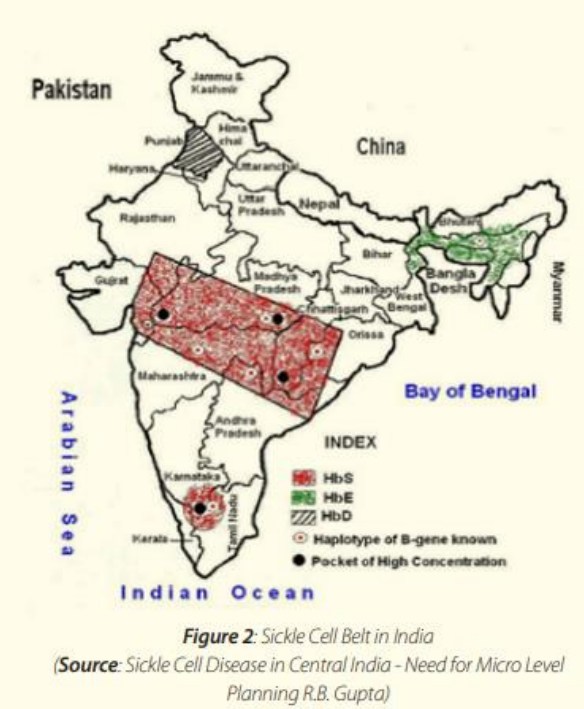
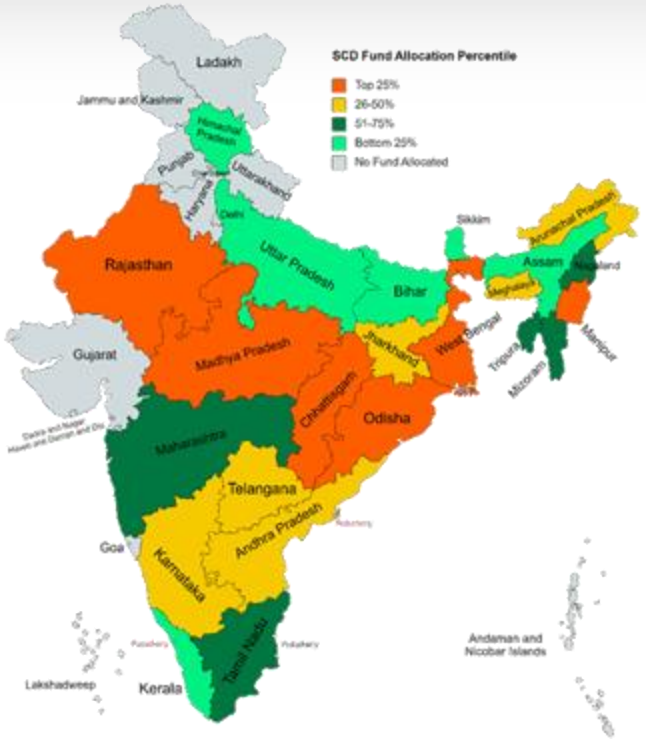


Figure 2: Sickle Cell Belt in India
(*Source*: Sickle Cell Disease in Central India - Need for Micro Level Planning R.B. Gupta)

- Presented in the operational guidelines for Sickle Cell, National Health Mission, Madhya Pradesh (2022) >>
- Depicts the central tribal of India covering the states of Gujarat, Madhya Pradesh, Chhattisgarh, Odisha and Maharashtra, and is consistent with our prevalence map

Evidence #2 – Central govt. allocation of funds to address SCD

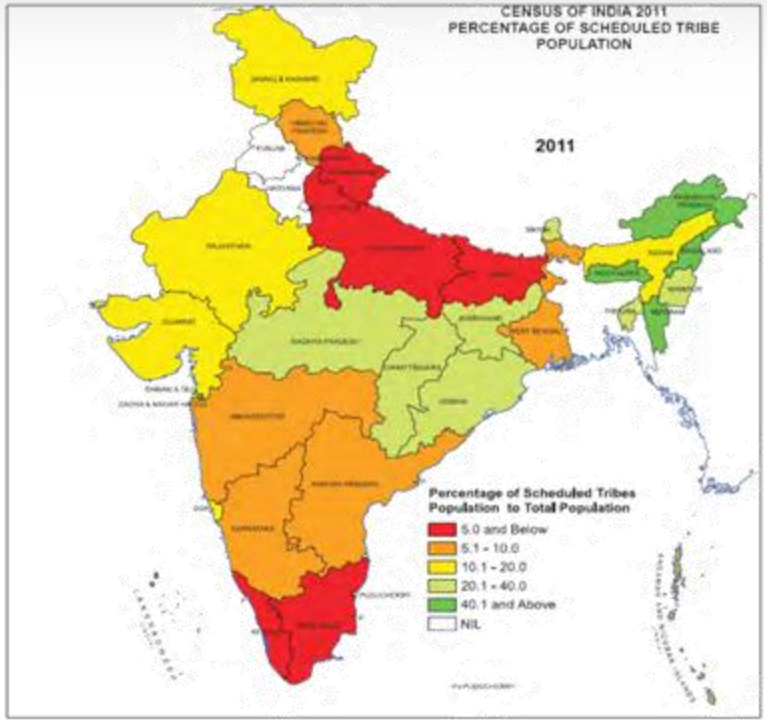


- % of funds released to states by Indian Government for tackling SCD between FY15 and FY20 >>
- Fund allocation is consistent with our analysis. 64% of the funds have been allocated to the states that we have categorized as “very high” and “high” risk

SOURCE: Team analysis

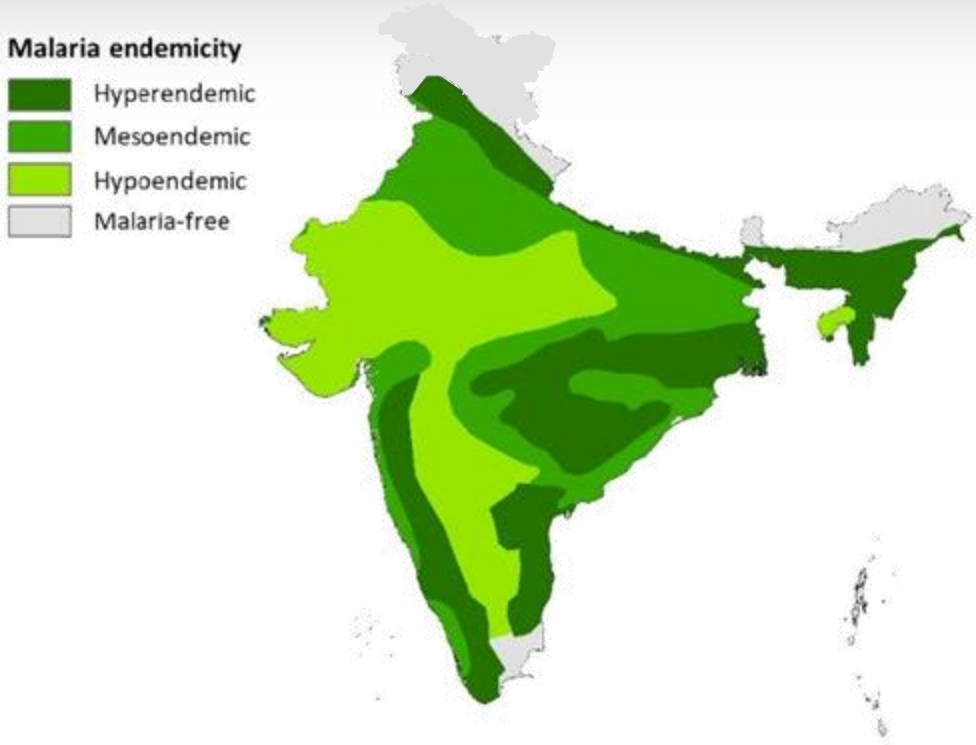
D Other relevant analyses support our conclusions (2/2)

Evidence #3 – Tribal population mapping



- Sourced form the "Statistical Profile of Scheduled Tribes in India 2013" document by Ministry of Tribal Affairs >>
- The states with "extreme" and "high" prevalence in our mapping consist of ~56% of the tribal population of India

Evidence #4 – Historical malaria map



- Sourced from "The spatial epidemiology of sickle-cell anemia in India", 2018 research paper >>
- The above represents the distribution of malaria when it was at its highest in India (approximately in 1900). Given the correlation between SCD and historical exposure to malaria, the map seems consistent with our mapping

SOURCE: Team analysis

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As of January 2024, the following treatment approaches are available in India against SCD (1/2)

Management and Treatment Approaches	Description	Availability in India
Hydroxyurea (HU) Therapy	▪ Tablet to be taken daily for life. Most commonly used drug for the clinical management of SCD and has been proven to decrease complications, such as pain crisis, acute chest syndrome and strokes ▪ For children, it helps to prevent organ damage, reduce transfusion requirement and improves overall survival ▪ As per the NSCAEM guidelines, 20% patients with SCD will not need Hydroxyurea while 20% of the patients will not respond well to it. Hence each patient needs to be evaluated for possible hydroxyurea therapy	**Availability** ▪ As per Indian Public Health Standards (IPHS), HU is available at Sub District Hospitals & District Hospitals. However, in states with high prevalence, HU can be made available up to the level of Primary Health Care **Cost** ▪ Costs are covered by the NSCAEM Program, with an average price of 1,000 INR/year/patient **Dosage** ▪ The starting dose of HU is 10-15 mg/kg/ day with other supportive care and followed for one year or more; maximum tolerance dose is 35 mg/kg/day ▪ Children below 2 years cases are to be referred to higher centers for pediatric consultation ▪ It is contraindicated during pregnancy and lactation **Follow-ups** ▪ A trained Medical Officer is advised to follow-up with patient with complete blood count every 2 weeks and for serum biochemistries every 2-4 weeks ▪ If the medicine does not show any signs of being toxic, dose is increased every 6-8 weeks **Approvals** ▪ The Central Drug Standard Control Organization (CDSCO) approved the marketing of HU tablets for treatment of SCD in December 2021 (FDA approved it in 1998 for adults and in 2017 for children from 2 years of age) ▪ Part of NSCAEM Program 2023
Blood Transfusions	▪ Blood transfusions reduce the risk of complications by decreasing the proportion of sickle red cells ▪ Required quite rarely for SCD patients; when needed, it is necessary every 2-4 weeks, depending on the patient ▪ Recommended in case of acute chest syndrome, strokes and transient ischemic attacks (TIAs) ▪ If children are receiving regular transfusions, serum ferritin monitoring and chelation therapy will be needed	▪ Transfusions can be performed in Community Health Centers (CHC) and District Hospitals (DH) ▪ Costs are not covered by the program, but states can ask for a budget allocation to cover the costs for the patients
Fever and pain management	**Fever management** ▪ Evaluation to include blood culture, complete blood count, reticulocyte count and chest X-ray ▪ Administration of antibiotics and penicillin ▪ Pain management ▪ Initial medicines usually prescribed include acetaminophen/paracetamol and non-steroidal anti-inflammatory drugs	**Availability** ▪ Fever and pain management medicines available at all healthcare facilities

SOURCE: Team analysis

As of early 2024, the following treatment approaches are available in India against SCD (2/2)

Management and Treatment Approaches	Description	Availability in India
Folic Acid Supplementation	▪ Folic acid helps to prevent deficiency resulting from increased cell turnover	**Dosage recommendations as per program guidelines** ▪ 5 mg daily for all SCD patients above 1 year of age ▪ 2.5 mg daily for al SCD patients below 1 year of age **Availability** ▪ Available at all healthcare facilities
Penicillin Treatment	▪ SCD patients develop functional hyposplenia, oral Penicillin is therefore recommended for children up to 5 years of age or lifelong for those who had splenectomy ▪ Mandatory routine penicillin prophylaxis has been seen to reduce the risk of mortality for SCD children	**Dosage recommendations as per program guidelines** ▪ Oral Penicillin V potassium 62.5 mg, twice per day for 1 year ▪ 125mg/day after 1 year until the age of 2 years ▪ 250mg/day till 5 years **Availability** ▪ Available at all healthcare facilities
Vaccinations	▪ SCD patients are at risk of severe infections, therefore early vaccination is advised to prevent infection and complications in later stages of life ▪ Mandatory routine Pneumococcal, meningococcal and HiB vaccination has been seen to reduce the risk of mortality for SCD children	**Schedule** ▪ For newborn children, vaccination advised as per schedule in the National Immunization schedule ▪ For adults vaccination, national guidelines are to be followed **Commonly recommended vaccines** ▪ Pneumococcal vaccine ▪ Meningococcal vaccine ▪ H-influenza vaccine ▪ Typhoid vaccine ▪ Influenza vaccine ▪ COVID-19 vaccine
Hematopoietic Stem Cell Transplant (Bone Marrow Transplant)	▪ Currently the only available curative therapy in India, but it comes with very high costs	**Availability** ▪ According to program guidelines, centers of excellence are expected to provide bone marrow transplant services for eligible individuals with SCD. Two centers are currently able to provide this service: Chhattisgarh Sickle Cell Institute in Raipur (Chhattisgarh) and RnT Medical College in Udaipur (Rajasthan) **Costs** ▪ As per NHM budget estimates, the total cost of an uncomplicated HSCT for a 12kg child may cost ~14 lakhs INR (~16,800 USD). Exact costs can vary depending upon the weight of child, disease class, etc. ▪ Serious complications after transplant can increase the cost to as much as ~25 lakhs INR (~30,000 USD) due to prolonged hospitalization, additional drugs, antibiotics and transfusion
Gene CRISPR Therapy	▪ Recently, in November 2023, UK regulators approved Casgevy, made by Vertex Pharmaceuticals (Europe) Ltd. and CRISPR Therapeutics, as the world's first gene therapy for SCD patients who are 12 years old and above. It is currently being reviewed by the U.S. Food and Drug Administration ▪ The medicine is based on the gene editing tool CRISPR-Cas9 from 2012, which won its makers a Nobel Prize in 2020 ▪ The manufacturers are yet to set a price for the new therapy but it is expected to exceed INR 1 Cr in India	▪ Not available beyond experimental settings ▪ Tata Institute for Genetics and Society (TIGS) in Bangalore is trying to reduce the cost of the procedure, which is estimated to be around 900k USD to 1.2 million. The procedure is not formally approved in India, yet

SOURCE: Team analysis

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The "National Sickle Cell Anaemia Elimination Mission" was launched in 2023 by the Government of India with the objective of eliminating SCD as a problem by 2047

The National Sickle Cell Anemia Elimination Mission

- Announced by Finance Minister Nirmala Sitharaman in the Union Budget 2023-2024 and officially launched by Prime Minister Narendra Modi in **July 2023**
- The program is led by Ministry of Health and Family Welfare (MoHFW), Government of India and implemented by National Health Mission (NHM) with the support of Ministry of Tribal Affairs in a mission mode
- The mission is being implemented in **278 districts of 17 states[1] in India**
- To date, the government has undertaken several initiatives under the mission:
  - Awareness modules have been launched to raise awareness about SCD among the population
  - Targets for screening have been established to increase the coverage of screening programs across the country
  - Software for data management has been developed to facilitate the monitoring of SCD screening program
  - Hydroxyurea availability has been increased, with the medication now included in the essential drug list, ensuring improved access for patients in need

Objectives of the mission

- Eliminate sickle cell disease as a public health problem in India before 2047
  - More in detail, the objective is to eliminate sickle cell genetic transmission by the year 2047 >>
- Quantify current burden and implement a robust monitoring system
- Increase **awareness** about the disease in the community
  - Primary prevention by focusing on awareness generation, pre-marital and pre-conceptional counselling
  - Secondary prevention by focusing on screening new-born and providing early diagnosis and care
- Implement **mass screening** activities for early identification
- Strengthen existing **primary health care** mechanism to incorporate SCD related strategies
- Provide **comprehensive care** and support to SCD patients

1. The 17 target states are Andhra Pradesh, Assam, Bihar, Chhattisgarh, Gujarat, Jharkhand, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Odisha, Rajasthan, Tamil Nadu, Telangana, Uttar Pradesh, Uttarakhand, West Bengal

SOURCE: NHM India – Operational Guidelines

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Policies and programs to manage SCD have been in place in the country since the early 2000s; higher national momentum only in the last 5-7 years

Geography	Program	Launch Year	Policies details
India	National Sickle Cell Anaemia Elimination Mission (NSCAEM)	2023	▪ Introduced in the Union Budget 2023 and launched in July 2023, the objective of the mission is provision of affordable and accessible care to all Sickle Cell Disease patients and eliminate sickle cell disease as a public health problem in India before 2047
India	Anaemia Mukt Bharat	2018	▪ Announced in 2018, the Anaemia Mukt Bharat initiative aimed to eradicate anemia in the country, which also included Sickle Cell Disease
Madhya Pradesh	Sickle Cell Anemia Control Mission	2021	▪ Madhya Pradesh launched its Sickle Cell Anemia Control Mission in 2021 to focus on screening in the eastern part of the state. The state govt. has established Integrated Centre for Hemophilia and Hemoglobinopathies in 22 Tribal Districts for treatment and diagnose of patient
Chhattisgarh	Sickle Cell Disease Control Program	2013	▪ Established a dedicated Sickle Cell Institute in 2013 at Raipur to provide treatment and counseling facilities to patients ▪ Developed large-scale data management systems to efficiently track sickle cell disease prevalence in the state and analyze the demographics of the condition ▪ Announcement of Sickle cell Institute of Health Department as a 'Centre of Excellence' in 2017 with facilities of Stem Cell Research, Blood transfusion and hemoglobinopathy
Odisha	Screening Program	2010	▪ Launch of mass screening for tribal and non-tribal population ▪ Provision of newborn screening program and free-to-access treatment facilities, including for bone marrow transplant
Maharashtra	Sickle Cell Disease Control Program	2008	▪ Sickle Cell Disease Control program is implemented in 34 high prevalence districts in phase wise manner by NHM since 2008 ▪ Activities under the project: – Creating Public awareness and screening general population -Target age group 1 to 30 years & pregnant mothers – Multiphasic screening - Identifying carrier & sufferer – Counselling - Carrier & sufferers of age group 12-20 years – Avoid marriage between colored card holders – Prophylactic & Symptomatic treatment - at Primary Health Centre, Rural Hospitals & District Hospitals – Training - Medical officers & other paramedical staff
Gujarat	Sickle Cell Anemia Control Program	2006	▪ Launch of Sickle Cell Anaemia Control Program in five districts of South Gujarat under a public-private partnership strategy by the Department of Health and Family Welfare
Kerala	Sickle cell Anaemia Project	NA	▪ Implemented by the Indian Systems of Medicine in the Wayanad district to reduce the severity of the disease, diagnose new cases and create awareness ▪ Kerala government also has a program to provide self-employment grant for SCD patients

Note: the list includes only SCD-specific policies. General policies which might indirectly have an impact on SCD patients as well are not included

The Ministry of Health and other concerned entities have issued multiple guidelines to reinforce the existing policies aimed at addressing Sickle Cell Disease

Geography	Material	Launch Year	Guidelines details
India	Guidelines for NSCAEM	2023	▪ Operational guidelines for National Sickle Cell Mission
India	ICMR Treatment Workflow	2023	▪ Guidelines on the prescribed medicines and procedures for the treatment of SCD
India	Awareness Campaign and Training of Trainers for the Elimination of Sickle Cell Anaemia	2023	▪ Training of grassroot level functionaries and engagement of community leaders to create awareness ▪ Translation of awareness documents into tribal languages
India	Provision for Hydroxyurea and Blood Transfusion	2023	▪ Support for Hydroxyurea and Blood Transfusion is given under National Health Mission for all Sickle cell patients as per State's proposal
India	Provision of services through Ayushman Bharat-Health and Wellness Centers (AB-HWC)	2023	▪ Regular follow-up of diseased individuals at frequent intervals ▪ Counseling regarding lifestyle management ▪ Nutritional supplementation support through distribution of folic acid tablets ▪ Conducting yoga and wellness sessions ▪ Management of crisis symptoms and referral to higher facilities
India	National Guidelines on Management and Control of SCD	2023	▪ Released by Indian College of Hematology (ICH) and Indian Council of Medical Research (ICMR), the guidelines present clinical protocols for management of SCD
India	Prevention and Control of Hemoglobinopathies in India	2018	▪ Guidelines released by Ministry of Health and Family Welfare for prevention and control of hemoglobinopathies including sickle cell anemia ▪ Aims to provide evidence-based treatment for patients and reduce the number of new-born children with sickle cell disease through initiatives such as the Sickle Cell Anaemia Control Program, screening and prenatal diagnosis

Note: the list includes only SCD-specific guidelines. General guidelines which might indirectly have an impact on SCD patients as well are not included

The National Sickle Cell Anemia Elimination Mission has key activities spanning all steps of the patients' care

Patient care steps	Key activities
1 Awareness and mobilization	▪ **Community engagement**: Actively engage with communities to raise awareness about SCD through culturally sensitive and accessible means ▪ **Healthcare worker education:** Provide comprehensive training for healthcare professionals to improve their understanding of SCD, diagnosis, management, and referral pathways ▪ **Public education campaigns:** Launch public education campaigns to disseminate accurate information about SCD and encourage early diagnosis and treatment ▪ **Multilingual resources**: Develop and disseminate educational materials on SCD in multiple languages to reach a wider audience and address linguistic barriers
2 Screening and diagnosis	▪ **Universal screening:** Implement universal newborn screening for SCD in 17 high and partial prevalence states of India to identify cases early and facilitate timely intervention ▪ **High-risk population targeted screening:** Establish screening protocols and guidelines for high-risk populations ▪ **Screening capacity building:** Strengthen screening capacity by ensuring adequate availability of screening facilities, trained personnel, and diagnostic equipment ▪ **Pre-natal screening:** Expand access to prenatal screening for SCD for pregnant women at risk ▪ **Point-of-care testing:** Promote the use of point-of-care testing for SCD in resource-limited settings to facilitate rapid diagnosis and early intervention ▪ **Data management and surveillance:** Implement robust data management and surveillance systems to track the prevalence, incidence, and outcomes of SCD in India
3 Treatment / management	▪ **Comprehensive care:** Provide comprehensive care for individuals with SCD, encompassing pain management, infection prophylaxis, psychosocial support, and educational interventions ▪ **Affordable treatment access:** Ensure access to effective and affordable treatments for SCD, including hydroxyurea, blood transfusions, and supportive care measures ▪ **Addressing complications:** Proactively manage and address SCD-related complications, such as pain crises, acute chest syndrome, and stroke. This involves preventive measures, prompt intervention, and ongoing monitoring ▪ **Clinical research:** Support and promote clinical research on new and improved treatments for SCD, including gene therapy ▪ **Genetic counseling:** Provide genetic counseling and family planning services for SCD patients and their families to inform reproductive decisions and risk management strategies

SOURCE: Team analysis

1 Deep dive on “Awareness and mobilization”

	Place	Key activities	Used tools and solutions
Community	**Home/village including Village/Urban Health Sanitation and Nutrition Days (VHSND)**	▪ Awareness for general population / eligible couples via home visits ▪ Identification and mobilization of eligible population for screening camps and facility-based screening	▪ -
	Bazaars	▪ Awareness mobilization of eligible population for screening camps and facility-based screening for general population through local events	▪ -
	Schools/ Anganwadis/ Ashramshalas/ Eklavya Model Residential School	▪ Awareness for school and college students incl . training programs for Eklavya Model Residential School teachers and school students ▪ Identification and mobilization of eligible population for screening camps and facility-based screening	▪ -
Healthcare Facilities	**Sub Health Centre (SHC)**	▪ Premarital and preconception counselling for eligible couples and pregnant women	▪ -
	Primary Health Centre (PHC) / Health and Wellness Centre (HWC)	▪ Premarital and preconception counselling for eligible couples and pregnant women	▪ -
	Community Health Centre (CHC)	▪ Premarital and preconception counselling for eligible couples and pregnant women (implied)	▪ -
	District Hospital (DH)	▪ Premarital and preconception counselling for eligible couples and pregnant women (implied)	▪ -
	Tertiary Centre / Centre of Excellence / AIIMS		▪ -

SOURCE: NSCAEM program guidelines, 2023

2 Deep dive on "Screening and diagnosis"

	Place	Key activities	Used tools and solutions
Community	**Home/village including Village/Urban Health Sanitation and Nutrition Days (VHSND)**	▪ Screening **in remote tribal hamlets** through outreach camps and mobile medical units (using PHC staff)	▪ -
	Bazaars	▪ -	▪ -
	Schools/ Anganwadis/ Ashramshalas/ Eklavya Model Residential School	▪ -	▪ -
Healthcare Facilities	**Sub Health Centre (SHC)**	▪ Screening of referred cases from the outreach camps ▪ Targeted screening on outpatient basis and on scheduled facility-based screening camps, subsequent referral of screened positive patients for confirmation to PHC/HWC	▪ Screening using solubility test
	Primary Health Centre (PHC) / Health and Wellness Centre (HWC)	▪ Opportunistic screening ▪ Confirmatory test for referred screened positive cases	▪ Screening using solubility test or confirmation using GoI approved electrophoresis based PoCT
	Community Health Centre (CHC)	▪ Screening of suspected individuals ▪ Confirmation of sickle cell diagnosis using HPLC/electrophoresis of individuals referred through PHC/SHC/Community screening	▪ Screening using solubility test or confirmation using GoI approved electrophoresis based PoCT
	District Hospital (DH)	▪ Screening of suspected cases ▪ Confirmation of sickle cell diagnosis using HPLC/electrophoresis of individuals referred through PHC/SHC/Community screening	▪ Screening using solubility test or confirmation using High-Performance Liquid Chromatography / Capillary zone Electrophoresis
	Tertiary Centre / Centre of Excellence / AIIMS	▪ **Prenatal screening** in select tertiary centers or Centers of Excellence	▪ Chorionic Villous Sampling (CVS) to be done to determine the disease status of the fetus

Opportunistic/targeted screening refers to screening of newborns, young children, adolescents, patient's spouse and extended family members of confirmed SCD patient
SOURCE: NSCAEM program guidelines, 2023

3 Deep dive on "Treatment / management"

	Place	Key activities	Used tools and solutions
Community	**Home/village including Village/Urban Health Sanitation and Nutrition Days (VHSND)**	▪ Motivate partner and extended family for screening ▪ Follow-up care for confirmed cases	▪ -
	Bazaars	▪ -	▪ -
	Schools/ Anganwadis/ Ashramshalas/ Eklavya Model Residential School	▪ Teachers to be educated to identify early symptoms of crisis in children	▪ -
Healthcare Facilities	**Sub Health Centre (SHC)**	▪ Counselling services: lifestyle modification ▪ Hydroxyurea follow-up and refill ▪ Teleconsultation services to higher centers	▪ Hydroxyurea, folic acid, NSAIDs, penicillin
	Primary Health Centre (PHC) / Health and Wellness Centre (HWC)	▪ Counselling services: lifestyle modification ▪ Preventive management and crisis episode management ▪ Follow-up and rehabilitation ▪ Referral to nearest secondary care facility (CHC / DH)	▪ Complete Blood Count (CBC) ▪ Hydroxyurea, folic acid, NSAIDs, penicillin
	Community Health Centre (CHC)	▪ Complication management ▪ Downward referral	▪ Complete Blood Count (CBC), transfusion services ▪ Hydroxyurea, folic acid, NSAIDs, penicillin
	District Hospital (DH)	▪ Complication management ▪ Downward referral ▪ Provide Hydroxyurea to PHC/HWC and CHC in states with high endemicity	▪ Complete Blood Count (CBC), transfusion services ▪ Hydroxyurea, folic acid, NSAIDs, penicillin
	Tertiary Centre / Centre of Excellence / AIIMS	▪ Complication management for confirmed SCD pregnant women	▪ Bone marrow transplant for eligible individuals with SCD

SOURCE: NSCAEM program guidelines, 2023

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Initiatives by government

Category	Organization	Type of work	Description
Government	Ministry of Health and Family Welfare (MoHFW)	Program implementation	• Introduced in the Union Budget 2023 and launched in July 2023, the National Sickle Cell Anaemia Elimination Mission (NSCAEM) focuses on addressing the significant health challenges posed by SCD, particularly among tribal populations of the country >> • Covers 17 high-burden states: Gujarat, Maharashtra, Rajasthan, Madhya Pradesh, Jharkhand, Chhattisgarh, West Bengal, Odisha, Tamil Nadu, Telangana, Andhra Pradesh, Karnataka, Assam, Uttar Pradesh, Kerala, Bihar, and Uttarakhand • Over a period of three years, spanning from the fiscal year 2023-24 to 2025-26, the program targets screening approximately 7.0 crore (70 million) people • Prior to the launch of the mission, the ministry's efforts were focused on raising awareness, data management, increasing screening and ensuring proper medical facility
	Ministry of Tribal Affairs	Program implementation	• Part of NSCAEM, the programme envisages training of grassroot level functionaries to create awareness among masses >> • Projects entails implementing a three-layer training programme at the State, District, and Village levels

	State Governments	Program implementation	• Health is a state subject – several governments have programs for Sickle Cell disease. E.g.
			  • Madhya Pradesh launched its Sickle Cell Anaemia Control Mission in 2021 to focus on screening in the eastern part of the state >>
			  • Kerala government has a program to provide self-employment grant for sickle cell patients >>

	The Council for Scientific and Industrial Research (CSIR) IGIB	Research and technology	• CSIR-IGIB is working on CRISPR CAS-9, a gene-editing therapy, to cure SCD >> • Indian government has been taking initiatives to develop this technology since 2017 and aims to make it affordable • The technology is claimed to have the potential to be a single dose cure for blood disorders such as SCD • As of March 2023, the research was in pre-clinical stage

SOURCE: Team analysis

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From our research, the following major challenges emerged (1/2)

Group	Sub-group	Description of major challenges
Lack of awareness / mistrust of institutions 	**Community and Patients**	▪ Affected populations have **limited awareness** about the disease and many hold incorrect beliefs, patients might be hesitant to seek support because of the **stigma associated with the disease** – *General population often lacks a proper understanding of the disease, leading to discrimination (interview with doctors, experts)* ▪ High **reliance on traditional healers in tribal areas across health areas** due to **low trust in public health system**
	Health care workers (including doctors, community health workers and local healers)	▪ **Doctors, nurses and other community health workers at primary health care centres** have **limited awareness and knowledge** of the disease, so less likely to diagnose it, refer and to provide proper treatment including monitoring and dosage – *Healthcare workers are unaware about SCD (patients' representative)* ▪ **Traditional healers and pharmacists** have low awareness and **often misdiagnose** condition
Lack of resources 	**Limited funding for research**	▪ Limited funding for research and development of tools (diagnostics, therapies)
	Not enough testing centres / diagnostic tools	▪ Challenges in conducting **pre-natal screenings due to limited diagnostic tools at facilities close to populations**; the screening techniques are invasive and carry a 0.5-2.0% risk of foetal loss (ICMR guidelines)
	Not enough treatment centres or treatment resources	▪ **Centres of Excellence for advanced treatment** not in place evenly

1. With the exception of Novartis' Crizanlizumab in those Indian states: Andhra Pradesh, Madhya Pradesh, Chhattisgarh, Gujarat , West Bengal, Odisha, Karnataka, and Rajasthan

From our research, the following major challenges emerged (2/2)

Group	Sub-group	Description of major challenges
Execution improvement opportunities	**Governance**	▪ Some **states may have limited capacity** to implement mission
	Program design	▪ Limited **access to quality care including medicines[1] close to patients for managing the disease** with limited support from community health workers leading to **adherence challenges** – *Lack of access to convenient quality care for managing the disease (interview with NGO)* ▪ **Lack of integration of local healers and pharmacists** into the system
	Program implementation	▪ **Stock-outs of key medicines** (hydroxyurea and vaccines) – *Vaccines and hydroxyurea are often not available (interview with patients' representative and NGO)* ▪ **Limited coverage of new-born screening** at health facilities
	Screening and diagnosis tools	▪ **Point of care diagnostics** have not scaled up yet; program may not be using the cheapest / best diagnostic solutions (e.g., Hemex Health's Gazelle, Mylab's PathoCatch, etc.) – *The solubility kits being used are of often of poor quality and result in a lot of false positives (interview with doctor)*
	Treatment tools	▪ **New drugs (Voxelotor and Crizanlizumab) are not available[2]** in India, but they **could benefit several patients** – *"Some patients do not respond to standard medication or do not tolerate side effects" (interview with doctor)* – *~10% patients can not use Hydroxyurea and would benefit from newer therapies (interview with doctor)* ▪ **Standard treatment might not be appropriate** for all patients – *"Due to the heterogenous nature of the disease, the severity and pattern of infections differ among patients. Therefore, a standard dose of any medicine does not work" (interview with doctor)* ▪ **Relevant vaccines** reach only a limited number of SCD patients (**catch up vaccines are not currently part of the program**) ▪ **Pediatric dosage** is not available – *500 mg dose of hydroxyurea is available in the market while a child requires 150 mg. Syrups are also not available for children (interview with NGO)*
Limited relevant evidence	-	▪ **Major gaps in evidence** to steer program: gaps in understanding burden, leakages in care cascade and impact of disease and treatment on Indian patients among others

1. As of January 2024, Hydroxyurea has been incorporated into the NHM Essential Drugs List and is being recommended for ensuring availability at PHCs and CHCs >>
2. With the exception of Novartis' Crizanlizumab in those Indian states: Andhra Pradesh, Madhya Pradesh, Chhattisgarh, Gujarat , West Bengal, Odisha, Karnataka, and Rajasthan

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From our research, it emerged that SCD patients face several challenges during their care journey

Impact on patients: Low Medium High

A Awareness

- Lack of awareness among all populations
  - **A.1** Tribal and rural
  - **A.2** Urban

B Screening and Care Seeking

- **B.1** Limited access to screening facilities in rural areas
- **B.2** Individuals hesitant to undergo screening tests due to associated stigma and misconceptions
- **B.3** High reliance on traditional healers who often provide symptomatic treatment, delaying professional medical intervention

C Diagnosis

- **C.1** Failure to access appropriate facilities and multiple referrals resulting in delayed diagnosis

D Treatment Initiation and Adherence

- **D.1** Limited access to quality care close to patients for managing the disease
- **D.2** Unaffordable permanent cure for Indian context
- **D.3** Limited patient education and significant attrition

Additional details about the specific challenges are shown on dedicated pages

SOURCE: Provided on deep dive pages, Team analysis

Deep dive on patients' challenges for "Awareness"

Extent of challenge: Low Medium High

Patients' Challenges	Description and Supporting Evidence
A.1 **Lack of awareness among tribal and rural population**	▪ According a multicentric intervention study conducted in 2021 across 24 primary health center areas of six high-prevalence SCD states, there is a gross inadequacy of knowledge about SCD in the tribal population >> – Only 32% of the 9,837 participants had heard of SCD, only 19% knew that a blood test can diagnose SCD and only 13% knew that SCD can be prevented – Individuals in Gujarat and Odisha reported a higher proportion of people with SCD-related knowledge compared to individuals in the state of Assam, Madhya Pradesh, Karnataka, and Andhra Pradesh ▪ Drivers of low awareness seems to be low literacy rates and poor socio-economic conditions of the tribal population >> – The literacy rate of Indian Scheduled Tribes (ST) is 63% as per the 2011 census, while the female tribal literacy rate is only 54% – As per SECC 2011 Census, the ST household earn monthly and average sum of only USD 61 >> – As per the 4th NFH Survey, only 73% of the tribal women received ante-natal care against 86% of uncategorized groups. Similarly, only 55% of the tribal children were fully immunized
A.2 **Lack of awareness among the urban population**	▪ Secretary, NASCO *"People in urban settings have a poor understanding of the disease and are unaware of the need for screening"* >>

SOURCE: in-line with text, Team analysis

Deep dive on patients' challenges for "Screening and Care Seeking"

Extent of challenge: Low Medium High

Patients' Challenges	Description and Supporting Evidence
B.1 **Limited access to screening facilities in rural areas**	▪ Insufficient screening infrastructure in remote and rural areas >> ▪ Due to unavailability of health centers close to them, many patients often try to manage the disease at home (KII) ▪ Logistical challenge to travel to cities for getting appropriate diagnosis, treatment and medicines (KII)
B.2 **Individuals hesitant to undergo screening tests due to associated stigma and misconceptions**	▪ Individuals diagnosed with sickle cell trait or disease are apprehensive about the stigma associated with being perceived as genetically inferior >> >> – *"Population screening is a futile exercise because those detected to have the sickle trait usually hide that for the marriage market, defeating the original purpose. What's worse is it stigmatizes STs and SCs to be genetically inferior,"* Tribal health expert in a letter to President of India in July 2023 after the launch of NSCAEM >> ▪ Individuals in the tribal population associate the cause of SCD to various misconceptions including infection, poverty or even myths such as "god's curse", "fate" or "black magic >> ▪ Patients who undergo screening are given sickle cell cards, creating a lasting label that marginalizes and stigmatizes the affected population. From the marriage perspective, the chief concern that emerged is diminished marriage prospects for girls having a "carrier" gene – *"In many of these States, cards of different colors are issued to the normal, trait carriers and diseased persons. Counselling is offered to the effect that persons who are gene carriers or have the disease should not marry those with the trait or the disease. These facts are also widely disseminated through information, education, and communication (IEC) materials. This is a human rights violation and a violation of confidentiality of the patients, and young girls are stigmatized,"* public health activist >> – *"The government's approach of issuing 'carrier cards' sends the message that two carriers should not enter a marriage. However, it is important to note that even if two carriers do marry, there is only a 25 percent chance of having an affected child. Denying the right to marriage based solely on carrier status creates a significant emotional burden for the entire community,"* Genetic Counsellor at JSS Medical College and Hospital>> – Senior Consultant, Pediatric Hematology and Oncology, Indraprastha Apollo Hospitals, *"Due to the social stigma, people are reluctant to undergo pre-marital screening and hence, we fail to identify sickle cell carriers"* ▪ Tribal community is apprehensive over the testing of their blood – Tribal Affairs Minister said, *"There is considerable suspicion in the target tribal population over why the government is testing their blood. In places I have visited, a common question from the target population is, 'why does the government want to test tribals' blood'?"* >> – *"Decades of mistrust in the public health system can be hard for the communities. People would ask us, 'Why are you taking our blood? Are you drinking it? Selling it?' They have even chased us away."* Genetic Counsellor at JSS Medical College and Hospital >>
B.3 **High reliance on traditional healers who often provide symptomatic treatment, delaying professional medical intervention**	▪ The acceptance of traditional healers is high in tribal communities and are readily available than any other type of healthcare ▪ In a research paper published in 2022, most traditional healers are unaware about the cause of SCD and give symptomatic treatment by providing herbal medicines and performing rituals >> ▪ Tribal population mistrust the public health system and government-run programs – NGOs implement projects that span one or two years, but their presence diminishes once funding is depleted, resulting in a lack of trust in such projects >> – *"The tendency to see tribal people as data points – or "guinea pigs" for scientific curiosity has left many of them wary of sickle cell programs conducted by researchers and the government",* Tribal Expert >>

SOURCE: in-line with text, Team analysis

Deep dive on patients' challenges for "Diagnosis"

Extent of challenge: Low Medium High

Patients' Challenges	Description and Supporting Evidence
C.1 **Failure to access appropriate facilities and multiple referrals resulting in delayed diagnosis**	▪ Patients in rural settings often live far away from hospitals and have no access to even basic health services in nearby regions – Secretary of NASCO: *"Patients in rural areas do not have access to proper healthcare infrastructure that leads to delayed diagnosis due to multiple referrals to numerous HCPs and institutions"* >> ▪ Most SCD patients do seek care for SCD-related health challenges but there are losses in the care cascade due to misdiagnosis (KII)

SOURCE: in-line with text, Team analysis

Deep dive on patients' challenges for "Treatment Initiation and Adherence"

Extent of challenge: Low Medium High

Patients' Challenges	Description and Supporting Evidence
D.1 **Limited access to quality care close to patients for managing the disease**	▪ Lack of basic health infrastructure in remote tribal and rural areas leads to improper or delayed treatment – Patients often face challenges when seeking primary care, as physicians may encounter difficulty in effectively managing a pain crisis or addressing the typical needs of someone with sickle cell disease >> – Treatment received often just hides symptoms and may worsen the condition for which the patients are eventually referred to district hospital – Private healers often give symptomatic treatment by providing herbal medicines and performing rituals >> ▪ To get the required treatment, patients thus must travel far distances and are often unable to due to the high cost of commute to hospital and poor road connectivity. Consequently, loss of wages becomes a concern >> >> >> – *"In Chhattisgarh, some patients come directly to the clinic, travelling distances of 200km or more—however, the loss of wages is their main concern"* Ex-Director Medical, Sickle Cell Institute Chhattisgarh, Raipur, Chhattisgarh >> ▪ Affordability and unavailability of medications affect proper treatment: Stock outs at public sector channels require patients to buy very expensive medicines in the private sector – Leader, health equity cluster at the Institute of Public Health, said, *"In 2022, the only small tablet we have [as a remedy], hydroxyurea, is still not securely supplied through the government channels. And molecular biology is far away from solving the problem."*,,, *"More people with sickle-cell anemia had died during the COVID-19 than in similar periods earlier, mostly due to poor access to public transport, high cost of private transport and drug shortage at community health centers""Even after being diagnosed, patients were not receiving a regular and free supply of hydroxyurea tablets to manage their pain, and many of them struggled to get a disability card, which would qualify them for pension, free blood transfusions and other benefits"* – A report by Adviser Health, MoTA, mentions about the gaps in availability of diagnostic and treatment at PHCs and CHCs in tribal areas • *"Without diagnosis and comprehensive care, children suffer crippling medical problem leading to lack of education, employment opportunities and integration into the society"* >> ▪ Because of the heterogenous nature of the disease, the severity and pattern of infections differ among patients. Therefore, a standard dose of any vaccine or medicine doesn't work for everyone – (KII)
D.2 **Unaffordable permanent cure for Indian context**	▪ Only permanent cure available in India is Bone marrow transplant, for which a closely matched donor is needed. Moreover, the treatment is expensive and can only be performed on some patients >> >> ▪ The new CRISPR-9 gene therapy is currently unavailable in India and if made available, it is expected to cost $2M per patient, in line with other gene therapies >>
D.3 **Limited patient education and significant attrition**	▪ Attrition – A clinician and patient representative, said *"although treatment is offered to sickle cell disease patients from remote villages, with clinics available to visit, they choose not to do so as they assume the disease is part of their life. They do not see the value of follow-up and miss appointments. Tracking them is a challenge."* >> ▪ Psychosocial support – SCD is a psychological challenge for young children, especially boys – (KII) – Even though Hydroxyurea is cheap, patients do not adhere to the daily dosage and only consume it when there's a pain crises (KII)

SOURCE: in-line with text, Team analysis

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The healthcare system faces various challenges in addressing the complexities of tackling Sickle Cell Disease

Team assessment on Extent of challenge: Low Medium High

1 Leadership and Governance

- 1.1 Lack of coordination in implementing SCD-focused policies and programs
- 1.2 Lack of attention to the disease prior to the launch of 2023 mission, currently slow implementation
- 1.3 Government not leveraging private and non-profit sector enough
- 1.4 Some states may have limited capacity to implement mission
- 1.5 Limited local evidence to steer program

2 Service Delivery

- 2.1 Limited resources on spreading awareness and busting myths
- 2.2 Lack of easy access to screening facilities
- 2.3 Lack of appropriate and accessible treatment at primary health care centers for diagnosis and treatment
- 2.4 Limited newborn screening (missed opportunities for identification)
- 2.5 Centers of Excellence not in place evenly

3 Health Information Systems

- 3.1 Inadequate systems for collecting and managing SCD-related data (prior to the launch of 2023 Mission)

4 Healthcare Workers

- 4.1 Lack of awareness among public healthcare workers leading to delayed or missed diagnoses
- 4.2 Misdiagnoses in the formal and informal (traditional healers) private sector

5 Medicines, Diagnostics and Equipment

- 5.1 Challenges in conducting pre-natal screenings due to limited diagnostic tools
- 5.2 Uncertain reliability of the solubility test's sensitivity and specificity
- 5.3 Losses of positive screened population who do not come to facilities for confirmatory testing
- 5.4 Catch up vaccines not in program
- 5.5 Newer drugs not in program (for patients not benefitting from hydroxyurea)
- 5.6 Stock-outs of hydroxyurea

6 Financing

- 6.1 Limited financial support for research and development in the field of SCD
- 6.2 Insufficient budget allocation for SCD-specific initiatives

Additional details about the specific challenges are shown on dedicated pages

SOURCE: Provided on deep dive pages, Team analysis

Deep dive on health system's challenges for "Leadership and Governance" (1/2)

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
1.1 **Lack of coordination in implementing SCD-focused policies and programs**	▪ "… *Government policy, which needs more streamlining… Funds for the SCD programs bounce around in various departments or return because of technicalities, and a lack of focus as multiple sickle cell groups operate simultaneously without adequate coordination",* Genetic Counsellor at JSS Medical College and Hospital >>
1.2 **Lack of attention to the disease prior to the launch of 2023 mission, currently slow implementation**	▪ *"Both sickle-cell anemia and thalassemia are outlier diseases for our public health system because they only impact certain groups of people in certain geographical areas. However, thalassemia has received comparatively more attention because it was also found in groups from affluent communities – such as Sindhis, Punjabis, Jains, etc., who were able to form their networks and advocate for an increase in the profile of the disease. Sickle-cell anemia, on the other hand, affects people born in tribal and Dalit families",* Health policy research scientist with Jan Swasthya Abhiyan, Karnataka >> ▪ Considered to be a disease that only affects tribal populations; non-tribal patients are often neglected – Very limited data on non-tribal population. ICMR-MoTA study 2016-2018 only focuses on tribal population – Doctors and medical researchers have pointed out that they have seen patients from non-tribal populations with extremely severe presentations of disease – a phenomenon that is relatively less known and accounted for in public health programs >>
1.3 **Government not leveraging private and non-profit sector enough**	▪ Limited activity by large NGOs and the private sector. Some exceptions include: – Unmukt program by Piramal Swasthya and Novartis >> The program is a three-year intervention on community-based screening of SCD through Mobile Medical Units in the backward districts of Jharkhand and Chhattisgarh – Gujarat government uses PPP model where NGOs carry out awareness and other programs in hard-to-reach areas

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Leadership and Governance" (2/2)

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
1.4 **Some states may have limited capacity to implement mission**	▪ Limited capacity to effectively implement the SCD mission is a notable challenge faced by some states in India. This constraint manifests in various forms, such as budget constraints impacting vital vaccination initiatives and frequent stockouts of essential medicines and vaccines. For instance: – One large state struggles with budget limitations, hindering critical catch-up vaccination efforts crucial for SCD prevention – Expert #12 – In another large state, frequent stockouts of essential medicines and vaccines significantly impede treatment accessibility, presenting formidable barriers to effective SCD management efforts (KII) ▪ Progress depends upon state government's intentions and will (KII) ▪ Some states have made good progress on SCD while some state are lacking behind (KII)
1.5 **Limited local evidence to steer program**	▪ The challenge of limited local evidence to steer the program arises from various knowledge gaps in understanding the burden, care cascade leakages, and the impact of disease and treatment on Indian patients. Evidence from interviews highlights several critical points: – Contrary to common belief, Sickle Cell Disease (SCD) is not exclusively prevalent among tribal populations; – it also affects Scheduled Castes (SCs) and some Other Backward Classes (OBCs), as indicated by experiences in Tamil Nadu and research findings (KII) – There is a misconception that SCD primarily affects tribal populations, whereas non-tribal populations also experience a significant burden of the disease - (KII) – Clinical understanding and severity assessment of SCD in Indian patients are lacking, with most studies based on non-Indian populations - (KII) – Experts emphasize the importance of conducting comparative studies to quantify the burden of SCD in terms of premature deaths, Disability-Adjusted Life Years (DALYs), and healthcare costs - (KII) – Additionally, there is a need for comprehensive studies to assess population beliefs about SCD on a state-by-state basis and develop strategies to dispel misconceptions - (KII) – The haplotype of SCD in India differs from that in other countries, necessitating unique treatment approaches tailored to Indian patients rather than replicating practices from Africa or the US - (KII)

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Service Delivery" (1/2)

Extent of challenge: Low Medium High

1 Leadership and Governance | 2 Service Delivery | 3 Health Information Systems | 4 Healthcare Workers | 5 Medicines, Diagnostics and Equipment | 6 Financing

Health System Challenges	Description and Supporting Evidence
2.1 **Limited efforts on spreading awareness and busting myths**	▪ There is a need to spread awareness among the affected population before screening them – *"The tribal communities often view sickle cell anemia screening as a source of shame and social ostracism. Evidence from Africa and American countries, which are almost 30 years ahead of India in addressing sickle cell anemia, has shown that if the government doesn't provide awareness to people and just start doing the screening, it could be more dangerous and may not even serve the purpose. Stigma is deeply rooted in information and lack of awareness"* Genetic Counsellor at JSS Medical College and Hospital >> ▪ Awareness about SCD is fairly high in endemic areas but not so much in non-endemic areas; awareness media material often poorly made (KII)
2.2 **Lack of easy access to screening facilities**	▪ Actual screening implementation is behind target, although it may be picking up pace – As per a report in the The Hindu, only 1% of the target to screen 10 million people for SCD was achieved in FY23 by the Health Ministry >> The target for FY24 is to screen 25 million people but as of Dec 2023, 7.6 million people were screened. Proportionately (assuming a linear trend), by Dec 13th, 2023, ~17.5 million people should have been screened >> ▪ Screening tests have logistical challenges – Blood samples collected at remote areas need to be shipped to labs in cities hundreds of of kilometers away >> ▪ Due to lack of testing facilities at the PHC and CHC level, the early detection of Sickle Cell in pregnant women is frequently missed >> ▪ The existing infrastructure for fetal screening is limited. States possess a limited number of Chorionic Villus Sampling (CVS) testing machines, primarily located in urban areas, distant from high-load districts (KII)
2.3 **Lack of appropriate and accessible treatment at primary health care centers for diagnosis and treatment**	▪ *"In tribal areas, even the primary health centers do not have enough doctors, nursing staff, pharmacy staff due to non recruitment, and no one wants to come and work in such interior areas. In such a scenario, the burden then entirely falls on the ASHA worker"* Genetic Counsellor at JSS Medical College and Hospital >>

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Service Delivery" (2/2)

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
2.4 **Limited newborn screening (missed opportunities for identification)**	▪ Newborn screening is not being conducted at scale in most states ▪ Key challenges include logistical issues such as same-day sample collection, availability of diagnostic tests, and follow-up procedures ▪ Resistance from parents against newborns being pricked during the screening process is also a significant barrier ▪ Additionally, high rates of home deliveries among tribal populations exacerbate the challenge of accessing newborns for screening
2.5 **Centers of Excellence not in place evenly**	▪ Operational guidelines specify Centers of Excellence (CoEs) for Sickle Cell Disease (SCD) but implementation remains lacking (KII)

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Health Information Systems"

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
3.1 **Inadequate systems for collecting and managing SCD-related data (prior to the launch of 2023 Mission)**	▪ "The State Governments, NGOs, Ministry of Tribal Affairs- Health have undertaken various screening programs in different pockets across country. However, there is no state level or central repository of such data", *mentioned in a report Adviser Health, MoTA* >> ▪ *"Urgent need of create mechanism so that after screening, the data of a SCD or carrier can go to a Central Data base and can be used for the databased planning and monitoring at district, state and national level" as noted in the MoTA report* >> ▪ A critical gap exists in terms of a systematic follow-up mechanism for patients (KII) ▪ Lack of follow-up provision in the government-provided software for patients (KII) ▪ **Efforts are now underway to build information systems**

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Healthcare Workers"

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
4.1 **Lack of awareness among public healthcare workers leading to delayed or missed diagnoses** (Medium)	▪ A paper published in 2022 reports the inadequacy of SCD-related knowledge and SCD management practices among the health workers working in tribal-dominated SCD-endemic districts in India >> – The study describes the knowledge and work experience of peripheral health workers as "poor" – *"No SCD-related activities are going on, and even primary care related to SCD management is not provided in the PHCs"* ▪ Patients are rarely advised about even simple strategies to manage the symptoms, such as avoiding dehydration, overexertion or high altitudes, all of which can trigger a pain crisis >> ▪ *"When they refer patients to a district hospital, due to lack of haematologist, and a general physician instead manages the case. There is need of training of paramedical and medical staff so that they can diagnose, treat, monitor and manage the complications of Sickle Cell Disease"*, *mentioned in a report by Adviser Health, MoTA* >> ▪ Lack of awareness about the disease among doctors in tier 1 cities (KII) ▪ Healthcare workers are unaware about SCD – Patients often given symptomatic treatment (KII) ▪ Medical practitioners lack awareness and training for managing SCD (KII) ▪ Clinicians are unable to interpret the result of the HPLC test resulting in false positives (KII) ▪ The non-distinctive nature of symptoms associated with SCD, including abdominal pain, anaemia, and strokes, often leads to misdiagnosis by healthcare professionals. Symptoms may be mistakenly attributed to conditions such as arthritis, or routine infections may be attributed to a perceived lack of hygiene >> ▪ *"Primary health centres typically don't do any interventions to sickle cell disease patients—they prescribe pain medication and refer patients to the next level of care if necessary"* Former Director In-Charge, ICMR-NIIH, Mumbai >>
4.2 **Misdiagnoses in the formal and informal (traditional healers) private sector** (High)	▪ Lack of awareness about the disease among doctors in tier 1 cities may lead to misdiagnosis in the private sector (KII) ▪ Traditional healers lack the necessary medical knowledge and tools to accurately diagnose SCD (KII)

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Medicines, Diagnostics and Equipment" (1/2)

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
5.1 **Challenges in conducting pre-natal screenings due to limited diagnostic tools**	▪ Advanced diagnostic facilities such as Chorionic Villus Sampling (CVS) are unavailable even in tertiary healthcare settings, as they involve substantial costs and necessitate specialized tests >>
5.2 **Uncertain reliability of the solubility test's sensitivity and specificity**	▪ There is uncertainty on the reliability of the solubility test among the healthcare professionals and experts – *Both in terms of sensitivity and specificity, the solubility test is not great, and it doesn't provide information about whether the patient is positive for sickle cell trait or disease," Associate professor at IISc* >> ▪ The confirmatory test, HPLC, is costly, necessitates an experienced medical professional, and is unavailable at the Community Health Center (CHC) level – *"The HPLC test is more expensive and requires a greater amount of blood (about 3-5 ml), which can scare off some patients, because it needs to be drawn from the vein by an experienced technician or nurse. And blood samples collected at remote locations in tribal areas need to be shipped to labs or district hospitals which can sometimes be hundreds of kilometers away. After we painstakingly collect the blood and take it to the district hospital, the person doing the HPLC will not be available, or will be on leave, or the machine will be broken down. Our effort of getting that 3 ml of blood from the patient would have gone to waste,"* Associate professor and nodal officer for a tribal sickle cell project, Bhopal >>
5.3 **Losses of positive screened population who do not come to facilities for confirmatory testing**	▪ Lack of awareness, stigma, or logistical barriers potentially contributing to the reluctance of positive screened individuals to seek confirmatory testing, leading to missed opportunities for early diagnosis and intervention

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Medicines, Diagnostics and Equipment" (2/2)

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
5.4 **Catch up vaccines not in program**	▪ Relevant vaccines for SCD patients (Pneumococcal, Hib, Meningococcal) are not procured at scale in most Indian states. Operational guidelines include them for children under 2 years old, but no catch-up vaccinations for adults are considered (currently they are only mentioned in technical guidelines, without budget allocation for most states)
5.5 **Newer drugs not in program (for patients not benefitting from hydroxyurea)**	▪ New treatments against SCD, complementing hydroxyurea, are not available at scale within the national program, yet. Several stakeholders mentioned that 10-20% patients can not use hydroxyurea
5.6 **Stock-outs of hydroxyurea**	▪ One large India state experiences frequent stockouts of medicines and vaccines, hampering treatment accessibility (KII)

SOURCE: in-line with text, Team analysis

Deep dive on health system's challenges for "Financing"

Extent of challenge: Low Medium High

Health System Challenges	Description and Supporting Evidence
6.1 **Limited financial support for research and development in the field of SCD**	▪ *"Innovation that IISc produces may have meaning in patients' lives, but without state support, it is tough. The number of people who might need a product like a low-cost screening test for SCD may be high, he says, but they are also less likely to be able to pay for it. In the interests of equity and justice, someone has to pay, and it has to be the state"*, said Leader at the health equity cluster at the Institute of Public Health >>
6.2 **Insufficient budget allocation for SCD-specific initiatives**	▪ Lack of funds for comprehensive sickle cell centers, Bone Marrow Transplant and comprehensive treatment (KII) ▪ Insufficient budgets for vaccine (only 2000 people budgeted for – those who get severe crises, ideally should be given to all known patients) (KII) ▪ Lower than needed budgets for PoC tests (funds for only 130k kits available) (KII)

SOURCE: in-line with text, Team analysis

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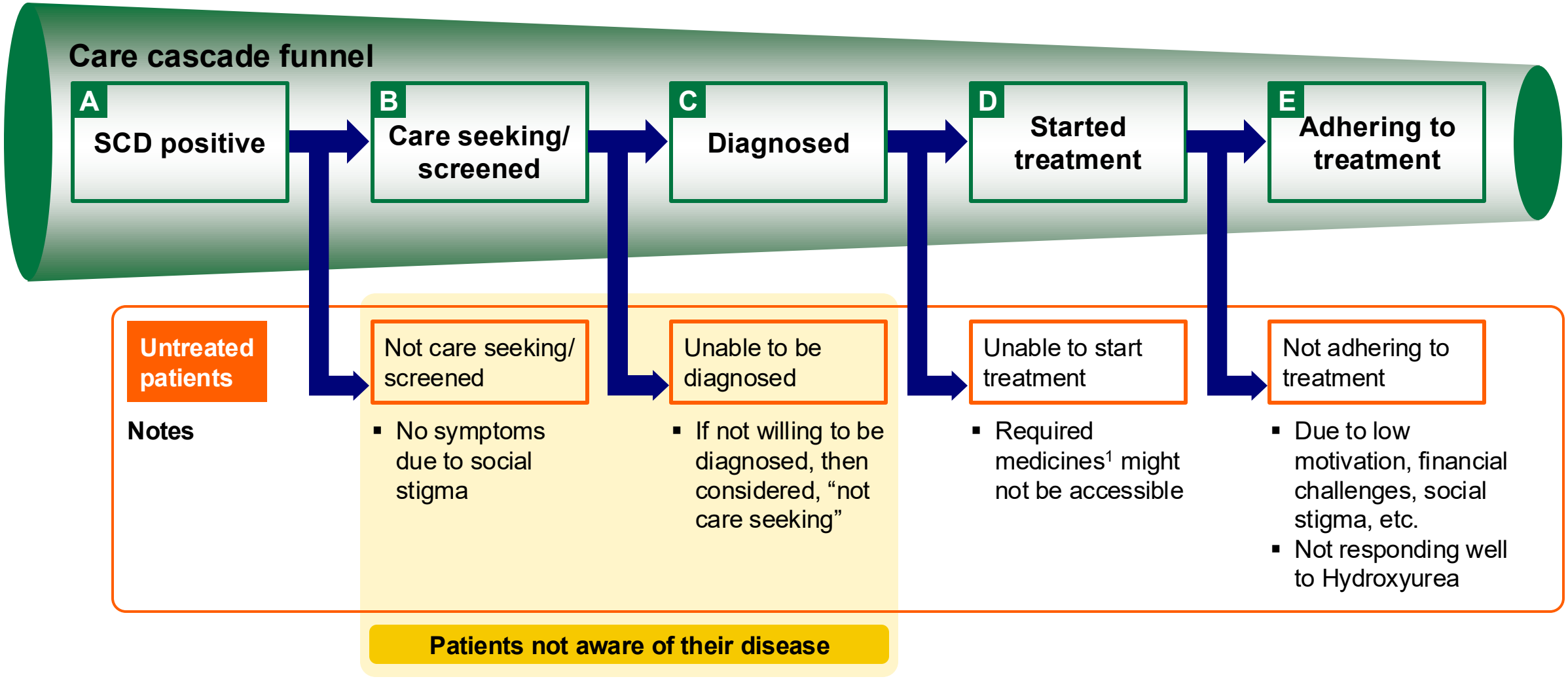
A detailed funnel was used to create the model for the care cascade

Structure for prevalence-based SCD care cascade

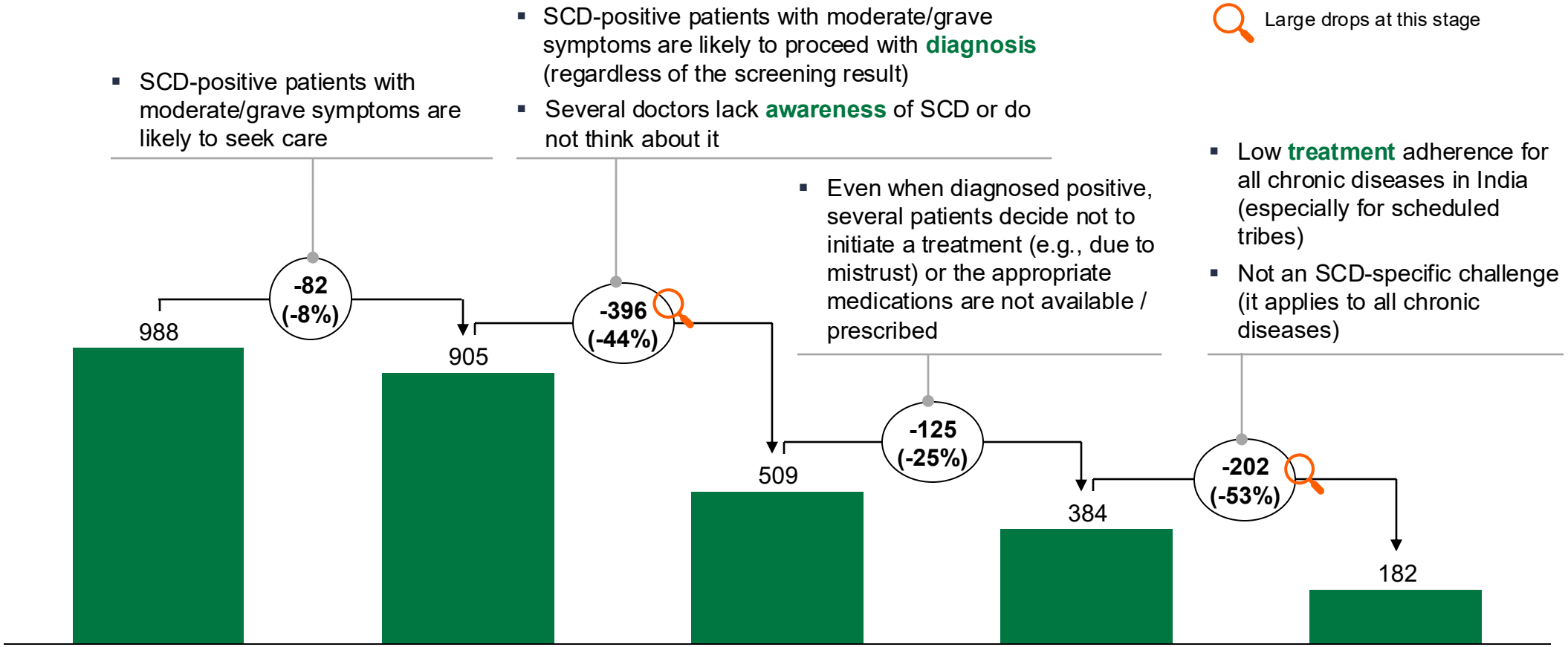


1. The majority of the patients will need Hydroxyurea, which is commonly available in India and its cost is meant to be covered by the government program. Nevertheless, in some cases, should the standard treatment not work, more advanced medicines could be needed, and they are not covered by the government program, and they might be inaccessible

SOURCE: Team analysis

Our assumption-based model estimates the biggest drops to be at diagnosis and treatment adherence, with lack of awareness playing a significant role

Patients through the steps of the care cascade, '000 people



% of SCD-positive patients	100%	92%	52%	39%	18%

1. "Treatment" includes SCD-specific medications. Symptomatic solutions (e.g., using pain killers) is not included

The calculations of the model are based on several inputs and assumptions, with different level of confidence (1/2)

Level of confidence
- **Higher**: based on research or multiple data points
- **Medium**: based on 1 data point
- **Low**: assumption only

Care cascade step	Parameter name	Value in the model	Level of confidence	Additional notes
[A] SCD positive	▪ Number of SCD positive patients	988 k patients	**Higher**	▪ Output of our updated model on the burden, based on several studies and data points (see dedicated section of more details)
[B] Care seeking / screened	▪ *Out of Gov. program:* % of SCD patients in India seeking active care	90%	**Low**	▪ Assumption based on the share of patients in India who are unlikely to have moderate/grave symptoms of 5% (source: interviews) ▪ Patients younger than 2 years old are unlikely to have moderate / grave symptoms (assuming life expectancy of 40 years, that is 2/40 = 5%)
[C] Diagnosed	▪ *Gov. program:* % of SCD patients identified positive in government screening camps and diagnosed correctly	70%	**Low**	▪ The same assumption of above is taken: regardless of the screening test result, patients are likely to get diagnosed only if they have moderate/grave symptoms, which justifies the effort
	▪ *Gov. program:* % among those going for confirmatory diagnosis who receive are positively diagnosed	94%	**Higher**	▪ A large Indian study showed solubility tests (in the previous screening step) to have a 93.8% sensitivity and a 100% specificity (source: ICMR report) ▪ Some patients might be tested only because the screening returned positive, but the solubility test used for screening is successful about 94% of the time
	▪ *Gov. program*: number of patients identified as positive to date	139 k patients	**Higher**	▪ Total number of patients identified as positive in the government screening initiatives to date (as of January 2024)
	▪ *Out of Gov. program:* % of SCD patients seeking active care and correctly diagnosed	50%	**Low**	▪ Qualitative evidence suggests several doctors are not aware of SCD at all ▪ For reference, in a small study it emerged that only 19 of 71 RHWs (27%) and 11 of 48 CHWs (24%) dealt with SCD cases in the past. The higher 50% value used in the model is justified by the fact that patients are likely to visit more than one doctor if not diagnosed properly

SOURCE: in-line with text, Team analysis

The calculations of the model are based on several inputs and assumptions, with different level of confidence (2/2)

Level of confidence:
- **Higher**: based on research or multiple data points
- **Medium**: based on 1 data point
- **Low**: assumption only

Care cascade step	Parameter name	Value in the model	Level of confidence	Additional notes
[D] Started treatment	▪ *Gov. program:* % of SCD patients identified positive in government screening camps and diagnosed correctly initiated on disease management	90%	**Medium**	▪ Based on the extrapolation of one small data point: of the 182 diagnosed SCD patients, 18 patients (9.8%) did not engage in care after initial diagnosis and were excluded from analysis (source: SEWA Rural Study) ▪ A small percentage of patients might reject the diagnosis (e.g., due to mistrust) or might not be able to access the right treatment
	▪ *Out of Gov. program:* % of SCD patients with who sought active care and diagnosed correctly who started on treatment post diagnosis	70%	**Low**	▪ Large drop-off between diagnostics and treatment (source: KII with Dr. Dipty Jain) ▪ In some cases, patients might reject the diagnosis (e.g., due to mistrust), or some private providers may not have the right treatment available or may prescribe the wrong medications
[E] Adhering to treatment	▪ % of patients who were diagnosed correctly, initiated treatment and adhere to that	48%	**Medium**	▪ From an extensive study on chronic diseases in India (not including SCD, but other diseases like Diabetes, Asthma, Hypertension, etc. link), it emerged the average treatment adherence to be about 51%, but lower at 46% for scheduled tribes, which account for 73% of the total estimated patient population. The weighted average of the figures gives an estimated 48% adherence rate ▪ Due to unavailability of any health center nearby, patients often try to manage the disease at home (source: KII with founder of ADEETECH) ▪ Most of the CHCs and district hospitals are operating as maternal and childcare centers and do not provide acute care for SCD patients (source: KII with founding member of Jan Swasthya Sahyog)

SOURCE: in-line with text, Team analysis

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Based on our findings, the following approaches to tackle SCD were identified

Approach type	Approaches
Program implementation	▪ The Indian government is working in mission mode to address the health challenges posed by SCD. The program builds upon the various state missions and central-level guidelines to tackle the issue in a collaborative manner across the whole country ▪ Various NGOs are working across the country to tackle SCD as per their capacity – JSS organizes patient supports group which has resulted in higher adherence among the affected patients. They have also developed a low-cost HPLC device to diagnose patients – SCAO and ASHWINI are providing free OPD services to patients – including pneumococcal vaccine and hydroxyurea
Advocacy	▪ NASCO has brought together 20+ advocacy groups that were spread across the country. The organization now organizes various state level meetings and workshops to raise awareness in the public and advocate for better quality life of SCD patients ▪ Other non-profits also conduct advocacy to support their implementation activities
Research and technology	▪ The Indian government has taken initiatives to develop CRISPR CAS-9, a gene-editing therapy, since 2017 and aims to make it affordable – CSIR-IGIB is making efforts to use the technology to cure SCD – While treatment for SCD using gene therapy have been approved by regulatory bodies in UK and USA, in India the research is still in the pre-clinical stage ▪ Various private sector organizations have developed low-cost, portable and high-quality point of care diagnostic tests that have the potential to be adopted as a screening tool for SCD in areas where health resources are limited

SOURCE: Team research

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Selected initiatives by philanthropists and non-profits (1/2)

Category	Organization	Type of work	Description
NGO	Piramal Foundation (with Novartis Funding)	Program implementation	• Piramal Swasthya Research and Management Institute is running a three-year intervention from June 2021 on community-based screening of SCD, called the Unmukt Programme, through Mobile Medical Units in the backward districts of Jharkhand and Chhattisgarh. • The screened positive population are referred to the health facility and provided health education and counselling on the disease (Novartis is funding the initiative. It aims to provide funds towards cost of procuring MMUs, medical equipment required for screening along with other administrative and operational expenses) >>
	Jan Swasthya Sahyog (JSS)	Program implementation	• Project for screening, diagnosis and management in eastern Madhya Pradesh in collaboration with National Health Mission, Madhya Pradesh >> • Started in 2018, the project is focused on 6 tribal districts of eastern Madhya Pradesh • The JSS team conducted ~20,000 screening tests in Madhya Pradesh in 2021-2022 period
	Thalassemia and Sickle Cell Society (TSCS)	Program implementation	• TSCS provides free consultation, free blood and transfusion facilities and counselling services to SCD patients in Telangana and Andhra Pradesh >>
	National Alliance of Sickle Cell Organizations (NASCO)	Advocacy	• A consortium of 20+ like minded organizations, NASCO is India's first registered, voluntary, non-profit, national organization constituted by patient advocate groups (PAGs) to educate and empower SCD patients and caregivers. Formed in 2020, NASCO is headquartered in Nagpur • NASCO mission is to increase awareness in the general public about SCD and advocate for better quality of life for SCD patients >> • It is a member of Global Alliance of Sickle Cell Disease Organization (GASCDO) and part of National Council of Sickle Cell Disease formed under aegis of Ministry of Tribal Affairs and FICCI
	Association for Health Welfare in the Nilgiris (ASHWINI)	Program implementation	• The organization runs a Sickle Cell Centre in Tamil Nadu and takes care of 300+ patients >> • The society provides screening facilities including newborn screening, counselling for patients and treatment including pneumococcal vaccination and hydroxyurea

SOURCE: Team analysis

Selected initiatives by philanthropists and non-profits (2/2)

Category	Organization	Type of work	Description
NGO	Sickle Cell Awareness Organization (SCAO)	Program implementation	• Based in Bharuch, Gujarat, the organization is dedicated to spreading awareness about SCD in the nearby villages and tribal areas >> • The foundation provides free OPD services, including, diagnosis, treatment and rehabilitation services. It is currently serving 200+ patients
	Sickle Cell Saksham Rajasthan Foundation (SCSRF)	Advocacy	• Member of National Alliance of Sickle Cell Organizations, SCSRF works alongside health care professionals, parents, and SCD patients raise awareness about the disease >>
	ADEETECH	Research and Advocacy	• Conduct SCD-related awareness campaigns at ground level in tribal areas, specifically in the state of Maharashtra state >> • Scientific achievements include reporting human parvovirus B19's impact on SCD in India and pioneering therapies in SCD mouse models in the USA

Other NGO working on the issue of SCD include Jan Swasthya Abhiyan – Karnataka, Valsad Raktdan Kendra – Gujarat, Jan Mitram Kalyan Samiti – Chhattisgarh, Sickle Cell Association – Nagpur, Maharashtra

SOURCE: Team analysis

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Selected initiatives by the private sector

Category	Organization	Type of work	Description
Private Sector	Mylab	Research and technology (Diagnostics)	• In June 2023, Pune-based Mylab Discovery Solutions launched a strip-based, rapid point of care test for SCD called PathoCatch Sickle Cell Rapid Test >> • The test is made up of 3 indicators which detect the presence of haemoglobin A, S and C • The test is claimed to have a combined sensitivity and specificity of 100%
	Lord's Mark Industries and IIT Bombay	Research and technology (Diagnostics)	• Lord's Mark Industries will invest Rs 25 crores to develop and distribute the technology-enabled PoC equipment, targeting revenue of Rs 100 crores by year 2026-27 >> • The company claims that it will offer sickle cell anaemia diagnosis at ₹120 per test, 10 times cheaper than the existing price of around ₹1,200 per test, and deliver the result within 30 minutes
	Voxtur Bio	Research and technology (Diagnostics)	• Maharashtra based-manufacturer, Voxtur Bio, launched a finger-pricking test kit in July 2023 • Evaluated by ICMR, the test kit is claimed to have 100% specificity, sensitivity and accuracy and provides results within 10 minutes, eliminating the need for skilled manpower (approved by ICMR) >>
	Pfizer	Vaccine	• Pfizer's Prevenar 13, the most widely used PCV in the world, was included in India's National's Immunization Schedule (NIP) in 2017
	SII	Vaccine	• Serum Institute of India (SII) released the indigenous PCV10 vaccine (Pneumosil) in December 2020. It's the world's most affordable PCV and has been included by the Indian government in NIP
	Hemex Health	Research and technology (Diagnostics)	• US-based health technology start-up Hemex Health has developed a portable diagnostic device, Gazelle that provides test results in under 15 minutes >> • A study was conducted on 960 Indian patients and published in the journal Frontiers in Medicine (study supported by Hemex health). The device demonstrated over 99% sensitivity and specificity to distinguish sickle cell disorders from normal • Researched concluded that the quick turnaround times and low-cost of the device can enable clinicians to perform widespread screening affordably and quickly

Novel drugs such as Endari (Emmaus Medical), Adakveo (Novartis) and Oxbryta (Pfizer) are not currently available in India

Note: The project will have a (marginally) lower focus on diagnostics and screening vs. therapeutics
Other popular diagnostic devices includes SickleScan and HemotypeSC

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Recent initiatives targeting health for tribal population in India do not focus on SCD, but can have a benefit on that dimension as well (1/2)

Organisation	Initiative description	Date and duration
CSIR-Advanced Materials And Processes Research Institute	Build a 6 beds hospital to handle Covid-19 and also other communicable diseases in a tribal district Jhabua, Madhya Pradesh >>	From November 2022-2023
India Health Action Trust	Project MANCH - aims to increase the availability, quality and utilization of critical MNCH services across the continuum of care in the tribal areas and capacity building of service providers (nursing officers & ANMs) of health care facilities and frontline workers to improve knowledge, skill & practice through trainings & mentoring	2021-present
Jan Swasthya Sahyog (JSS)	Strengthen quality standards in maternal health services in public health facilities in the states of Chhattisgarh and Madhya Pradesh >>	Several projects; most recent: 2016-2022
Jhpiego	Provide end-to-end operationalization support for mobile health vans in Jharkhand >>	2022
M.S. Swaminathan Research Foundation	Support community led Interventions for Tribal Health Resilience in Koraput, Odisha >> >>	From October 2023-2026
Parivaar Education Society	Run full day mobile clinic service in the tribal villages in Madhya Pradesh. Qualified doctors are employed who visits 4-5 villages daily and examine around 100-150 patients. Free medicines are also provided to the patients >>	2023

SOURCE: In-line with text, team Analysis

Recent initiatives targeting health for tribal population in India do not focus on SCD, but can have a benefit on that dimension as well (2/2)

Organisation	Initiative description	Date and duration
Partnership for Health (USAID, PATH, Piramal Swasthya, Jhpiego, Deloitte)	Creating customized models of patient centered TB care in tribal communities >>	Various project dates (almost all are currently ongoing)
Piramal Swasthya	Setup a collaborative platform that will work to improve health and nutrition in tribal districts >>	From November 2021-2023
Savitribai Phule Mahila Ekatma Samaj Mandal	Provide doorstep Maternal Health Care to 84 remote Tribal Villages using a sound network of health-workers with smart tools and point-of-care diagnostic devices >>	2015-2019
Society for Education Welfare and Action Rural (SEWA Rural)	Supports an intervention-research project that deploys internet and mobile phone solutions to improve the coverage and quality of maternal health interventions through village-level health workers in tribal and rural areas in the state of Gujarat >>	1998-2015
Tata trusts	Improve the quality and coverage of services in the Integrated Child Development Services (ICDS) and National Health Mission by focusing on trainings, demand generation, monitoring and a management information system that helps in managing the process >>	2017-2021
	Grants supporting building infrastructure in tribal hospitals and creating centers of excellence >>	Unclear - article from 2021

SOURCE: In-line with text, team Analysis

Agenda

- About Alstonia Impact
- Executive Summary
- Summary report
- **Detailed findings**
  - Disease context
  - Burden analysis
  - Current prevention and treatment approaches
  - Current health system response
  - Key challenges faced by patients and health system
  - **Mapping of efforts from the non-profit and corporate foundation system**
    - View by organizations' types
    - Additional on-going additional initiatives
    - **Identified innovative practices**
  - Recommendations for the ecosystem

Various organizations are implementing innovative practices to address the challenges of SCD (1/2)

Patient Journey	Innovative Practices Identified	Practicing Organization
Awareness	▪ Using social media platforms such as Instagram, Twitter, and Facebook to raise awareness about SCD, share patient stories, and disseminate latest developments in the field	▪ National Alliance of Sickle Cell Organization (NASCO), India
	▪ Sensitizing public, state, and central government by organizing state-level round-table conferences	▪ National Alliance of Sickle Cell Organization (NASCO), India
	▪ Raising public awareness through various knowledge dissemination mediums such as video presentations, street plays, and marriage counseling	▪ Sickle Cell Awareness Foundation (SCAF), Bharuch, Gujarat
Screening and Care Seeking	▪ Conducting newborn screening programs to identify infants with SCD early, allowing for timely interventions and treatments	▪ Gujarat Government; Odisha Government; Ghana
	▪ Ensuring availability of ambulance services in areas where health resources are limited	▪ Sickle Cell Awareness Foundation, Bharuch, Gujarat and ASHWINI, Tamil Nadu
	▪ Using telemedicine solutions for remote consultation and monitoring of patients, enabling patients in remote areas or those with limited mobility to seek care more conveniently	▪ Novartis, Ghana
	▪ Integrating tribal healers that are willing to use scientific tools into the healthcare system to enable right guidance for screening and care seeking	▪ Piramal Foundation, Tribal areas
Diagnosis	▪ Using reliable and portable point-of-care diagnostic tests to screen the population in areas with limited health resources	▪ Sickle Cell Awareness Foundation, Bharuch, Gujarat
	▪ Training healthcare staff on the proper usage of diagnostic tools including the HPLC machine	▪ ICMR-NIRTH and AIIMS, Delhi

1. Based on secondary research and expert interviews; the list is not comprehensive

SOURCE: Team analysis. Not enough evidence is available to be able to provide a qualitative or quantitative assessment of the impact of these initiatives

Various organizations are implementing innovative practices to address the challenges of SCD (2/2)

Patient Journey	Innovative Practices Identified	Practicing Organization
Treatment initiation and adherence	▪ Running a Sickle Cell Centre that provides comprehensive services including pre-natal diagnosis, genetic counseling, and clinical services	▪ Sickle Cell Foundation, Nigeria and ASHWINI, Tamil Nadu
	▪ Ensuring a consistent and reliable supply of essential medications, such as hydroxyurea including regular follow-ups and monitoring	▪ SCAF, ASHWINI and GMC Medical College, Nagpur, Maharashtra
	▪ Forming Patient Support Groups (PSGs) to support knowledge sharing and regular follow-ups	▪ Jan Swasthya Sahyog, Madhya Pradesh
	▪ Collaborating with donors and corporate foundations to leverage financial and human resources	▪ Novartis, Ghana
	▪ Providing catch-up pneumococcal vaccination to SCD patients	▪ ASHWINI, Tamil Nadu and AIIMS, Delhi
	▪ Ensuring availability of human health resources in tribal areas	▪ ASHWINI, Tamil Nadu
	▪ Providing specialized training for healthcare workers on the diagnosis and management of SCD	▪ Novartis, Ghana and ICMR-NIRTH

1. Based on secondary research and expert interviews; the list is not comprehensive

SOURCE: Team analysis. Not enough evidence is available to be able to provide a qualitative or quantitative assessment of the impact of these initiatives

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- Executive Summary
- Summary report
- **Detailed findings**
  - Disease context
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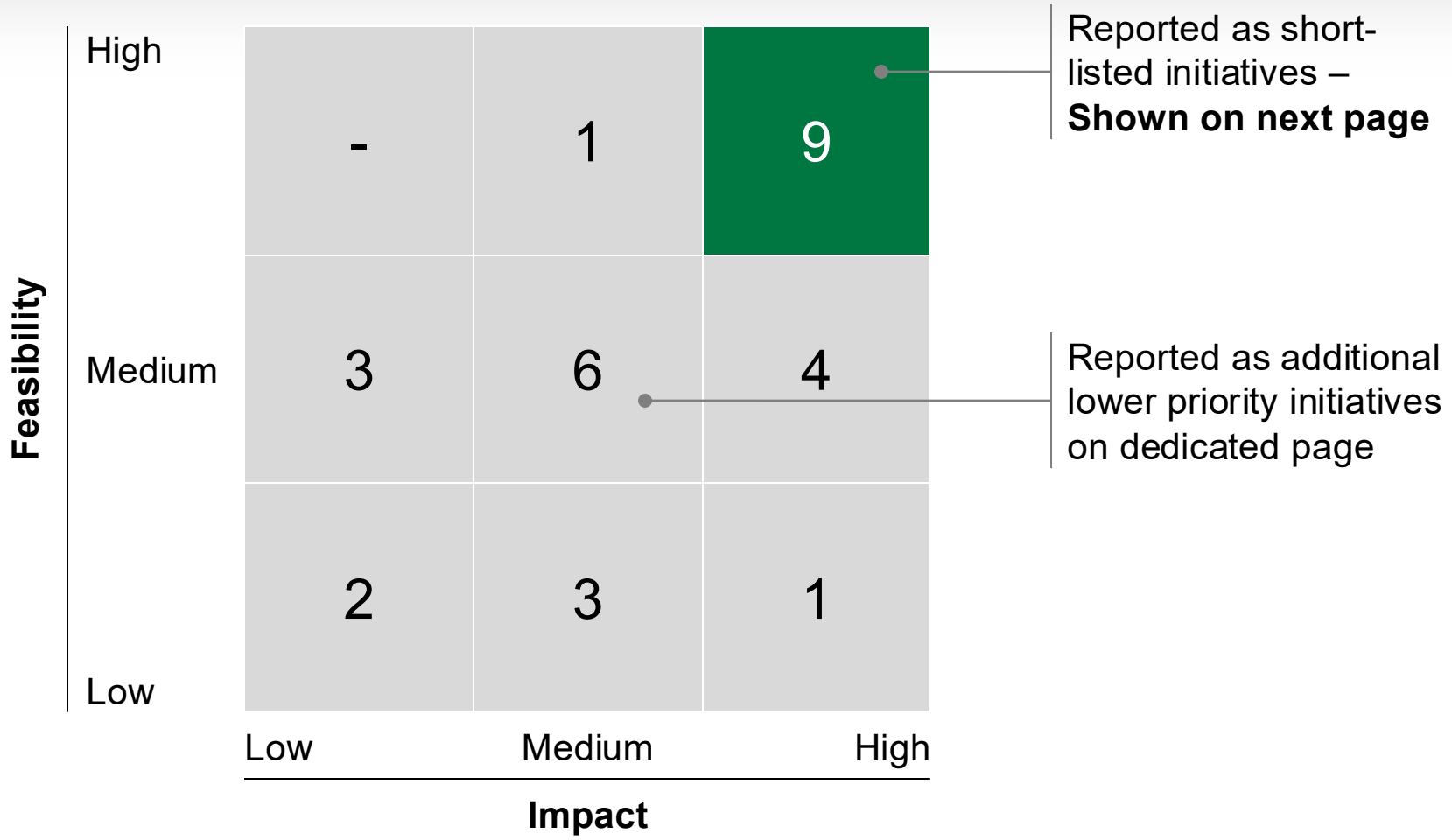
  - Mapping of efforts from the non-profit and corporate foundation system
  - **Recommendations for the ecosystem**

All identified recommendations were mapped in an impact / feasibility matrix; only those scoring high on both dimensions were kept as a main recommendation

Count of identified recommendations



SOURCE: Team analysis

Based on our research, we identified several key recommendations for donors and key stakeholders to tackle the SCD challenges at system level

Group	Sub-group	Suggested recommendations (shortlisted)
Improve awareness / trust for institutions	Community	1 Run / Fund mass media campaigns for community to fight social stigma and build trust in the public system, learning from the TB and Polio programs
	Healthcare workers[1]	2 Run training campaigns focused on doctors and relevant healthcare workers in high prevalence areas, including when and how to provide vaccines, hydroxyurea and other treatments
Provide more resources	Not enough treatment centres or treatment resources	3 Support in building and scaling Centres of Excellence for advanced treatment and training lower-level facilities (e.g., using a phased approach, creating working role models to scale up, etc.)
Improve execution	Program implementation	4 Investigate opportunities to strengthen systems to improve coverage of new-born screening in public facilities 5 Provide technical assistance to the government program to prevent stock-outs of key commodities (e.g., hydroxyurea), manage human resources effectively, measure program progress and success (e.g., number of successful follow-ups, etc.) 6 Strengthen health system for tribal populations as a whole; investigate synergies with other programs *(not SCD-specific)*
	Treatment and disease management	7 Consider including catch-up vaccines and new therapies in the program
Build relevant evidence	Evidence generation	8 Conduct interventional studies to discover the definition of an optimal operating model for providing care close to the communities and scale up model 9 Understand how beliefs and myths vary by region and tribes to be able to design better SBCC (Social and Behaviour Change Communication) efforts

x Deep dive on dedicated pages

These recommendations are those which scored “High” / “High” in the impact vs feasibility matrix. De-prioritized initiatives and additional details are available in the appendix

1. Including doctors, community health workers and local healers

1 Run / Fund mass media campaigns for community to fight social stigma and build trust in the public system, learning from the TB and Polio programs (1/2)

Recommendation: Run / Fund mass media campaigns for community to fight social stigma and build trust in the public system, learning from the TB and Polio programs

Challenge to be addressed

- *Social stigma surrounding Sickle Cell Disease (SCD)*: Communities often hold deep-rooted cultural beliefs and misconceptions about SCD, viewing it as a curse or punishment. These beliefs contribute to the stigma around the disease, leading to discrimination and social exclusion of affected individuals and their families. Such attitudes lead patients to hide their status, which in turn affects care seeking, diagnosis and treatment. Myths about the disease vary by state and tribes; for example, in Maharashtra, the prevailing myth is that SCD occurs due to eating non-vegetarian food, in Jharkhand due to black magic, and in Chhattisgarh and Gujarat because of consuming old rice.
- *Mistrust of public health system, especially in tribal areas*: Past negative experiences, perceptions of inadequate services, and cultural beliefs contribute to scepticism among affected communities. This mistrust can lead individuals to avoid seeking necessary care and hinder efforts to effectively manage and combat SCD

>>

Target geography

- Tribal regions across multiple states, with a focus on areas where SCD prevalence is high and where social stigma surrounding the disease is particularly pronounced
- Within those areas, focus should be on population as a whole (not patients specifically)
  - Leveraging mass media: in national urban centres with high internal migration, and at state level in Chhattisgarh, Madhya Pradesh, Maharashtra and Odisha
  - Leveraging Mid-media/digital: for high-burden districts with low mass media reach, focusing on tribal / community leaders as well as community members

Recommendation description

- Run or fund mass / mid media / digital campaigns aimed at:
  - Dispelling myths, raising awareness about SCD, and fostering acceptance and support for affected individuals.
  - Empowering people with knowledge of prevention and appropriate care-seeking
  - Building awareness of services provided by the public health system
- Tribal communities (patients well as non-patients), community leaders and healthcare workers in high-burden areas should be targeted, in local languages where appropriate
- Leverage tribal influencers in campaigns where possible

Practical & immediate next steps

- Align with government (centre and selected state, including the Ministry of Tribal Affairs, which has a major role in awareness building) stakeholders to secure support and ensure complementarity with their efforts. Discuss with them possible initiatives to start within the programme to fight the mistrust of the public health system
- Onboard a media agency, to develop strategy for campaign development
- Note: additional research might be needed to articulate appropriate messages *(see next page)*

SOURCE: in-line with text, from interviews, Team analysis

1 Run / Fund mass media campaigns for community to fight social stigma and build trust in the public system, learning from the TB and Polio programs (2/2)

Recommendation: Run / Fund mass media campaigns for community to fight social stigma and build trust in the public system, learning from the TB and Polio programs

Potential partners

- Government (central / state level esp. Ministry of Tribal Affairs): approve content and potentially provide airtime through IEC division
- Media agencies and communication experts, to develop the communication strategy and content for mass media communication
- Local community-based organizations / advocacy groups, to leverage existing resources, to connect with tribe / community leaders and to ensure communication is culturally sensitive and effective for the target audience + mid-media efforts

How to measure success

- Increase in awareness about SCD among the tribal communities
- Reduction in level of stigma associated to SCD
- Indicators such as media reach, engagement, and audience feedback can be used to monitor the reach of the campaign
- Increase in healthcare-seeking behaviour (especially in public health settings) among tribal community members could also be measured

Possible additional research

- Investigate what can be learnt from successful campaigns addressing other health issues like HIV, tuberculosis (TB) and polio, where stigma was a major issue
- Better understand the diversity and specificity of cultural beliefs, attitudes, and perceptions surrounding SCD within tribal communities. This research can inform the development of targeted messaging and communication strategies tailored to the unique needs and preferences of these communities
- Quantify baseline for level of awareness of the local communities, to size the problem and to be able to monitor progress

Timeline and priority

- **Immediate**: it can be started immediately, but a better knowledge of the awareness or myths about SCD in the different geographies will be required to design an effective programme

SOURCE: in-line with text, from interviews, Team analysis

2 Run training campaigns focused on doctors and relevant healthcare workers in high prevalence areas (1/2)

Recommendation: Run training campaigns focused on doctors and relevant healthcare workers in high prevalence areas, including when and how to provide vaccines, hydroxyurea and other treatments

Challenge to be addressed

- Public sector doctors and Community Health Officers (CHOs) at primary and secondary health care centres have limited awareness about SCD, which can lead to delays in recognising the root cause of symptoms and, thus to improper diagnosis
- They also have limited knowledge about the appropriate treatment to prescribe the patients, including the right dosage of hydroxyurea, the value of vaccines in patient management, paediatric treatments (including penicillin), awareness of the new treatments
- Governments are attempting to change this through trainings, but trainings are often under-budgeted and not always delivered well

Recommendation description

- Trainings can be developed and delivered to the CHOs and to Medical Officers working at the primary health care centres and district hospitals
- For CHOs, the training should be focused on recognising SCD symptoms and on how to refer the patients properly, for correct treatment
- For Medical Officers, the training should be based on the official government guidelines and focused on treatment (right dosage of hydroxyurea, paediatric dosage) usage of vaccines and of the new treatments, ability to read results of HPLC tests (where relevant). This could be developed in a way that helps doctors complete Continuing Medical Education (CME) requirements. The content should be visual and interactive, and in local languages, where required. Stakeholders have mentioned that current training material is not engaging.
- Trainings can be delivered by NGOs or government medical colleges

Target geography

- Areas with higher SCD prevalence within the states with the highest absolute prevalence: Odisha, Maharashtra, Madhya Pradesh, Jharkhand
- Areas where CHOs and Medical Officers have lower awareness should be prioritized (data to support this prioritization are not available)

Practical & immediate next steps

- Connect with:
  - Implementation partners with existing relationships with relevant state governments would be best positioned to start developing the content of trainings and designing how to deliver them
  - State governments or state medical councils

SOURCE: in-line with text, from interviews, Team analysis

2 Run training campaigns focused on doctors and relevant healthcare workers in high prevalence areas (2/2)

Recommendation: Run training campaigns focused on doctors and relevant healthcare workers in high prevalence areas, including when and how to provide vaccines, hydroxyurea and other treatments

Potential partners

- NGO partner, government medical colleges or medical councils: experts and implementation partners to develop and to execute the training
- Content development partners: for creating engaging content
- State government: To provide access to public doctors and facilities
- Monitor and Evaluation (M&E) partner: to set up the M&E processes

How to measure success

- Progress can be quantified measuring the higher awareness of doctors and healthcare workers about appropriate treatments and the improved ability to read HPLC's reports

Possible additional research

- An awareness study in target locations can help to identify target population and priorities, highlighting in detail the gaps to be addressed by the training program

Timeline and priority

- **Immediate / medium term**

SOURCE: in-line with text, from interviews, Team analysis

3 Support in building and scaling Centers of Excellence for advanced treatment and training lower-level facilities (1/2)

Recommendation: Support in building and scaling Centres of Excellence for advanced treatment and training lower-level facilities (e.g., using a phased approach, creating working role models to scale up, etc.)

Challenge to be addressed

- Centers of Excellence (CoEs) in India specifically dedicated to addressing sickle cell disease (SCD) are not operational. There is still a major gap in specialized facilities equipped to provide comprehensive interdisciplinary care for complicated cases, advanced treatments, and specialized training for healthcare professionals as articulated in the operational guidelines. CoEs also have a role in training lower level facilities
- This absence also creates a scenario where patients often have to navigate through multiple healthcare facilities and undergo numerous referrals to receive appropriate care. This fragmented approach to healthcare not only adds to the burden on patients but also leads to delays in diagnosis, treatment, and management of SCD

Recommendation description

- Support the establishment and scaling of Centers of Excellence through:
  - Funding or in-kind support towards equipment and medicines
  - Funding for HR expertise (beyond sanctioned staff, where appropriate)
  - Access to software and necessary other resources
  - Where CoE is operational: Funding for specific research studies and international collaborations as well as associated logistics and travel costs
  - Funding / lending for construction of facilities (for financial institutions or donors)
  - Fund / Support the preparation of appropriate and engaging training material, meant for other health care workers (not in the CoEs)

Target geography

- The first phase of CoEs could focus on the ones that are already in development, including ICMR-NIRTH, Sickle Cell Institute, Chhattisgarh and GMC Medical College, Nagpur

Practical & immediate next steps

- Initiate discussions with nascent / planned CoEs directly or via state governments to identify areas of support and articulate priority requirements

3 Support in building and scaling Centers of Excellence for advanced treatment and training lower-level facilities (2/2)

Recommendation: Support in building and scaling Centres of Excellence for advanced treatment and training lower-level facilities (e.g., using a phased approach, creating working role models to scale up, etc.)

Potential partners

- CoEs in development (ICMR-NIRTH, Sickle Cell Institute, Chhattisgarh, GMC Medical College, Nagpur): they will be receiving support
- State/central governments: CoEs generally under their operational command
- Technology Vendors: they need to provide the necessary tools and equipment (e.g., manufacturers of PoC diagnostic tests, HPLC machines, etc.)

How to measure success

- Higher number of fully operation CoEs, patient numbers and satisfaction

Possible additional research

- Investigate key gaps in the development of proposed CoEs (ICMR-NIRTH, Sickle Cell Institute, Chhattisgarh and GMC Medical College, Nagpur), reasons behind the gaps and challenges they are facing for ramp up

Timeline and priority

- **Immediate / mid-term**: CoEs are identified and ramping up now, external contributors can help in the ramp up of activities. Long-term sustainability should be kept in mind

SOURCE: in-line with text, from interviews, Team analysis

4 Investigate opportunities to strengthen systems to improve coverage of new-born screening in public facilities (1/2)

Recommendation: Investigate opportunities to strengthen systems to improve coverage of new-born screening in public facilities

Challenge to be addressed

- Newborn screening programs for sickle cell disease (SCD) in high prevalence areas is a challenge in many public healthcare facilities. This leads to missed opportunities for early intervention and treatment initiation which is crucial for SCD
- Key challenges include:
  - Logistical issues such as same-day sample collection, availability of diagnostic tests, and follow-up procedures
  - Resistance from parents against newborns being pricked during screening
  - Higher priority given for mass screening

Recommendation description

- Provide funding or in-kind support for the procurement of:
  - HPLC machines (costs ~INR 30-40 lacs per machine) and required personnel at facilities with high number of deliveries or procurement / other PoC diagnostic tests (costs to be explored, likely lower) at high-load facilities OR
  - Outsourced tests and sample collection if required for same day
- Fund/Offer training programs for healthcare professionals on newborn screening protocols, sample collection techniques, and results interpretation. Train on soft-skills to persuade parents to consent to sample collection
- Advocate for prioritizing newborn screening as a fundamental aspect of routine healthcare services (Especially with the Reproductive and Child Health group at NHM central level)

Target geography

- Tribal regions, across multiple states, with a focus where SCD prevalence is high
- Public facilities which see high-load of deliveries (primary and secondary)

Practical & immediate next steps

- Identify states open to support (and collaborate with NGOs in this space)

SOURCE: in-line with text, from interviews, Team analysis

4 Investigate opportunities to strengthen systems to improve coverage of new-born screening in public facilities (2/2)

Recommendation: Investigate opportunities to strengthen systems to improve coverage of new-born screening in public facilities

Potential partners

- Government (policy level) with NHM, RCH division at central level among others
- Public healthcare facilities (Primary health centers, district hospitals, and maternal and child health centers): place of intervention
- Technical partners (Academic institutions, research organizations, non-profits): to support the implementation and required training for new processes
- Technology Vendors (Manufacturers of PoC diagnostic tests and screening equipment) to provide necessary tools and equipment
- Advocacy partners: raise salience of the value of focusing on new-born screening

How to measure success

- Number of screened new-born in public facilities vs total number of new-borns in target areas

Possible additional research

- Investigate the share of new-born screens which are not performed due to resistance from the parents

Timeline and priority

- **Mid-term**: identifying the needs, securing the funding and the procurement of new tools and equipment and embedding them into new processes is likely to take some time

SOURCE: in-line with text, from interviews, Team analysis

5 Provide technical assistance to the government program at the central and/or state levels (1/2)

Recommendation: Provide technical assistance to the government program to prevent stock-outs of key commodities (e.g., hydroxyurea), manage human resources effectively, measure program progress and success (e.g., number of successful follow-ups, etc.)

Challenge to be addressed

- Ambition of the program is not matched by resources and implementation strength at the state-level. Several symptoms are apparent:
  - Sub-optimal commodities utilization: Despite regulatory improvements, such as hydroxyurea inclusion in the essential medicines list, cautious prescribing practices among doctors, stock-outs and low adherence among patients
  - Human resources: There is a dearth of trained personnel on the ground for conducting screening and awareness campaigns, hampering reach of programs
  - Program management: Managing the program effectively and measuring success is impeded by a lack of robust data collection (especially after screening) and follow-up mechanisms to ensure regular medication intake among patients, resulting in suboptimal treatment outcomes

Recommendation description

- Provide support to states (and potentially to the center) through a Technical Support Unit that can holistically support government leadership in executing its mandate. Personnel could include specialists in program management, supply chain and forecasting, and monitoring and evaluation

Target geography

- States with the highest SCD prevalence and express interest in receiving support
- Central government (MoHFW) if interested in receiving support

Practical & immediate next steps

- Conduct workshops with government stakeholders at the central and state levels to identify gaps and priorities as well as appetite for receiving support via Technical Support Units

SOURCE: in-line with text, from interviews, Team analysis

5 Provide technical assistance to the government program at the central and/or state levels (2/2)

Recommendation: Provide technical assistance to the government program to prevent stock-outs of key commodities (e.g., hydroxyurea), manage human resources effectively, measure program progress and success (e.g., number of successful follow-ups, etc.)

Potential partners

- Government health departments at the central and state levels, responsible for overseeing SCD programs and implementing interventions at the grassroots level
- National or global organizations and technical agencies with expertise in healthcare supply chain management, human resource development, and program monitoring and evaluation

How to measure success

- Success of the TSU will be measured by how government's own outcome / output metrics are achieved

Possible additional research

- n/a

Timeline and priority

- **Immediate**: needs assessments and stakeholder consultations can be performed immediately (potentially leveraging this document) to identify priority areas for technical assistance and develop tailored interventions to address identified challenges

SOURCE: in-line with text, from interviews, Team analysis

6 Strengthen health system for tribal populations as a whole; investigate synergies with other programs (1/2)

Recommendation: Strengthen health system for tribal populations as a whole; investigate synergies with other programs

Challenge to be addressed

- Many challenges associated with Sickle Cell Disease (SCD) are also prevalent in other health domains, largely attributed to frail health systems. This includes issues such as the limited reach and access to quality healthcare in remote and hard-to-reach regions
- Support for tribal communities is not a major priority for many donors despite the recent government push, and there is low donor funding in this area. The few existing donor-funded initiatives do not have SCD as a focus area

Recommendation description

- Explore collaboration opportunities between the Indian government and potential donors like BMGF, USAID, and others to address tribal health comprehensively, including SCD. For example, initiate discussions to advocate for incorporating SCD into existing initiatives (such as Piramal Foundation's Tribal Health Collaborative)

Target geography

- Focus on the geographical areas covered by existing initiatives and government priorities for tribal health, including regions across Chhattisgarh, Madhya Pradesh, Maharashtra, and Assam

Practical & immediate next steps

- Initiate discussions between the Indian government and potential donors like BMGF, USAID, and others to explore partnership opportunities for addressing SCD within existing tribal health initiatives

SOURCE: in-line with text, from interviews, Team analysis

6 Strengthen health system for tribal populations as a whole; investigate synergies with other programs (2/2)

Recommendation: Strengthen health system for tribal populations as a whole; investigate synergies with other programs

Potential partners

- Government stakeholders at state and central levels, including health divisions, Ministry of Health and Family Welfare, and Ministry of Tribal Affairs
- Community / tribal leaders or local NGOs, to be willing to accept a scope extension of the existing programs
- BMGF, USAID, and other donors providing funding and technical assistance

How to measure success

- Short-term: Increased donor funding available for tribal health
- Mid-term: Higher attention to this topic, more innovations tested and mainstreamed
- Long-term: improved outcomes for tribal populations

Possible additional research

- Investigate specific modalities for strengthening health systems in tribal-dominated areas

Timeline and priority

- **Immediate: I**nitiate discussions with other funders and governments, with ongoing efforts to advocate for SCD inclusion in tribal health programs

SOURCE: in-line with text, from interviews, Team analysis

7 Consider including catch-up vaccines and new therapies in the program (1/2)

Recommendation: Consider including catch-up vaccines and new therapies in the program

Challenge to be addressed

- *Low coverage of recommended vaccines among patients, limited availability of new treatments*
  - *Vaccines*: relevant vaccines for SCD patients (Pneumococcal, Hib, Meningococcal) are not procured at scale in most Indian states. Operational guidelines include them for children under 2 years old, but no catch-up vaccinations for adults are considered (now they are only mentioned in technical guidelines, without budget allocation by states)
  - *New treatments*: new treatments against SCD, complementing hydroxyurea, are not available at scale within the national program, yet. Several stakeholders mentioned that 10-20% patients can not use hydroxyurea

Recommendation description

- Government: Consider inclusion of catch-up vaccines and new therapies into the SCD program.
- Non-profits/researchers: Fill evidence gaps, support in testing programs to help reach patients for vaccines (catch-up vaccines will need a diverse set of platforms given limited touchpoints with children > 2 years old)

Target geography

- India-wide, where the on-going National Sickle Cell Program is operational. Specific high-burden states such as Odisha, Maharashtra, Madhya Pradesh and Jharkhand may also be focused on in addition to national engagement

Practical & immediate next steps

- Non-profits: Fill evidence gaps and raise salience of issue

SOURCE: in-line with text, from interviews, Team analysis

7 Consider including catch-up vaccines and new therapies in the program (2/2)

Recommendation: Consider including catch-up vaccines and new therapies in the program

Potential partners

- Non-profits: For testing models to reach patients for catch-up vaccines

How to measure success

- Inclusion of catchup vaccines for adults and new treatment in the operational guidelines and in the national SCD programme

Possible additional research

- n/a

Timeline and priority

- *Vaccines*: **short term**, products are already available and related recommendations are already present in general guidelines, plus already included in operational guidelines for children under 2 years old
- *New treatments*: **medium term**, since significant effort for scaling up existing therapies such as Hydroxyurea needed

SOURCE: in-line with text, from interviews, Team analysis

The following recommendations may have a positive impact, but they were considered lower priority (1/2)

Lower priority recommendations

Group	Sub-group	Suggested recommendations (de-prioritized)	Score (Impact / Feasibility)
Improve awareness / trust for inst.	**Healthcare workers**[1]	▪ Awareness program for local healers and pharmacists and to advice patients with relevant symptoms to get screened	▪ High / Medium
Provide more resources	**Not enough testing centres / diagnostic tools**	▪ Support the government with CVS equipment (fetal) in relevant facilities ▪ Support screening efforts via MMUs (Mobile Medical Units) in places where there are gaps	▪ Medium / Medium[3] ▪ Medium / Medium
	Not enough funds for research	▪ Fund research into new diagnostics and therapies (e.g., Support research efforts on gene therapy and other treatments to push the costs down)	▪ Medium / Low
Improve execution	**Program design**	▪ Roll out a holistic and convenient treatment package that addresses adherence challenges, making most services and drugs made available close to the patient (relevant follow up tests to monitor treatment should also be covered) ▪ Introduce counsellors for patients' support at primary care facilities ▪ Leverage traditional healers and pharmacists to bring patients into the government program. Investigate synergies with other programs (e.g., TB) ▪ Support states that have high prevalence but are not priority states due to low absolute burden	▪ High / Medium ▪ High / Medium ▪ High / Low ▪ Low / Medium
	Screening and diagnosis	▪ Make sure the best tools[2] from the technical point of view are used for testing (cheaper, more portable, less invasive, etc.).	▪ Medium / Medium

1. including doctors, community health workers and local healers
2. PCV vaccine to SCD patients was already suggested by the Indian National Technical Advisory Group on Immunization (NTAGI) inJuly 2023 >>
3. During an interview with a representative from the Maharashtra government, supporting fetal screening was mentioned as an area they would be interested to get support on. Feasibility was scored as "medium" driven by this point, but considering that this is only one data point and equipment remains expensive

The following recommendations might have a positive impact, but they were considered lower priority (2/2)

Lower priority recommendations

Group	Sub-group	Suggested recommendations (de-prioritized)	Score (Impact / Feasibility)
Improve execution	**Treatment and disease management**	▪ Consider including newer therapies in the program	▪ Medium / Medium
		▪ Support patients with nutrition and mental health support and assist patient support groups	▪ High / Medium
		▪ Support patients economically	▪ Low / Low
		▪ Support bone-marrow transplants	▪ Low / Low
		▪ Develop convenient dosages for children	▪ Medium / High
Build relevant evidence	**Evidence generation**	▪ Conduct research studies to build a more accurate care cascade to understand burden and leakages better	▪ Medium / Medium
		▪ Create local evidence of variations of disease across the different Indian areas	▪ Low / Medium
		▪ Fund evidence generation to prove vaccines are an effective way to improve quality of life of patients	▪ Low / Medium
		▪ Investigate reasons for lack of treatment adherence (note: this is a problem in India for all chronic diseases, it should be addressed holistically)	▪ Medium / Low
		▪ Support roll out of development of data systems for disease management	▪ Medium / Medium
		▪ Research on new molecular drugs, as Hydroxyurea might not be as effective anymore in the next 10 years	▪ Medium / Low

1. including doctors, community health workers and local healers
2. PCV vaccine to SCD patients was already suggested by the Indian National Technical Advisory Group on Immunization (NTAGI) inJuly 2023 >>

Alstonia Impact

Thank you!