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A Framework for Enabling Predictive Genomics to Improve Public Health in India

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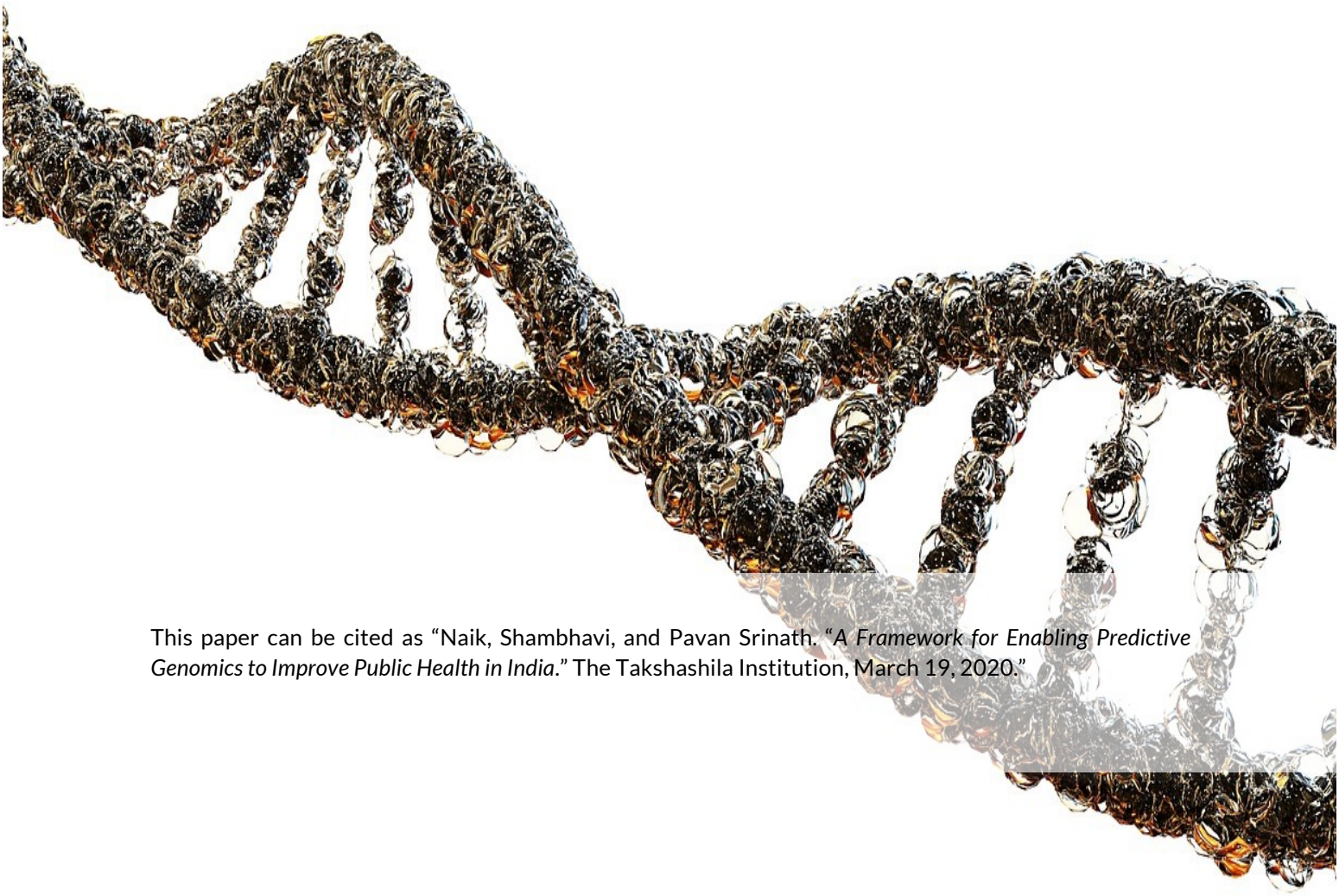

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Executive Summary

Heritable genetic diseases, particularly rare diseases, contribute to a significant disease burden in India. In India's urban areas, congenital malformations and genetic disorders are the third most common cause of mortality in newborns[1]. Rare diseases by themselves are expected to afflict 70-96 million Indians currently.

Guided by a few core principles, this document provides a governance framework for collecting, analysing, and prioritising genomic data for engineering diagnostics and therapeutic solutions. At an estimated cost of INR 1600 crore per year over the next 5 years the "Indian National Genome Project" is made up of the following steps:

1. **Seeding the National Genome Platform with the full genome sequencing of 1 million Indians –** this seeding will represent the approximately 5000 genetic sub-populations present in India. There are provisions for co-opting private players to leverage existing infrastructure for completion of the sequencing exercise.

2. **Developing and Maintaining a National Genomic Database as Public Infrastructure -** anonymized and annotated data to be made publicly available. This would ensure access and effective use of the data by multiple players for designing diagnostic/therapeutic products.

3. **Governing outputs from the National Genome Platform –** the project will lead to vast amounts of data. The document presents two frameworks to prioritise diseases for diagnostic/therapeutic product development through publicly funded projects.

On the genetic front, India comprises over 5000 sub-populations and individual sub-populations may be pre-disposed to specific diseases. A comprehensive study of the genetic layout of these sub-populations would reveal their disease predispositions and help make informed decisions on preventing or managing disease outcomes. A publicly funded database of the genetic data at the sub-population level would help make correlations between genetic mutations and diseases and also create diagnostic/therapeutic solutions. The resulting public awareness about genetic diseases and creation of solutions would lead to reduced healthcare issues and costs. This would further improve productivity, standards of living, and greatly contribute to India's GDP.

This document presents a template which funding agencies could use for creating their own governance frameworks, both for collecting data and making the data publicly available. The data can inform on disease predisposition and enable Indian citizens to make more informed decisions on their health in the future.

Background

Improvement in public health has many positive implications for India – increased human productivity (through reduction in sick leaves), poverty mitigation (through reduced personal expenditure on healthcare), improved standard of living (through promotion of preventive self-care) and overall growth in GDP (through reduced healthcare expenditure compounded by increased productivity).

At 1.28% of GDP[2], India's public health spending is one of the lowest in the world – this includes both maintaining public health and healthcare spending. Apart from this, more than 60% of the healthcare costs are paid by consumers out-of-pocket[3]. Patients prefer spending on private healthcare leading to Indians being the sixth biggest out-of-pocket health spenders[4] in the low-middle income group of 50 nations. A study[5] reported that about 55 million Indians were pushed into poverty every single year because of having to pay healthcare costs and 38 million fell below the poverty line from spending on medications.

Precision medicine is fast becoming a gold standard for targeting diseases and this is particularly relevant to genetic diseases that are driven through mutations in single genes. Genetic and congenital abnormality is the second most common cause of infant and childhood mortality and occurs with a prevalence[6] of 25-60 per 1000 births in India.

Precision medicine involves identifying the genetic drivers of a disease through analyses of large, curated genomic databases and creating specific therapeutic strategies to target the underlying causes. Table 1 provides an overview of other countries who have invested in setting up a healthcare related genomics database.

Country	Project Name/Year of Launch	Target Number of Genomes	Target population	Total Allocated Cost
UK	100,000 Genome Project	100,000	NHS patients	$408.4 million
Japan	Initiative on Rare and Undiagnosed Diseases, 2015	2000	Rare diseases	$5.4-$6.3 million
China	100,000 Genome Project, 2017	100,000	Not specified	$13.2 million
Australia	Australian Genomics Health Futures Mission	Not specified	Rare diseases	$370 million
Saudi Arabia	Saudi Human Genome Programme, 2013	100,000	Normal and diseased	$200 million
USA	All of Us Research Programme	100,000	Across population groups	$130 million
Estonia	Personalized Medicine Programme, 2016	100,000	Across population groups	$5.8 million for 2018
France	France Génomique, 2016	Not specified	Rare diseases and cancer	$782 million
Turkey	Turkish Genome Project, 2018	100,000	Across population groups	Not specified

Table 1: Countries which are investing in developing national genomics databases.

Two Indian governmental funding agencies – CSIR and DBT- have announced their inclination to create an India-wide genome repository with the purpose of uncovering disease prevalence and origins. While the DBT[7] project is yet to start, the CSIR project, christened IndiGen[8], has sequenced 1008 genomes in its aim to cover 10,000 Indian genomes. The genomes have so far been sourced from volunteers from across India.

Precision medicine[9] is much easier to accomplish in monogenic diseases (where disease is caused by a single gene mutation) such as thalassemia. However, this causality relationship is more complex in conditions that arise because of polygenic defects – aging-related conditions or cardiomyopathies for example. Ongoing research will create necessary tools and scientific knowledge to explore such polygenic disorders in the near future.

However, currently it is possible to determine the molecular basis for a range of genetic diseases and this document argues that there is a need to systematically collect and analyse genetic data to prevent, diagnose or cure these diseases.

This document outlines the guiding principles and governance frameworks for the creation of an Indian National Human Genome Platform and its applications. The creation of this platform will create a data repository that could be used for designing diagnostic tools, therapeutics, and lifestyle management practices to improve public health and productivity.

Genetic Disease Burden in India

Various genetic diseases contribute to the genetic disease burden in India. The underlying causes of these genetic disease define their inheritance patterns, ease of diagnosis and treatments.

Types of Genetic Diseases

a. *Single Gene Inheritance* – where the defect lies in a single gene and can be inherited in an autosomal dominant, autosomal recessive or X-linked patterns. For example, cystic fibrosis, sickle cell anaemia, etc.

    i. Autosomal dominant diseases are those where even one mutated gene is sufficient to result in the disease. If such a mutation is lethal, it gets selected out by its very lethal nature.

    ii. Both genes require to be mutated for an autosomal recessive disease to be manifested. As a result, carriers for the disease (individuals who have only one mutated gene and therefore do not have complete disease manifestation) may not be even aware of the mutation and can lead healthy lives.

    iii. X-linked diseases are caused by mutations on the genes contained within the X-chromosome. Since human males have only one copy of the X-chromosome, any defect becomes dominant since there is no healthy sister gene. Females carry two copies of X-chromosome and are therefore, more likely to be carriers for the disease. For example, Hemophilia.

b. *Multifactorial inheritance* – arising out of defects in multiple genes. For example, breast cancer, diabetes, etc.

c. *Chromosomal abnormalities* – caused by malformation of the chromosomes. For example, Down Syndrome, Turner Syndrome, etc.

Presence of founder mutations in genetic subpopulations is one cause contributing to inherited genetic disorders. A cohort of these diseases are autosomal recessive in nature, that is they can be mapped to mutations in the autosomes and they can show phenotype (symptoms) only when both chromosomes contain the mutation. Below, we highlight the evidence for genetic sub-populations in India and present an example of how founder mutations can contribute to genetic disorders.

Identity-By Descent

Identity-By-Descent (IBD) score represents the amount of genetic information shared by individual descendants of a common founder. **Communities which practice endogamy have a higher IBD score than communities which consider mates from outside the group.** Communities with higher IBD also risk sharing genetic mutations which the founder members carry. Any dominant mutation, that is a mutation where a single gene copy can cause disease, usually gets identified and selected out of the population. However, for diseases which are manifested only when both genes are mutated, carriers who do not suffer from the disease continue to exist. The disease will only manifest if two carriers mate and then too at a probability of 1 out of 4 children. When IBD scores are high, there is an increased risk of carrier mutations in the population that could result in a diseased child. A study of India's community groups found 81 groups to have a higher IBD score than those of Ashkenazi Jews – a population that has been extensively studied for its high IBD level[10].

Genetic population and Disease prevalence

An example of founder mutation in genetic subpopulation was highlighted in the case[11] of Vysya community of Andhra Pradesh. Members of the community were discovered to be fatally allergic to some anaesthetic preparations. Further research showed that these members lack the enzyme (butyrylcholinesterase) needed to break down the anaesthetic preparation and hence they could not recover. This community has not seen any major gene flow for 108 generations

and therefore, the observed 100-fold high rate of butyrylcholinesterase deficiency can be attributed to a founder mutation. This is an apparent case for a community's predisposition to a condition, which can now be easily avoided. Doctors recommending anaesthesia to patients of this community now administer other preparations that can be broken down in the patient's body. A simple knowledge of community-spread genetics resulted in a non-invasive strategy that has saved many lives.

Similarly, a thorough study of the genome of various Indian sub-populations can lead to the identification of other genetic diseases which may be rare at the level of national population but are prevalent in the endogamous communities. The knowledge of these diseases can enable communities to take proactive steps to improve health outcomes. The identification of these diseases will underpin a national program of predictive genomics to prevent the birth of diseased children and improve the health of current and future generations in India.

Benefits of Genetic Screening

Pre-emptive genetic screening is the most cost-effective way to reduce healthcare expenses and improve overall health of the society. Autosomal recessive diseases can be prevented through informed mate selection based on genetic screening. Autosomal dominant diseases, X-linked patterns and chromosomal abnormalities can be determined through pre-implantation genetic diagnosis of embryos to identify healthy embryos. The cost of preventing the birth of a diseased child is much lower than the cost of disease management.

For example, consider the case of thalassemia. The cost of genetic screening of prospective parents for presence of mutation associated with thalassemia is roughly INR 20,000. The cost of embryo testing for presence of thalassemia mutation is approximately INR 5000/embryo in addition to the INR 1,50,000 cost for IVF. However, both costs are much lower than the cost of the only known bone marrow transplant which alone costs INR 15,00,000. Additional costs of hospitalisation, blood transfusions and medications make thalassemia management extremely costly. This is true of most other genetic conditions, where treatments, if available, are extremely costly. Thus, the economic argument of how genetic screening can help lower healthcare costs is apparent. In addition, the loss of productivity because of medical conditions can also be alleviated further impacting individual income, savings as well as national productivity.

On the other hand, if genetic screening reveals the presence of mutation in the BRCA1 gene, the affected individual could resort to increased breast screening to ensure that the disease can be diagnosed in the early stages when the probability for treatment and recovery are higher. Further, as gene editing technologies are further developed, it may even become possible to rectify these mutations to prevent genetic diseases.

An excellent case study of the use of informed decision making based on genetic screening is that of Dor Yeshorim. The non-governmental organisation works with teenagers of Jewish descent and helps identify potential pre-disposition of a child borne to tested parents. The exercise has helped eradicate the lethal Tay Sach's disease from two Jewish communities in the United States. Appendix 1 details the operations and principles followed by Dor Yeshorim.

Challenges to Genetic Screening and Databasing

The premise of improved health outcomes is based on the analysis of large genomic and medical databases. Questions relevant to other databases holding sensitive information are also relevant to the genomic database – that is the entity which would house the database, who would have access to the data and how the data will be potentially used. Any attempt to create such a database should address these concerns before collection of data.

Data privacy is of utmost importance and the database should have mechanisms to separately hold sensitive and non-sensitive information. Access to the database should not divulge information that can lead to identification of the sample donor. The consent form should clearly address the use of the data – whether it is only for research or for creation of commercial diagnostic or therapeutic solutions.

Assuming the exercise would need at least one million genomes to adequately cover the various genetic subpopulations, this project will result in massive amounts of data. Since this is a publicly funded project, the data should be made publicly available (*sans* any sensitive information) to optimally use the data set. Mechanisms for researchers and private companies to access the database and share any publications/commercial solutions that arise from the data need to be agreed upon.

There are also thousands of genetic mutations that are co-related with disease prevalence but may not be direct causal factors. As of yet, we have incomplete

understanding of the underlying mechanisms of multiple diseases. While such a database seeks to address this gap in knowledge, premature deduction between mutation and disease without adequate scientific proof should not be made. Thus, it is very important that the data is properly analysed before findings are disseminated. Burdening individuals with the knowledge that they might be at risk of a disease may push them into lifestyle changes or expensive medical tests/treatments that might not be necessary. Thus, any findings from the database need to be carefully validated.

Finally, the biggest challenge to a project of this scale is capacity and training. Capacity will need to be built for sequencing genomes, storage of data sets, and analyses of the data. Clinicians will need to be trained to understand genetic data and interpret the data to best guide their patients on their lifestyle managements or medications.

The case for a Publicly Funded Indian Genome Project

The current cost of whole genome sequencing is INR 1.2 lakhs. This will decrease over time. However, it is still unrealistic to expect all individuals in India to be able to afford such sequencing to determine their disease susceptibilities. Instead identifying diseases common to the Indian population would make individual screening faster and cheaper. Thus, it makes sense to create a National Human Genome Platform that hosts whole genomic data as a common national good for use by authenticated agencies to design diagnostics or treatments for genetic diseases.

In the context of Indian population, it has already been identified that various genetic sub-populations are present. Thus, it is prudent to have genetic datasets from these sub-populations to get accurate understanding of disease prevalence. Further as founder mutations are a cause for autosomal recessive diseases, it would be wise to group data from genetic sub-populations for analysis. The building of this platform with sub-population level information could then inform the molecular signatures of various diseases and disorders. This platform would be utilised for building further solutions not only for established genetic diseases, but other maladies such as malnutrition, stunted growth, etc.

Together the prevention and targeted medication of genetic diseases will propel India as a global leader of precision healthcare. It will help us achieve our health targets at the lowest cost and streamline healthcare offerings based on genetic disease burden. This platform would not only be valuable in the short term but it will also be the building block for the genomic foundation for future.

If India does not establish a national platform, Western countries which can already access the Indian genome through the Indian diaspora will outpace Indian solutions that cater to our local problems. These foreign solutions may not be best tailored to local environments. Thus, it is in national interest to create a platform that can harness the knowledge of the Indian genome and use it to create effective solutions for India's health issues.

Predictive Genomics as an Instrument for Improved Public Health

Predictive genomics, based on identification of founder mutations in genetic sub-populations could help improve public health in the following ways:

1. Informed Mate Selection: When mates are chosen within the community, the individuals could profile themselves for the presence of common disease mutations. They could then make informed decisions on the basis of their genetic makeup and the risk of having diseased off-springs.

2. Genetic Counselling: If individuals having genetic incompatibility do decide to have progeny, they can have recourse to genetic counselling and Preimplantation genetic diagnosis to prevent the birth of diseased off-springs.

3. Improved Lifestyle Management: If individuals are aware of mutations that increase pre-disposition to certain diseases, they could take steps to prevent or delay those diseases through lifestyle management.

The cost of genomic sequencing has reduced significantly over the last few years. Today, the cost of whole genome sequencing is around INR 1.2 lakhs while the cost of testing individual genetic mutations is around INR 5000. On the other hand, management of genetic diseases can be extremely expensive. For example, thalassemia which is also an autosomal recessive disease can be managed through blood transfusions or bone marrow transplant. In addition to the cost of time and

effort, the primary cost of the treatment itself is about 8.5 – 10 lakhs per patient. The cost of avoiding a diseased child through informed mate selection is around 10,000. The cost of PGD is also about INR 5000 per embryo.

Guiding Principles for a Publicly Funded Indian Genome Project

1. **Genomic testing cannot be discriminatory:**

   Genome testing can reveal personal characteristics including family history and susceptibilities to health conditions. As further understanding of the genome increases, it is likely more facets of an individual could be unravelled from genomic information. However, this information cannot be grounds for discrimination against the individual. Therefore, any application built using genomic testing has to contain safeguards that protects personal information and prevents discrimination.

2. **Privacy and protection of personal data is paramount:**

   DNA information is sensitive personal data and maintaining its privacy and protecting individual rights is of utmost importance.

3. **Policymaking should be scientific and inclusive:**

   Genomic information can provide a lot of information and therefore policies around which information should be revealed must be scientifically grounded.

4. **Citizens have a right to enjoy the benefits of scientific progress (WHO-Guiding Principles)**

   Communities which have used predictive genomics are seeing benefits through reduced rate of diseased off-springs. Since this is a tested solution, citizens in India too should be able to benefit from this scientific progress and have the freedom to make informed decisions about their future generations.

5. **Citizens have a right to adequate standard of living (WHO-Guiding Principles)**

Finally, Indian citizens also have a constitutional right to health that the government should facilitate.

A Proposed Workflow for Predictive Genomics in India

Based on the above principles, we propose that the Government of India invests Rs 1,600 Crore per year for a period of 5 years on the National Genome Mission for Health Transformation, to enable 21st Century Predictive, Precision Medicine for all Indians.

The National Genome Mission will entail three broad things. One, the complete genome sequencing of 1 million Indians. Two, the development of a **National Genome Platform** which will house all the annotated, anonymised genomic data in an accessible format. Three, an access mechanism that allows private or public researchers access to the data for exploratory therapeutic or diagnostic studies.

The Government of India under the National Genome Mission should set up the National Genome Authority as an Apex body that is in-charge of the National Genome Platform. The National Genome Authority shall then identify 15-20 **Nodal Agencies** from top academic institutions in the country who have demonstrated expertise in genome analysis for sequencing and annotating whole genome sequences. These nodal agencies can employ in-house facilities or partner with private companies to fulfil the sequencing requirements. The National Genome Authority will perform quality control of data on the National Genome Platform, regularly update the annotations on the Genomic platforms, and publish reports for the public and for healthcare providers on improving predictive and precision medicine in India.

Seeding the National Genome Platform with the full genome sequencing of 1 million Indians

India has close to 5,000 distinct genomic populations with distinct genotypic and phenotypic tendencies. At least 200 representative human genomes from each genomic population will be needed to understand the full population genetics of diseases and disorders. Altogether, the full genomes of one million Indians will

need to be sequenced, quality-approved, annotated and added to the National Genome Platform database along with relevant metadata on demographics, clinical information, and anonymisation.

This can be achieved in four broad steps:

1. The National Genome Authority will constitute a Steering Committee with nominees from Nodal Agencies, the Government of India and other Eminent Individuals. The Steering Committee shall come up with a sampling plan and priority plan for collecting genome samples from 1 million Indians over 5 years.

2. The National Genome Authority will grant Nodal Agencies funds annually for collection of genome samples and metadata, sequencing, and quality control. The respective Nodal Agencies can either conduct the sequencing themselves, or work with private partners in order to meet the National Genome Platform goals in a timely and cost-effective manner. The Nodal Agencies will be responsible for the genomic data and for its input into the National Genome Platform. The Nodal Agencies may also set up their BioBanks to cryogenically store the biological samples collected for sequencing, for any future use.

3. The National Genome Authority will govern all incoming data inputs via three mechanisms. One, publish frequently updated standards for genome data quality, formats, collection and sequencing protocol. Two, have a standing committee to review the quality of all inputs from Nodal Agencies. Three, appoint a 3rd Party Anonymised Evaluation setup for incoming genomic data, where a second Nodal Agency will review the data quality.

4. The National Genome Authority shall create a Genomic Annotation Committee, comprising of scientists and nominees from Nodal Agencies. The Genomic Annotation Committee shall:

    i. Come up with an Annotation plan and annotate the Genomic database

    ii. Conduct quarterly reviews of new research on genetic links to health risks, and update the annotations on the National Genome Platform

    iii. Publish annual reports

Provision for private seeding of data

As an open platform, the National Genome Platform can also enable private individual Indians, communities and Indian diaspora members to submit their genomes and biological samples to the platform at their own cost. Since there will be no sequencing cost associated with the data, the Platform could charge only for the annotation and reporting of genomic data to the donor.

Further private companies or clinics should be able to feed in demographic data about the genetic mutations on the platform so that comprehensive information of disease incidence and changing trends of prevalence can be captured.

Development and Maintenance of a National Genomic Database as a National Common Good

Several efforts are already underway in India which are collecting thousands of genome sequences of Indians. These are being done to study ageing, mental health, cancer, and other health objectives. Currently, there is no common, open genomic database where annotated genomes can be stored and accessed easily by researchers.

After sufficient anonymisation to uphold the Constitutional Right to Privacy of all the individuals, genomic data should be available easily to researchers, academics in India free of cost. In stages, anonymised genomic data could also be opened up for private pharmaceuticals so that they can conduct research for Indians, as well as come up with therapies for Indians at a cost in cash or kind.

Governing outputs from the National Genome Platform:

From a public health perspective, information for diseases should be made publicly available. For example, the information of prevalence of thalassemia in genetic sub-populations and the mutation that causes it can empower individuals to screen themselves for thalassemia. This would bring down the cost for individuals who can pick which mutations they want to be screened for instead of screening whole genomes.

Academic researchers or private companies who want to access the raw data can apply to the National Genome Authority with a research proposal. There would be a cost attached to the data if used for commercial purposes.

The national genome platform will result in massive data sets and could be used for assessing many conditions – from diseases to physical attributes. Opening up this data would lend it for use by private companies to create diagnostic or therapeutic solutions. But the government, as the primary funder of research and development, may also like to prioritise areas to actively invest in.

There are two main areas in which public funds could be used –

a. For research and development on key disease areas

b. Creating a diagnostic disease panel similar to the Dor Yeshorim panel for communities to then self-test at lower costs.

The below section details frameworks that can be used to assess disease conditions. The frameworks can be used to determine diseases that need to be prioritised under the two areas.

Priority disease areas for research and development: To address which diseases should be considered, we suggest the following framework–

Priority panel: This framework analyses diseases on the basis of the risk that the mutated gene results in the disease and lethality of the resulting disease. Diseases in the upper right quadrant are for highly debilitating or lethal mutations where the risk of gene mutation causing these disease is the highest. Thus, treating these mutations will most likely lead to alleviation of the disease. Similarly, improved diagnostics may help identify the disease earlier. Thalassemia is an example of a disease where medical intervention could not only help the individual sufferer, but perhaps a treatment like gene editing could eliminate the disease in future generations.

Upper left quadrant contains diseases which are lethal but the mutation and disease co-relation is not completely understood. BRCA1 mutations are co-related to breast cancer, but there are other variables that contribute to the disease. These diseases should also be studied.

On the other hand, genetic mutations leading to baldness are not lethal and may not be the best use of public funds.

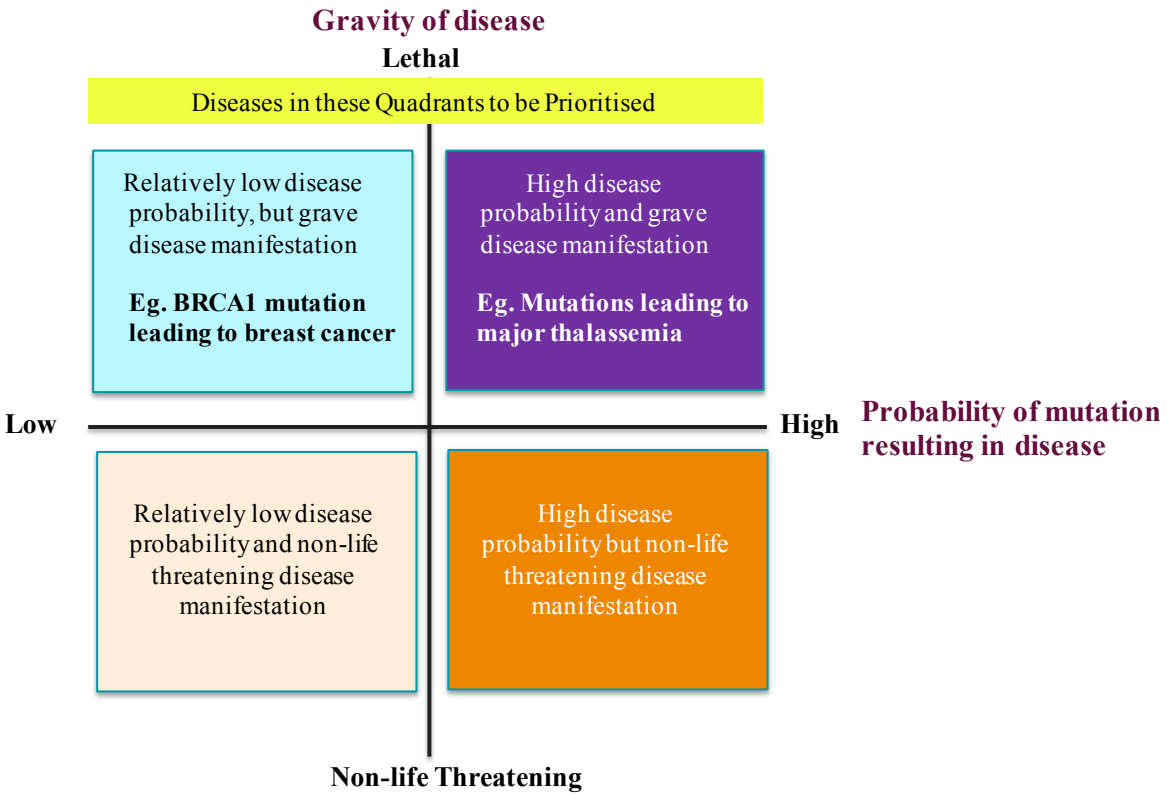

Figure 1: Framework for Priority Diseases.

A panel for diseases where communities can self-test

Much like the Dor Yeshorim panel, this panel will be for those diseases where there the mutation is known to increase predisposition to a disease. People can test themselves for select diseases at lower costs instead of getting their whole genomes sequenced. It would be most effective to include diseases which could be managed through lifestyle changes.

For example, those suffering from thalassemia could choose to opt for preimplantation gondal diagnosis to ensure their children do not carry the defective gene. Someone diagnosed with BRCA1 mutations could opt for increased breast cancer screening, to diagnose the disease early enough for medical intervention.

Diseases in the upper right quadrant of the below framework should be ideally considered for the panel followed by upper left.

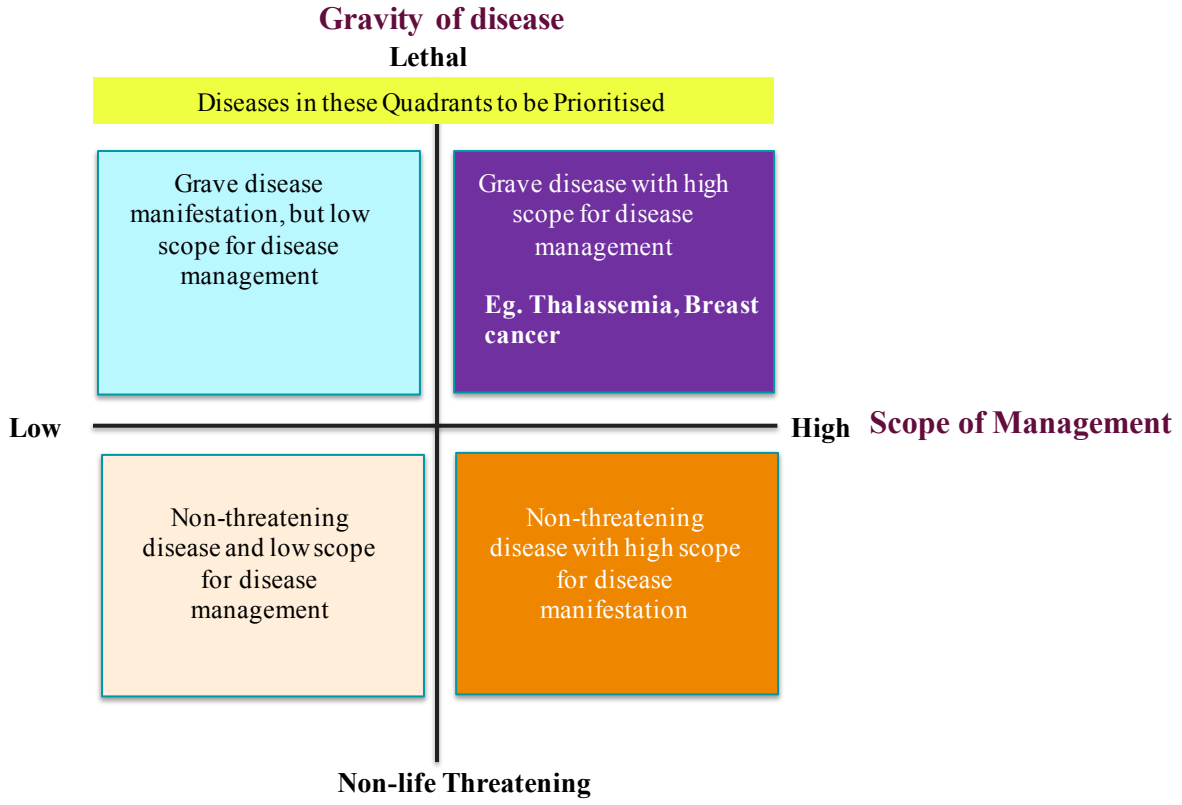

Figure 2: Framework for lifestyle management diseases

Once the panel of diseases have been ascertained, private companies could be accredited to undertake the genomic tests for individual citizens. A governance framework for streamlining the laboratories would help prevent any violations of data privacy.

Development and Maintenance of a Distributed BioBanks

It is important to also store biological genome samples of all individuals on the National Genome Platform, apart from the sequenced and annotated genomic data.

Bringing India's States on Board

Health is a State List subject according to the Constitution of India. The Government of India must take the lead on building a National Genome Mission for Health Transformation as the National Genome Platform has large inter-state externalities and requires high investment.

However, the Government of India must involve State Governments as stakeholders, and help states establish State Genome Mission Centres such that state governments develop capacity and competence in providing genomic services to their citizens. The Government of India and state governments can jointly fund the creation of State Genome Mission Centres with a Nodal agency attached as a technical and scientific partner.

Budget Allocation

A breakdown of costs for the project across the various budget heads is detailed below. Overall the project will require an investment of INR 1600 crore/year over 5 years.

Budget Head	Cost
Sequencing Costs for 1 million sample	At INR 1 lakh per sample, total cost to be INR 10,000 crore. Given the scale of the project, the costs could be reduced to INR 7000 crores
Platform Development	INR 200 crores
Biobank	INR 200 crores
State level centres	INR 600 crores (across 20 centres)
Total Project Cost	INR 8000 over 5 years

Conclusion

Predictive genomics can help identify and prevent many congenital diseases. This strategy would help improve health standards of Indian citizens while reducing healthcare costs. In a country where most healthcare expenses are borne out-of-pocket, the prevention of congenital diseases could result in improved standard of living. Even lifestyle changes when prescribed correctly can help prevent unnecessary disease exacerbation and associated medical costs. A healthy population will not only help people stay out of poverty but also result in a healthy, productive population.

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Appendix I: Genetic Screening – A case study of Dor Yeshorim

The organization, Dor Yeshorim[12] offers genetic screening for members of the Jewish community for a panel of debilitating diseases found commonly in their population. Informed mate selection based on genetic compatibility and genetic counselling has reduced the disease burden in the community. This is an example of how scientific use of genetic screening can be applied for reducing human suffering and improved community health.

Dor Yeshorim, is an organization offering genetic screening to Jewish community members with the objective of eliminating debilitating genetic disorders from the community. Ashkenazi Jews, for example have a relatively high score of Identity by Descent and the consequently the community suffers from common genetic disorders. Orthodox Judaism generally opposes selective abortion. By avoiding marriages between "carriers", the incidence of the disorders decreases without having to resort to these methods.

Dor Yeshorim employs the following methodology:

1. The organisation screens Jewish children for a panel of genetic disease-causing mutations that have been pre-identified on the basis intensive research. These mutations are either lethal or extremely debilitating to the diseased individual.

2. While gather DNA sample, no identification details of the children are documented. The organization does not hold any personally sensitive information, such as name, age or social security number.

3. Each screened child receives a unique id number.

4. Dor Yeshorim does not reveal the individual health report.

5. When two individuals of the community contemplate marriage, they contact the organisation with their unique id numbers and the organization only reports if the match is compatible or incompatible based on their mutations. Thus, if one partner has a mutated Tay Sac's gene but the other partner does not carry a mutation, they would receive a compatible health report.

Through this mechanism, the Dor Yeshorim achieves its goal of helping individuals make informed mate choices while addressing following concerns:

1. Data protection: Since the organization does not possess any other sensitive personal data, the questions of data protection and privacy are mitigated.

2. Right to Not Know: The organization believes that the knowledge that you are a carrier of a disease may burden people. Hence, they do not divulge genetic information to individuals.

3. Discrimination: Since no information of carrier status of individuals is released, it prevents them from being discriminated about in society.