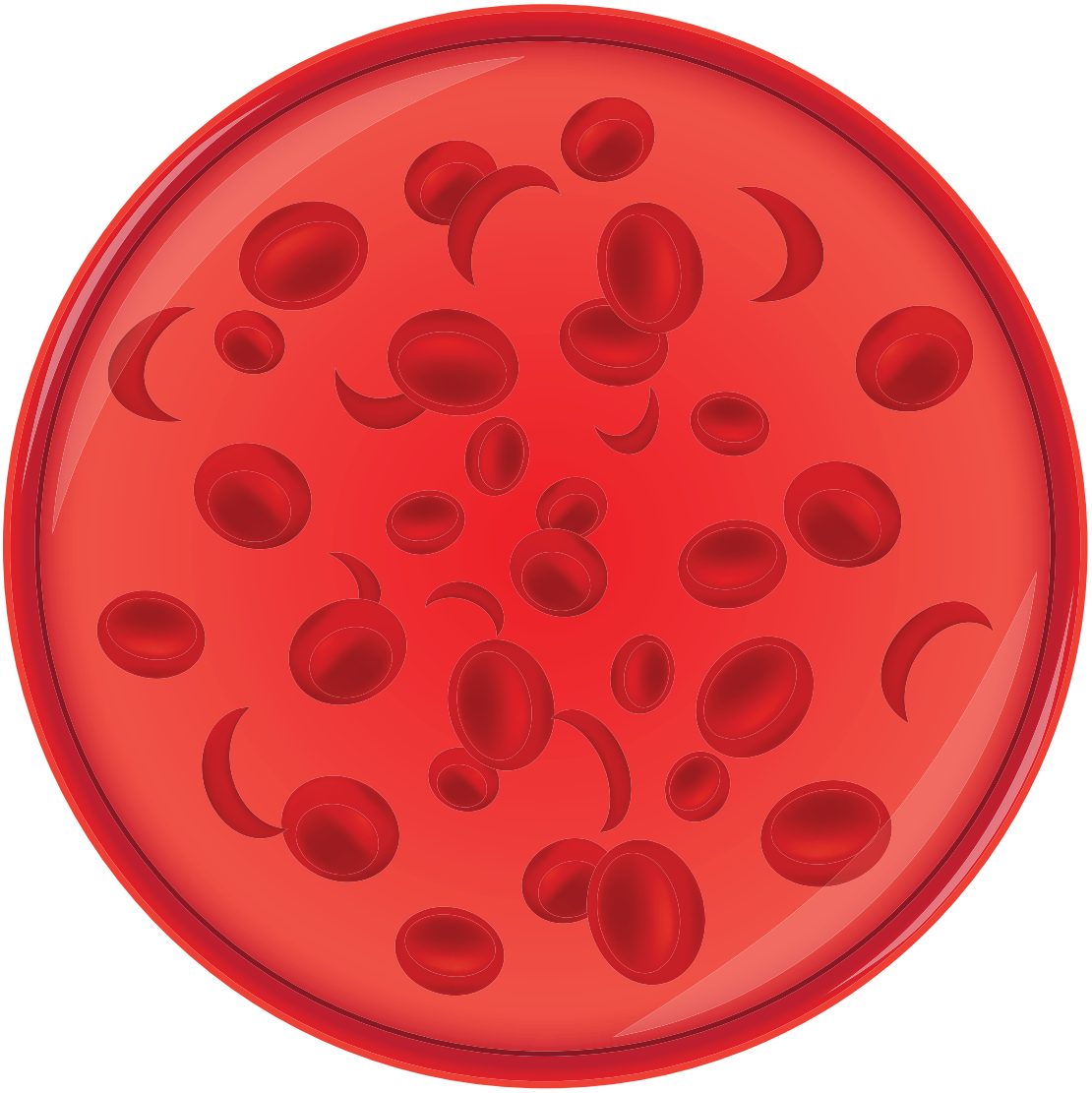
The Economist INTELLIGENCE UNIT | HEALTHCARE

Stepping out of the shadows
Combating sickle cell disease in India

A report by The Economist Intelligence Unit



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Contents

About this report

"Stepping out of the shadows: Combating sickle cell disease in India" is a report by The Economist Intelligence Unit. The report examines key elements of sickle cell disease in India, which includes challenges, opportunities and policy-related responses. The findings of this report are based on a structured literature review, an expert panel, and in-depth interviews with healthcare professionals, patient groups, academics, epidemiologists and policymakers. The report is sponsored by Novartis.

Many people kindly contributed to the report, either by agreeing to be interviewed and/or contributing to our advisory board. Our thanks are due to the following for their time and insights:

- **Anil Khatri**, Member of Managing Committee, Indian Red Cross Society, Gujarat State Branch
- **Anuradha Shrikhande**, President, Sickle cell Association Nagpur
- **Dexter Patel**, President, Sickle Cell Awareness Foundation, Gujarat
- **Dipti Jain**, Head and Professor at Department of Pediatrics, Government Medical College, Nagpur
- **Lalit Dandona**, Distinguished Research Professor, Public Health Foundation of India (PHFI)
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- **Suman Jain**, Chief Executive Officer, Thalassemia and Sickle Cell Society, Hyderabad
- **Tarun Kumar Agrawal**, Ex-Director Medical, Sickle Cell Institute Chhattisgarh, Raipur, Chhattisgarh
- **Tulika Seth**, Professor, Department of Haematology, All India Institute of Medical Sciences (AIIMS), New Delhi
- **Vinita Srivastava**, National Consultant, Ministry of Health and Family Welfare, Government of India

The EIU team field also visited a centre of excellence, the Sickle Cell Institute in Raipur. We took the opportunity to interview the Director Medical, patients and pathologists, and reviewed the facilities provided at the centre. The centre has improved the quality of life of sickle cell patients significantly and is increasing the state screening programme to cover high prevalence tribal areas. We thank all those who we spoke to for offering their time and insights so generously.

The findings and views expressed in this report are those of the Economist Intelligence Unit. They do not necessarily reflect the views of the sponsor.

Executive summary

Sickle cell disease predominately affects disadvantaged communities and is a significant public health challenge

Sickle cell disease, an inherited blood disorder, is a major health burden in India. It is a debilitating disease that affects every part of the body. The disease is most prevalent across central India: states of high prevalence include Chhattisgarh, Bihar, Uttar Pradesh, Madhya Pradesh, Jharkhand, Assam, Meghalaya, Arunachal Pradesh and Rajasthan. While most common in tribal groups, sickle cell disease is increasingly found throughout the country because of migration into the cities.

People with sickle cell disease suffer from social stigma. This not only adds to patient burden, but also reduces the effectiveness of screening programmes: people don't want to know. For those who are diagnosed, their best chance of treatment may be hundreds of miles away. Healthcare facilities, particularly in rural areas, are often ill-equipped and so unable to support timely diagnosis and management of the condition. Children with sickle cell disease often have to drop out from school, and parents providing care to their kids inevitably miss out on work, causing economic hardship.

The disease is characterised by repeated episodes of debilitating pain. These episodes are caused by vaso-occlusive crises, which are a common and repeated cause of morbidity and hospitalisations among sickle cell patients. Twenty percent of tribal children with sickle cell disease die before reaching the age of two, and 30% children die before reaching adulthood.

Sickle cell disease is associated with significant costs to the health system and to patients and wider society. Medical costs come from medications, primary and emergency care visits, hospitalisations, blood transfusions and bone marrow transplantation procedures. Societal costs are primarily caused by lost productivity as a result of parents' missed days of work while providing care for their children, plus future workforce loss to the economy arising from early deaths. Total costs are unclear because of a lack of data, but are likely to run into hundreds of millions of rupees a year.

India's policy and health system response has been fragmented to date, with isolated examples of good practice

India drafted a national-level policy and guidelines in 2018 on the prevention and control of haemoglobinopathies, covering sickle cell disease along with haemophilia and thalassemia. Given differences in disease burden, states will be responsible for implementation. However, the draft policy has yet to be adopted. While there is little clarity on timelines, the government is currently working with various stakeholders to publish a revised version.

We argue that the implementation of an updated policy is urgently needed. This would help to announce that policymakers are finally focussed on the disease. A dedicated national programme should be set up to coordinate activities and ensure momentum is maintained. Part of the programme should include the creation of patient registries to collect and manage large-scale data. Awareness also

needs to be improved to increase public acceptance of pre-marital counselling and help reduce social stigma.

Sickle cell disease centres of excellence oversee state level care and screening programmes, provide training and deliver care to severe cases. They are a vital cog in India's fight against sickle cell disease. However, it is also necessary that primary and local healthcare facilities are suitably equipped to ensure equitable access to care. Improvement is needed in staffing, information technology, and the development of complementary packages of proven, cost-effective interventions. Good examples of this can be seen in Gujarat and Chhattisgarh.

The world of sickle cell disease is at last getting its share of innovation. There are local developments in point of care technologies which promise to improve early detection rates in a rural setting. There are also global developments, with many novel drugs recently approved or in the pipeline. India not only needs to be ready for these new innovations to arrive, but should also establish itself as a centre of innovation, for example through increased participation in global clinical trials.

Changes in diagnosis and treatment are on their way—we describe a series of actions that would reduce burden and improve outcomes

Issues such as social stigma, rural isolation, staffing pressures and support for the poor, will not be solved overnight. However, a number of principles of good practice emerged from the research, and we have laid out a draft "roadmap to success" in India. While not a detailed policy programme, it describes the building blocks around which a sickle cell disease policy programme in India could be designed: it describes actions that would help India to better understand the burden of sickle cell disease, reduce its incidence, and improve outcomes and quality of life for people with the disease. The focus should be to:

1 Recognise sickle cell disease as a priority	2 Strengthen implementation at national and state level	3 Adopt innovative technologies and processes
• **Tackle** stigma • **Improve** data collection • **Expand** screening programmes	• **Improve** and implement the 2018 draft policy • **Invest** in local infrastructure • **Strengthen** centres of excellence	• **Work** with local and global innovators • **Embrace** disruption • **Recognise** that the treatment and diagnosis landscape in sickle cell disease is changing

The delayed implementation of the 2018 draft policy on haemoglobinopathies is acting as a brake in the bid to ensure that sickle cell disease is recognized in India as a public health challenge. Once national policy moves, it then needs to be adopted at state level, especially in states with a high burden.

While there is much to applaud in India's response to sickle cell disease, particularly at state level, the condition continues to blight people's lives. India's best chance of success will come from focussing on packages of simple, complementary sets of interventions, while keeping the door open for disruptive, innovative practices. Much of the suffering in sickle cell disease is avoidable, and we believe that there is both an economic and moral case why more can, and should, be done.

Introducing sickle cell disease

"Doctors don't share the correct information about the disease with us, and so we face delays in getting treated"

Sickle cell disease patient

A chronic, debilitating disorder

Sickle cell disease, an inherited blood disorder, is a major health burden in India. It is a debilitating disease that affects every part of the body. The disorder tends to be most common in poor and rural communities—although is increasingly an urban problem too, due to migration into cities. While the precise burden remains unclear, India is estimated to have the second highest national burden of sickle cell disease, after Nigeria.[1]

Common acute complications of the condition include excruciating episodes of pain, also known as vaso-occlusive crises, and fever. Longer-term complications extend to organ damage, chronic kidney disease and functional disability.[2] Patients with sickle cell disease are also more susceptible to infections, stroke, acute chest syndrome, fatigue, leg ulcers and a range of other complications.

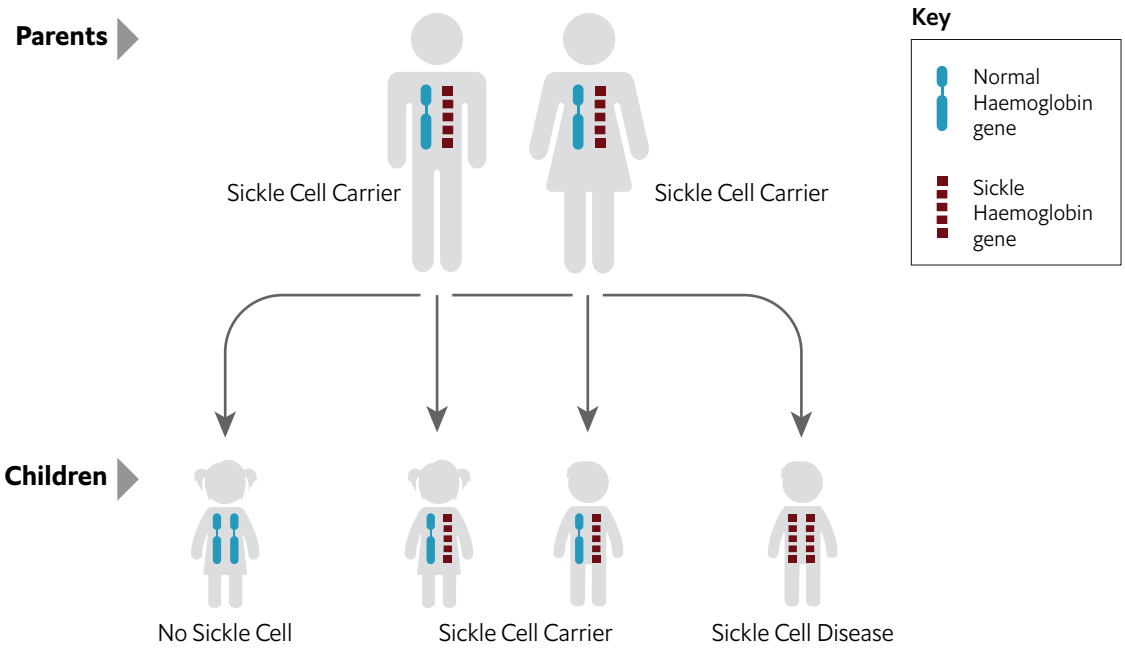
Treatment, when it is available, typically involves undergoing repeated blood transfusions and bone marrow or stem cell transplantation. Vaso-occlusive crises are largely managed by a combination of hydration, anti-inflammatory agents and analgesics, with the patient often having to visit an emergency room or undergo hospitalisation. Hydroxyurea, an anti-cancer agent, has also become an increasingly important component of care, as it can reduce complications such as pain crises.[3] Other therapies for people with sickle cell disease include the prescription of antibiotics to combat infections and vitamin supplements to help generate red blood cells.

Who does sickle cell disease affect? Genes, carriers and inheritance

Sickle cell disease is a group of genetic disorders in which red blood cells take on a sickle shape: a change called 'sickling'. These sickled cells unsettle the normal flow of blood through the vascular system, leading to blockages and other complications. Sickle cell disease is a recessive condition, meaning that you have to inherit the sickle form of the defective haemoglobin gene from both parents. If a child receives a sickle haemoglobin gene from one parent and a normal haemoglobin gene from the other, then they are called carriers (or alternatively they have a sickle cell 'trait'). Sickle cell carriers do not suffer from the disease, but may pass the gene to their children.[4]

When both parents possess a sickle cell gene there is a 1 in 4 possibility that their child will inherit both sickle cell genes and therefore develop sickle cell disease. Equally, there is a 1 in 4 chance that they inherit two normal genes, and there is a 1 in 2 chance that they will inherit one normal gene and one sickle cell gene, thus becoming a carrier **(Figure 1)**.[5]

Figure 1: Sickle cell disease gene inheritance chance when both parents are sickle cell carriers.



Source: The Economist Intelligence Unit.

There are different haplotypes of sickle cell disease—these are different variations of the sickle cell gene that can lead to more or less severe forms of the disease. The 'Arab-Indian' haplotype is considered the most common form in the Indian population, although testing is not always performed.[6] Dr Dipty Jain told us that "Although the identification of haplotypes are not carried out on newborns, it may be 91% Arabic [Arab-Indian]"

The Arab-Indian haplotype is associated with higher foetal haemoglobin (HbF) levels, and although it seems to be associated with fewer vaso-occlusive crises compared to the Benin haplotype (observed in North and West Africa) and the Bantu haplotype (observed in Central and East Africa) its clinical profile is very variable.[7] The long-term clinical impact of the Arab-Indian haplotype, compared to other sickle cell haplotypes, is not currently well understood.

A growing, yet neglected, burden in India

Sickle cell disease in India has been largely undocumented.[8] Reliable estimates of burden are unavailable, but the condition is thought to be most prevalent along a central "sickle cell belt", stretching across central India from South-Eastern Gujarat to South-Western Odisha (although estimates vary: see Figure 3). The disease is particularly prominent in scheduled populations in India: designated tribal groups that have been given reservation status, guaranteeing them political representation. These tend to be socioeconomically disadvantaged communities. Reports in the 1990's emerged that showed that the sickle cell gene was more prevalent throughout society than previously thought.[9,10] This observed shift was partly due to the migration of people from tribal or rural

backgrounds into urban areas, and the consequent intermarriages. Dr. Tulika Seth pointed out that "the map we used to have pointed sickle cell disease to certain pockets. However, that map is becoming diluted as people are intermarrying." When sickle cell disease is found outside tribal areas, it is often more clinically severe. This has raised the suggestion of possible geographic variation in the disease's clinical manifestation across the country.[9]

Because sickle cell disease has historically been neglected, progress in terms of diagnosis, treatment and the adoption of innovation has been slow. However, with new treatments in the pipeline, and national policy discussions on-going about how India can improve the quality of life of sickle cell patients and their families, this is an ideal time to take stock of the current situation. The objective of this report is to investigate what is known about the burden of sickle cell disease in India, how it varies from state to state, and what are some of the local and national initiatives to mitigate its burden. We shall then look at where the gaps are in India's current policy response, and propose a roadmap to improve outcomes and reduce suffering.

The public health challenge

"Even when we have a smart card, there is lack of immediate treatment provided by the hospital. There's a lot of trouble caused by the blood bank staff, lack of cooperation, delay in blood provision, poor facilities provided within the hospital..."

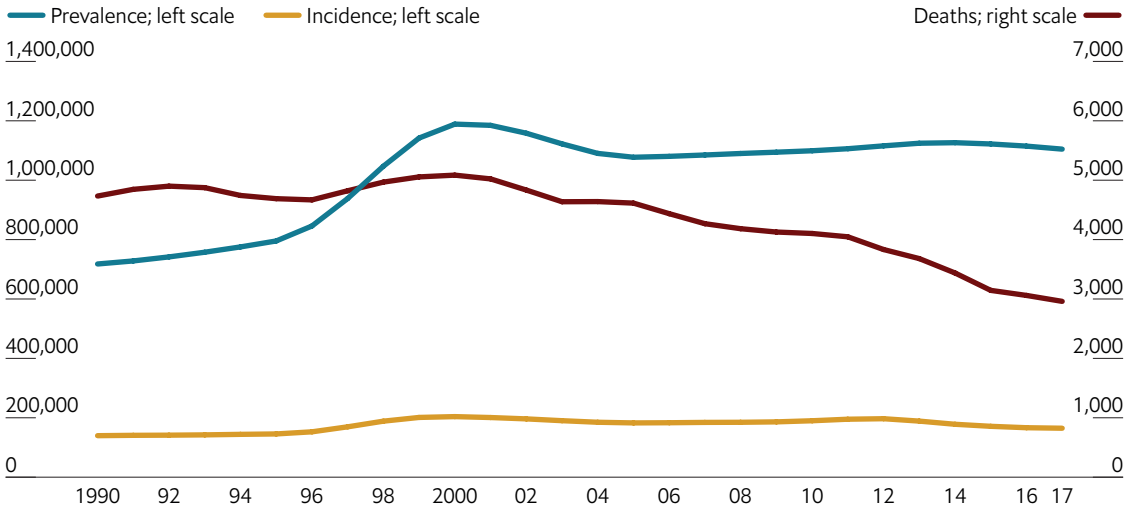
Sickle cell disease patient

Estimates of burden are hampered by a paucity of data

Estimating even basic epidemiological statistics for sickle cell disease in India is challenging. According to estimates from the Global Burden of Disease (GBD)—a global research programme that estimates mortality and burden from major diseases across the globe—prevalence and incidence of sickle cell disease in India in 2017 was 1,104,634 and 195,166, respectively **(Figure 2)**. The GBD's estimates that the number of deaths has decreased from 1990 to 2017, although prevalence and incidence have increased during the same period by a remarkable 51.8% and 32.3%, respectively.[11] The GBD have also published estimates at state level.[12, 13] They suggest that the highest prevalence of sickle cell disease is found in Chhattisgarh, Bihar and Uttar Pradesh **(Figure 3)**.

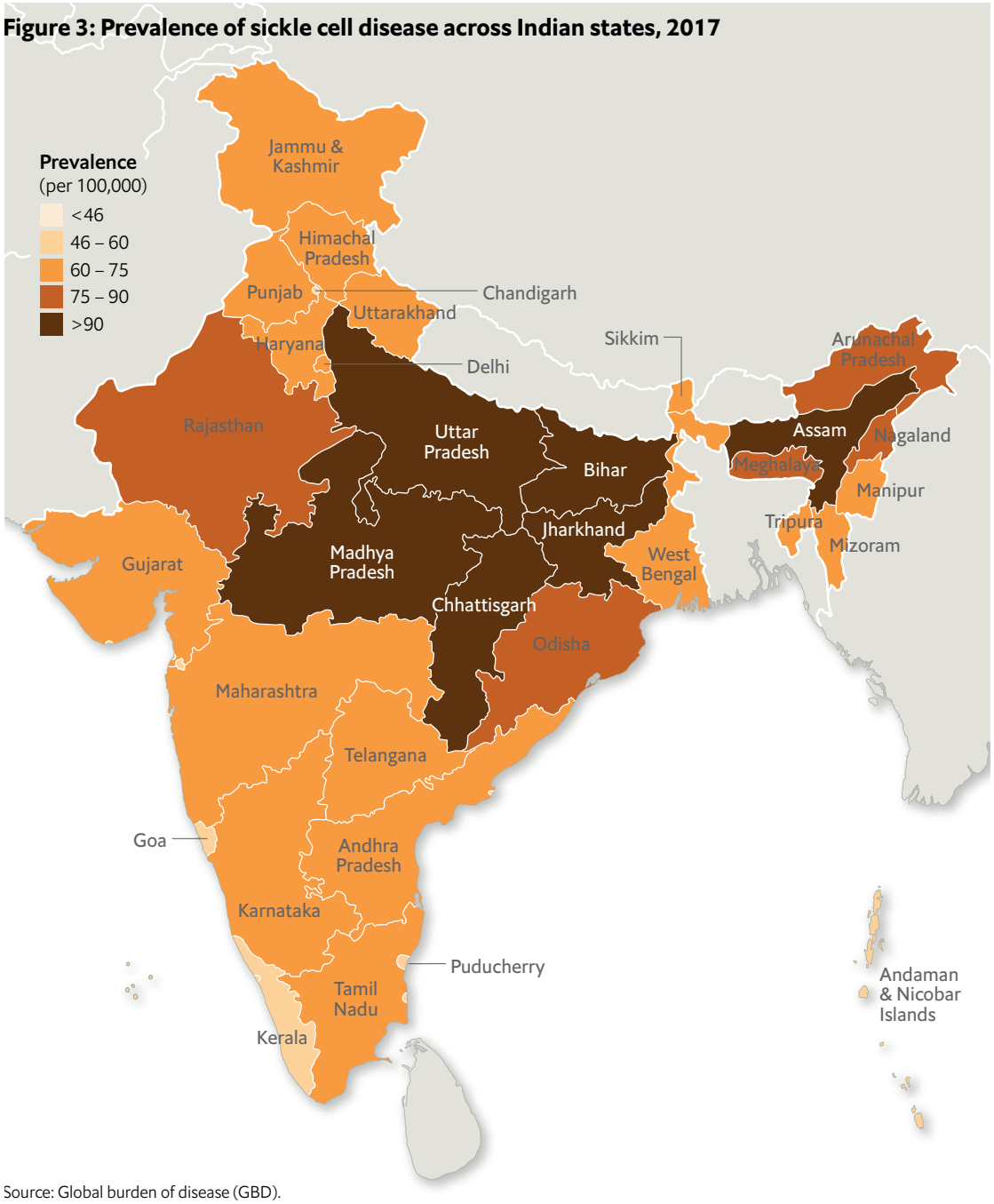
However, some stakeholders in India consider the GBD to have underestimated prevalence of the condition. Certainly estimating burden does require some guesswork. "There is a dependence on indirect methods because not all patients with sickle cell disease are able to access the health system", says Professor Lalit Dandona. "For instance, estimates for diarrhoea are based on large scale surveys which happen in India on a regular basis and it is relatively easy to get the historical data. On the

Figure 2: Sickle cell disease prevalence, incidence and deaths numbers from 1990 to 2017



Source: Global burden of disease (GBD).

Figure 3: Prevalence of sickle cell disease across Indian states, 2017



Source: Global burden of disease (GBD).

contrary, sickle cell disease diagnosis can be made only after confirmation at a health facility and that too, only in facilities that have adequate laboratory diagnostics."

In addition to the GBD estimates, many state level studies have been conducted in India, mostly through screening programmes. While there isn't a consensus on which provides the most accurate estimates, **Table 1** shows a range of estimates from these screening programmes.

Table 1: Primary data from published studies

State	Programme	Total screened	Carrier	Sickle cell disease	% with Sickle cell disease trait	% with Sickle cell disease
Maharashtra[14]	Non-tribal, infants of maternal carriers	2,134	978	113	45.83%	5.30%
Chhattisgarh[15]	Tribal and non-tribal infants	1,158	61	6	5.27%	0.52%
Odisha[16]	Tribal and non-tribal infants	1,668	293	34	17.57%	2.04%
Odisha[17]	Tribal infants	761	112	13	14.72%	1.71%
Tripura[18]	Tribal and non-tribal infants	2,400	15	0	0.63%	0.00%
Tamil Nadu[19]	Tribal population under 30	9,646	1,089	137	11.29%	1.42%
Rajasthan[20]	Garasia tribals	416	31	7	7.45%	1.68%
Madhya Pradesh[21]	Pregnant women	416	31	7	7.45%	1.68%
Chhattisgarh[22]	3-15 years aged school children	1,704,749	169,307	6,816	9.93%	0.40%

The National Health Mission of Gujarat estimated national figures by extrapolating findings from data taken from the state's screening estimates **(Table 2)**. Compared to the GBD estimates, these show a higher number of people living with sickle cell disease. There is a risk that the figures published by the Government of Gujarat are an overestimate as Gujarat is a high burden state and they have extrapolated their state estimates to the whole of India. Overall, aggregating available data from GBD and the sickle cell disease programme in Gujarat, the 2017 prevalence is estimated to be 1,104,634 or 1,339,684, respectively.

Table 2: Estimated national figures.

Subject	Gujarat (2011)	India (2011)
Total population	60,383,628	1,210,193,422
Tribal districts	12	593
Tribal population	8,912,623	178,624,549
Suspected sickle trait	891,262	17,862,455
Suspected sickle cell disease patients	66,845	1,339,684

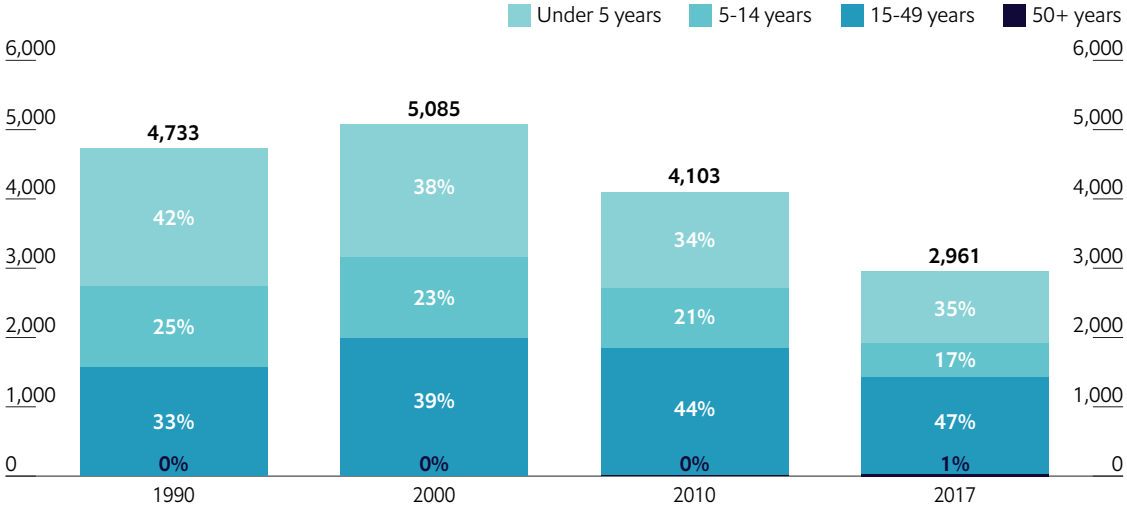
Source: Sickle cell anaemia control program manual, Gujarat

Survival rates are improving as infant mortality declines

Average survival for people with sickle cell disease in India is reported to be about 40 years.[23] State-level data, again, are limited. In Gujarat's southern region, 20% of tribal children with sickle cell disease die before reaching the age of two, while 30% children die before reaching adulthood.[24] In Odisha, a study of sickle cell disease patients above the age of 14 found that the mortality rate was 48% for the age group of 15 to 25 years, 24% for 26 to 35 years, 20% for 36 to 45 years and 8% for above 45 years of age.[25]

The GBD has estimated that the total number of deaths from sickle cell disease fell by 37% from 1990 to 2017 **(Figure 4)**. While similar mortality proportions have been observed in 1990, 2000 and 2010, there is a general trend that infant mortality is declining slightly, and people are living longer with the disease. No definitive cause for this trend in improved survival has been identified, although a number

Figure 4: Number of deaths from sickle cell disease across age groups, from 1990 to 2017



Source: Global Burden of Disease (GBD).

of influences have been suggested. There has been growing awareness of the condition, partly due to events such as World Sickle Cell Day, which first started in 2009. Specifically in India, other sickle cell non-profit organisations and government programmes have also launched awareness programmes. Treatment has also improved. The use of hydroxyurea to manage sickle cell disease began being reported in studies in 1995 in the US, while in India such studies emerged after 2010. Other contributing factors include improvement to access to care in rural India, the establishment of screening programmes, and a better understanding of disease. Healthcare spending also increased in India from $18 per person in 2000 to $63 per person in 2016, as did the number of doctors, from 0.5 to 0.8 per 1,000 of the population.[26]

Patient perspectives

"Entire body pain, pain in the backside, stomach pain, night time pain—unable to sleep—pain in the legs—unable to move. It really impacts basic day to day activities, and it has an emotional impact on the rest of my family."

Sickle cell disease patient

Stigma, missed schooling and poverty

People with sickle cell disease suffer from stigma. This not only adds to the patient burden, but also impacts the implementation of programmes: people don't want to know. "Pre-marital screening has not been accepted due to the associated social stigma", says Dr Roshan. Therefore sickle cell carriers—who do not suffer from the disease—do not go for pre-marital screening and hence are not identified. This lack of awareness, coupled with increased migration from rural to urban areas and a culture of endogamous marriages, makes prevention difficult.[14, 15, 27, 28]

Children with sickle cell disease often have to drop out from school. When this happens they don't receive any support; there are no supporting national organisations, private or public. This can be contrasted with the experience of children with haemophilia or thalassemia disease, where support groups do exist. As a result, 60-70% of school children with sickle cell disease are unable to complete past 11th grade, impacting their education and lowering their life chances. Many girls with sickle cell disease don't want to visit the dedicated centres for diagnosis and treatment. Dr. Agrawal reports that "girls hide their disease, because if their community knows that she is affected with sickle cell disease, then her marriage will be seen as a problem to her new family. Why? Because she will transfer the disease to their offspring".

Pain and vaso-occlusive crises

Vaso-occlusive crises (VOC) are a common complication of sickle cell disease. They occur when blood vessels to a part of the body become blocked by sickled red blood cells. Consequences can include debilitating pain, lasting for up to a week, anaemia, organ damage and early mortality.[29] Frequency of pain episodes is unpredictable and varies from patient to patient. It isn't clear what the trigger for these episodes is, but evidence suggests that they can be caused by changes in weather, dehydration, stress or vigorous exercise.[30] For example, a majority of hospital admissions for vaso-occlusive crises are seen during the monsoon season.[23, 31] Tribal populations may have fewer pain episodes: vaso-occlusive crises have been found to be significantly higher in non-tribal individuals from Nagpur compared to tribal populations from Valsad.[9, 32]

Vaso-occlusive crises are a common and repeated cause of morbidity and hospitalisations among sickle cell disease patients. Painful episodes have been found to be the most prominent clinical complication faced by babies with sickle cell disease, followed by blood transfusions and acute fever.[33] These complications in turn have a large influence on the mortality rate.[33] Similarly, vaso-occlusive crises have also been found to be a common cause of early mortality in adult sickle cell disease patients.[25]

Research on these episodes in India is often of low quality. Most publications are hospital-based observational studies. Main outcome measures tend to be presence, absence or number of episodes and number of blood transfusion. Episodes themselves are often not characterised further, with symptoms not clearly defined nor pain scores used, neither are cost estimates of treatment reported. Nonetheless, vaso-occlusive crises clearly cause much of the burden for patients and caregivers as they are implicated in repeated and chronic morbidities.

Other complications are commonplace

Sickle cell disease patients suffer from several other complications. The blocking of small blood vessels can result in anaemia, functional asplenia (impaired spleen function) and other residual organ damage.[34] Secondary infections are also common, particularly pneumococcal sepsis, a leading cause of death in children with sickle cell disease.[33] Patients furthermore suffer from acute fever, particularly during the monsoon season, because of the increased prevalence of water borne infections.[35] Early mortality can be due to infections resulting from a consequent of lack of treatment.

Like pain crises, non-tribal patients have been found to be more likely to suffer from infections such as high fevers, upper respiratory or urinary tract infections.[36] In 85 children analysed in Maharashtra, hospitalisation caused by acute febrile illness was the most recurring cause of morbidity, closely followed by severe anaemia and pain crises.[31]

Finally, sickle cell disease takes a terrible toll on pregnant women, who often suffer from anaemia. Stillbirths are more common in women with sickle cell disease (9.9% vs 3.6% in the general population). More than half of mothers with sickle cell disease needed blood transfusions with 8.4% needing three or more. Weight of the newborns also varied; almost 70% of sickle cell disease deliveries were low birth weight and 46% of deliveries were preterm.[37]

Getting treatment is often a marathon, not a sprint

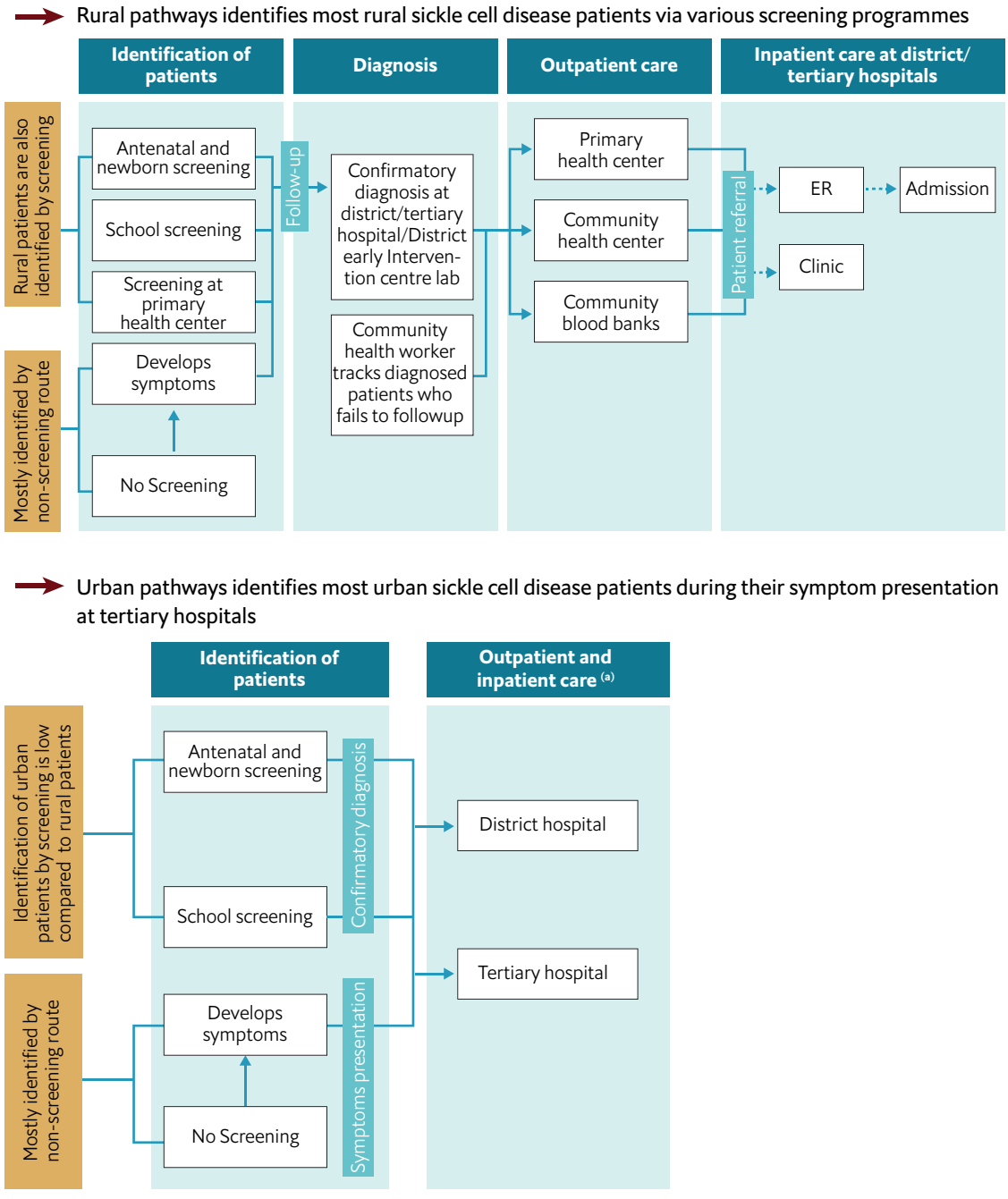
Many of these problems are due to a delay in diagnosis and treatment, and pathways to care vary between urban and rural patients **(Figure 5)**. People in urban settings can go straight to district and medical college hospitals if they experience symptoms. If they haven't already been identified through a screening programme, this is where they are diagnosed and where they can have their follow-up treatments as necessary. Patients in rural settings, on the other hand, often live much further away from hospitals and typically visit primary or community health centres for immediate medical attention. They are commonly prescribed pain killer medications and antibiotics.

Patients that cannot be treated in such centres, such as those undergoing a pain crisis, are often referred to district hospitals or tertiary hospitals. Patients are usually there given hydroxyurea medication. More complex cases, such as those involving bone marrow transplantation, are typically referred to sickle cell disease centres of excellence. These patients are identified at district early identification centres (DEIC) or at the paediatrics department of district hospitals or medical colleges. Only a few government centres provide transplantation services—although a number of private centres do offer this procedure.

Hematopoietic stem cell transplantation remains the only curative option for sickle cell disease patients. However, it is often not considered by haematologists in India. This is likely because the

success rate of the procedure remains unclear in the country; so many healthcare professionals consider it not worth the risk. Furthermore, there is a disparity between demand and donors, and finding a matched donor is hard.

Figure 5: The key difference between urban and rural patient pathways



(a) Interviewees suggested that for follow-ups, urban patients visit district and tertiary hospitals directly. It is also common to follow-up directly at sickle cell centres of excellence.

Source: The Economist Intelligence Unit.

A national priority?

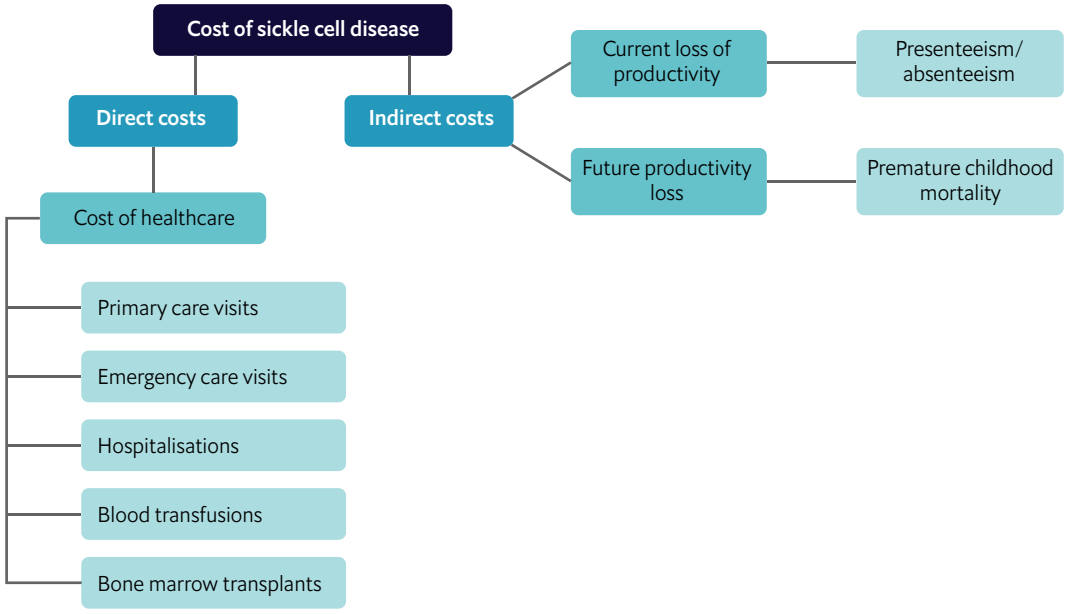
"When I'm stuck in hospital, my day to day work suffers. Business is stopped… my education is impacted. There's also a lack of family support, as no family members are able to support me during the crisis."

Sickle cell disease patient

Shining a light on the impact of sickle cell disease

Sickle cell disease hits the weakest and vulnerable, lending a strong moral case for action. Here we ask what impact the disease has on the healthcare system and wider society. Calculating the economic impact of a disease involves understanding both the direct and indirect costs of the disease. Direct costs are those that are met by the healthcare system: for sickle cell disease these include the cost of screening, primary and emergency care visits, hospitalisations, blood transfusions and bone marrow transplants. Indirect costs are those met by families and wider society. We have estimated two kinds of indirect costs. The first is due to lost productivity as a result of parents' missing days of work to look after their children. The second is the future loss to the economy as sickle cell disease deaths mainly occur in children and early deaths erode the future workforce (**Figure 6**).

Figure 6: Major contributing factors to direct and indirect costs of sickle cell disease



Source: The Economist Intelligence Unit.

A significant barrier to understanding the economic burden of sickle cell disease in India comes from the lack of a standard patient pathway to see where direct costs are accrued. The care pathways in **Figure 5** provide an overview of how sickle cell disease patients move through the health system and

where differences occur in urban and rural settings. Rural patients are mostly identified by screening programmes at community or primary health centres, or at programmes run at schools. Although local level screening programmes that encourage premarital screening exist, the associated stigma results in low uptake. Patients may also be identified when presenting with symptoms at a community health centre: commonly a pain crisis, anaemia or fever.

The burden on the healthcare system

The patient pathways allow us to estimate where the majority of direct costs accumulate. For primary care visits, costs are accrued from medications such as penicillin prophylaxis and pain medications (acetaminophen, ibuprofen and opioids). Costs of emergency visits are associated with the management of complications—such as pain crises—where hydroxyurea medications add to the cost. Blood transfusions include costs from serum ferritin monitoring and chelation therapy, and bone marrow transplantation costs vary depending on the donor. Unrelated donors tend to be more expensive compared to a related donor, such as siblings, which is less expensive and thus more common. Aside from procedure related expenses, iron chelation also adds to the costs.

Previous estimates have found that, without taking into account costs of transfusions and managing pain crises, annual healthcare costs including penicillin prophylaxis are about 3,000 rupees per child.[38] Data based on estimated costs from 2008 for transfusions and iron chelation found that, for a child weighing 30 kg, the costs were 200,000 rupees per year.[39] Additional costs result from hospitalisation and emergency and outpatient visits.[40]

Data on spend from the 2015 survey on Social Consumption **(Table 3)** offer cost estimates for general blood diseases and infections. Though this data aren't explicitly attributable to sickle cell disease, they give a broad insight into costs for related disorders. Cost estimates for infections have also been reported due to patients' increased risk.[41]

Table 3: Cost estimates for general blood diseases and infections

	Average medical expenditure per hospitalisation case (Rupees)		Average total medical expenditure for non-hospitalised treatment per person (rural / urban) (Rupees)			
	Public	Private	Public		Private	
			HSC / PHC and others	Public hospital	Private doctor clinic	Private hospital
Blood diseases (including anaemia)	4,752	17,607	290 / 119	1507 / 1150	846 / 761	979 / 2432
Infections	3,007	11,810	262 / 456	338 / 193	477 / 533	727 / 782

Source: Key indicators of social consumption in India Health 2015 (can download the report from here)[42]

Many patients present with symptoms associated with complications such as pain crises. Depending on the type of hospital that a patient may visit, there is a big difference in cost. In 2010-11, a visit to an outpatient department ranged between 94 rupees and 2,213 rupees, a visit to an emergency department fell between 385 rupees and 21,873 rupees, while the cost of a bed day in an inpatient department was between 345 rupees and 6,996 rupees.[43] Charitable district hospitals are in general cheaper, while private hospitals are much more expensive; however in rural areas, patients often have little choice of which hospital to travel to.

Blood transfusions are often required to provide the patient with normal red blood cells, reducing the percentage of sickled red blood cells. **Table 4** shows the regulated price of drugs, although it is reported that many blood banks do not follow the restrictions and charge significantly higher prices.[44]

Table 4: Approximate cost of regulated drugs under government and non-government blood banks.

	Rupees	USD
Non-governmental blood banks	1450	21-25
Governmental blood banks	1050	15-18

Source: Access to safe blood in low-income and middle-income countries: lessons from India[44]

Finally, although bone marrow transplants are the only known cure for sickle cell disease, their high cost makes them unaffordable for many. The Government's 2016 guidelines on hemoglobinopathies estimate that a haemotopietic transplant would cost 1.4 million rupees per patient, roughly US$19,500.[3]

Estimating indirect costs

Sickle cell disease deaths result in future losses in the economic output of countries due to the erosion of the workforce. We have estimated future GDP losses attributable to deaths from sickle cell disease in one year (2017), based on the method of Kirigia and Muthuri (originally used to estimate productivity losses associated with TB deaths).[45] We believe that the methodology can be applied to analyse the losses attributed to sickle cell disease because the disease predominantly affects young people, causing early mortality.

We calculated the number of life years lost from sickle cell disease in each age group—1-14 years of age, 15-59 years, and 60 years and over—to understand how sickle cell disease affects the future and current labour force **(Table 5)**. We applied a 3% discount rate to the number of years to calculate the non-health GDP losses from deaths in 2017. Due to uncertainty in prevalence figures, we have calculated the losses using both estimates from the GBD and the Government of Gujarat. Since the number of annual deaths wasn't available from the Government of Gujarat's figures, we have extrapolated the mortality rate from the GBD. Using the GBD data for 2017, we estimate that deaths attributed to sickle cell disease will result in future GDP losses of approximately US$139 million (900 crores). The same calculation using the Government of Gujarat's figures leads us to estimate a loss of US$169 million (1100 crores). However, both these sets of figures are likely to be underestimated due to underreporting.

Table 5: Indirect cost estimate from the lost of life years due to sickle cell disease

Age bracket	Number of deaths	Non health GDP loss (USD)	Non health GDP loss (Rupees)	Number of deaths	Non health GDP loss (USD)	Non health GDP loss (Rupees)
0-14	1,544	81,667,705	5,318,329,576	1,872	99,045,354	6,449,989,442
15-59	1,415	57,351,548	3,734,823,134	1,716	69,555,088	4,529,536,875
60+	2	37,856	2,465,242	3	45,911	2,989,770
Total	2,961	139,057,109	9,055,617,953	3,591	168,646,352	10,982,516,088

Source: Estimated from mortality data from GBD and the Government of Gujarat.[3, 13]

Sickle cell disease also causes productivity losses through lost days of work. Although sickle cell disease mainly affects children, losses attributable to parents and carers' lost days of work have to be taken into account as absenteeism is associated to loss of GDP. Thus, we have calculated a range of costs on productivity losses **(Table 6)**. We used prevalence estimates from both the GBD study and Government of Gujarat. The prevalence was applied to the proportion of parents who had their work affected to estimate the number of parents affected. In absence of India specific data, we obtained the proportion of parents affected from a Nigeria based study. Here, the study found that 56.8% of parents lost between 1 and 48 work days to look after their child, while 2.7% of parents had lost their jobs (a total of 251 days of lost work).[46] We assumed the GDP contributed by a working person per working day to be US$21.20. Overall, the total productivity loss, considering the average work days lost and a loss of job, would give a range from US$ 484.6 million (3155.8 crores) to US$587.7 million (3827.2 crores).

Table 6: EIU calculation of indirect costs due to lost days of work from sickle cell disease

Number of working day(s) lost	Rationale of using the corresponding working day(s) lost	Productivity loss estimates			
		Total costs (US$)		Total cost (Rupees)	
		GBD	Government of Gujarat	GBD	Government of Gujarat
1	Minimum possible number of work day lost	13,301,635	16,132,021	866,223,435	1,050,542,637
48	Maximum possible number of work days lost	638,478,490	774,337,024	41,578,724,886	50,426,046,570
24.5	Average work days lost	325,890,063	395,234,523	21,222,474,160	25,738,294,603
251	Assume loss of job	158,706,306	192,476,600	10,335,204,612	12,534,379,314

Source: GBD and the Government of Gujarat

The overall burden: bigger than it seems?

How much does sickle cell disease cost India? The short answer is, we don't know. Data limitations mean that any attempt to provide a single number will likely be far from the truth. However, we can estimate from the above calculations and data points where the main costs are likely to fall. Multiplying up the figures from tables 3, 4 and 5 with the epidemiological data presented in the previous chapter suggests that national primary care costs for people with sickle cell disease are likely be in the tens of millions of dollars, while hospital visits and emergency care add up to hundreds of millions. Indirect costs are also in the hundreds of millions per year.

The impact of these costs is not merely financial. Compared to sickle cell disease, other conditions cost more: conditions such as heart and respiratory diseases, diarrhoea, cancer and tuberculosis. But the impact of sickle cell disease is acutely felt by the poor and disadvantaged, and the condition is life-long, with little hope of seeing an improved quality of life. Coupled with these realities is the stigma and isolation that so many sufferers have to face.

India's policy response

"A major problem is with pain management. Often with a Tramadol capsule there is no effect after two hours, but then the doctor will only use an injection of it after 6 or 8 hours observing the pain. Some doctors deny me an injection as it might damage on kidney. I then have to force them to give me the injection."

Sickle cell disease patient

The prevention and control of haemoglobinopathies draft policy, 2018

The Ministry of Health and Family Welfare of India drafted a policy on prevention and control of haemoglobinopathies in 2018, including sickle cell disease and thalassemia.[1] Given state-level variation in disease burden and healthcare infrastructure, the policy guidelines recommended being adopted in different states with the necessary modifications. The policy 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.[47] Existing public health facilities are expected to provide services through a hierarchical infrastructure, including the development of centres of excellence to meet advanced care requirements. Recommendations include training healthcare professionals, forming haemoglobinopathy units in government medical colleges and tertiary care centres, and the development of innovative technologies to improve early detection in rural areas.

The policy recommends creating improved information about sickle cell disease through the National Health Portal, and the establishment of a patient registry to keep track of how sickle cell disease affects patients. There is a recognised need for a multi-disciplinary approach to include patients, academic institutions, the healthcare industry, non-profit organisations and parent support groups. The policy advocates providing medications to cover vulnerable patients at no or reduced cost, and supports the wider development of excellence in sickle cell disease in India. Innovative treatment and diagnostic methods are supported by encouraging research and development within the country.

Screening programmes: today and tomorrow

India has already implemented a range of regional sickle cell programmes in high burden states, including Chhattisgarh, Gujarat, Maharashtra and Odisha **(see figure 7)**. Programmes include prenatal, neonatal and premarital screening and counselling. The draft policy plans to push the screening programme out further. Carrier screening is a specific programme that focusses on the prevention of the disease through early detection, although there is a need to raise community awareness in order for such screening programmes to be accepted. Prenatal diagnosis is offered to carrier couples to reduce the likelihood of a child being born with a clinically severe form of the disease. Neonatal Screening is relatively recent, with pilot screening programmes that started in 2008; there are only six published reports on neonatal screening in India across five states.

Screening programmes are set to be extended to include premarital screening and the screening of students. Adolescent students have been targeted for screening, to allow informed decisions to be made around marriage. Although the effectiveness of such programmes has not been studied, they have provided records of clinical presentations such as severe anaemia, infections, pain and acute febrile illness.[22] Efforts to expand screening programmes are supported by the strengthening of information infrastructure to handle large scale clinical data through electronic medical systems.

Large-scale data management in Chhattisgarh

Chhattisgarh has created efficient management and analysis tools for the data its sickle cell programme has generated over the years. The state has implemented two main electronic systems: 1) the State Wide Screening Data Interface (SWSDI) to manage data from screening programmes and 2) the Sickle Cell Patients Temporal Data Management System (SCPTDMS) to handle patients' data at outpatient departments.[23] As of April 2015, the screening interface had data from 1,294,558 subjects; 121,819 were found to be carriers and 4,087 had the disease. The data management system had records from 3,760 individuals, including 923 sickle cell disease patients and 1,355 sickle cell carriers.

The screening interface has helped Chhattisgarh to efficiently track sickle cell disease prevalence in the state and analyse the demographics of the condition. Complementing the screening data, the state's data management system keeps track of clinical information. These include signs and symptoms, medications administered and their effectiveness, and laboratory diagnostic data. These data management tools help plug holes in the data gaps that are so commonly found in sickle cell disease in India, and may serve as a model for elsewhere.

Public-private partnerships in Gujarat

In 2006, the Sickle Cell Anaemia Control Programme was initiated in five districts of South Gujarat under a public-private partnership strategy by the Department of Health and Family Welfare. The programme was later extended to 12 districts and The Gujarat Sickle Cell Anaemia Control Society established.[30] Since the society was formed, state screening programmes continued to diagnose increasing numbers of sickle cell patients.

The increasing awareness of the burden of sickle cell disease in the state revealed a growing challenge: how to improve access to quality care for people from poor and vulnerable rural areas. To address this challenge a Sickle Cell Comprehensive Care Programme was initiated by SEWA Rural, a voluntary development organization, to deliver quality healthcare services in resource-restricted settings in rural South Gujarat.[48] This non-profit programme, supported by the Government of Gujarat in partnership with private organisations, employed a comprehensive care model delivering simple, cost-effective interventions. These included education initiatives, screening, standardised outpatient and inpatient care—such as prophylactic penicillin, regular follow-up and treatment with hydroxyurea for severe cases—through its 150 bed sub-district hospital. Patients were given the pneumococcal vaccine, monthly folic acid supplements, pain killers and blood transfusions for free. SEWA Rural has had a tremendous impact on improving health outcomes of the community, including a 90% reduction in maternal mortality and 75% reduction in neonatal mortality.[49]

Figure 7: Sickle Cell Disease control programmes in India

State 1- Gujarat	
Total number Screened	55,510,494
Confirmed Cases	29,584
Initiated in (year)	2006
Type(s) of screening	New born , adolescent, prenatal, Mass screening
Population coverage	All Tribal population

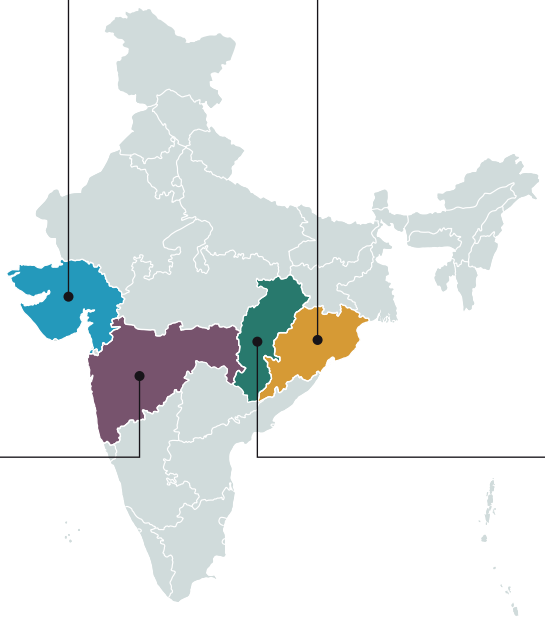
Other initiatives include:

Ongoing work of the Gujarat Sickle Cell Anaemia Control Society by SEWA Rural and the inclusion of sickle cell screening in annual "Mamta Divas", special immunisation days hosted in villages in tribal areas.

State 3- Odisha	
Total number Screened	11,062
Initiated in (year)	2010
Type(s) of screening	Mass screening
Population coverage	All Tribal and Non-Tribal population

Other initiatives include:

The provision of newborn screening programmes and the free-to-access treatment facilities, including for bone marrow transplant.



State 2- Maharashtra	
Total number Screened	95,543,493
Confirmed Cases	6267
Initiated in (year)	2007
Type(s) of screening	Antenatal, adolescent, Mass screening
Population coverage	Target age group 1 to 30 years, Pregnant women, family members, Symptomatic individuals of all ages

Other initiatives include:

A range of state level innovations, including day-care centre facilities, sickle cell counsellors, provision of HPLC, telemedicine, and screening of schoolchildren and Anganwadi children (a type of rural child care centre).

State 4-Chhattisgarh	
Total number Screened	1,050,440
Confirmed Cases	2742
Initiated in (year)	2007
Type(s) of screening	Mass screening, adolescent
Population coverage	Children age group 3 to 15 years

Other initiatives include:

The implementation of electronic systems such as the State Wide Screening Data Interface (SWSDI) and Sickle Cell Patients Temporal Data Management System (SCPTDMS). In 2014 the state produced a "Handbook on Sickle Cell Disease", setting out guidelines on recognition, management and couselling.

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Adopting disruptive innovation

The lesson from SEWA Rural is that relatively simple, cost-effective interventions, delivered at the right time and place, can massively improve sickle cell outcomes. This should form the bedrock of future initiatives in India. However, the reality is that care often fails to reach sufficient quality standards. For example, timely diagnosis is often hindered by a lack of diagnostic equipment in rural laboratories. When the diagnostic kit does exist, its operation requires expensive and trained laboratory personnel, who are often unavailable.

New and innovative technologies can mitigate these challenges and disrupt the entire care pathway. An emerging diagnostic technology is the HemoTypeSC, a rapid and affordable point-of-care (POC) tool. Its deployment in remote tribal areas has shown promising results, correctly detecting sickle cell hemoglobin using a droplet of blood. The device has the potential to be used for bedside screening at primary health centres without requiring the complex, expensive equipment that is in short supply.[50] Portable devices and personalised technologies have the potential to transform care for people with sickle cell disease.

In addition to innovative devices, novel treatments are also being developed. There are no less than 17 new medicines currently being developed for sickle cell disease, produced as a result of an improved understanding of genetic diseases.[51] These include potentially curative cutting-edge gene therapy technologies, which replace the defective haemoglobin gene with a corrected gene. This approach effectively turns patients into carriers. Another development is a monoclonal antibody that has been shown to reduce the number of painful vaso-occlusive crises.[52] Further therapeutic options are being developed with the application of antioxidant agents, which have been found to reduce pain crises when used with or without hydroxyurea.[53]

While many of these innovations are not immediately going to impact practice in India, they will increasingly become available, and they have the potential to revolutionise sickle cell management. Health systems in India need to be aware of global trends, and prepare how they will ensure the sustainable and equitable distribution of these new technologies.

Barriers to progress

"The government should follow initiatives such as seen in Chhattisgarh. There are 2.5 Lakh patients with sickle cell disease and now two more diseases have become common: thalassemia and haemophilia. Blood transfusions are required."

Sickle cell disease patient

Urban and rural patients remain a world apart

Two distinct groups of sickle cell disease patients exist in India: urban and rural. They have their own challenges and unmet needs. Generally, urban patients have a poor understanding of the disease and are unaware of the need to attend screening. Furthermore, the focus of screening programmes in urban areas is often on haemophilia and thalassemia, not sickle cell disease. Regardless of what it's for, urban patients tend not to attend such screening programmes. This leads to diagnostic delays—often at a crucial time, when swift action could be most beneficial. Dr. Roshan noted that "in urban areas, most patients don't go for screening and most screening programmes are focused on other hemoglobinopathies. They normally present with symptoms at district hospitals."

In remote tribal or rural settings it is more difficult for patients to visit healthcare centres. Access to even basic health facilities is challenging, resulting in low screening rates and poor follow-up. Some large tribal populations, such as in Jharkhand and Madhya Pradesh, have no access to even basic health services. Late diagnosis is common, and patients have typically suffered greatly before sickle cell disease is confirmed. While there are empowerment programmes targeted at tribal populations, sickle cell disease is rarely a focus area, although the Ministry of Tribal Affairs may be able to mitigate some of these challenges by investing in mobile health services. Screening programmes have lacked focus on particular sub-populations and have consequently missed vulnerable age groups. There is also a lack of prenatal screening.

Late diagnosis and loss to follow-up is commonplace

Because disease understanding is poor, most patients only visit a clinic when they're unwell. Much of the suffering associated with sickle cell disease is therefore unnecessary. Moreover, in remote regions of India there are typically not enough sufficiently trained healthcare providers able to diagnose patients or provide acceptable levels of care. Many tribal patients are poor, and so unable to travel for higher quality treatment. Thus, with poor reachability, financial constraints and lack of awareness, tribal patients regularly miss follow-up appointments. "In Chhattisgarh, some patients come directly to the clinic, travelling distances of 200km or more—however, the loss of wages is their main concern", reported Dr. Agrawal.

But it's not only physical remoteness that is a concern. There is also a sense of resignation among some patients. Dr. Ratna Devi, 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."

Staffing and equipment at primary health centres are often missing

Sickle cell disease requires specialist care, and the disease is sometimes misdiagnosed in non-specialised centres. It's not only a lack of manpower and experience in primary health centres that leads to misdiagnosis; functional equipment is also often missing in action, and machines to perform procedures such as complete blood count may be broken. "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" reported Dr Roshan.

Primary care physicians are therefore often unable to manage a pain crisis or the typical needs of a sickle cell patient. And when they refer patients to a district hospital, the nearest could be hundreds of miles away. Well-off patients may choose to travel to a nearby private hospital for treatment: although the treatment they receive there often just hides symptoms, and may actually worsen the condition, for which they are eventually referred to district hospital. Even in district hospitals there may not be a haematologist, and a general physician instead manages the case. Finally, the patient may be sent to a medical college hospital. In short, poor management results in delays and can cause many patients to experience complications, sometimes leading to life-long disability.

A lack of staffing also impacts screening programmes, which tend to be labour intensive. Antenatal screening in rural locations is hard to deliver as facilities require gynaecologists and obstetric facilities. Healthcare professionals and counsellors—backed up by robust data management systems—are then needed to ensure that patients with positive screens are followed-up for treatment. With these logistical challenges, mass screening campaigns have historically had limited success in India.

Sickle cell disease remains a low priority

The haemoglobinopathies draft policy from 2018 has yet to be implemented. The major challenge is funding. The government is currently consulting stakeholders in order to publish a revised version of the policy. Although there is little clarity on timelines, progress is anticipated to take place in 2020. While funding is an important issue, another obstacle is the need for sickle cell disease to be recognised as a public health challenge. Thalassemia and haemophilia have recently received attention, through allocated funds from the central government, due to successful campaigning by non-profit organisations and patient groups. Aspects of sickle cell disease could be prioritised in a similar manner.

The need for a greater priority to be placed on sickle cell disease by policy makers was supported by a number of interviewees. Dr Tulika remarked that "India had faced and is still facing disease burdens from infectious disease and non-communicable diseases year on year. Currently, policymaker focus has included hemoglobinopathies and sickle cell disease, however there is still more that can be done". She also noted that lessons from other countries should be considered. For example, in Italy there is a programme to control the number of babies with thalassemia. She explained that "similarly, if we have good programmes, we can improve the quality of life of sickle cell disease patients. It is important to continue pointing out the disease burden so that things will progress forward. The policy must also be rolled out in a timely manner to allow patients to benefit."

Roadmap to success

"I used to have to go every two or three months for a blood transfusion. Now with the treatment centre available I don't need to go so often..."

Sickle cell disease patient

India needs to take steps to better understand the burden of sickle cell disease, reduce its incidence, and improve outcomes and quality of life for people with the disease. Although plans under development are welcome, such as the policy for haemoglobinopathies, more can be done. Paying attention to the following priorities would help ensure policy progresses in the right direction.

1 Recognise sickle cell disease as a priority	2 Strengthen implementation at national and state level	3 Adopt innovative technologies and processes
• **Tackle** stigma • **Improve** data collection • **Expand** screening programmes	• **Improve** and implement the 2018 draft policy • **Invest** in local infrastructure • **Strengthen** centres of excellence	• **Work** with local and global innovators • **Embrace** disruption • **Recognise** that the treatment and diagnosis landscape in sickle cell disease is changing

Recognise sickle cell disease as a priority

Sickle cell disease has typically been under the shadow of thalassemia and other haemoglobinopathies: it needs to be recognised as a public health issue in its own right. In practical terms this means there needs to be a suitably resourced national programme, supported by capacity building at the local level, so that states can deliver localised plans according to their specific needs.

One of the first priorities must be to improve the quality of the conversation around sickle cell disease. Stigma is found in the general public and even among family members, hampering the implementation of programmes such as pre-marital screening. Building on lessons learnt from Gujarat's programmes, the media should be used to help raise awareness of the seriousness of sickle cell disease. Awareness can and should start at an early age, with credible educational material about sickle cell disease being incorporated into the school curriculum. The biggest investment needs to be made in rural communities: unless awareness is increased, prevalence will continue to rise.[16]

Accompanying school and prenatal screening programmes, there is the need to continue to improve new-born screening. This will not only help earlier identification, but also collect incidence data. Certain states, such as Chhattisgarh and Gujarat, have already expanded their screening programmes from hospital to school-based screenings. Extrapolating such screening efforts and implementation strategies to other states will help map the prevalence of the disease.

Understanding burden and policy impact requires the collection of data on matters such as incidence, numbers of hospitalisations and vaso-occlusive crises. While some of these data are collected at local level, methods vary between states. There needs to be a commitment to measuring a minimum set of standardised outcomes, with well-defined methods for their collection. Indicators like hospitalisation and mortality rates, though important, only reveal part of the picture of living with a chronic disease. In order to design effective outcomes measures it is necessary to engage patients and their families through focus groups or patient councils.

Data collection through registries could also improve follow-up. Gujarat's experience emphasises the need for an integrated sickle cell disease management strategy. Improvement in health data capturing was witnessed with the use of Aadhar, India's 12-digit identification number, to link screening camps to other levels of healthcare such as primary health centres, district hospitals, medical colleges and sickle cell disease centres of excellence. Similarly, Gujarat hospitals have also established web-based records of all patients; as a result, Gujarat experiences a (relatively) low rate of 25% lost to follow up.

Strengthen implementation at national and state level

National and local policies are a good start. But they need strong implementation and rigorous evaluation to understand their impact on patients. While the 2018 draft policy draws upon the success of many regional interventions, stakeholders have noted that gaps remain, including how local and state level actors will work together. Other concerns include the need for impact assessments of sponsored programmes, involvement of patient groups in policy decisions, and addressing quality of life. The policy also needs to clarify how it will raise awareness about the disease and its burden on individuals and their families.

Sickle cell disease policy implementation must be recognised as a priority by state governments—particularly those in the sickle cell belt. Technical equipment and medications should be provided at the most local level possible, with referral centres being used only for complicated cases and research purposes. The supply of basic treatments and expertise at district hospitals would often remove the need for patients to travel hundreds of miles to a centre of excellence.

The availability of funding was identified by interviewees as a primary challenge facing policy implementation. Innovative strategies, such as public-private partnerships, could alleviate such concerns. This model is being utilised in Ghana.[54] Dr Tulika noted that "funding investment to advance healthcare facility infrastructure should be considered so patients don't have to travel across states to receive good quality of treatment."

Dedicated sickle cell disease centres, or centres of excellence, play a pivotal role in providing technical support for all levels of care. Such centres are more developed in some states than others. They should support the implementation of other initiatives, such as state-level screening programmes and patient registries. Each state should minimally have one sickle cell disease centre; more could be developed depending on the local disease burden. Alternative arrangements could be considered in cases of budgetary constraints, such as the collaboration of hospitals and laboratories to share resources.

Adopt innovative technologies and processes

Because sickle cell disease has historically been neglected, there has been little in the way of innovation. This, however, is changing. There are on-going research programmes conducted by the Government and private organisations that offer innovative ways of managing the disease. Current programmes include the Mobile Application based health program (TeCHO-Plus) in Gujarat state and the Sickle SCAN for diagnosis of sickle cell anaemia.[55] Many of these technologies are home grown: Dr Desai remarked that "we have developed mobile apps by partnering with government and an IT provider to develop mobile apps to provide care in tribal areas, focusing on maternal, child and adolescent care."

Fast and easy to use, diagnostic point of care tools are increasingly being introduced in primary care facilities. Supporting the provision of portable and mobile health technologies into the primary healthcare system will increasingly remove the need for patients to make regular visits to far-flung centres of excellence. These innovations, backed up by the delivery of simple but effective packages of care interventions, will improve sickle cell outcomes.

Aside from point of care tools, new and exciting drugs are in the pipeline, driven by an increased understanding of the disease. These include gene and cell therapy, humanised monoclonal antibodies and antioxidant agents. In addition to planning how the country will adopt and fund these developments, in a sustainable and equitable manner, India should also take an active role in collaborative international clinical trials.

Taking the first steps

"With the establishment of the specialised centre, my hospitalisation visits are reduced and medicine is available for free".

Sickle cell disease patient

Sickle cell disease is a major health issue in India that is both neglected and largely undocumented. The burden is not evenly spread, with the disease highly prevalent in the poor and relatively isolated tribal and scheduled populations in central and western regions. While survival rates have improved since 1990, access to the health system is inequitable, and the impact of the disease on the day to day lives of sufferers remains unknown. Stigma remains commonplace. Finally, estimates of the cost of the disease remain hampered by a lack of standard patient pathways to grasp where direct costs are accrued.

Issues such as social stigma, rural isolation, staffing pressures and support for the poor, will not be solved overnight. However, a number of principles of good practice emerged from the research, and we have laid out a draft "roadmap to success" in India. While not a detailed policy programme, it describes the building blocks around which a sickle cell policy programme in India could be designed.

The delayed implementation of the 2018 draft policy on haemoglobinopathies is acting as a barrier in the bid to ensure that sickle cell disease is recognized in India as a public health challenge. Such recognition is a priority. Once national policy moves, it then needs to be adopted at state level, especially in states with high burden. While much can be learnt from overseas experience, there is already good practice in India.

We set out in **Table 8** how some components of the roadmap might be taken forward: the first steps to success. While there is much to applaud in India's response to sickle cell disease, particularly at state level, the condition continues to blight people's lives. Much of this suffering is avoidable, and we believe that there is both an economic and moral case why more can, and should, be done.

Table 8: The main actions required, justification, and examples of supporting activities

Action	Why?	What's to be done?
Recognise sickle cell disease as a priority	Sickle cell disease affects over a million people, affecting rural populations the hardest	Implement an improved version of the 2018 draft policy without unnecessary delay
Ensure effective policy implementation	To have an impact, the national policy has to be effectively implemented via adequate resourcing and political prioritisation	Set up a central office to oversee implementation and ensure adequate support is provided to states. Where there are budget constraints, public-private partnerships could be considered
Coordinate nationally; implement locally	National policy can improve public health goals only if effective treatment and preventive measures are implemented at state level	The draft policy for haemoglobinopathies should continue to supported by state-level organisations
Support stakeholder collaboration	A holistic approach is needed to fill knowledge gaps, especially as sickle cell disease has historically been neglected	In addition to policymakers and healthcare organisations, an alliance should be formed that also include patient groups, counsellors, academics, industry and the media
Increase awareness and reduce stigma	Social stigma delays patients seeking care and discourages people attending pre-marital screening programmes	Raise of awareness through evidence-based information both in schools and through national and local media channels
Focus on rural and tribal populations	Difference in pathways exists between rural and urban patients, with rural patients facing more delays	Equip local primary health or community health centres with resources and trained staff to ensure care is not delayed
Inform via data collection	India suffers from incomplete epidemiological data, plus loss to follow-up a major issue	Record patient information at healthcare facilities and screening sites – this could be done through Integrated sickle cell disease management with improvement in health data capture by using (e.g.) Aadhar
Expand the screening programmes	Early detection of sickle cell disease vastly improves mortality rates and reduces the number of pain crises	Hospital and community based screening should be supported to expand within and across states, including pre-natal and new-born screening
Establish dedicated sickle cell disease centres	Advanced facilities can provide comprehensive care to hard-to-treat patients	Centres should be supported with sufficient equipment and help co-ordinate training programmes for primary healthcare professionals
Provide patient (and family) centred care	Patient needs varies, such as with different age groups and location	Treatment needs to be delivered in a timely manner and complications better managed. Patient priorities need to be understood and acted upon
Innovate in care and diagnosis	Disruptive technologies can improve quality of life and have the potential to save money	India should take a more active role in international trials and build up a reputation of being an supporter of innovation

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Appendix: Methods for calculating indirect cost

Estimation of future non-health GDP losses due to early mortality

To calculate the future losses to the economy due to a single year of deaths from sickle cell disease in India, we followed the method from Kirigia and Muthuri, which used a human capital approach. This method calculates the amount that a person could have contributed to the economy in terms of non-health GDP had they not died prematurely. These losses in the macroeconomic outputs of countries result from the erosion of future labour and productivity, as well as the reduction in investments in human and physical capital formation.

The key variables utilised in these calculations and their sources included (most recent available data used):

- Deaths from sickle cell disease by age (0-14, 15-59 and 60+)
- Life expectancy at birth
- GDP per capita
- Health expenditure per capita
- Key assumptions
- People's contribution to GDP starts from age 15+ and continues throughout their lifetime
- The rate used to discount future losses was 3%
- The average age of death being the mid-point of the age bracket
- Non-health GDP is calculated by subtracting health expenditure per capita from GDP per capita

Estimating the annual indirect impact on the economy of working days lost owing to receiving treatment for sickle cell disease.

Over 90% of sickle cell disease suffers are under 20 years old and so we have quantified the number of days parents have lost from work to care for their child. We estimated the number of parents that had lost days of work by taking the findings from a study based in Ekiti, Southwest Nigeria which aimed to calculate the financial burden of sickle cell disease on households in the area. One of the findings was that of the 111 patients followed, parents of 63 children lost between 1 and 48 working days due to their child's heath, and 3 parents lost their jobs. These figures were multiplied by GDP per employed person per working day to calculate the cost from losing one day of work because of treatment for their child's sickle cell disease.

Data for the labour participation rate, labour force, GDP estimates and population figures came from the World Bank. We assumed 251 working days in a year in 2018.

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