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RESEARCH

# Public Health Genomics – Treading Two Parallel Tracks

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**Abstract.** Against the backdrop of a decrepit healthcare system, where health for all is still a ‘distant’ dream, exposing stark gaps and shortfall of crucial inputs at various levels in catering to the health needs and requirements of a large population has compelled a review of the existing system and innovative course corrections. It has invoked a functional vision based on two parallel tracks; one, to rejuvenate and efficiently manage existing healthcare infrastructure and associated healthcare professionals at the village, tehsil and district level; and, the other of providing the modern facilities of diagnosis, prognosis, and preventive investigations with requisite interventions across all sections of the society. For more precise interventions to advance health the proposed two-pronged approach would ensure and safeguard the health, and inter alia reduce morbidity and mortality. Precision medicine in public health is predicated on OMICS technologies along with big data, machine learning and artificial intelligence for disease risk predictions and management in future. The capital intensive character of such technologies does raise concerns about their affordability, demanding an inter-institutional effort to generate simple and cost-effective high-throughput technology and tools for the diagnosis of diseases. The necessity to adopt modern medical biology technologies including Genomics has been amply evident in the COVID-19 pandemic through variant characterization of SARS-CoV2, and anticipated variations in the human host for differential susceptibilities and outcome of the disease.

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## Introduction

Resolving the hiatus in the availability and accessibility of healthcare across socio-economically disparate groups has been a challenge for the Indian health system. Government efforts invariably face several impediments in the provision of basic health facilities and services across large swathes of rural and semi-urban areas. An inherent paradoxical situation that we confront is, neglect and deprivation in the villages, tehsils, small districts and semi-urban extensions; while urban areas present a case of plenty. Beset with myriad problems ranging from lack of safe clean water, unhygienic living conditions, equity in opportunities to education and health, the disadvantaged regions testify to a failed promise of health for all.' In glaring contrast, urban mega-polis can claim most modern and state-of-art technologies available for diagnostic and therapeutic interventions, which at times burden patients with exorbitant and unrelated medical procedures. Many of the urban and privileged class also live in pathetic civic conditions of ill-organized sewerage system and cess-pool of unregulated garbage with health implications. This is a carryover of the legacy of the decrepit public health planning unattended by impervious local municipal corporations dating back to the 19<sup>th</sup> century.

A major chunk of public health issues is entrenched in the unhygienic and deteriorating environmental conditions. Better sanitation practices along with immunization programmes have resulted in a dramatic improvement in health and life expectancy as in the USA and around the world long back.<sup>1</sup> Whereas in India and the rest of the developing world challenges of deteriorating physical environment, socio-political factors, and lifestyle behaviours have remained peripheral to the public health agenda ([Park and Park 1977](#); [Molster et al. 2018](#)). Bridging this wide gap requires the creation of an ecosystem where essential basic amenities, as well as modern healthcare facilities, are easily accessible and affordable to all sections of the populace in an equitable manner.

Taking cognizance of basic public health issues of safe water, hygiene and nutrition, and concomitantly introducing novel approaches in the system have found resonance and legitimacy, especially in dealing with the health crisis during the COVID-19 pandemic. Apart from variegated experiences, world-over of preventive aspects of COVID-19 and preparedness in dealing with the heterogeneous presentation of disease in people, knowledge-both traditional and modern- can mitigate adverse health outcomes and provide an impetus to public health initiatives in India. The future road map requires preparedness for a holistic healthcare plan, focusing on the wellness of an individual, a family and the population groups as a central plank. To ensure quality healthcare, evidence-based cost-effective and modern

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[1] Ten great public health achievements – United States, 1900–1999. *MMWR Morb Mortal Wkly Rep* 1999; 48:241–243.

medical biology technologies for diagnosis, prognosis, and precise intervention could work as the pivot for achieving universal healthcare and wellness.

## ***Dynamic Digitization and Networking Operations for Overhauling Health System***

The National Health Mission Report (<http://nhm.gov.in>) proposes to reinvigorate the ill-equipped primary healthcare set up by setting up health and wellness centres<sup>2</sup> in a bid to revolutionize the healthcare infrastructure and provide efficient healthcare delivery. Since health outcomes are influenced by a range of socio-cultural-political, economic, environmental, behavioural, and biological (including, genetic) (Wilkinson et al. 2011) factors, mechanisms to ensure health and well-being require a reassessment. Admittedly some determinants of health, such as age, ethnicity are given and cannot be changed; while others, such as weight, habits, lifestyle could be influenced and the behaviour modified (Molster et al. 2018). Mapping and real-time analysis of these determinants necessitate a nationwide comprehensive survey at regular intervals, eschewing multiple surveys which have proven inadequate in involving all stakeholders in covering the changing trends of disease burden in India (Dandona et al. 2016).

A decentralised and reliable repository of health conditions, wellness status, and disease burden in real-time would require automation of the system as a reverse flow of data from the sub-centre up to the district level. Efficient centralized monitoring of the network would essentially provide the macro and meso level policy and programmatic oversight in the devolution of services and facilities. Districts should get positioned as hubs where top-down and bottom-up approaches converge. In the past telemedicine had largely failed to induct both doctors and patients because of a fledgling digital network system, lack of standard diagnostic facilities and an aversion to the distant mode treatment protocol. Today possibilities of dovetailing of basic with advanced healthcare need at the sub- and primary- health centres (future health and wellness centres) can be ensured through the network of specialists at the tertiary level. This would allow collation and free access to data sets in enjoin six lakh villages, seven hundred-odd districts in 28 states, 8 UTs, into a nationwide network. Appropriate matching of different matrices comprising of the area to be traversed, population coverage, manning of sub-centres, PHCs, district hospitals, tertiary hospitals-both private and government, and the facilities existent and non-existent, would provide a comprehensive database for micro-and macro-level planning. In the proposed 'twin track' paradigm network, the flow of information should be accessible and functional to ensure: (i) availability of diagnostic tests, (ii) access to consultants and specialists across the nationwide healthcare networks for facilitating unhindered access to treatment. The current system of data collection remains in siloes and remains delinked from decisions highlighted by the evidence gathered.

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[2] Ayushman Bharat-Comprehensive Primary Health Care through Health and Wellness Centers- Operational Guidelines-National Health Systems Resource Centre, MoHFW.

NITI Aayog Health Vertical document<sup>3</sup> endorses how surveillance functions in vertical siloes of programmes and institutions. Deficiency in the delivery of quality care can be bridged with automated facilities for remote, inaccessible, rural and semi-urban areas. The aim is to supplant the decrepit and the disorganized system and randomized flow and rush of public seeking cure by attending to access to basic and advanced healthcare needs, in a symbiotic manner virtually or physically.

The mechanism of the weekly reporting system in the majority of districts under IDSP<sup>4</sup> (Integrated Disease Surveillance programme, NCDC, MoHFW; [www.idsp.nic.in](http://www.idsp.nic.in)), should also involve real-time analysis rather than record-keeping to achieve universal and effective healthcare coverage. Setting up real-time monitoring at state, UT and central levels would facilitate epidemiological surveys, ensure data analysis of the prevalence of infectious and non-infectious diseases, and be used as the basis for priorities formulation and budget allocation. Simultaneously, the disparate information manually collected, if digitally collated using IDSP infrastructure, could add to the pool of useful information about local and remote areas, their trends and patterns, ensuring appropriate intervention. Regular monitoring by IDSP centres at the district level could help in dealing with specific disease surveillance and operational bottlenecks and propel local performance. The proposed approach could add efficiency to the Comprehensive Primary Health Care through Health and Wellness Centres under the Ayushman Bharat Scheme,<sup>3</sup> and provide a template for managing the pandemics or any other health-related emergency.

Linkages and automated communication in sharing availabilities, strengths and patient databases between hospitals, small and big, rural or urban areas, and government bodies could have prevented the crisis, inconvenience and mitigated the intense sufferings of the COVID patients and their families. The Integrated Health Information Platform (IHIP), supported by the National Digital Health Blueprint,<sup>3</sup> proposes to strengthen the citizen electronic health record (HER) with the help of the Unique Health Identity Number (UHID). However, such an integrated platform suffers from a lackadaisical approach in expanding the network across the country and is reduced to a mere collection of data without redirecting it back into the system for ground-level action. If such an efficient network was operational, it would have optimized and scaled up attention and intervention adequately within villages, districts, small cities to meet the challenge of the two waves of COVID pandemic and reduced the lethality of the infection.

During the COVID pandemic, virtual access to the point of treatment became a reality. Many patients, who never met their doctor face to face, were examined virtually; thereby enabling timely treatment without admission to the hospital. Involvement of the private partners, as proposed in the Comprehensive Health Care document, is a compelling proposition for a larger population who are deprived of access to good healthcare. Subsidizing health spend by the marginalised sections of the society through Pradhan Mantri Jan Araogya Yojna (PMJAY)<sup>2</sup>

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[3] Vision 2035 Public Health Surveillance in India –A white paper by NITI Aayog and the Institute for Global Public Health, University of Manitoba, Canada.

[4] Integrated Disease Surveillance programme, National Centre for Disease Control, Directorate General of health Services, MoHFW; [www.idsp.nic.in](http://www.idsp.nic.in)

<sup>3</sup> and improvising the health facilities in the form of proposed 150000 wellness centres (HWCs) <sup>2</sup> <sup>3</sup> augurs well but would require community partnership and universal availability without pilferage.

## Public Health Genomics and Challenge of COVID-19 Pandemic<sup>5</sup>

The COVID-19 pandemic offered a unique challenge in recent history; never before had governments and the public alike confronted an unprecedented threat physically and socially on a global scale. Faced with an unimaginable daunting task, the situation further tested the ability to muster resources, mount logistics and facilities for a billion-plus population. In this situation, we were subjected to a litmus test for the public health policy in India and learnt a few lessons as a tradeoff. The preventive approach of COVID-appropriate behaviour was a rational choice in the absence of any specific drug or uncertainty of the vaccination drive. Required momentum and motivation were the keys to keep the medical and essential services operational. The government played a proactive role along with the health and front-line workers, a majority of whom volunteered to offer their services despite the risk to their lives. Glitches in hospital admissions and the fear of a high number of infections not commensurate with the available facilities did create unease and curbs on free movement. Treating the suspected or affected cases at home with aggressive campaigns and social media messaging met part of the challenge. Mass-media blitz to update people in adapting to social conduct was launched to deal with the pandemic effectively, though lowering of guard and inappropriate behaviour became a recurrent cycle after the lockdown, especially before the second wave, engendering risks of mortality and morbidity for many. However, the focus was not lost in mitigating the situation with the development of the vaccine. The scale at which the public, in general, should have been vaccinated and the inability to meet the demand have led to distrust and disbelief about the adequacy of the health system and made public health experts rethink future challenges in healthcare delivery.

As a vaccine production hub, India was one of the few countries which mobilized its R&D efforts for vaccine generation by producing Oxford-AstraZeneca vaccine, COVISHIELD by Serum Institute of India, Pune, and manufacturing its own Make-in-India vaccine-COVAXIN by Bharat Biotech, a pharmaceutical company of Hyderabad. Additionally, the production of Russian-made Sputnik V by Reddy's Lab, Hyderabad, and Genetic (DNA) vaccine from Indian Zydus-Cadilla, and a few more subunits and getting mRNA based vaccines in the pipeline, were initiatives undertaken to meet the challenge. Prior experience of conducting the nationwide immunization programmes through social mobilization have stood us in good stead through this time the challenges of vaccination are immense. Despite a good number of

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[5] National Webinar on PANDEMIC COVID-19 and PUBLIC HEALTH POLICY OF INDIA organized by the Delhi School of Public Policy & Governance, Institution of Eminence, University of Delhi. <https://youtu.be/L5BscQzTyh4>

trained manpower, impediments ranging from inadequate diagnostic infrastructure, uncertainty about vaccine efficacy and safety, lab to field translation, and public resistance in adherence to advisories, have hampered the initiatives.

From the Public Health Policy perspective, the need was of ‘preparedness’ in diverse ‘working vaccine platforms’ ([Kumar et al. 2018](#)) to meet the desired scale. The dearth of such scientific platforms within the higher education or research institutions has not augured well for R&D efforts in setting up the vaccine development programme. An adequate presence of a whole virus, protein subunit, or genetic (viral vector and DNA/RNA) vaccine platforms would have reduced the gestation period in generating vaccines, and transfer of technology to multiple industries and pharma companies. The same scale and speed in such industries would have accelerated the production process for a timely and sufficient quantity of the vaccine for the country and the rest of the world. Timely and coordinated engagement of the research expertise early in the first wave of the pandemic could have enlightened us about the cytokine storm, a cardinal feature in some of the critical patients, before their admission to the ICUs. Production within the country and the ease of availability of the reagents, apart from the proficiency to carry out detection procedures, could have saved many lives. Expertise to isolate or characterize the CoronaVirus-2 for genomic variations and mutant populations, arising within the country or coming from outside, was creditworthy, though did not correspond with the spread of the pandemic and the country of our size. Imagine if we were to confront another pandemic of an unknown infection how we would brace up to the challenge! Apart from ensuring bare minimum infrastructure and trained manpower, such state-of-the-art diagnostic facilities with requisite support are essential at all tertiary and secondary level-district hospitals and CHCs to attend to any evolving emergency but equally resolutely for routine purposes as a part of the Public Health Policy imperative.

In retrospect, assessing the government's management of the first wave of COVID-19 pandemic scored reasonably well in the initial phase but the healthcare system was ill-prepared for the mounting cases and spree of deaths during the second wave. Although we do have a reasonably large public health infrastructure with >24 thousand PHCs and >145,000 sub-centres serving 72 per cent of the rural population, but their functional status is compromised in terms of physical infrastructure, manpower, equipment, drugs and other logistical supplies. In the past, health research activities have not matched with public health priorities, however, the challenge of the COVID-19 pandemic has changed that perspective. The intent and preparedness were evident in making a quick transition from an insignificant tally of 6,500 RT-PCR tests conducted on March 13, 2020, averaging not more than 200 tests/state and UT to rounding up more than 10-12 lakhs/day tests with an average of 20 to 35,000 tests/day/per state and UT. This was obviously a phenomenal feat, but not adequate to cover the entire adult population of the country.

Against this background, it is incumbent to reassess the fault-lines in critical areas of health system, management and delivery. A ‘twin track development model’ is being proposed which rests on two major pivots: (i) upgrading and equipping the PHCs, sub-centers/Health and Wellness Centers, District and Tertiary Hospitals, with essentials as proposed in policy



documents; and (ii) concomitantly set-up uniform state-of-the-art diagnosis and treatment in all 28 States and 8 UTs. A proper description of both viral and host genetic factors, affecting infectivity and disease outcomes, would help gauge the scope of a genomics and OMICS-based approach in the next phase of prevention and control of the current pandemic, and other health afflictions. Detailed understanding of the disease, novel ways of drug and vaccine development attains importance to contain unexplained fatality, resistance to infection in higher age groups and rare idiopathic severe disease in the young. Post-Covid morbidities-genetic susceptibilities need to be attended to as an on-going process for management of future infections and non-infectious diseases to ensure tenable health outcomes.

## Symbiotic Relationship Between Genomics and Comprehensive Healthcare

Genomic knowledge over the past few decades has enabled building our understanding about health and susceptibility towards a variety of diseases; and a prospective approach in precision treatment. These studies involve exploring the complete genetic makeup of a cell and a living being at an individual or population level to improve our ability to comprehend disease aetiology, diagnosis, risk, treatment or prevention. Appropriate public health services require an understanding of health status and wellbeing indices, factors affecting morbidity patterns and socio-economic determinants of health. Considering the 4635 anthropologically well-defined population groups ([Chakrabarty et al. 2016](#)) as distributed among ~40,000 endogamous caste groups with ancient admixture and phylogeography, it is imperative to identify their vulnerability to a diverse set of infectious or non-infectious diseases. Effective and sustainable integration of genomics into the healthcare system must be mandated for an organized approach ([Molster et al. 2018](#)). Genomic information is expected to expand the understanding of diseases and predicate an alignment with public healthcare policies.

Over the years, public health genomics has evolved into integrative genomics linking the field of personalized and precision medicine and public health ([Khoury 1996](#); [Beskova et al. 2001](#); [Molster et al. 2018](#); [Roberts et al. 2021](#)). Incremental progress in the use of OMICS tools and techniques, including genomics, has resulted in precise and improved therapies. Based on the information related to pharmacogenomics, genomic variations in a gene or a group of genes involved in metabolizing a given drug efficiently or responding to vaccination differentially can prove efficacious in managing patients and the disease efficiently. Apart from the utility of genomic tools in public health practice, integrating them with artificial intelligence, machine learning and big data analytical tools could help to establish the prognostic factors.

Conventionally, clinicians have either depended on their experience or limited available investigations for diagnosis and management of a patient. This approach does work, but *inter alia* entails a limited understanding of the aetiology of the disease in absence of markers or needed characterizations, resulting in either mortality or morbidity due to adverse drug

reaction. Modern medical biology has expanded its knowledge base and tools to differentiate many such susceptible individuals either in a population or a hospital setting, lending it a cutting edge as a therapeutic treatment. Meticulously working out its execution on the ground, induction of trained manpower, and provision of basic infrastructure in sync with the existing structures of health delivery would be the prerequisites. Characterization of Corona virus-2 variants and strains leading to the quick spread of the virulent infection and causing hospitalization and mortality have drawn attention to the critical relevance of genomic information to the health condition. Molecular characterization of any infecting agent and its host has, therefore, attained significance in the context of a current pandemic; and highlighted the importance of genomic epidemiology in public health. The capital intensive character of such technologies does raise concerns about their affordability at individual, community, or even at the national level. Innovative R&D in India, as part of the translational research, need to shape such technologies that are simple, affordable, and suitable in the field conditions.

With genomics becoming increasingly integrated into population-level health initiatives, maintaining efficiency, effectiveness, ethics, and equity requires a strategic approach. A functional approach would be to establish a knowledge network of biomedical research to create information commons of data sets on large populations of patients for validation, suggested as the New Taxonomy. This information then could be processed for accurate diagnosis, targeted treatment and improved health outcomes.<sup>6,7,8</sup> Giving credence to this perspective, the European Union member states and Norway have given a call for introducing cooperative development and harmonization of policy on genomics in healthcare to provide comprehensive and customised services (Mazzucco et al. 2016). The group on “Beyond Health Genomics” recommended the improved facilitation of translation research through greater engagement between public health professionals, geneticists, and scientists. Similarly, the Australian Government's Department of Health has released the *National Health Genomics Policy Framework 2018–2021*<sup>2</sup> to harness the health benefits of genomic knowledge and technology into the Australian health system. This framework provides a shared direction and commitment between all levels of governance in Australia to consistently and strategically integrate genomics into the Australian health system through five strategic priority areas: person-centred approach, workforce, financing, services, and data. The cohesive strategy is expected to integrate genomics in healthcare for appropriate health benefits which would translate into an efficient and sustainable health system. Genomics Health Futures Mission has announced to invest \$500 million over 10 years in genomic research to improve testing and diagnosis for many diseases, help personalise treatment options to better target and improve health outcomes, and reduce unnecessary interventions and health costs to transform clinical medicine.<sup>2</sup>

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[6] Institute of Medicine. 1988. *The Future of Public Health*. Washington, DC: The National Academies Press.

## ***Traditional Medicine and Genomics: Ayurvedomics as an integral part of AYUSH and Comprehensive Health Care***

In keeping pace with developments in medical biology and technology, modern Ayurved and other AYUSH systems can be seen in conjunction with OMICS knowledge and technology in the provision of customized diagnosis and treatment. The traditional wisdom of AYUSH, especially Ayurved, to enhance the body's natural system in augmenting the immune response as a prophylactic measure, apparently has proved efficacious and has gained global recognition due to its accessibility, affordability and prophylactic effectiveness (Dahanukar and Thatte 1997; Valiathan 2006; Patwardhan and Bodekar 2008; Mukherji 2011); even in COVID afflicted condition (Saggam et al. 2021; Joshi et al. 2021).

According to Charaka, in Ayurveda, the diseases originate either from physical or mental health, the former due to the derangement of *tridosha* and the latter by *Doshas* of mind. The *Tridosha* theory of Ayurved deals with three principal forces, called doshas, determining the physiology of each individual. *Vata-dosha* is responsible for the principles of motion and is involved in the transportation of molecules and nerve impulses. *Pitta-dosha* accounts for the process of digestion and metabolism inside cells and the body. *Kapha-dosha* governs structure and cohesion in the body. Each one of us is born with a combination of these three doshas, which is *Prakriti*, which are of seven types: *Vata*; *Pitta*; *Kapha*; *Vata/Pitta*; *Pitta/Kapha*; *Vata/Kapha*; and *Vata/Pitta/Kapha*. These are the *Prakriti* phenotypes. Phenotype based classification in humans offers a challenge to look for underlying genetic variations among the phenotypic datasets (Valiathan 2006). *Prakriti* phenotypes have also been reported for different responses to medication (Dahanukar and Thatte 1997), similar to what has been observed in pharmacogenetic variations in human genetic studies. Ayurgenomics is an integrative approach of Ayurveda and Genomics for the discovery of predictive markers for preventive and personalized medicine (Mukherji 2011).

*Prakriti* has been proposed to be genetically determined and responsible for differential normal state and susceptibility to various diseases. A correlation was shown between HLA alleles and *Prakriti* types, providing a proof of concept for the genotype-prakriti-phenotype relationship (Patwardhan et al. 2005; Patwardhan and Bodekar 2008). However, how do the catalogue of genes and linked biological processes and pathways result in a given *Prakriti* phenotype in a

[7] Public Health Functions Steering Committee. 1994. Public Health in America, Fall 1994, online. Available at <http://web.health.gov/phfunctions/public.htm>.

[8] Committee on A Framework for Developing a New Taxonomy of Disease. 2011. In *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*. The National Academies Press, USA. <http://nap.edu/13284>.

[9] National Health Genomics Policy Framework 2018–2021. 2017. Commonwealth of Australia as represented by the department of health. <https://www1.health.gov.au/>

normal and diseased state is still not clear, although there is no contradiction between traditional medical practices and genomic medicine ([Prasher et al. 2016](#)).

In India, experiments in introducing traditional medical practice as a standalone or part of the district health services have had tepid success. It needs to be resurrected and shaped into an integrative exchange of introducing traditional medical practice as a standalone or part of healthcare and wellness with supportive modern molecular characterization.

## ***Simple Cost-Effective Genomic and OMICS Technologies***

Modern high-throughput testing facilities have become basic to healthcare today, especially in the current COVID pandemic. This would become possible if the simultaneous emphasis is laid on R&D to innovate simple and cost-effective high-throughput methods, executable in field situations, even at the sub-centre level. Efforts in this direction in the country are minimal and need to be encouraged in institutions with such high-throughput facilities. The advances made in these research institutions have remained elusive for public health. The huge amount of knowledge generated only finds a place in publications with the little translational outcome. If in sync with the molecular epidemiological characterization of the prevalent diseases in the country, it would prove to be of great benefit to the community. Concurrently, dissemination of easy to comprehend information and skilled manpower ready to empathise and provide a healing touch, as part of the holistic healthcare-delivery machinery, is vital. After-all ‘art of healing’ began thousands of years ago in human evolution, when attending to sickness and suffering was motivated by feelings of sympathy and kindness ([Park and Park 1977](#)).

There is an increasing recognition that precision in diagnosis and intervention based on molecular characterization can advance health at a population-level. Projections in this direction have been initiated within India and some neighbouring countries<sup>10</sup> ([Chakrabarty et al. 2016](#); [Riaz et al. 2019](#); [GenomeAsia100K Consortium 2019](#)) which give confidence and legitimacy in redirecting our attention to changing the structure and dispensation of health. This provides an opportunity to execute “the right intervention to the right population at the right time” by translating basic-science discoveries to the population level ([Roberts et al. 2021](#)). At this juncture, India and the developing world must learn how to navigate twin tracks of strengthening the existing healthcare infrastructure and introducing an affordable and accessible modern diagnostic and intervention facility, to achieve the goal of universal healthcare for all.

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[10] International Symposium on Human Genomics and Public Health along with the XXXI Annual Conference of Indian Society of Human Genetics. 2006, at JNU, New Delhi, February 27-March 1.

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