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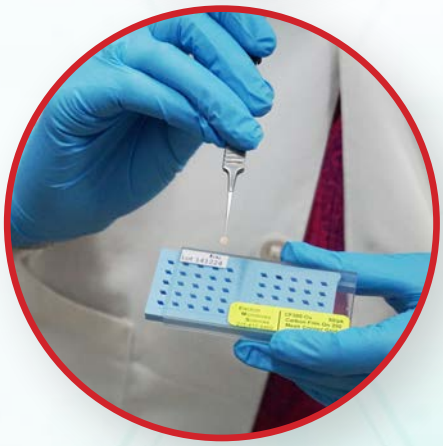

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nature INDIA

April 2018

FROM THE EDITOR

India is headed towards an astonishing population surge. With 1.34 billion people recorded in early 2018, the country is estimated to add another 100 million by 2024 overtaking China, currently the most populous nation in the world.

Therefore, her daunting demographics are integral to any discussion around the challenges faced by India. The mammoth population coupled with limited resources, and growing urbanization and energy needs are important factors behind many socio-economic issues.

Be it poverty, healthcare delivery, literacy, pollution or waste management — each of India's problems can be directly linked to and are intensified by its teeming millions.

Some of the most pressing challenges raised by a large population are in the public healthcare, energy and sanitation sectors. Successive Indian governments have made tremendous efforts to meet public needs and expectations. However, health concerns such as tuberculosis, maternal and infant mortality, vector- and water borne-diseases, malnutrition, hygiene and sanitation remain major problems.

The *Nature India* special issue on Grand Challenges takes a closer look at some of these hazards, which are experienced across the developing world. What are the grand challenges for the country's 1.3 billion people? Can science help find solutions to some of the public health problems? Can innovation provide long-term answers?

Through in-depth commentaries by subject experts, this special issue looks at the state of affairs in malaria management, maternal and child health, malnutrition and tuberculosis. It also looks at the science-led innovations and solutions already on offer. In a reprint section, we compile some recent articles from across Nature Research publications that highlight the grand challenges and research-based solutions that India and the rest of the developing world have adopted.

The volume also features a special photo section curated from top entries to the 2017 *Nature India* photo competition, themed 'Grand Challenges'. These pictures are compelling visual narratives of some deeply moving and familiar circumstances.

With examples and case studies of evidence-based solutions, the *Nature India* special issue on Grand Challenges hopes to be an enlightening read for scientists, policy-makers, business leaders, and societies across the developing world.

SUBHRA PRIYADARSHINI
EDITOR

SUBHRA PRIYADARSHINI

India's daunting demographics are a central consideration in solving her biggest challenges.

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A baby born in India today has twice the life expectancy of one born 70 years ago, but there is much still to be done to improve health measures.

MATERNAL AND CHILD HEALTH

In search of a good start for our mothers and babies

Adverse birth outcomes still too common, with a legacy of growth issues that last a lifetime.

MAHARAJ KISHAN BHAN
SHIRSHENDU MUKHERJEE

The Grand Challenges project aims to command the attention of world-class researchers and to focus funding and research on solutions to the biggest public health and development problems we face. Grand Challenges India has the same mandate on a domestic scale — directing Indian innovation to solve our specific challenges, which can be taken to the rest of the world.

A child born in India today has a life expectancy of 68 years, more than twice that of a child born in 1947. More mothers survive birth today than they did even a decade ago. These are markers of slow, yet steady progress in improving the lives of our mothers and children.

This is where the good news ends The stillbirth rate and neonatal mortality are still high in India and other low and middle-income countries (LMICs). Around 20% of our babies come into the world with low birth weight as a result of prematurity, fetal growth restriction alone or in combination. A high proportion of Indian newborns experience wasting and become stunted by their second birthday. This increased risk of linear growth retardation occurs both in low birth weight and those weighing 2.5kg at birth, but the risk is many fold higher in the

former category. We therefore have the challenge and the opportunity to improve both child survival rates and growth, and prevent this exceptionally high rate of stunting in Indian children.

There are gaps in our knowledge of what causes these adverse outcomes, as much as the unaddressed concern of relatively lower coverage and quality of current interventions. Research is important for both.

The factors associated with adverse birth outcomes, such as prematurity and low birth weight explains about a third to a half of the variation in these outcomes. These include under nutrition and specific nutrient deficiency, hypertensive and thyroid disorders, anemia, infections and inflammation particularly of the reproductive tract, complications related to pregnancy involving mother and fetus. Sanitation, hygiene, water supply increase risk of infection and inflammation. Psycho social factors may have direct and indirect effects on gestation and growth, but there are knowledge gaps. Many of these and other factors also affects placental function which is related to fetal growth and development.

On the implementation side, there is inequitable and inadequate intervention, and only low to moderate compliance by mothers and families.

How do we engage and initiate the research community, working alone, and through interdisciplinary teams to generate applicable knowledge, innovative tools for measuring gestation, fetal growth, pregnancy complications, placental function, postnatal growth and development? On the nutrition front, there is uncertainty about which are the most critical nutrients for mother and child. And how do we measure and address sub-clinical infection and inflammation that impairs linear growth in the fetus and the child. On the basis of new knowledge we can improve existing measures and add new interventions.

Research is needed on how to improve intervention delivery to achieve high coverage and quality on a wide scale.

Investments in promoting research and innovation on these issues is a high priority, given the link between adverse birth outcome, stunting at two years of age and eventual education attainment, income, and health (particularly risk of chronic diseases such as coronary artery disease and diabetes).

This is where the value of programmes such as Grand Challenges India lies. It encourages innovation to address some of these challenges through two mechanisms, open calls for solutions and through the policy thinktank KnIT.

The 'Achieving Healthy Growth through Agriculture and Nutrition' (AGN) and the 'All Children Thriving' (ACT) threw open the challenge to researchers from across the country. The AGN call targeted the interrelationship between nutrition and agricultural practices to reduce the high incidence of low birth weight, early stunting and wasting among Indian infants and mothers. The ACT call was envisaged to investigate measurement tools and mechanisms to tackle unhealthy birth, growth and development in infants and children.

The linear growth study, under the ACT grant, is being carried out by the Society for Applied Studies to understand the causes of stunting in India, and to develop mechanisms to address them. There are many possible explanations as to why stunting rates haven't improved in India, despite significant socio-economic progress, and this study intends to investigate many.

"There are markers of slow, yet steady progress in improving the lives of our mothers and children."

Specifically the study evaluates the impact of a package of interventions targeted at known risk factors on prematurity, fetal growth restriction and stunting and wasting at two years of age. The study will assess the role of intergenerational factors, such as maternal height, play in modulating the effectiveness of intervention packages. The study is designed as a randomized control intervention trial in low-income areas in New Delhi and will deliver the intervention package from pre-pregnancy, through pregnancy and the first two years of life.

It comprises of host of interventions addressing nutrition, medical disorders, infection and inflammation, psycho social support and timely detection and care of pregnancy complications. Postnatally, it provides evidence-based intervention for the mother and infant during the first two years. We will learn how much reduction in childhood stunting is feasible with evidence based intervention.

Another ACT project, implemented by THSTI in collaboration with Regional Centre for Biotechnology (RCB) and National Institute for Biomedical Genomics (NIBMG) is creating and using a biobank generated from a large pregnancy cohort to find new ways of predicting, detecting and addressing premature birth. The study uses omics technologies and imaging in search of new tools and ideas.

Another programme working in nutrition and maternal and child health is the Knowledge Integration and Translation Platform or KnIT. This is a policy thinktank which collates, analyses and synthesize secondary data and evidence on child survival and thriving to inform policy-makers on various aspects of health policy that are relevant and targeted to the Indian context. It works to synthesize and disseminate Indian evidence derived from routine surveillance, periodic health and nutrition surveys, intervention trials and programme evaluation. The output is helpful in reshaping policy and strategies in maternal child health and in assisting state governments in programme redesign and systems improvement. This platform is designed to ask the right questions and rigorously evaluate evidence supporting different interventions. It will provide state policy-makers with a holistic view of the challenge in their states with tailored interventions that may help mitigate the problems.

Today, KnIT is working on important questions in the area of nutrition and maternal and child health such as possible interventions for low birth weight babies, interventions to reduce anemia rates, and understand the facility level demands and supply for the care of sick and small newborns at the district level in the country. KnIT is assessing equity and impact of existing nutritional and health programmes for women and children at national and state level.

The agri-nutrition linkage programme supports innovative ideas in agriculture and food sector that could

improve the nutrition of the very same communities that produce food.

Many interesting projects are testing innovation to reduce postharvest losses, preserve nutrition quality of seasonal vegetables and fruits, and reengineer distribution to ensure access to sustenance for the poorest communities.

Grand Challenges for healthy growth and birth is identifying a new generation of young investigators and providing an opportunity to support and nurture them.

The programme, it is hoped will generate as many solutions and tools as there are insightful and creative young researchers.

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Shirshendu Mukherjee is mission director, Grand Challenges India, BIRAC, New Delhi.

MALNUTRITION

To end hunger, we must make smarter use of land and sea

Better systems, information sharing and technological progress are vital for nutrition security.

MONKOMBU S SWAMINATHAN

A recent issue of *National Geographic* (February 2018) raises the question of who will feed China. We have to ask a similar question about India. The answer lies in the integration of ecological principles, technological advancement and information sharing.

Nutrition security comes under the following categories.

INADEQUATE DIETARY CALORIES

Wheat, rice, millet, and other food crops are available. The development and implementation of an effective distribution system is essential.

PROTEIN HUNGER

Protein hunger can be overcome through the greater production and consumption of pulses. Indian farmers have shown that they can produce much larger quantities of pulses provided there is a certain and remunerative market. Poultry, milk, and fish also provide necessary protein. We are fortunate to be the world's largest producer of milk. We have a large programme of inland and coastal fisheries, along with aquaculture infrastructure.

MICRONUTRIENT DEFICIENCY

A dietary shortage of micronutrients such as vitamin A, vitamin B12, iron, and iodine could be eased through growing biofortified crops like sweet potato and moringa. Genetic gardens should be established in order to introduce farmers to crops which are rich in badly needed micronutrients. A national grid of genetic gardens of biofortified crops will make a major contribution to overcoming hidden hunger.

The three forms of hunger can be addressed through appropriate farming systems. The Farming Systems for Nutrition (FSN) initiative involves agricultural solutions for nutritional problems. Agriculture, nutrition and health are currently being dealt with separately, and FSN helps to integrate the three.

Our aim should be to achieve the second of the United Nation's Sustainable Development goals: 'End hunger, achieve food security and improved nutrition, and promote sustainable agriculture". To achieve this, we must pay attention both to sustainable agriculture and to farming systems for nutrition.

Sustainable agriculture involves increased productivity without ecological harm. To make the transition from a green to ever-green revolution, we need to attend to the following.

1. Soil health, paying attention to the physics, chemistry and microbiology of soil.
2. Better management of ground water, surface water, rain water, coastal water resources, and water recovered through waste recycling.

NOAH SEELAM/AFP/GETTY IMAGES

Homeless people gather at a feeding programme in Hyderabad.

BIJU BORO/AFP/GETTY IMAGES

A farmer dries harvested rice from a paddy field at Burha Mayong village in Morigaon, Assam

PRICE VOLATILITY

Instead of adhoc steps to appease consumers, we should find a permanent solution. One method is the promotion of peri-urban horticulture, making use of considerable areas of available land, within cities and on their fringes. A movement to encourage cultivation on rooftops and vacant land with essential food crops, such as tomato, onion, and chilli. This will confer a double advantage; price stability and nutrition security.

SEAWATER FARMING FOR COASTAL AREA PROSPERITY

India's 8,000 km coastline offers a great opportunity for seawater farming, as practiced in the Kuttanad region of Kerala. Both crops and fisheries can be included in a seawater agroforestry system. India should become a world leader in demonstrating how seawater can be used to cultivate crops. The M S Swaminathan Research Foundation is a hub for the technologies for seawater and below-sea level farming, and will undertake training and capacity building in this area. A genetic garden of halophytes, including mangroves, has been established for this purpose.

NATIONAL YEAR OF MILLETS

The Indian government has declared 2018 as the National Year of Millets. Tamil Nadu are leaders in the cultivation of millet crops like samai, thinai, kezhvaragu, panivaragu, kambu and several other minor millets. Kolli Hills has a rich germplasm of such grains. It would be useful to establish a **millet biovalley** for the conservation of varieties, along with small production industry for a wide range of processed millets, like breakfast cereals.

EMPOWERMENT OF WOMEN IN AGRICULTURE

I made proposals to the Rajya Sabha legislation regarding the technological empowerment of women in agriculture. Several features of this legislation could be incorporated in a Tamil Nadu Act for the empowerment of women in farming. Tamil Nadu will become a leader in promoting gender equity in agriculture.

ANIMAL HUSBANDRY AND FISHERIES

Kisan credit cards should be given not only to those cultivating crops, but also promoting the cultivation of poultry and marine and inland fisheries. Animal husbandry such as rearing of goat, sheep and poultry products can give substantial addition income to farmers. These can also augment the income of fisher families during seasons when catching fish is prohibited in order to promote regeneration.

RICE BIOPARK

This will show farmers how to increase their income through biomass utilisation, creating value-added products from the rice straw, husk, brawn and grain. Similar bioparks can be organised for pulses. This will help the farmers to derive income and employment from every part of biomass.

ADAPTATION TO CLIMATE CHANGE

It is important to set up many more climate risk management R&D centres. Such centres should be supported by trained Climate Risk Managers, a man and woman from each panchayat.

Climate change could lead to catastrophe, and there is need for immediate steps in the areas of mitigation and adaptation. Training manuals are available with MSSRF which can be used as a tool for an education programme.

ESTABLISHMENT OF FARM SCHOOLS

Farmer-to-farmer learning through **farm schools** should be established in the fields of outstanding farmers, to spread agrciultural knowledge and skill.

Another urgent requirement is greater investment in research on these 'orphan crops', so that the yield potential is substantially enhanced. Both higher yield and assured marketing will increase the attractiveness of these crops to small farmers.

There is presently a mismatch between production and post-harvest technologies which leads to losses for both producers and consumers. In this part of the cycle, food processing industries are urgently needed. The 2018-19 budget provides substantial support to food safety and food processing. Value-added products will have to be prepared in order to promote greater investment in post-harvest technology. Cold storage and cold chains are needed. The recent potato crisis in West Bengal, Uttar Pradesh and Bihar could have been avoided had there been cold storage available in the Punjab's Haryana region.

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The author is the founder and chairman, M S Swaminathan Research Foundation

Fumigation using a fogging device to control the menace of mosquitoes at Ulsoor Lake in Bangalore, India.

JAGADEESH NV/EPA/REX/SHUTTERSTOCK

DISEASE

BASIC RESEARCH THE BEST WEAPON IN THE AGE-OLD MALARIA BATTLE

The developing world needs a tool to distinguish *falciparum* from *vivax* cases

GOVINDARAJAN PADMANABAN

More than 100 countries have eliminated malaria in the past century, and 35 countries have joined the malaria-eliminating category. These countries have reduced their malaria burden by an impressive 90% from 1.6 million cases to 0.16 million, and cut death rates by 87%. The WHO has described various strategies for decreasing the global burden in terms of death and incidence by 90% by 2030[1]. A strong surveillance system to identify and classify all foci of transmission, aggressive and timely intervention to block transmission, methods of characterizing high-risk migrant and mobile populations, early capture of drug and insecticide resistance, real-time response for diagnosis and treatment, regional cooperation and data sharing, advocacy for political and financial support have all been addressed[2].

Malaria is a major problem in India. The country did have a major success through the National Malaria Eradication Programme (NMEP) which brought down malaria incidence of 75 million cases and death of 0.8 million cases in 1953 to 0.1 million cases and no death, respectively, in 1965. However due to technical, operational and financial complexities, incidence had shot up to 6.4 million cases in 1976. Various programmes of intervention have brought this to a figure of 1.1 million cases

Policy recommendations

India needs to aggressively pursue strategies described in the National framework for malaria elimination in India (2016-2030) (NFEMI) document to change its status from a malaria-controlling country to malaria-eliminating country, to eventually become free of malaria by 2030. Emphasis on operational research and translational basic research is essential. Strategies to prevent entry and spread of artemisinin resistance, quick diagnosis and treatment of *falciparum* and *vivax* cases, emphasis on research with *vivax* malaria, strategies to block transmission and vector control measures, and tackling insecticide resistance are among the priorities.

and 562 deaths in 2014, although the death figures have been debated. Even if death rates are not considered as a major factor, the morbidity, loss of man hours and economic burden are considered very high, since the country is a target for both *falciparum* and *vivax* malaria. India also runs the risk of being a malaria-exporting country since neighbouring Sri Lanka has been malaria-free since 2012, and other nearby countries have malaria-eliminating status.

Malaria interventions are considered highly cost-effective, representing large returns on investment in public health. Therefore, in line with the WHO Global technical strategy 2016-2030, the Ministry of Health and Human Welfare, the government has delineated a strategy for malaria elimination in India. The approaches described are very similar to the strategies described by the WHO, as applied to Indian states falling in three categories representing low, moderate and high transmission rates.

Operational research must be an integral part of the Grand Challenges programme. There are many challenges, well described in the NFMEI document[3]. To quote a couple of examples, an aggressive intervention in high transmission areas of Odhisha, Chattisgarh, Jarkhand, MadhyPradesh, Maharashtra and the northeast states, which contribute to 70% of all the malaria cases in the country, is a priority. Intensification of control activities in forest, hilly, tribal and conflict-affected areas will be the challenge. Another example is to eliminate *vivax* malaria. India accounts for 80% of global *vivax* cases contributed by three countries. As the NFMEI document[3] states: "The parasite can survive in cooler climates, is less responsive to conventional methods of vector control, is more difficult to detect using conventional diagnostic tools, treatment of liver stage parasites requires a 14-day course of primaquine which can produce some serious side-effects".

The use of spurious drugs and artemisinin-based monotherapy have been described as contributing to drug resistance in the malaria origin centres in Southeast Asia[4]. Surveillance in this context in India is also essential.

There are many aspects that need to be addressed through basic lab research as well. In my opinion, the biggest threat is entry and spread of artemisinin resistance in the country, even as a combination therapy. Resistance to this most effective drug in the greater Mekong Subregion, which includes Cambodia, Laos, Myanmar, Vietnam and China's Yunnan province[4] is a real threat to the already-affected NE states and further spread. Slower clearance of parasites to Artesunate-SP (Sulfadoxine-Pyrimethamine), approved combination to treat *falciparum* cases in India, is already being reported. A policy is in place to introduce artesunate-lumefantrine combination. Our own studies in animal models have established the efficacy of artemisinin-curcumin combination, both in uncomplicated and Experimental Cerebral Malaria cases[5,6]. This is a unique combination, where curcumin has been shown to act through activating host immune mechanism, despite low bioavailability and rapid metabolism. Curcumin can delay the onset of resistance to artemisinin. It would help significantly if this combination is taken through clinical trials at the earliest.

"Bugs are smarter than scientists, and this human-pathogen is as old as evolution."

A bigger global challenge is to find a new antimalarial that is as effective as artemisinin. There are candidate molecules undergoing trials, but may not be ready in the next three years. The Grand Challenge has to give priority to study of *vivax* malaria. More virulent cases are being reported even in *P. vivax* infection, although chloroquine-based therapy seems to work. Thus, a diagnostic to distinguish between *falciparum* and *vivax* cases in the shortest time is needed. Most often, *vivax* detection is by ruling out falciparum infection. Mixed infection can pose major challenges. Imaging techniques for microscopy need to be upgraded.

Can we find an alternate to primaquine, that involves a 14-day treatment in *vivax* cases with side-effects? The main difficulty in studying *P vivax* is the inability to culture this parasite. Partial success for short-term culture has been reported, but the patient remains as the main source for the parasite. The emergence of simian parasites, *P. knowlesi* and *P. cynamolgi* as potential human parasites in the region needs to be studied carefully, although the reports may be considered as outlying cases at present. The vacuum created by the elimination of *P. falciparum* and *P. vivax* may provide an opportunity for the simian parasites to spread. Bugs are smarter than scientists and this human-pathogen conflict is as old as human evolution!

Most laboratories are carrying out studies with *P. falciparum* cultures to understand the pathology. These studies need to be taken through a translational mode. *P. berghei* infected mouse model is the most popular to carry out studies *in vivo*. It is important to create facilities to use humanized mouse models to study *P. falciparum* infection and even *P. vivax* infections as such. Very few laboratories in India study parasite development in the mosquito. Intervention in the sexual stages of

DEBAJYOTI CHAKRABORTY/NURPHOTO/GETTY IMAGES

Official blood testing at a dengue and malaria clinic in Kolkata.

parasite development is important in the transmission stage and crucial for malaria elimination.

Creation of more insectories to study malaria parasite development in the mosquito would be useful. While, *P. berghei* development in the mosquito can give important leads, *P. falciparum* development studies in the mosquito would need appropriate containment conditions.

I do not believe that an effective malaria vaccine will be available in the next decade, although the RTS,S vaccine may still be introduced in Africa with less than 40% efficacy. The sporozoite vaccine seems to have tantalizing success, but I do not know how it can be made available on a global scale even for *falciparum* cases. Perhaps, it will have limited application in specific geographical regions.

The best option seems to be quick and correct diagnosis, immediate appropriate drug therapy, vector control measures, strategies for intervention in the transmission stage and 'Swachh Bharat' initiatives.

I have already described the priority for basic research. More investments in these areas rather than in more 'fashionable' studies based on gene drives to eliminate mosquitoes are welcome. Gene Drive will have huge environment and regulatory issues in India, even if the several technical challenges are successfully addressed. I would like to see India as a malaria-eliminating country rather than as a malaria-controlling country. Malaria eradication is feasible, but not the mosquitoes.

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ENGAGEMENT

Maintaining momentum

Interest in tuberculosis research is high, but a quantum leap in funding must follow.

SOUMYA SWAMINATHAN

It is heartening to note the heightened political interest and engagement on TB in the past year. What started at the Berlin G20 meeting was followed by the Moscow Declaration to End TB: a promise to increase multisectoral action as well as track progress, and build accountability. The first UN General Assembly High-Level Meeting on TB in September 2018 will seek further commitment from heads of state, which some, like the Prime Minister of India, have already made. At the recent End TB Summit in Delhi, PM Modi announced an ambitious plan to eliminate TB, with a slew of new interventions, including a social support scheme for all TB patients.

Modi also pointed out that the fight against TB must start in communities, villages and towns — a true people's movement.

The World Health Organization's End TB Strategy adopted by all member states in May 2014 aims to reduce TB deaths globally by 95%, and to cut new cases by 90% between 2015 and 2035, and to ensure that no family is burdened with catastrophic expenses due to the disease.

Tuberculosis still kills more people than any other infectious disease and the growing burden of multidrug resistant (MDR) TB is a challenge. Seven countries account for 64% of the total burden. India leads the count, followed by Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa. In fact, India accounts for a quarter of the world's TB cases and a third of its deaths. For the

MOHD ZAKIR/HINDUSTAN TIMES/GETTY IMAGES

Prime Minister Narendra Modi addresses the END-TB Summit and launches the TB Free India campaign in Delhi, March 2018

year 2015, the updated estimate of incidence (new and relapse TB cases per year) is 2.8 million cases, of which the RNTCP diagnosed and notified 1.7 million incident TB patients, leaving approximately 1.1 million presumptive patients whose fate was unknown. The 2015 estimate of the number of TB deaths is 478 000 — making it one of the leading causes of death in India. Of the estimated 79,000 cases of multi-drug resistant (MDR) TB, about 31,000 were diagnosed and the majority put on treatment, leaving a large number of patients undetected with the possibility of further transmission.

While the disease is caused by a bacterium *Mycobacterium tuberculosis,* socio-economic determinants are important and the incidence rate of TB among people in the lowest socioeconomic quintile is at least three times higher than those in the highest quintile. A recent systematic review found that the total cost of TB for patients and affected families on average represented more than half their yearly income. Major drivers of TB in Asia include poverty, overcrowding and under-nutrition, while HIV is the main risk factor in sub-Saharan Africa. Other risk factors include diabetes, smoking and exposure to indoor air pollution, and alcohol consumption.

In Europe, TB rates began to decline in the 1920's, well before any effective vaccine or drug was available, mainly due to living standards improvements.

Tuberculosis infects people mostly via the respiratory route and establishes a nidus of infection, where the organism can survive in a dormant or latent form for many years or decades. An imbalance in the immune control system allows the infection to progress to active disease and the infection progresses faster and is more severe/widespread in young infants and children, those with HIV infection and other immunosuppressive conditions.

There have been great advances in genomics, proteomics and immunology in recent years, but major gaps remain in understanding of pathogenesis of some forms of TB. There is much to learn about the interaction between mycobacterial lineage and host genetics, determinants of virulence and transmission, biomarkers that can predict progression from latent to active disease and correlates of protective immunity. This has slowed down the development of a newer, more effective vaccine for TB, as well as tests that can easily identify individuals most at risk of disease progression who could be targeted for treatment of latent infection. Ultimately, for elimination, latent TB treatment would have to be scaled up, in addition to identification and treatment of active cases.

Major challenges in India include the disparity of treatment providers, many of whom do not follow standard diagnostic or treatment algorithms, the lack of awareness about TB symptoms, and the fact that free diagnosis and treatment are available at government health centres, causing stigma which prevents people from seeking care.

The National Strategic Plan 2017-2025 addresses many of these challenges and provides cash incentives for TB patients who are regular with therapy as well as for physicians who report TB. A national prevalence survey is planned in 2018 to provide a baseline prevalence rate — ideally, complete notification of TB by private and public providers will negate the need for such surveys and enable the programme to monitor progress.

"The total cost of TB for patients and families represents half their annual income."

After relying on sputum smear microscopy for diagnosis for more than a hundred years, a cartridge based nucleic acid amplification test has become the standard of care, enabling rapid diagnosis and detection of Rifampicin resistance simultaneously. There are more affordable diagnostics on the horizon, mainly from India and China, and it is now possible to imagine that every patient with suspected TB could have a molecular diagnostic test, with susceptibility testing for at least Rifampcin, even at a remote primary health centre, with no electricity or highly qualified staff.

After a gap of 40 years, there are now two new drugs to treat TB, though currently these are reserved for multidrug resistant cases. There is a small pipeline of novel molecules that must undergo further clinical development.

More data are likely to become available on the combination of Bedaquiline and Delamanid in treating extensively drug-resistant TB. In the case of TB, it is novel drug combinations (rather than individual drugs) that need to be tested for safety, efficacy, affordability and convenience. This will require the involvement of research institutes, pharmaceutical companies, regulatory agencies and funders, including middle-income countries. The paradigm of drug development needs to be different for diseases like TB, which predominantly affect the poor and do not have a market in the West.

Research to identify specific immune cell core regulatory pathway disruptions caused by pathogens must be increased to efficiently develop new host directed therapies for treatment and prevention. Already, some host directed therapies like the antidiabetic drug, Metformin, and leukotriene antagonists are being tested as adjunct therapies. There needs to be a quantum increase in investment in research in TB — right from basic science to better understand biology and transmission dynamics, to translational research on biomarkers, clinical trials of new drug combinations, and operational research to address blocks in programme delivery. The India TB Research Consortium was launched in 2017 by the Indian Council of Medical Research, in partnership with the Department of Biotechnology and other science ministries, international agencies, and WHO, to undertake translational research to develop and validate new tools (diagnostics, drug combinations and vaccines) needed to fulfill the TB elimination goals.

A national mission to end TB has been launched in India. A concerted effort by all stakeholders — government, private sector, and the patient community — is required, with regular surveillance. The ministry of health has developed a seven-year national strategic plan. Additional investments in research through the India TB Research Consortium will hopefully deliver new and better tools to prevent, detect and treat TB.

The author is deputy director-general of programmes, World Health Organization.

A pavilion at the 'Make in India' week in Mumbai

INDRANIL MUKHERJEE/AFP/GETTY IMAGES

INNOVATION

BIOTECH NATION: SUPPORT FOR INNOVATORS HERALDS A NEW INDIA

The country is uniquely poised to deliver effective and affordable solutions

RENU SWARUP

Innovation is key to solving many problems faced by communities, societies, nations or humanity as a whole. Nurturing innovation requires special attention to maximize benefits for those with the greatest need.

An innovation ecosystem models the economic dynamics of the complex relationships between entities, which in this case are the material resources and humans whose goal is to enable technology development and innovation.

Innovation is believed to be the fundamental source of significant wealth generation within an economy. An innovation ecosystem is thriving and healthy when the resources invested in the knowledge economy (either through private, government, or direct business investment) are replenished by innovation induced profit increases in the commercial economy. The interdependence of innovation and entrepreneurship is therefore a clear one.

India is undergoing a revolution in the area of innovation, whether it is in the areas of science, technology or others. The emphasis of Make in India, Stand Up India, and Startup India launched by the government is on creating a conducive environment for home-grown innovation and entrepreneurship to solve some of the biggest challenges that India faces.

A penchant for frugality, combined with public and private support for entrepreneurship and innovation, mean that India is uniquely poised to deliver effectve and affordable solutions in areas of medicine, healthcare, agriculture, energy, industry and others.

In science and technology, this thrust for innovation and entrepreneurship has been possible because of the systematic and unflagging support of the government. Since independence, until the 1980s, India had built a substantial scientific infrastructure through public funding and some private funding. By the early 1980s, India had a fledgling biotechnology sector with a few biotechnology focused companies that manufactured vaccines, enzymes and other biotechnology products intended primarily for the domestic market.

It was during this time that the true growth potential of the biotechnology sector was realized by science policy-makers and the government, to deliver valuable and affordable solutions to some of India's challenges. This spurred public investments first in academia for basic research which has now expanded to include translational research and development and the entire innovation ecosystem.

Systematic government support for the biotechnology sector began in the 1980s with the National Biotechnology Board (NBTB) and followed by the Department of Biotechnology (DBT) in 1986.

Biotechnology today well poised, because of the excellent base created by DBT in the last 30 years. There are more than 500 laboratories to 16 autonomous institutes each strategically positioned to contribute to a special high-risk area of research. They are part of a focus on creating the translation ecosystem through bio-clusters and connecting with industry, startups and entrepreneurs through BIRAC. It is because of this that India is today a preferred partner for all international collaborations in biotechnology, which we currently have with more than 80 countries.

Biotechnology's role is crucial for the Indian knowledge economy to grow. Establishing and growing an innovation product driven biotech industry was a significant need in India which led to creation of BIRAC by the Government of India. Biotechnology Industry Research Assistance Council (BIRAC) is a not-for-profit public sector enterprise, set up by the Department of Biotechnology (DBT) as an interface agency to strengthen and empower emerging biotech to undertake strategic research and innovation, addressing nationally relevant product development needs. BIRAC is a new industry-academia interface and implements its mandate through a wide range of initiatives, be it providing access to risk capital through targeted funding, technology transfer, IP management and handholding schemes that help bring innovation excellence to the biotech firms and make them globally competitive. In its four years of existence, BIRAC has initiated several schemes, networks and platforms that help to bridge gaps in the industry-academia innovation research and facilitate novel, high-quality affordable product development. BIRAC has also initiated partnerships with several national and global partners.

"India enjoys a penchant for frugality, and support for innovation."

In recent years BIRAC has had very positive impact on the whole ecosystem for startups and entrepreneurs, and the industry academia interface has greatly benefitted. We have more than 1,000 startups and 500 industries engaged in the network. The ecosystem has been empowered by creating over 30 bio-incubator centers with 300,000 sq.ft of incubation space. More than 1000 products or technologies have been developed, many of which are in the market, and more than 150 new IP's have been filed. The focus is also on skill development, training, employment and market access.

An important part of encouraging entrepreneurship is assuming the business risk that a young business developing an innovative scientific idea faces specially in its nascent stages. As products move along the value chain, only the level of their risk changes. Therefore, funding bodies such as BIRAC need to create support through the market value-chain to ensure that ideas don't fail for the want of support. Government funding has also plugged several holes where venture capitalists and angel investors were typically unwilling to invest before, such as early-stage research, during which private investors were more wary. India is moving towards high-risk funding, encouraging for many scientists to take up research on disruptive technologies.

Our recent focus on retaining and attracting scientists with high-level experience and our recent investments in high-tech infrastructure gives us the confidence to support disruptive technologies.

Biotechnology is an intrinsic component of the 21st century knowledge economy. The Indian government has set an ambitious target of US$ 100 billion for the biotechnology industry by 2025. DBT along with BIRAC is committed to work alongside all partners in the endeavor to create an innovation driven biotech ecosystem and amplify the growth of Indian biotechnology.

The vibrant ecosystem we see today gives us the confidence that our innovators will be recognized globally for providing solutions for addressing major societal problems.

The recent government impetus on Make in India and Startup India have given a major boost to this sector, and the biotechnology industry will contribute immensely to the enhanced GDP and employment opportunities.

The industry is poised to leverage its strength and capacity to bring in transformational change and the making of a new India by 2022.

Renu Swarup is BIRAC's managing director.

The challenge of improving sanitation demands a pipeline of technological solutions from India's best minds, along with sustained funding.

JONATHAN RAA/GETTY IMAGES

PHILANTHROPY

A strong foundation for progress

Supporting and enabling groundbreaking projects from inception to results on the ground.

TREVOR MUNDEL

The words science and technology can conjure images of things far from our everyday experience: ISRO's Mars orbiter or theoretical physics, for instance. But science and technology are both intuitive and immediate, and they are key to addressing the most pressing challenges India faces.

As part of Swachh Bharat, for example, the government of India set a deadline of 2019 for Indians to stop dumping untreated waste into the environment. The government has called for "measurable results" on malnutrition by 2022, and it has pledged to eliminate tuberculosis as a serious national health challenge by 2025. That is a lot to do in a short time, which is why India is committed to an innovation agenda.

At the Bill & Melinda Gates Foundation, we agree that innovation and India's future are inextricably linked. We believe the world is getting better, and can get better still, in large part because scientific and technological innovation can help solve difficult problems, especially those faced by the poorest. We have been working closely with the government of India for more than a decade as it implements its

innovation agenda, and one of our most effective collaborations to date is Grand Challenges India.

The Grand Challenges programme dates back to the very beginning of the Gates Foundation. Bill and Melinda Gates had spent their careers in the software industry, where the best minds came together to unleash an almost-constant stream of innovation that revolutionized the way people lived and worked. They did not see the same focus on innovation in global health and development, and they were convinced that a little attention after years of neglect could unlock big improvements. As a result, they worked with partners to create a programme that turned the usual grant-making paradigm on its head. Instead of selecting grantees and prescribing their activities, Grand Challenges would explain the end goal — for example, to discover treatments that don't lead to drug resistance — and then invite innovators from everywhere to propose ideas for how to achieve it. The hope was to encourage more ideas from more places and push the best ones forward fast.

India had always been a part of our vision for Grand Challenges, both because many of the problems the programme was designed to solve exist on the subcontinent and because so many world-class innovators come from India as wel. As a result, we decided to host the 2011 Grand Challenges annual meeting in New Delhi. In the run up to that meeting, we forged a strong relationship with the Department of Biotechnology, which was interested in creating a Grand Challenges India to engage more Indian innovators to work on India-specific challenges. In 2012, we signed a memorandum of understanding, the newly formed Biotechnology Industry Research Assistance Council (BIRAC) was given responsibility for the programme, and in 2013 Grand Challenges India issued its first calls for proposals, with funding provided jointly by the government of India and the Gates Foundation.

Many Grand Challenges projects that generated impressive early results are now being scaled up. Together, they offer hope that Prime Minister Narendra Modi's ambitious targets for improving the quality of life for the poorest in India are within reach.

Consider sanitation. Though open defecation is a problem in rural areas, most people in urban areas use pit latrines or septic tanks. While the waste is contained initially, most of it is eventually dumped, untreated, into the environment. Consequently, one of the first two calls issued by Grand Challenges India was for proposals to "reinvent the toilet"—that is, to create technologies appropriate to the situation on the ground in Indian communities that can prevent the pathogens in human waste from circulating. One of the Reinvent the Toilet grantees, BITS Pilani, is developing what it calls the empowered septic tank. Run on photovoltaic power, the system uses electricity to change the pH levels in effluent, killing pathogens and helminth eggs. The team is now pilot testing its technology in a community setting, in preparation for scale-up.

"The hope was to encourage more ideas from more places, and push the best ones forward first."

To achieve the results promised on malnutrition, India will need to continue to improve routine immunization, since enteric infections can prevent children from absorbing nutrients from food. Improving routine immunization requires improving the supply chain. The old-fashioned paper records were sometimes inaccurate, and even when they weren't, information traveled slowly, which meant it could take weeks to address stockouts. One Grand Challenge project supported a start-up company in Bengaluru called Logistimo, which created a cloud-based mobile supply chain platform so that anyone with a smartphone can instantly check stock anywhere in the system. Logistimo is now deployed in five countries and has over 12,000 stores in its network with a stock availability of more than 95 percent.

Fighting tuberculosis is another priority our foundation shares with the government of India, and almost 15 years of Grand Challenges-funded research has produced a better scientific understanding of latency, which is helping drug developers accelerate their research. We have also supported programs to promote adherence to the current treatment regimen, including 99DOTS, an ingeniously simple and inexpensive monitoring system. Each time a patient takes a pill from a specially designed packet, it reveals a number for the patient to call, toll-free. That phone call feeds into a system that dispenses reminders, incentives, and counseling for patients who are having trouble sticking to the regimen.

The impact of each of these innovations is significant. But what's just as significant is that the government of India is supporting a platform that is producing innovations on an ongoing basis to overcome a vast array of obstacles standing in India's way. We are proud to work alongside the nation as it addresses the priorities of today to create the India of tomorrow.

Trevor Mundel is the president of the Bill and Melinda Gates Foundation

nature
INDIA

Photo contest 2017

Grand Challenges

Deepak Bhau Kumbhar

Ricky Patel

Avinash Surendran

Dipankar Ghosh

Preethi Krishnamoorthy

Samrat Mukherjee

Nature India held its first photo contest in 2014. We received about 50 entries, but the quality and passion of our entrants was enough for us to make the contest an annual affair.

Four years later, *Nature India* has a rich archive of stunning science pictures from across the world. We've even put together a travelling exhibition curated from some of the winning pictures. The large number of scientists participating in these contests also got us thinking about the importance of visual elements in communicating science.

In 2016, this sparked our 'Visualising Science' workshop where more than 80 selected Indian scientists received hands-on training in photography, illustrations, infographics, film-making and virtual reality. The two-day workshop at the National Institute of Immunology, New Delhi was supported by *Nature India*'s long time partners Wellcome Trust DBT India Alliance.

The theme for the 2017 photo contest was Grand Challenges. Dan Ferber, who was then executive editor, Grand Challenges, for Springer Nature, called for entries:

"Droughts. Typhoons. Rising seas. Refugees. In this big, crowded world of ours, the challenges we face can sometimes seem daunting. Indeed, we must address the complex global problems we face — the world's grand challenges — to ensure humanity a healthy and sustainable future. But first we must see them clearly. That's where photography comes in.

We must see the vast sweep of the flooded landscape in the aftermath of the typhoon, as well as the man carrying his belongings on his back through the waist-deep floodwaters. We must see the woman walking two kilometres to obtain drinking water for her family, as well as the young child, wan with fever from a treatable disease like pneumonia or diarrhoea.

But we must also see images of ingenuity and resilience: a scientist testing an improved form of wastewater treatment, a green skyscraper that not only cools the air, but grows food as well, a nurse vaccinating rural children.

Addressing the world's grand challenges will require scientists — and all of us — to reach beyond our comfort zone, collaborate across disciplines and across sectors, focus on solutions. It's a big, crowded world, but ultimately it's a small one, and we're all in it together."

We received more than 300 entries from around the world. Scientists and non-scientists, professional photographers and amateurs, high-end digital camera operatives and mobile phone users all vied for the top spots. A team of editors and art directors from across Nature Research judged the entries for novelty, creativity, quality and printability. The photos were also rated in part by the engagement they received from the online science-loving community on *Nature India*'s social media channels.

We present some of the winning pictures, as well as some very worthy contenders.

Deepak Bhau Kumbhar, Maharashtra, India

Just one world

These beautiful caterpillars face severe competition from one another, trying to nibble into a single piece of leaf. That's what is happening to mankind as we greedily consume the world's limited resources. It is time we realise that soon there won't be enough left for all of us. Though that realization has dawned among many, out of sheer habit we continue to nibble into the same leaf.

I am a science teacher at a high school, passionate about micro wildlife photography. I photograph nature's amazing creations and show them to my students with various messages.

Dipankar Ghosh,
Minnesota, USA

Fishy tales

A dramatic increase in population, along with climate change, are depleting global natural resources at an alarming rate. Fishermen on the Puri coast in Odisha, India depend on the ocean's natural resource for their livelihood. But meeting the daily targets of fish needed to earn a living is often a big challenge.

Ricky Patel,
West Bengal, India

Cleaning up my abode

Can we please use biodegradable material or adopt safer waste disposal practices, at least inside the national parks? My friends and I living in the Ranthambore National Park (Rajasthan, India), have a hard time cleaning up after careless tourists. I imagine this would be the message of this Royal Bengal Tiger, with a plastic bottle in its mouth, if it could speak to you. Incessant use of non-biodegradable polymers makes a mockery of our national programme of 'Clean India', even in highly protected zones.

Avinash Surendran, Bengaluru, India

Children of the Sun

Enough sunlight hits the Earth in an hour to power it for a year. Why aren't we using this resource enough? Even five years ago, powering homes or industries using solar power would be the realm of a billionaire philanthropist. However, in the last five years, the cost of solar energy has fallen by a fifth, making it cheaper than fossil fuels in many countries around the world. The story of solar energy is not just about sunlight. Its success includes sound technology, innovation and the political will to solve the grand challenge of cheap sustainable energy. It is a story of democratization of energy and leaving the planet a better place for our children. The next generation should be the children of the sun.

This photo was taken from the terrace of the Indian Institute of Astrophysics, Bangalore. I am a PhD student there and contributed to the installation of a solar rooftop power plant which offsets the energy usage of the entire institute, while providing cheaper electricity than that available from the grid. This photo for me is symbolic of the opportunity we have in solving the problem of cheap sustainable energy for all.

Preethi Krishnamoorthy, Bengaluru, India

Poverty inherited

I was having my morning cup of tea at the window in a quiet Bengaluru neighbourhood when I saw this little boy. He was confidently running around the street without fear of the moving vehicles. He walked over to a woman, perhaps his mother, among some workers mending the road, tugged on her sari for attention and made a sad face when she refused. For her, leaving work to attend to him would probably mean no dinner for him that night. She went back to work, and he to play with a little girl he found. She readily shared a packet of chips with him. All was well again in his little world, but there were a lot of questions in mine. Would he grow up to get formal education or have a healthy life? Would the underprivileged ever be able to break their inherited cycle of poverty? The burden of these questions should weigh heavily on our collective conscience.

Samrat Mukherjee, Mumbai, India

Home alone

Every year the rains are more unpredictable. Traditional ways of living are unable to cope with this change.
This image was taken in the Nadia district of West Bengal, crippled after a spell of heavy cyclonic rains, a phenomenon that's more frequent in the Bay of Bengal in recent times.

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Funding to address India's pressing challenges

Technology holds the solution to many pressing problems. BIRAC and Grand Challenges aim to HARNESS LOCAL INGENUITY.

Bio-incubation centers across the country are important for encouraging young entrepreneurs and researchers.

Agriculture, nutrition, sanitation and maternal and child health are some of the biggest challenges India faces.

A solar dehydrator to help famers preserve excess produce and a toilet that cleans itself and creates biogas for cooking are just two of many Grand Challenges projects helping to meet some of the most daunting development issues in India.

Despite reductions in child mortality rates, increased immunization levels and improved nutrition, India and its population of 1.3 billion still face immense challenges.

Grand Challenges India was launched in 2012 to address some of the most difficult issues. Specifically, it focuses on three critical areas: improving mother and child health; reducing malnutrition; and improving sanitation.

Set up as partnership between the Indian Department of Biotechnology and the Bill & Melinda Gates Foundation, Grand Challenges India is hosted by the Biotechnology Industry Research Assistance Council (BIRAC).

A not-for-profit company of the Indian Government, BIRAC was established in 2012 to nurture the Indian biotechnology landscape, through the development of startups and entrepreneurs in the biotechnology sector.

BIRAC works across a wide range of products, processes and technologies spanning the fields of healthcare, agriculture and industrial biotechnology. "We fund across the whole value chain — from research idea, to proof of concept — to scale up to innovative products. We also work with successful projects to help them launch products in the market," says Renu Swarup, BIRAC's managing director.

BIRAC and Grand Challenges India work with early-career and established researchers as well as entrepreneurs from both academia and industry. It provides financial, technical and administrative support. Grand Challenges India also provides special support for implementing out-of-the-box ideas for projects that lack sufficient funds to generate preliminary data through the Grand Challenges Explorations India program.

RESEARCH PRIORITIES

Since its inception, BIRAC has initiated a number of programs that support biotechnology from the earliest stages of idea generation through to providing early stage seed grant to reach proof-of-concept stage. BIRAC's Biotechnology Ignition Grant has become one of the largest early stage programmes and has supported more than 500 start-ups and entrepreneurs. Some notable products and technologies from this scheme include the development of a protein which acts as a molecular drilling machine, drug candidates for diseases and water potability solutions.

BIRAC's other flagship schemes such as Small Business Innovation Research Initiative, Biotechnology Industry Partnership Programme and Contract Research Scheme have also contributed immensely to connecting industry and academia and taking ideas to product development.

The council also plays an important role in the implementation and delivery of the flagship programmes of the Indian Government, especially **'Make in India'** and **'Start-up India'**.

Within Grand Challenges India, research priorities

Products such as Sohum, a hearing test for babies, are some of the novel products that have been supported by BIRAC schemes.

focus on the critical problems of mother and child health, malnutrition and sanitation.

An example is understanding how farmers' inability to store fresh produce can ultimately contribute to malnutrition. When produce is abundant, the glut means farmers have difficulty selling all their produce, which is then wasted. If the season is poor, food prices go up and the farmers themselves can no longer afford to buy a wide range of foods, which can result in malnutrition.

A solution to this problem is a domestic solar food dehydrator designed by Vaibhav Tidke. A study of 200 female farmers who were given the solar dehydrator found that the women who sold dried food doubled their profit, compared with selling only fresh produce.

Meanwhile, the Grand Challenges' Reinvent The Toilet program has been investigating toilets that don't depend on connection to the grid or the sewer. One such toilet, the Eram eToilet is designed to use recycled water for autoflushing and floor cleaning. In the pilot test, the school test site even used the biogas generated from the waste for cooking.

HOW TO APPLY FOR FUNDING

BIRAC and Grand Challenges India funding is available through many of the schemes that the organisation advertises on **www.birac.nic.in** and **www.birac.nic.in/grandchallengesindia**. Seed funding or larger amounts are available depending on the project theme and mandate. Support may come from Grand Challenges India, the Biotechnology Industry Research Assistance Council or program partners such as the Bill & Melinda Gates Foundation or the Wellcome Trust.

Applying for funding is a route for addressing some of India's most important challenges and tapping into the extensive mentor and peer network of BIRAC and the other partners.

"We are working on real challenges. When a challenge is accomplished it can really touch human lives. It provides a great sense of satisfaction," says Shirshendu Mukherjee, mission director, Program Management Unit at BIRAC. ■

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Grand Challenges India

A shot at contraception

In India, a nonagenarian renews testing of a birth control vaccine

By Killugudi Jayaraman

Matt Hansen/SpringerNature

The idea to try to revolutionize birth control came to Gursaran Pran Talwar during a trip in 1972 to the holy city of Varanasi on the banks of the Ganges. There, in the crowded streets, the Indian biochemist bumped into groups of emaciated women herding their large broods of children.

Why did they not limit their family size when the government offered a basket of birth control methods for free, Talwar, who then worked at the All India Institute of Medical Sciences (AIIMS) in Delhi, wondered. A brief conversation with them revealed the reasons: using birth control pills required remembering to take them daily and the intrauterine devices (IUDs) available at the time caused excessive bleeding. A surgical procedure involving ligation of the fallopian tubes, known as 'getting your tubes tied' in other parts of the world, caused permanent infertility and was therefore not preferred until later in their reproductive lives. Their husbands, meanwhile, were reluctant to use condoms.

That set Talwar thinking. Why not devise a reversible contraceptive option for women that didn't require daily dosing and was free of many of the side effects associated with traditional birth control, such as unexpected mid-cycle bleeding, mood changes and headaches?

He believed that a vaccine targeting the hormone called human chorionic gonadotropin (hCG) would be ideal. hCG is made by the embryo early after fertilization and isn't produced until the onset of pregnancy. This unique aspect of hCG is the very reason why it is used as a reliable test of pregnancy. Importantly, hCG is essential for implantation of the embryo in the uterine lining. So, if a vaccine were to generate antibodies neutralizing hCG, Talwar reasoned, implantation of the embryo would be blocked, thereby preventing development of a fetus.

Now, after more than four decades and having developed three different successively improved versions of an anti-hCG vaccine, Talwar, 91, thinks his idea is finally becoming reality.

In late November, he got the news he was eagerly waiting for. The Indian Council of Medical Research (ICMR), the country's primary funding and coordinating body for biomedical research, informed him it would fund and conduct the clinical trials of his latest vaccine. A total of 120 women will participate in the testing—50 in the phase 1 trial and 70 in the phase 2 trail—at two hospitals in Delhi. Talwar expects the phase 1 trial to start by March, and, according to the ICMR letter he received, the trials are approved to "determine the safety and immunogenicity of the vaccine in sexually active healthy women and prove its ability to prevent pregnancy without impairment of ovulation and derangement of menstrual regularity and bleeding profiles."

Other scientists have taken note of the upcoming trials. "It is gratifying to hear the hCG vaccine has been revived," says John Schiller of the US National Cancer Institute, who a decade ago had considered hCG as a potential 'payload' for a vaccine platform that he had developed, although he did not end up moving ahead with this particular application. Jeffrey Jensen, director of the Women's Health Research Unit at Oregon Health & Science University in Portland, who has followed Talwar's work since the late 1980s, is also watching to see what happens. Although he stresses that some of the immune system's reactions to the vaccine have to be better understood, he told *Nature Medicine* that "a vaccine approach could become an additional option for birth control in India" and would likely be accepted in other countries, too.

But Sharon Batt, a bioethicist at Canada's Dalhousie University, fears that the vaccine, if it becomes available, will inevitably be deployed among the poor where large families are most common. "It masks, rather than addresses,

the social and economic reasons that poor, undereducated women have large families, including a dependence on children for economic security," she says.

For his part, Talwar hopes that the vaccine, when released, will have women opting for it because of its contraceptive benefit without the unpleasant side effects of 'the pill'. "I am sure there would be plenty of women who would like to take three or four doses of vaccine and be free for about two years," he says. "A role for vaccines undoubtedly exists as an aid to birth spacing, particularly in developing countries."

Gursaran Pran Talwar

Forging ahead: Talwar in his office with a photo of his aunt, Vimal Raghuraj, who raised him.

An alternative choice

References to fertility regulation in women exist in historical records stretching back to ancient times, but it was only in the twentieth century that a basket of efficient and secure methods of birth control became available. The first oral hormonal pill of this sort, Enovid, was first marketed as a contraceptive in 1960. IUDs appeared in the 1920s, but it was only in 1988 that the new-generation copper IUD was first introduced to the US market, and hormonal IUDs came later in 2001. Altogether, 18% of the world's contraception users rely on hormonal methods. But Talwar says that his vaccine offers an advantage in that it doesn't control women's menstruation cycles or hormones as the pill does. And he believes that modulating the immune system should be better for temporary contraception than IUDs, which require surgery for implantation and removal.

The number of women using contraception globally has already surpassed 770 million[1], with high growth in use projected for all regions of Africa and in southern Asia. However, according to the World Health Organization (WHO), 214 million women of reproductive age in developing countries who want to avoid pregnancy are not using a modern contraceptive method. The need for increasing contraceptive options was noted in a December study[2] by the Guttmacher Institute in New York. This study found that, in India, half of the 48 million pregnancies in 2015 were unintended and that more than 15 million ended in abortion. "Our findings confirm and reinforce the need for more effective contraceptive methods for women to choose from," Susheela Singh, the study's author and the institute's vice president for international research told *Nature Medicine*.

Talwar's vaccine targets hCG, which has two subunits—alpha and beta. Ideally, a contraceptive vaccine would use both to stimulate an immune response, but the alpha subunit of hCG is common to other non-pregnancy hormones produced by the pituitary gland, so its incorporation in the intended vaccine could provoke an autoimmune response against this whole range of vital pituitary hormones. Talwar therefore chose to make the vaccine out of the beta subunit and chemically attached it to the tetanus toxoid protein to help trigger the body to become immunized against this subunit.

In1974, he launched a phase 1 clinical trial that included four Indian women who had completed their families and had their fallopian tubes tied to prevent further pregnancies. In these women, the vaccine made antibodies against both hCG and tetanus with no disruption of regular menstruation. Their antibody levels steadily rose to reach a plateau, which was maintained for about three months, after which antibody levels began to decline, indicating that the vaccine's effects wear off over time[3,4]. The safety and ability of the vaccine to induce anti-hCG antibodies were confirmed by Population Council–sponsored trials in the late 1970s using the same vaccine in Finland, Sweden, Brazil and Chile[5] on 15 healthy women.

Besides Talwar, another scientist named Vernon Stevens at the Ohio State University had been working since the early 1970s on a similar approach for birth control. However, unlike Talwar who designed his vaccine to employ the whole beta subunit, Stevens ultimately designed a vaccine based on only a tiny fragment of the beta subunit for the WHO Task Force on Vaccines for Fertility Regulation.

Even though the idea of a birth control vaccine was gaining traction outside India, this did not assuage all skepticism to the approach in Talwar's homeland. "Back home, people felt that this was a crazy idea that could make women permanently sterile," he says, reminiscing about the early days that, fairly or not, generated significant debate on ethics. "Vaccines were made against infections and not contraception," Sarojini Nadimpally, a feminist bioethicist and the founder of Sama, a Delhi-based resource group for women and health, told *Nature Medicine*. The result, says Talwar, was that he "could get no research grant or support from his peers to go ahead." Talwar's distress was, however, short-lived. The break came in 1983 when he became the director of the newly established National Institute of Immunology in Delhi, where he resumed the voyage that he started a decade earlier at AIIMS.

Talwar was aware of the main drawback of his prototype vaccine: the antibody levels it produced were insufficient to neutralize hCG. To make it more powerful, in 1988, he combined the hCG beta subunit (which was prepared from hCG purified from the urine of pregnant women) with a sheep-derived version of the alpha subunit of another reproductive signaling molecule known as luteinizing hormone. The rationale behind the updated design was that the latter hormone, being a foreign molecule, would stir a greater immune response in humans.

In a 1990 phase 1 trial, this second-generation anti-hCG vaccine produced higher antibody titers than its predecessor. The phase 2 efficacy trial on 148 women during 1991–1993 in three centers in India demonstrated the feasibility of preventing pregnancy in a reversible manner without impairment of ovulation. The women had IUDs implanted until it was demonstrated that their antibody levels were high enough to prevent pregnancy. Once the IUDs were removed, there was only one implanted pregnancy (which was terminated upon the subject's request) occurring in 1,224 menstrual cycles[6]. The response to the vaccine was reversible. Four women in the trial, who desired another child and who did not take a booster after having remained protected for a year or more, did conceive and delivered normal babies[7]. A news report in *Science*[8] described the

trial as a "landmark" and hailed it as the "first demonstration that women can be vaccinated against pregnancy."

Evoking a response

Although the phase 2 trial of Talwar's second-generation birth control vaccine provided proof of concept, only about two-thirds of women in the trial produced antibodies above the desired threshold, thought by Talwar to be sufficient to prevent pregnancy, for a duration of at least three months. So, it was Talwar's next task to enhance the vaccine's ability to evoke an immune response. But he suddenly faced another barrier that again held up the vaccine's progress: in October 1994 he had to retire from the National Institute of Immunology, whose authorities could not extend his emeritus position nor provide him working space. Parting from the institute also meant that he had to leave behind a Canadian grant he had received for developing the vaccine.

The bad news kept coming. Around the same time, news arrived that a WHO task force trial undertaken on women in Sweden testing the vaccine developed by Vernon Stevens was suspended because the first seven of the 30 trial participants all experienced severe and unexpected side effects[9]. The study was not published.

Talwar says he "was left injured" when asked to quit midway. But a remedy arrived quickly in the form of a new grant from the Rockefeller Foundation in New York and an offer of laboratory space by the National Institute of Immunology's neighbor, the International Centre for Genetic Engineering and Biotechnology (ICGEB). The honeymoon, however, lasted for just four years, as the space given to him was subsequently needed to house the National Brain Research Centre. The prospect of an imminent ouster from ICGEB when his project was midway completed put him in a fix.

But nothing could deter Talwar, an incurable optimist who is no stranger to difficulties. He lost his mother when he was eight days old and, as a youth, had to flee to Delhi from riot-torn Hissar—his birthplace—following the partition of India. Talwar completed his final year of college by staying in a camp set up for migrants. All this didn't stop him from winning a fellowship for graduate studies at the Pasteur Institute in Paris, where he got his doctorate, and becoming the second faculty member to join the newly launched AIIMS in Delhi in 1956.This indomitable spirit drove him to carry on working on his dream vaccine, even after eviction from ICGEB, in a laboratory he built near his residence with his own funds. Thanks to a grant from the Indo-US Committee on

Gursaran Pran Talwar

Early days: Talwar as a graduate student at the Pasteur Institute.

Contraception Research in 2006, his research program that had remained inactive for about 12 years was revived.

His third-generation vaccine, now awaiting clinical trial, is a recombinant vaccine that consists of the hCG hormone's beta subunit fused with a portion of a protein derived from *Escherichia coli* bacteria that is thought to be more capable of stirring an immune response than the inactivated tetanus toxin used as a carrier in earlier versions. This version of the vaccine passed toxicological studies in rodents and marmosets and was ready in 2010 for human testing, but it has taken eight years to pass through India's National Review Committee on Genetic Manipulation and the Drugs Controller General of India to reach the clinical trial stage. Bharat Biotech in Hyderabad will produce the vaccine and make it available free of charge for the clinical trials.

Will it prevent pregnancy? Talwar is optimistic but adds that "how long the protection will last will only be clear after the trials." He notes that, in clinical trials of the second-generation vaccine, many women remained protected for as long as two and a half years by taking boosters an average of every three months to maintain the desired antibody levels[6]. Talwar does not believe there is a risk of long-term infertility from the vaccine and says a woman can conceive a child by skipping the boosters and waiting until her antibody levels drop below a certain level.

"It is exciting news," Rajesh Naz, who is vice chair of research and professor of obstetrics and gynecology at West Virginia University's School of Medicine, says of the new trial launch. "If successful," adds Naz, who was Talwar's PhD student decades ago, this vaccine "will revolutionize the field of contraception all over the world, especially in India where presently the population explosion is a pressing issue."

But not everyone is buoyant about the vaccine's prospects. Aaron Hsueh, a reproductive biologist at the Stanford University School of Medicine who is familiar with the story of the hCG vaccine, says he is "surprised that Talwar is still working on this project." He questions the need for a vaccine given the safe contraceptive options available for women, including the so-called 'morning after pill'. Sharon Batt of Dalhousie University says that, although there is no evidence of harm from the earlier versions of the vaccine to animals, mothers or offspring, the numbers of subjects and extent of follow-up are not adequate to conclude safety. "If this trial goes ahead," she says, "Talwar and his colleagues would be advised to welcome a very public system of external oversight."

There are still skeptics in Talwar's home country as well. "I do not think there is any likelihood of this vaccine being accepted as a reversible form of contraception," says Jacob Puliyel, a pediatrician at St. Stephens Hospital in Delhi and a member of India's National Technical Advisory Group on Immunization. But all this doesn't worry Talwar. "When it was decided to conclude the phase 2 trial in 1993, many participants offered to pay for the vaccine to continue to be immunized," he says, even though he and his fellow scientists could not continue administering the vaccine after the trial's end. "It reflects in a way that they were happy and satisfied with this mode of contraception."

Reflecting on his decades-long scientific journey, which began in the holy city of Varanasi, the nonagenarian Talwar posits that another hand might be helping to bring this type of vaccine forward: "Maybe God has given me long life to see this vaccine become the first birth control vaccine for preventing pregnancy, if it succeeds in the clinical trials."

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SUZANNE LEE/PANOS

Kamla Devi, Rajasthan's first female solar engineer.

Rethink India's energy strategy

Address the needs of poor and rural households, target subsidies and support low-carbon industries, urge **Arunabha Ghosh** and **Karthik Ganesan**.

India's policy-makers have three big energy goals: providing everyone with access to energy, securing energy supply and trying to limit carbon emissions without encumbering the nation's growth. These important concerns miss the point.

Energy access cannot be assured by progress towards a simple target such as supplying power 24 hours a day, 7 days a week, nationwide. India has deep divides in the quantity and quality of energy consumed across income groups and between rural and urban households. Fuel subsidies are poorly designed and the strategies to reduce them to enhance energy security are heavy-handed. And because of limited action by the world's largest emitters, there is little left in the global carbon budget before planetary safety limits are breached. Clean energy and alternative growth is imperative.

India's energy priorities should be reframed as follows: to cater to the different energy demands of citizens of various economic strata; to direct energy subsidies to benefit the poor; and to promote low-carbon industry.

DISPARATE DEMAND

Urban India aspires to have a reliable 24/7 electricity supply — voltages currently drop at peak demand times such as during evenings. Meanwhile, more than one-third of India's households, mostly poor and rural, are not connected to the electricity grid. For those that are, blackouts last 4–16 hours a day. The poorest households consume one-quarter of the energy of those at the highest income levels. Urban centres are in effect subsidised by rural areas, which are being overcharged for substandard service[1]. The poorest households pay 30% more per unit of useful energy than the richest[2].

Renewable-energy applications can provide heating, cooling, cooking, mechanical power and electricity.

One solution to these disparate demands is to deliver more electricity through the grid while adopting cleaner energy sources. The Indian government has announced ambitious plans for renewable energy: up to 175 gigawatts (GW) of installed capacity by 2022. There are many challenges to achieving this target, from the availability of resource data on which to base decisions and managing risks to the high cost and the huge variability across the grid in terms of energy sources and infrastructure.

Meanwhile, the promise of reliable electricity through centralized infrastructure

SOURCE: REF. 7

and systems remains unfulfilled. This is in part because most electricity utilities suffer financial difficulties — they lost more than US$19 billion in 2012–13 (ref. 3). One solution is to tap smaller-scale distributed renewable energy sources, primarily solar, biomass and small-scale hydropower. Off-grid power based on these technologies has advantages such as network resilience, flexibility and environmental and health benefits[4].

More than one million households in India rely on solar off-grid systems for lighting. A further 20 GW of energy capacity could be achieved if 15% of irrigation pumps were converted to solar energy. Renewable-energy applications can provide heating, cooling, cooking and mechanical power as well as electricity[5].

More than 250 companies across India, with long supply chains and networks of village-level entrepreneurs, operate in the decentralized clean-energy sector already. They demonstrate that putting power in the hands of poor people can begin a transformation in how energy access is understood and delivered. At the same time, such rapid growth and geographical spread could result in variable quality of service and expensive energy for poor people. More training would help to keep up standards.

The challenge is to balance two types of investment: those in the centralized grid, which are key to the aspirations of millions of higher-income households, and funds for standalone systems in isolated and underserved areas or for integrating such systems to the grid.

RATIONAL SUBSIDIES

Another reason for pursuing renewable energy in India is to avoid the pitfalls of a growth strategy mostly based on fossil fuels. Already, imports account for more than 80% of India's crude oil and 25% of its coal and gas, raising worries about supply and price volatility[6]. Petroleum constitutes nearly 30% of all commodity imports, leaving India little fiscal room to shrink its large current account deficit.

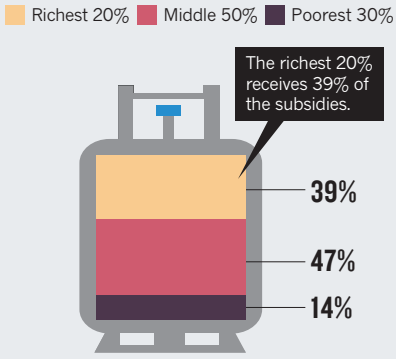
India hands out generous energy subsidies, most of which are not means-tested (see 'Energy imbalance'). For example, in 2013–14 the government gave away $8 billion worth of subsidies for liquified petroleum gas (LPG)[7]. Yet less than half of urban households and only 6% of rural ones exclusively use LPG for cooking. Traditional biomass fuels such as wood account for 20% of Indian households' energy use. The government must rationalize subsidies and target them better.

"The poorest households pay 30% more than the richest per unit of useful energy."

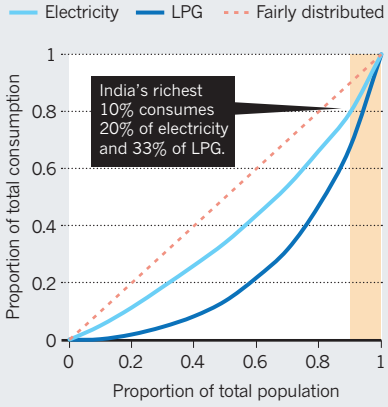
ENERGY IMBALANCE

Liquified petroleum gas (LPG) fuel is heavily subsidized by the government, even though it is used mainly by high-income families. A rural electrification programme started in 2005 has improved the fairness of electricity consumption.

1 **Share of LPG subsidy, by income bracket**



2 **Energy-consumption inequality**



A well-designed programme would increase access to modern cooking energy (electricity and gas) for the same budget. For instance, reducing subsidized LPG to 9 cylinders (instead of 12) per year per connection could save the government $724 million. Excluding the richest 15% of households from the subsidy could save $1.18 billion annually. The savings should be redirected to increasing the availability in rural areas of cleaner cookstoves and biogas, and could extend LPG provision to 30 million more households.

WHAT TO MAKE IN INDIA?

Energy and climate policies are closely tied to industrial policy. Even on a low-carbon energy pathway, total primary energy consumption in India will at least double by 2030 (compared to 2011 levels). Energy efficiency alone — in industry, residential and commercial spheres — cannot mitigate climate change.

Although unemployment rates in India are low (less than 5%) nearly 35% of employment is casual labour. The government's Make in India campaign, launched in September 2014, calls for aggressive job creation through rapid growth in the industrial sector.

Manufacturing consumes nearly one-third of India's primary energy supply, and contributes to 16% of gross domestic product (GDP) and more than 20% of direct emissions[8]. These emissions would grow, should India achieve its target of 25% contribution to GDP from manufacturing.

The best opportunity for decarbonization, therefore, is the power sector — which contributes nearly 38% of overall emissions[8]. Here, renewable energy could account for about 30% of the electricity mix by 2030.

In sectors such as metal production, non-metallic minerals, chemicals and textiles, which contribute most to manufacturing GDP, fuel accounts for 9–23% of all input costs compared to the industrial-sector average of 5%. Energy efficiency and alternative fuels should play a key part in decarbonizing these sectors. India's cement industry, for instance, is one of the world's most efficient, but it also accounts for 7% of the country's emissions. Here, technological advances such as refuse-derived fuels could save 600 million tonnes of coal, 550 billion units of electricity and 3.4 gigatonnes of carbon dioxide emissions between now and 2050.

A shift to a different industrial mix is required: away from such energy-intensive sectors and towards metal fabrication, manufacture of computers and electronics, electrical and mechanical machinery, advanced materials, biotechnology, nanotechnology and photonics. This would lower the energy footprint of India's industrial growth. ■

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A man with mental health problems talks to a volunteer psychiatrist from the Institute of Human Behaviour and Allied Sciences (IHBAS) in Delhi.

STUART FREEDMAN/PANOS

Action on mental health needs global cooperation

As threats to populations transcend national boundaries, it is crucial that responses to mental-health problems do too, say **Pamela Y. Collins** and **Shekhar Saxena**.

Mental-health disorders are the leading causes of disability worldwide. Nearly 30% of people around the world experience a mood, anxiety or substance-use disorder in their lifetime[1]. The resources required to address these conditions are inadequate, unequally distributed, inefficiently used and static[2]. The widespread incarceration of people with mental-health disorders persists.

The need and demand for mental-health care is increasing as vulnerable populations expand. Notable are the tens of millions of migrants fleeing persecution, conflict and violence, as well as the survivors of Ebola and other recent threats. Yet there are only 9 mental-health providers per 100,000 people globally; an extra 1.7 million mental-health workers are needed in low- and middle-income countries alone.

Mental health does not lack political support. This month, the World Bank and the World Health Organization (WHO) will together address the broader development community to make the case for investment in mental health. In the past three years, the importance of mental health has been highlighted by the WHO, in its Mental Health Action Plan for 2013–20; by leaders of countries in the Asia-Pacific Economic Cooperation (APEC); and by the health ministers of the Commonwealth nations. In September 2015, mental health was incorporated into the United Nations' Sustainable Development Goals.

Five years ago, we, as members of the ▶

Grand Challenges in Global Mental Health initiative, called for an equitable and global approach to reducing the burden of mental disorders[3]. The visibility of the issue has come a long way since then. And although there continue to be problems with the delivery of mental-health services, funding for research and innovation in mental health in low- and middle-income countries has increased substantially (albeit from a small base). Since 2011, new investments estimated at US$79.3 million have been made by the three largest funders of mental-health research in low- and middle-income countries (Grand Challenges Canada, the UK Department for International Development and the US National Institute of Mental Health).

Researchers in such countries are tackling the dearth of mental-health professionals by testing the delivery of care by non-specialists — such as peers, community health workers or primary-care providers. Others are developing and testing applications on smartphones and tablets to extend access to screening and treatment[4].

Now, clinicians, patients, caregivers and researchers need to learn from each other. The knowledge gained in all countries must be evaluated, disseminated and adapted for local use everywhere. Crucially, everyone involved must start with the same mindset: when it comes to mental health, all countries are developing countries.

Of course, the resources available are drastically different in the developing and developed worlds: a teenager in Afghanistan seeking mental-health care does so in a country that has 1 psychiatrist for every 10 million people, not 1 per 5,000, as in, for instance, Belgium. But no country has sufficient numbers of trained mental-health-service providers. Nearly one-third of the US population lacks adequate access to mental-health-care providers. There are similar shortages in parts of countries as diverse as Australia, Canada, Finland, France, Japan, New Zealand and Slovakia. Even in wealthy countries, 40–60% of people with severe mental disorders do not receive the care they need[5].

Across all settings, those with the fewest social and economic resources are least likely to receive quality mental-health services, be they in Arctic areas of Canada, inner-city Glasgow or rural Sierra Leone. Today's global mental-health research must lead to interventions developed in and for such underserved communities.

MOVING FORWARD

Mirroring the global community's commitment to sustainable development, the world needs a global commitment — financial as well as moral — to mental health that supports the translation of ideas and interventions between poor and rich settings while taking into account local needs. If an intervention shows great promise in Iran, for instance, can it be adapted for Poland or Indonesia?

In the 1980s and 1990s, global collaborative research led by the WHO enabled cross-national comparisons of the incidence, prevalence and long-term course of mental disorders, as well as cross-cultural conceptualizations of mental illness and traditional modes of understanding and management. Over the past 15 years, many of the efforts in global mental health have focused on introducing high-quality research in low- and middle-income countries to establish an evidence-base for the delivery of services in these nations.

More-recent research has focused on efficacy, effectiveness and implementation in low- and middle-income countries. Local research teams frequently collaborate with colleagues in rich countries. Yet, the relevance of this work to underserved populations in high-income countries is not routinely part of the global conversation. In low-income countries, the limited infrastructure for community mental-health care and the dismal budgetary allocations for mental health are significant obstacles to implementing research findings.

The status quo is not working — and innovations are needed urgently. The following case studies are exemplars of the approaches we advocate.

South–south learning. The Programme for Improving Mental Health Care (PRIME) is a consortium of research institutions and ministries of health funded by the UK government. PRIME aims to scale up mental-health services in Ethiopia, India, Nepal, South Africa and Uganda by integrating these into primary care. Together, these countries have developed locally relevant mental-health plans informed by community advisory boards that include district health administrators, service users, traditional healers and police. The consortium observes cross-country differences and similarities in the evolving mental-health-care systems.

"If an intervention shows great promise in Iran, for instance, can it be adapted for Poland or India?"

The shared framework for developing and implementing plans with local adaptations is a powerful tool. Adaptations included change-management interventions for district managers in South Africa, a mental-health case manager in India, and new assessment tools in Nepal. All country teams have recognized the need for systemic changes. The next phase of the study is evaluation, to assess whether and how these changes affect disease burden.

North–north learning. The Arctic Council, an intergovernmental forum for the circumpolar states, has emerged as an avenue for launching collaborative efforts to reduce suicide rates in those countries. Young Alaska Native men experience the highest rates of suicide of any demographic group in the United States. Similarly high rates also occur among some indigenous Arctic communities in Canada, Greenland and Russia. Local responders can benefit from what has been learned and shown to be effective elsewhere.

An Arctic Council initiative that ran between 2013 and 2015, led by Canada, identified promising practices for suicide prevention and mental-health promotion, and mapped the evidence across circumpolar communities, noting what interventions were acceptable where. Teams identified common threads that made a programme scalable and adaptable across the region. These included having sustained funding and dedicated physical spaces for services; easy access for community members; having skilled workers who were based in and were knowledgeable about the community; and creating forums for talking about suicide. Crucially, the effort continues in the US-led RISING SUN initiative, which engages researchers, community-members and decision-makers to identify shared tools.

South–north learning. BasicNeeds is a global mental-health charity, established in 2000 in Britain, that facilitates access to employment and mental-health care for people with mental illness. The organization refined a model for helping people into care and work and to advocate for their problems in African and Asian countries, including Ghana, Tanzania, Nepal, China and Vietnam.

In Nepal, for example, a local charity that specialized in community-based rehabilitation adopted the BasicNeeds model. Working closely with government-funded mental-health clinics, the programme conducted community outreach and facilitated access to mental-health-care services. It reduced expenses for families with ill members. Eligible families received training and financial support for developing and implementing a business plan for income generation. People who received support were all earning money 6–12 months later. BasicNeeds received funding last year from the Robert Wood Johnson Foundation in Princeton, New Jersey, to translate the model to a deprived, inner-city environment in the United States.

This kind of translation of practices is just beginning. Technology is increasingly enabling innovators to make their ideas and projects public. One venue for sharing ideas is the Mental Health Innovation Network (MHIN), funded by Grand Challenges Canada and managed by a research team at the London School for Hygiene & Tropical

DAVID KOHN/THE NEW YORK TIMES/REDUX/EYEVINE

Brochures and handouts on depression, anxiety and mental health in Goa, India. In India, as in much of the developing world, depression and anxiety are rarely diagnosed or treated.

Medicine and the WHO's Department of Mental Health and Substance Abuse (of which S.S. is director). Another virtual community is the WHO's Global Clinical Practice Network. This online platform allows thousands of clinicians from around the world to contribute to and benefit from mental-health research. Through it, more than 12,000 clinicians from 139 countries have participated in field trials, testing diagnostic guidelines in a wide range of settings. Such networks also break national, professional and linguistic boundaries to facilitate global conversation and learning.

NEXT STEPS

To meet the mental-health needs of vulnerable people everywhere, we must develop, study and practise the translation of knowledge and ideas in all directions. How? Here are six suggestions.

Determine which innovations will scale up. Sometimes local application is enough. The community must distil guiding principles that enable practitioners to decide what is right for which contexts. This requires health planners to consider system-level issues (such as human resources and financing) and community-level needs (including acceptability and feasibility of care practices). In all contexts, cost, complexity and fragmented services can curtail wider implementation.

Train scientists to translate research findings. A new cadre of global mental-health researchers is needed to adapt treatments to fit local health systems. They must be able to assess needs and must be equipped with the collaborative skills to engage decision-makers, clinicians and community members. They need to generate knowledge that informs cross-cultural translation.

Use the community's knowledge. The growing evidence base on effective low-cost mental-health treatments is underused. Scientific knowledge is often inaccessible to practitioners, because they lack the time and resources to review information. We need to develop ways to synthesize new global mental-health findings routinely, and present this information so that users can apply it. The global fight against HIV/AIDS presents one model to draw from: networks of funders, researchers, clinicians and patients have been able to achieve standardized care protocols by sharing information through international working groups, society representatives and UNAIDS, the UN programme for HIV/AIDS. Similar networks exist in vaccine and contraception research.

Sustain effective mental-health treatments. A major problem is that research funding does not support continued delivery of services on the ground — this requires a greater commitment from local and national governments and aid agencies to invest in mental health. The WHO Mental Health Action Plan specifically calls for stronger leadership and governance for mental health at the national level, including adequate funding. Around $1.6 billion is needed in low-income countries, and between $6.6 billion and $9.33 billion in lower-middle-income countries, to provide a basic package of mental health services; this is eight and six times more, respectively, than current investments[6]. The message that poor investment in mental health is costly for all countries must be communicated to leaders with the power to invest[7].

Evaluate the outcomes of treatments. Globally, we lack adequate information on the impact of services because clinics and health systems often lack the funding, capacity, motivation and protocols for monitoring and evaluation. Rarer still is a mechanism for using the results of evaluation to improve services. So people need to be trained to monitor and evaluate new and established approaches. Collaborative research networks can facilitate this kind of capacity building. The WHO Mental Health Action Plan sets out six global targets to achieve by 2020. For example, it calls for a 20% increase in service coverage for severe mental disorders and a 10% reduction in suicide rates globally. Mental-health advocates, clinicians and patient groups in each country must track progress towards these targets.

Disseminate successes and failures. The risks that result from sharing information about programme weaknesses must be minimized. Researchers rely on journal publications to disseminate information, but it is much harder to publish unsuccessful trials or evaluations. We need options beyond research databases. Online platforms such as the MHIN could be used here, especially by those who are not researchers who develop new solutions to local problems.

In a world where mental-health innovations cross borders as people do, a mother migrating from Khayelitsha in South Africa to New York could meet a community health worker who delivers a depression treatment in her home, much like the community counsellor at her maternal health clinic in South Africa. People move because of needs and opportunities — so, too, must knowledge. ■

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The views expressed here do not necessarily represent those of the US National Institute of Mental Health, the US National Institutes of Health, the US government or the World Health Organization.

Akshay Kumar plays the lead in *Pad Man*, a fictionalized biopic of sanitary-pad innovator Arunachalam Muruganantham.

BOLLYWOOD TAKES ON MENSTRUAL STIGMA

Subhra Priyadarshini lauds a biopic of an inspired Indian sanitary-pad innovator.

COLLECTION CHRISTOPHEL/ALAMY

Frugal innovation is a new norm in India, emerging sporadically in pockets of brilliance — from rural hamlets to technology labs. It has even spawned a word in Hindi: *jugaad*.

Thanks to *jugaad*, bioengineer Manu Prakash is flooding rural schools in India with his US$1 'foldscope', an origami-inspired microscope teaching science to tens of thousands of children.

It is also in this spirit that, in 2000, school dropout Arunachalam Muruganantham created a do-it-yourself unit in Coimbatore, Tamil Nadu, to manufacture the world's cheapest sanitary pads. Now, Muruganantham's story hits the big screen in *Pad Man*, billed as the first feature-length film on menstrual hygiene.

'Period poverty' is a health issue affecting women in countries across the globe. In Britain, 1 in 10 girls and women aged 14–21 cannot afford sanitary products, according to London-based charity Plan International UK. In India, according to a 2015–16 government health survey, just 58% of women aged 15–24 can afford to use a hygienic method of menstrual protection: 78% in urban areas and 48% in rural ones. And the average varies wildly between states — from 91% in Tamil Nadu to just 31% in Bihar. The rest resort to rags, leaves and even ash. This can result in serious health risks, such as toxic shock syndrome, and lead to absence from school or work.

"PERIOD POVERTY IS A HEALTH ISSUE AFFECTING WOMEN IN COUNTRIES ACROSS THE GLOBE."

Pad Man attempts to open up this taboo topic for much-needed discussion through narrative sparked by melodrama and music. Like Shree Narayan Singh's 2017 film *Toilet: Ek Prem Katha*, centred around the problem of open defecation, it has captured the imagination of a nation grappling with a massive burden of women's health issues.

Directed by R. Balki, *Pad Man* has a starry cast. Muruganantham (renamed Lakshmikant) is played by renowned Bollywood action-hero-turned-character-actor Akshay Kumar; the powerful theatre actor Radhika Apte plays his wife, Shanthi (called Gayatri). There is even a jingoistic cameo from superstar Amitabh Bachchan, who, playing himself, declaims: "India should not be seen as a country of one billion people. India should be seen as a country of one billion minds."

Muruganantham's is the inspiring story of an unconventional and tenderhearted man. In the early 1990s, he was an assistant in a hardware workshop. His wife's use of rags during menstruation concerned him, so he experimented with materials — first cotton, then cellulose fibre — to make a pad that wouldn't leak, in a process of reverse engineering. At first, when it came to testing his prototypes, "the only available victim was my wife", Muruganantham said in a 2012 TED talk. In *Pad Man*, we see Lakshmikant perfecting the scientific steps of pulverizing cellulose fibres, compressing them, sealing the pad with non-woven fabric and sanitizing the whole with ultraviolet light. And it was all accomplished using four ingenious, makeshift machines that cost peanuts, compared to the giant assembly lines used by multinational companies.

At the cost of being ostracized for openly tackling a hidden issue, he worked doggedly on the pad's design. The biggest challenge was finding volunteers to test it. "Everyone thought I had gone mad," he says. He finally realized that he could turn guinea pig himself. He wore a pad, and used a deflated football filled with goat's blood and fitted with a tube. It took him six years to isolate cellulose as the core adsorbing medium. That roller-coaster journey won him a national innovation prize, a spot on TIME magazine's '100 most influential people' list in 2014, and one of India's highest civilian awards, the Padma Shri, in 2016.

Pad Man makes Muruganantham's unusual journey relatable, although it often descends a little into preachiness. It falters, too, with a laboured first half, in which the risk to women's health is not clearly delineated, and the stigma associated with the subject of menstruation is signalled by bursts of "Sharam!" (shame) from the female actors. Endorsing Bollywood's unapologetic love affair with song and dance, the demure Gayatri suddenly breaks into an exaggerated, hip-swaying number to celebrate the puberty of a girl next door.

The rest of the film brings in the usual elements of a potboiler — a love angle, the rise and rise of the protagonist and Gayatri's forgive-and-feel-proud reconciliation. Bachchan delivers the applause-inducing line: "America has Superman, Spiderman and Batman. India has *Pad Man*!"

Over the past decade, Muruganantham has travelled across villages in India — first selling his sanitary pads, and then setting up self-sustaining pad-making units in collaboration with women's self-help groups and cooperatives. He has spawned close to 2,500 such centres, in India and a dozen other developing countries. His pads retail at a fraction of the cost of those from multinational brands.

Although *Pad Man* captures the essence of grass-roots innovation and benefits from true-to-life portrayals by a brilliant set of actors, the instructive overtone mars the narrative. If it wants to reach other countries affected by period poverty, the song-anddance might be a dampener. The film is also currently an urban sensation. Reaching its target audience in India's rural hinterland might be difficult, given the taboo — unless Balki and team have a plan for that.

Meanwhile, a social movement is now associated with the film. Muruganantham has mentored a biologist, Maya Vishwakarma, who came home to rural Madhya Pradesh from California four years ago to spread menstrual-hygiene awareness. Vishwakarma has now received backing to distribute free pads to tribal women. Her mission has earned her the sobriquet Pad Woman. The buzz created by *Pad Man* might help her small non-profit organization to get international donors and become a national movement.▪

Subhra Priyadarshini *is chief editor of* Nature India.

INNOVATION

Waste mountain

Subhra Priyadarshini examines the wide-ranging impacts of India's throw-away culture.

People collect recyclable material at a dump in Guwhati, India.

Waste of a Nation: Garbage and Growth in India
ASSA DORON & ROBIN JEFFREY
Harvard University Press: 2018.

In *Waste of a Nation*, an in-depth investigation of India's feeble fight against mountains of consumerist waste, are robust statistics, compelling history and telling case studies. The authors, anthropologist Assa Doron and historian Robin Jeffrey, also throw the occasional philosophical curve ball, such as: "waste is in the eye of the beholder". The result is both beguiling and disturbing.

As Doron and Jeffrey show, waste in India has generated a vast recycling culture — a world apart, of *kabaadiwalas* (garbage buyers), scavengers and 'rubbish rajas'. The authors reveal the complex cultural, social, political and religious hurdles that hamper the country's struggle with waste, from unjust pressure on 'low-caste' Dalits to collect human excreta to unenforced environmental regulations.

Meanwhile, the mountain builds by an average 100,000 tonnes a day — a fraction of the US tally, but problematic nevertheless. India has few mechanisms for dealing with sewage and hazardous, wet, medical or electronic waste. And, like many other countries, it is losing the battle with megamounds of plastic. Until 1985, the country did not even have an urban-development ministry.

Municipal bodies are responsible for managing waste. But tradition — and the labour-intensive nature of the sector — means that unorganized waste-pickers do most of the dirty work. Their job is to collect and segregate household, commercial and industrial waste for processing in centres where it is sorted for composting, recycling or energy generation. However, the reality rarely reflects this orderly progression.

Non-compliance is rife: waste is often not sorted at source. Ultimately, around 90% of unsorted waste is thrown into dumps. Meanwhile, the millions of scavengers and cleaners are not part of any organized waste-management system, and lack health, safety and legal cover. They face harrowing occupational hazards. Urban dumps in megacities such as Mumbai, Delhi and Kolkata can be clogged with excrement, rotten food, and liquid and solid household wastes that can promote infectious diseases and attract flies, rats and other vectors. Dumps can catch fire; burning tyres, for instance, emit volatile organic compounds and particulate matter. Doron and Jeffrey cite a suspected outbreak of bubonic plague in Surat in 1994 as an example of the breakdown of civic waste management. They point, too, to a community in the brass-working centre Moradabad who extract metals from electronic waste. The illegal operation suffuses their lungs with metallic dust and chemical fumes, and chokes the nearby rivers with mercury and arsenic. In these lands of waste, humans end up being treated as waste.

Sewage, as *Waste of a Nation* underlines, is a prime concern in a country where more than 560 million people defecate in the open. In 2014, the government of Prime Minister Narendra Modi set out to tackle the problem with the Swachh Bharat ('clean India') campaign, pledging to build 120 million toilets across rural India by 2 October 2019 — the 150th anniversary of Mahatma Gandhi's birth. In 2017, the project achieved a remarkable 70% coverage of rural areas. Significant challenges remain, however. Untreated sewage is choking the mighty Yamuna river and parts of the lake system around Bangalore, for instance.

Despite India's tradition of frugality, the rise of consumerism contributes to these issues. The dark side of the economic liberalization of 1991 is the generation of new waste from mines, factories and industrial agriculture. The gradual switch from natural, biodegradable materials to plastics is changing behaviour even among the rural poor. For instance, twigs (*daatuun*) of the medicinal neem tree (*Azadirachta indica*), once used to brush teeth, have given way to plastic toothbrushes. The latter are a recycling nightmare: separating bristles from the handle is labour-intensive and unrewarding.

Doron and Jeffrey also discuss India's waste market. The world's largest 'ship-breaking' industry is in Alang. Here, retired ships are imported and dismantled, and their parts and materials — primarily steel — are sold for profit. India is also a leading exporter of hair, a market worth almost US$400 million. Many Hindus have their hair cut in temples to demonstrate devotion, and much of the waste hair is sent to China to be made into wigs.

Doron and Jeffrey analyse the isolated, small-scale attempts of large Indian companies such as ITC and the Ramky Group to recycle waste profitably as well as hygienically, through state-of-the-art containment, neutralization and disposal technologies. For instance, Ramky's first project in 2000 was managing medical wastes for disposal at government-approved centres. By 2016, the country had just 198 approved disposal centres for more than 169,000 hospitals and clinics.

The authors rightly call for a sustainable system. To be practical, this must be motivated by profit, discipline, need, pride or better still, a combination of these. In 2013, China signed up to a 'circular economy' model devoted to recycling as much as possible. This is one approach to sustainability. But India has, as *Waste of a Nation* emphasizes, other strengths that could unite municipalities and individuals. One is its 40,000 civic organizations and action groups that could catalyse coalitions between *kabaadiwalas*, professionals, scientists, engineers, ethical businesses and, importantly, politicians. ▪

SUSHAVAN NANDY/BARCROFT MEDIA/ GETTY IMAGES

A child carries bricks on her head as a part of her daily job in West Bengal, India. Thousands of migrants from Bihar and Jharkhand work as unskilled labourers in the brick fields of West Bengal.

Understand young people in low-income countries

For most of the world's adolescents, poverty and social marginalization influence health much more than risk-taking does, argue **Robert Blum** and **Jo Boyden**.

Nearly 90% of current evidence about adolescence comes from research in high-income countries. Yet nine-tenths of people aged between 10 and 24 live in low- and middle-income countries (LMICs), where this life stage looks very different (see 'Worlds apart').

In LMICs, young people's health and well-being tend to be more severely affected by cultural, socio-economic and environmental risk factors than in high-income countries, and there are fewer resources to mitigate such risks. Adolescents in LMICs also tend to have many more family responsibilities than their peers in high-income countries.

Currently, millions of young people in LMICs are condemned to poor health,

Opportunities for education can be just as important as nutrition for adolescent health.

impaired development and premature death. In fact, since 1990, there have been fewer improvements in health for adolescents (aged 10–19) and young people (aged 15–24) in these countries than for any other age group[1].

We need to better understand the everyday realities of adolescents' lives in LMICs and how this affects their health. This would enable targeted investment to improve well-being and productivity globally — but it

means abandoning Western assumptions about adolescence being predominantly a time for risk-taking. It also means finding better ways to reach adolescents — for instance, through the use of mobile phones, social media and community-based strategies — and applying approaches such as web-based surveys and interactive data-collection methods to build a richer picture of the forces shaping young people's lives.

POVERTY TRAP

Studies show that adolescents in LMICs who are subject to poverty and restricted access to health, education and other services are also more likely to be exposed to environmental toxins and extreme weather events, such as droughts, than their wealthier peers.

And this pile-up of multiple stressors is likely to worsen in the coming years. According to the Notre-Dame Global Adaptation Initiative (http://gain.nd.edu), out of the 100 countries most vulnerable to climate change, 42 are low-income countries, 33 are lower middle-income countries and 14 are upper middle-income countries. Meanwhile, rapid and unplanned urbanization is driving more overcrowding, road injuries, noise pollution and the accumulation of toxins such as lead[2].

In LMICs, adolescents from minority communities tend to be significantly more disadvantaged than those in majority populations. A 2009 study of the health and well-being of more than 10,000 individuals in Vietnam aged 14 to 25 found that young people from ethnic minorities fared worse than those from the Kinh majority in every measure[3]. For example, 10% of young people from ethnic minorities reported being illiterate, compared with 1% of Kinh young people.

Gender is another major determinant of health differences. The pilot of the ongoing Global Early Adolescent Study (www.geastudy.org/), which R.B. is directing, collected predominantly quantitative data between 2015 and 2017 from about 35 families in 15 countries on 5 continents. These data indicate that, compared with their brothers and male peers, girls in LMICs tend to experience more social isolation as they move from childhood to adolescence, and have fewer opportunities in education, recreation and exploration.

Opportunities for education can be just as important as nutrition for adolescent health. According to a 2014 study, for instance, there is a strong link between teenage pregnancy and low levels of literacy in Africa[4]. And a wealth of literature shows that deficiencies early in life cast a long shadow.

As part of Young Lives (www.younglives.org.uk), an ongoing longitudinal study directed by J.B., researchers have been collecting information about 12,000 children in Ethiopia, India, Peru and Vietnam for 15 years. In all four countries, children whose growth is stunted when they are around one year old are likely to remain so until they are at least 15 (ref. 5). Those who experience an early nutritional disadvantage are more likely to have difficulty progressing through school. And stunting at age 8 correlates with lower scores on measures of self-efficacy, self-esteem and educational aspirations at age 12 (ref. 6).

"Adolescents are the least likely of any age group to access conventional health services."

Another characteristic of life for poor adolescents in LMICs is combining the pursuit of education with work. Young Lives data suggest that the time devoted to education remains broadly constant for girls and boys aged 8 to 15. But as they grow older, adolescents tend to do more work, either for pay or as part of family life. Indeed, they are frequently the primary carers of younger siblings or incapacitated adults. Some are even the principal breadwinners in their households (see 'Age of responsibility').

Employment can affect health during adolescence in many ways. Young workers commonly suffer more accidents than adult workers, and they are particularly susceptible when exposed to chemical toxins from mining or agricultural work, for example[7].

NO TIME TO PLAY

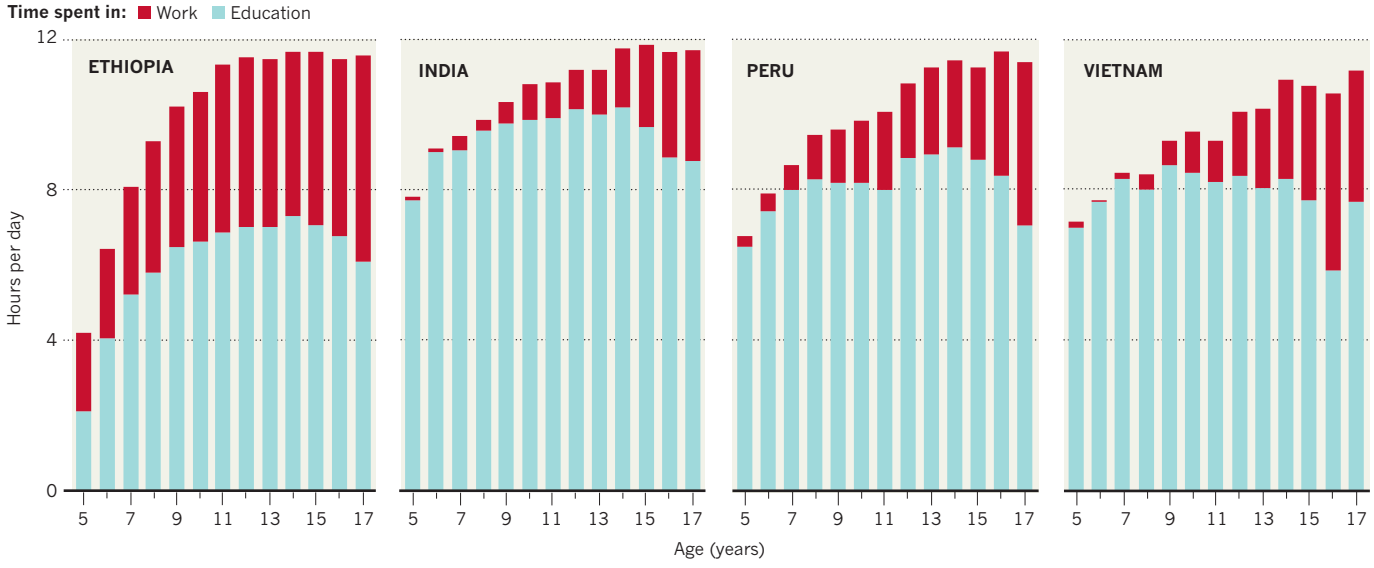
Experts in the Global North generally assume that adolescence is a carefree time of emerging independence, social exploration and risk-taking. This way of thinking carries over to adolescent-focused health programmes and policies in LMICs, which regularly focus on violence, sexually transmitted infections and teen pregnancies.

Too many programmes fail to understand what drives behaviour in the first place, and ignore the broader risks that young people face from poverty, work, social stigma or exclusion from quality services. Also, many centre around the provision of clinical services, even though adolescents are the least likely of any age group to access conventional health services[8].

With the right approach, community-based interventions geared towards reducing a behavioural problem such as violence can also improve the overall health and well-being of young people. Reducing violence

AGE OF RESPONSIBILITY

As they grow up, young people in low- and middle-income countries tend to devote more of their time to work that helps sustain their families. Under-reporting of work is likely because those surveyed described 'a typical day last week' when school was in session.



SOURCE: P. ESPINOZA REVOLLO & C. PORTER, UNPUBLISHED DATA

SAJJAD HUSSAIN/AFP/GETTY IMAGES

A street child uses a cellphone outside a closed shop in New Delhi.

and the incidence of HIV/AIDS are among the principal aims of South Africa's activity-based Waves for Change surf schools, Soul Buddyz Clubs and AMANDLA EduFootball programmes, for example. But these programmes also improve young people's fitness, psychological well-being and ability to form friendships and take responsibility for others.

Donors, governments and non-governmental organizations in LMICs are expanding their repertoire of approaches. But better research tools and more community-based initiatives are needed that focus specifically on understanding and enhancing resilience among adolescents.

Digital technologies offer fresh ways to improve health and well-being (see page 432). Various surveys conducted over the past decade indicate that young people in LMICs value the unrestricted access to information and the privacy that the Internet affords, and prefer digital media over other delivery channels for health information[9]. Several investigators have already tried to exploit these preferences. In a recent randomized trial in Ghana, for instance, text messages improved girls' knowledge about reproductive health[10]. Evidence on the effectiveness of digital health information in changing behaviours is needed, however.

Importantly, researchers, policymakers, practitioners and others must deploy a bottom-up approach in which adolescents are treated as partners in improving their health and well-being, not just the recipients of change. Likewise, the design and implementation of interventions must draw on evidence of what works, for whom and why.

This means that investigators must work in communities and across all settings — not just in hospitals and clinics — to understand how young people spend their time, how they access resources, who controls their earnings, and so on. Researchers must also work out how health measures can be integrated into schools or mobile-phone applications, rather than delivered solely through medical facilities. This is not simply about making schools a hub for health education and services; greater flexibility in timetables or the provision of catch-up classes and vocational measures, for example, could encourage more working adolescents to stay in school for longer.

Finally, international organizations, such as the World Health Organization, the International Labour Organization and the United Nations Children's Fund, should direct much greater effort towards economic analyses and surveys of occupational and environmental hazards, exposures to social risks and the mental health of young people in LMICs.

The second decade of life presents an extraordinary opportunity to improve people's health over the long term. And threats to human health and well-being are becoming more acute in our rapidly urbanizing, industrializing world, with rising environmental risks and the potential for reductions in youth employment opportunities as a result of expanding technologies.

Only with a realistic understanding of the lives of young people in LMICs, grounded in the social, economic and political contexts of their everyday lives, do we stand a chance of shaping their futures for the better. ■

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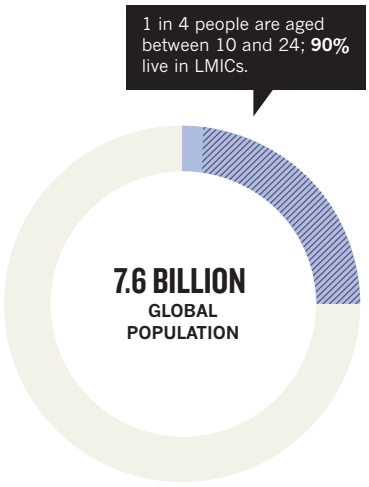
WORLDS APART

Most research on 10- to 24-year-olds comes from high-income countries. But nine-tenths of this age group live in low- or middle-income countries (LMICs).



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nature energy

Challenges and gaps for energy planning models in the developing-world context

Kumar Biswajit Debnath * and Monjur Mourshed

Energy planning models (EPMs) support multi-criteria assessments of the impact of energy policies on the economy and environment. Most EPMs originated in developed countries and are primarily aimed at reducing greenhouse gas emissions while enhancing energy security. In contrast, most, if not all, developing countries are predominantly concerned with increasing energy access. Here, we review thirty-four widely used EPMs to investigate their applicability to developing countries and find an absence of consideration of the objectives, challenges, and nuances of the developing context. Key deficiencies arise from the lack of deliberation of the low energy demand resulting from lack of access and availability of supply. Other inadequacies include the lack of consideration of socio-economic nuances such as the prevalence of corruption and resulting cost inflation, the methods for adequately addressing the shortcomings in data quality, availability and adequacy, and the effects of climate change. We argue for further research on characterization and modelling of suppressed demand, climate change impacts, and socio-political feedback in developing countries, and the development of contextual EPMs.

Human activities have led to rapid changes in atmospheric concentrations of greenhouse gas (GHG) emissions[1], contributing to and amplifying global climate change[2]. Fossil fuels and land-use change (for example, through deforestation and farming) are two primary sources of GHG emissions, of which the emissions from land use has been nearly constant[3], while the emissions from fossil-fuel based energy systems increased by 50% between 2000 and 2013 (ref. [4]). Current energy and transportation systems can result in substantial GHG discharges[5], with a likely global mean temperature increase between 2.0–4.9 °C, with a median of 3.2 °C by 2100 (ref. [6]). Even if current GHG concentrations remain constant, the world will experience a few centuries of rising temperature and ocean level[7,8]. Therefore, substantial reductions in global GHG emissions are essential for mitigating climate change.

In addition to the infrastructural elements of national energy systems (that is, generation, distribution, and transmission), access to grid electricity and purchasing power of the population influence energy end-use and GHG emissions. Figure 1a illustrates that both access to electricity and per capita CO_2 emissions are more significant in high-income countries, compared to low-income and middle-income developing countries. Most developed countries can ensure 100% access to electricity, which only a few developing countries can match. In 2010, annual per capita CO_2 emissions ranged from 0.02–15.14 tCO_2 in low and middle-income countries, compared to 1.6–42.63 tCO_2 in high-income ones. In general, there is a positive association between electricity access and GHG emissions. One notable exception is Costa Rica, an upper middle-income country, which had 98% access to electricity but per capita CO_2 emissions of 1.7 tCO_2, well below the average of 2.09 tCO_2 for all low and middle-income countries in 2010. This is because 93.3% of Costa Rica's energy was from renewable resources, of which hydroelectric sources accounted for 75.8% (ref. [9]).

As a result, future energy planning objectives of developed and developing countries are distinctly different. In developed countries, the focus today is on reducing emissions while enhancing energy security, primarily characterized by a shift from fossil fuels towards more renewable resources. However, developing countries are concerned with increasing access to electricity, which is considered a prerequisite for development and economic empowerment, as reflected by the inclusion of energy as a goal in the Sustainable Development Goals[10]. The current CO_2 emissions per capita of developing countries are low, often much below the global average (Fig. 1c). Hence, emission reduction is not always on the agenda for developing countries, even at a cursory level, except for a few large countries such as China and India[11].

Energy planning models (EPMs) play an essential role in the development of the energy sector at global, national and regional levels by enabling informed decision-making. EPMs are especially crucial as significant investments in innovative energy research and planning are required for decarbonization[12]. The development of EPMs started in the late 1950s and early 1960s (ref. [13]) but intensified after the oil crisis of the 1970s in light of the realization of the effects of exogenous political events on global and national energy supply[14]. It was necessary, then, to critically assess the interrelationships between the sources of energy supply and demand, as well as to identify pathways for long-term development of the energy sector[15]. The drive for global sustainability in the 1990s — spurred in particular by the Rio Earth Summit in 1992 and the 1995 report of the Intergovernmental Panel on Climate Change (IPCC)[16] — brought forward the issue of GHG emissions and their impact on the environment. As a result, further models were developed for projecting climate change and investigating the environmental impact and its mitigation. However, given that some two-thirds of global GHG emissions come from the electricity, heat, and transportation sectors[4], the integration of the environmental aspects of energy demand and supply within EPMs became necessary, providing a comprehensive picture of the interrelationships between energy, environment, and climate change.

Over the past four decades, a substantial number of EPMs have been developed by researchers and organizations in different countries, with various objectives and scopes. EPMs range from the holistic — modelling the partial or whole energy system of a country, region or the world — to the more sectoral — providing projections of the energy needs of, for example, transportation or industry.

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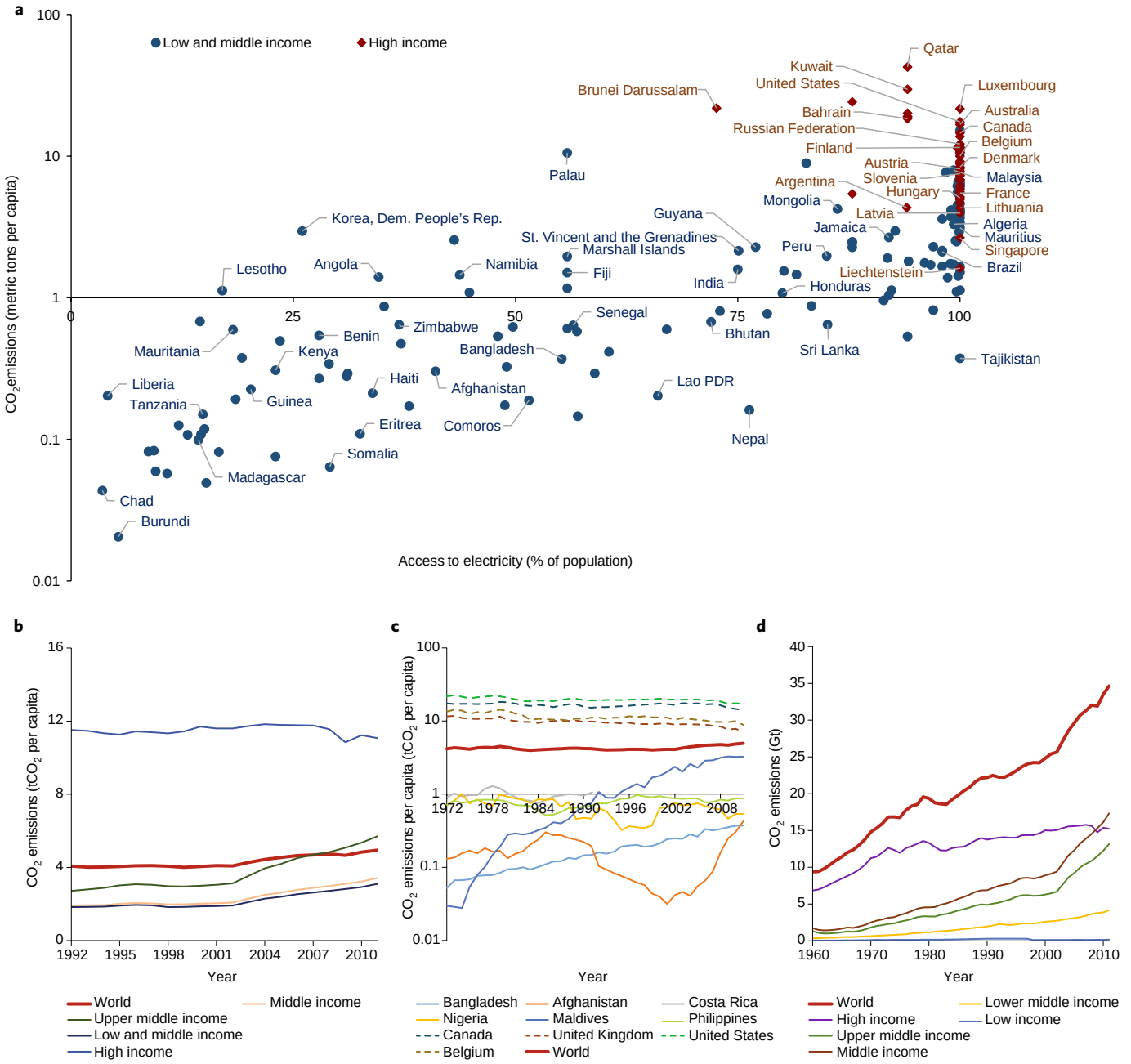

Fig. 1 | CO_2 emissions characteristics. a, CO_2 emissions versus access to electricity in high-income and low-income countries in 2010. Access to electricity in low-income and middle-income countries ranges from 3.5–100% of the population. In contrast, the figure is 72.6–100% in high-income countries. **b**, CO_2 emissions per capita for the period 1992–2011. **c**, CO_2 emissions per capita in selected developed and developing countries for the period 1972–2011. **d**, CO_2 emissions in countries by income group in the period 1960–2011. The income group classification used here is that from the World Bank list of economies (July 2015): low income, US$1,045 or less; lower middle income, US$1,046–4,125; upper middle income, US$4,126–12,735; and high income, US$12,736 or more. Data is taken from ref. [9].

Given that the IEA estimates the growth in energy demand over the next 23 years will be higher in developing Asian countries than the rest of the world[17] and future emissions from growth regions will be critical in the current 1.5 °C temperature discourse[1], it is essential to understand how EPMs reflect the challenges being faced by decision-makers in different parts of the world.

Previous work has reviewed EPMs of different types. Suganthi et al.[18] categorized energy demand projection models based on their methods but misclassified bottom-up and top-down approaches. Bhattacharyya et al.[19] analysed available EPMs for application in developing countries but did not present details on relevant socio-economic parameters and their effect on policies. Pfenninger et al.[20] categorized EPMs into four types: energy system optimization; energy system simulation; power system and electricity market and qualitative and mixed methods. They recommended further development and integration of innovative approaches into EPMs to address the complex interactions among disciplines such as social science, ecology, finance, and behavioural psychology. Urban et al.[21] analysed twelve EPMs to investigate their suitability for developing contexts and suggested that critical characteristics of developing

countries such as the informal economy and supply shortages were overlooked. The study identified a bias towards industrialized countries in the EPMs, yet specifics were not offered on socio-economic drivers such as political stability (or lack thereof) and corruption in energy markets in developing contexts.

In light of this, there is a lack of evidence-based analysis of contextual variations, model structures, and relevant emerging socio-economic variables for EPMs in the developing world context. To that end, we reviewed thirty-four current, highly used, macro-level EPMs to investigate their applicability and deficiencies for energy systems in developing countries. Our focus is on the factors that affect the demand and supply of energy, as well as the rational development of the energy sector in a developing country.

Typology and structure of energy planning models

We conducted a systematic survey of published literature on EPMs. Our study focuses on models predominantly used for the planning of energy systems and infrastructures and that are more strategic, as opposed to operational. First, a preliminary study was conducted to gather an overview of the topics related to EPMs that resulted in the identification of two main themes: energy demand and supply, and energy information and emission models. Electronic databases — namely Google Scholar, ScienceDirect, JSTOR, IEEE Xplore, Scopus, Web of Science, and other official websites with energy databanks, specifically United Nations (UN), World Bank, International Monetary Fund (IMF), International Energy Agency (IEA) and Energy Information Administration (EIA) — were searched for relevant publications using the keywords listed in Table 1. The keywords were categorized into five-word groups, which were combined using the Boolean operator 'AND', for example, 'Energy planning model' AND 'Forecasting' AND 'Input variables' AND 'Organization' AND 'Global'. Based on the search and the available literature, thirty-four models developed by international organizations or institutions were selected for analysis (Table 2). In addition to the published journal articles and books, manuals of different models were investigated to explore their structure and key components. The reviewed models were categorized based on model objectives to contextualize the subsequent analysis and discussion. Model structures were then analysed to investigate their relevance and deficits in developing contexts. For the categorization by model objective, four categories were used: energy information systems, energy demand–supply, energy–economic and energy emissions models. Table 2 illustrates EPM types, and their inputs, outputs, and underlying methods. Five characteristics of input variables were analysed: qualitative, quantitative, financial, aggregated and disaggregated. Although financial data are typically classed as 'quantitative', based on the extensive use of these variables in different models it was deemed worthwhile to include them as a separate characteristic. The underlying methods were categorized into accounting framework, regression, optimization, economic, simulation, and equilibrium methods. Output variables were classified into energy, emissions, and cost measures.

Among the analysed 34 models, quantitative and financial data are utilized in 34 and 32 models respectively. 27 models used disaggregated data as input variables. In the case of the output variables, most of the model's outputs are energy (30 models), emission (29 models), and cost (28 models). Model outputs are often normalized; for example, cost per unit GDP, cost per capita, cost per unit generated, and emissions per unit GDP. Reviewed models adopted different underlying methods for estimation and projection. Optimization methods are widely utilized (13 models), followed by simulation (11 models) and economic (10 models) methods. Optimization methods are mostly applied to energy demand and supply, and economic models.

EPMs have three common components and a basic workflow: input variables → underlying estimation or projection methods → output variables. Key variations, however, lie in the type, resolution (temporal and spatial), scope and timeframe of the input and output variables. Model objectives and the nature of the data most often determine the choice of estimation or projection methods.

Primary input variables in the studied EPMs are quantitative, financial and disaggregated. EPMs are numerical models and utilize quantitative data for calculation. Qualitative parameters are typically interpreted as ordinal data for modelling purposes. While modelling energy infrastructure in a holistic approach to cover a broader context, the supply, demand and socio-economic sectors require disaggregated data for a better interpretation of the existing systems.

In the case of underlying methods, optimization was utilized in thirteen models because they would create an optimization loop as a way of testing whether the selected output satisfies the defined constraints. In some models, especially energy demand and supply models, the primary objective is to find the least-cost solution for the energy market. Optimization methods in such models would render the opportunity to test different policies against the least-cost option. However, simulation methods were also utilized in a significant number of models.

Developing country characteristics not addressed in EPMs

Almost all EPMs were constructed in developed countries (Table 3) and considered their energy systems, economic assumptions, and the extent to which GHG emissions need to be reduced. While CO_2 emissions per capita in high-income countries are decreasing (Fig. 1b), they are increasing in the developing upper-middle and middle-income countries, whose primary objective often is to improve access to convenient forms of energy. Despite the fact that some EPMs have been widely adopted for energy system planning in developing countries, they lack consideration of a substantial number of issues affecting developing contexts; for example, the effects of a lack of innovation, and the varying nature of privatization,

Table 1 | Searched keywords and associated groups

Model	Objective	Components	Origin of development	Geographical applicability
Energy planning	Forecasting	Input variables	Organization	Global
Energy information	Projection	Estimation methods	Country	Regional
Energy economic	Demand and supply; demand; supply	Output variables		Country
Energy supply and demand	Economic			
Energy supply	Emission control			
Energy demand				
Emission reduction				

Table 2 | Characteristics of existing energy planning models

Model	Input variables[a]					Method[b]						Output variables[c]			Total	Ref.
	Qul	Qua	Fin	Agg	Disaag	RE	OP	EC	SM	EQ	AF	En	Em	Co		
Energy information system																
E3		✓	✓						✓			✓	✓	✓	6	67
CO2DB		✓	✓						✓				✓	✓	5	68
Energy economic model																
MAM		✓	✓	✓				✓[d]						✓	5	69
MARKAL-MACRO		✓	✓	✓	✓		✓	✓[e]		✓		✓	✓	✓	10	70
MICRO-MELODIE		✓	✓	✓	✓		✓	✓[e]				✓	✓	✓	9	71
TIMES- MACRO		✓	✓	✓	✓		✓	✓[e]				✓	✓	✓	9	72
Energy demand-supply model																
DECPAC		✓	✓	✓			✓		✓			✓	✓	✓	8	73
IKARUS	✓	✓	✓	✓	✓		✓		✓			✓	✓	✓	10	74
ENPEP		✓	✓	✓	✓			✓[e]		✓[f]		✓	✓	✓	9	71,75
LEAP		✓	✓	✓	✓			✓[d]	✓		✓	✓	✓	✓	10	76–78
POLES		✓	✓		✓			✓[d]		✓		✓	✓		7	79
MESSAGE-III		✓	✓		✓		✓					✓		✓	6	80
WASP		✓	✓		✓	✓	✓					✓		✓	7	81
MARKAL		✓	✓		✓		✓					✓	✓	✓	7	82
TIMES		✓	✓		✓		✓					✓	✓	✓	7	83
MEDEE		✓	✓		✓	✓					✓	✓			6	84
MAED		✓			✓	✓						✓			4	85
NEMS		✓	✓		✓		✓					✓	✓	✓	7	86
ENERPLAN		✓						✓[d]	✓			✓	✓		5	71,75
MESAP		✓	✓	✓	✓		✓	✓[d]	✓		✓	✓	✓		10	71
Energy emissions model																
UK 2050	✓	✓	✓		✓				✓			✓	✓	✓	8	87
BD 2050	✓	✓	✓		✓				✓			✓	✓		7	51
MESAP PlaNet		✓	✓		✓	✓			✓			✓	✓	✓	8	88,89
EFOM-ENV		✓	✓		✓	✓	✓					✓	✓	✓	8	90
IMAGE		✓	✓		✓	✓							✓	✓	6	91
AIM		✓	✓		✓	✓						✓	✓	✓	7	92
ASF		✓	✓						✓				✓	✓	5	93
GREEN		✓	✓		✓					✓		✓	✓	✓	7	94,95
ERM		✓	✓		✓					✓		✓	✓	✓	7	96
IEA		✓	✓		✓			✓[d]				✓	✓	✓	7	96
CRTM		✓	✓		✓					✓		✓	✓	✓	7	95,96
MR		✓	✓		✓		✓					✓	✓	✓	7	96
WW		✓	✓		✓					✓		✓	✓	✓	7	96
SGM		✓	✓	✓		✓						✓	✓	✓	7	97
Total	3	34	32	10	27	8	13	10	11	7	3	30	29	28		

[a]Input types: Qul (qualitative); Qua (quantitative); Fin (financial); Agg (aggregated); and Disag (disaggregated). [b]Methods: RE (regression); OP (optimization); EC (economic–econometric, macroeconomic); SM (simulation); EQ (equilibrium); and AF (accounting framework). [c]Output types: En (energy — demand/supply); Em (emissions); and Co (cost). [d]Econometric. [e]Macroeconomic. [f]Economic equilibrium.

decentralization and competition in the energy industry[22]. Policy priorities in EPMs need to be more country-specific or regional, because of the differences in objectives due to the common socio-economic vulnerability or conditions, and geographical and climatic characteristics. Indicators relevant to most developing economies include[22]: issues regarding resource management; assessment of energy alternatives; the economic and technical challenges associated with the transformation of the energy infrastructure from a centralized one to an intelligent and decentralized one; and financial vulnerabilities in households. Addressing these in EPMs is necessary to provide higher reliability of estimates.

In the following sections, the issue of suppressed demand in developing countries is analysed, followed by a discussion of the difference in socio-economic characteristics such as corruption and political stability, as well as their effect on the economy. The following section explores the influence of data inadequacy on the

Table 3 | Origin and use of EPMs

Model	Developer	Country of origin	Applied to or adopted in developing countries	No. of countries applied to or adopted in	Ref.
E3 Database	Ludwig-Bolkow-Systemtechnik GmbH	Germany	-		67
CO2DB	International Institute for Applied Systems Analysis (IIASA)	Austria	-		68
DECPAC	International Atomic Energy Agency (IAEA)	Austria	-		73
IKARUS	Former German Federal Ministry of Education, Science, Research, and Technology (BMFT)	Germany	-		74
MAM	US Department of Energy	USA	-		69
MARKAL-MACRO	International Energy Agency (IEA) and ETSAP	France	Yes		70
MICRO-MELODIE	US Department of Energy	USA	-		71
TIMES- MACRO	Brookhaven National Laboratory	USA	-		72
ENPEP	Commissariat à l'énergie atomique et aux énergies alternatives (CEA)	France	Yes	60	98
LEAP	Energy Technology Systems Analysis Program (ETSAP) and International Energy Agency (IEA)	France	Yes	190[a]	99
Mesap PlaNet	International Atomic Energy Agency (IAEA)	Austria	-		88
EFOM-ENV	Stockholm Environmental Institute, Boston	USA	Yes	20	100
POLES	First developed by CNRS (France), and now by CNRS, UPMF University, Enerdata, and IPTS (Spain, European Commission Research Center)	France	Yes	57[a]	101
MESSAGE-III	International Institute for Applied System Analysis (IIASA)	Austria	Yes		102
WASP	International Atomic Energy Agency (IAEA)	Austria	Yes	100	98
MARKAL	International Energy Agency (IEA) and ETSAP	France	Yes	70[a]	102,103
MEDEE	Institut Economics et Juridigue de l'Energie (IEJE), Grenoble	France	Yes		100
MAED	International Atomic Energy Agency (IAEA)	Austria	Yes	40	85
NEMS	US Department of Energy	USA	-		86
ENERPLAN	Tokyo Energy Analysis Group	Japan	Yes		102
MESAP	Institutes für Energiewirtschaft und Rationelle Energieanwendung (IER), University of Stuttgart	Germany	Yes		104
UK 2050	Department of Energy and Climate Change (DECC)	UK	Yes	24 [a,b]	105
IMAGE	PBL Netherlands Environmental Assessment Agency and Utrecht University	Netherlands	-		91
AIM	National Institute of Environmental Studies (NIES)	Japan	-		92
CRTM	Joint Center for Satellite Data Assimilation (JCSDA)	USA	-		96
SGM	Pacific Northwest National Laboratory (PNNL), and maintained by the PNNL Joint Global Change Research Institute (JGCRI)	USA	-		97

[a]Including all the countries that utilized the specific model. [b]Several 2050 pathways models have been constructed for the following developing countries: Vietnam, Bangladesh, Thailand, Nigeria, Mexico, Mauritius, Indonesia, India, Colombia, China and Brazil. These models are roughly based on the principles of UK2050 Pathways[106], albeit with some minor country-specific additions. Most models lack the consideration of socio-economic parameters except BD2050 where electricity consumption is modeled against various scenarios of GDP and population growth. Political instability, corruption, suppressed demand and climate change effects are not modeled in any of these developing country pathways.

development of EPMs. Afterwards, the impact of climate change is discussed focusing on the effect of energy planning on land development and food production, as well as the role of extreme weather events on EPMs. Finally, the impact of poor characterization of variables on EPMs is discussed.

Suppressed demand in developing countries. Suppressed demand refers to the incapability of the people, community or nation to meet minimum services levels (MSL) necessary for human development[23], such as clean and safe drinking water and adequate energy for cooking and lighting because of some host barriers[24]. Barriers can be a lack of infrastructure, low technology penetration, and poverty, particularly the high costs of energy services compared to household incomes[25]. Energy infrastructure barriers such as the lack of access to grid electricity can lead to minimal or no use of electrical appliances. The barriers can also interact to produce a situation where the population cannot afford energy for basic needs because of low income and high unit cost. On the other hand, studies show that

the reduced unit cost often results in higher demand for energy. For example, the transition from kerosene to electric lighting in developing countries reduced the unit cost of light by more than 90% but augmented the consumption of lighting services (lumens) by a factor of 40 (refs [25–27]). In the case of the technology barrier, the penetration of specific technology among the population can be hindered by the higher initial cost. This cost can be compensated by high income, and policy incentives by governments (such as tax reduction on the technology or subsidies).

Emissions from developing countries are much lower than the global average because of suppressed energy demand. Energy consumption of many household needs, such as heating and cooking, and lighting, may not reflect the real demand. The lack of consideration of suppressed demand can result in an inaccurate estimation of baselines for Clean Development Mechanism (CDM) projects[28]. More specifically, CDM rules state that "the baseline may include a scenario where future anthropogenic emissions by sources are projected to rise above current levels, due to the specific circumstances of the host party"[29]. However, a UNFCCC report[30] encouraged the CDM Executive Board "to further explore the possibility of including in baseline and monitoring methodologies, as appropriate, a scenario where future anthropogenic emissions by sources are projected to rise above current levels due to specific circumstances of the host party". These guidelines explicitly differentiate energy contexts between developed and developing countries. None of the reviewed EPMs considered the CDM guidelines, which may increase error in future energy planning strategies for developing contexts.

Difference in socio-economic characteristics. Developed countries have different socioeconomic attributes than those of developing countries. The literature suggests that political instability affects the economic growth of a country[31], especially GDP growth[32]. The rate of change of stability is lower in developed countries that are often characterized by steady GDP growth (Fig. 2a–e). However, all developing countries do not necessarily demonstrate a similar association between GDP growth and political stability, which varies substantially (Fig. 2f–j). There are also exceptions. Despite the negative progression of political stability, some countries have positive GDP growth (for example, Japan, Germany, and Bangladesh). Developed economies mostly maintain steady progress on the positive side of the political stability scale (that is, they have a political stability score of 0 to 2.5), while the same parameter is on the negative side of the scale in most of the developing countries (that is, the score ranges from 0 to −2.5). In most developed country EPMs, GDP is the only socio-economic parameter for demand projection. Considering GDP growth or GDP volume alone is unlikely to represent the nuances of the economic structure of a developing country. More integrative modelling is, therefore, required for predicting future energy demand while accounting for the structural changes in the economy. The increasing share of industry and services in the economic output with a corresponding rise in energy use and emissions in developing countries has the potential to further augment world GHG emissions, despite the decreasing trend for emissions in high-income countries.

Along with the stage of economic development, the intensity and distribution of economic activities influence a country's energy consumption. The analysis of GDP per capita against electricity consumption in Fig. 3 shows a positive relationship; that is, electricity consumption increases with the growth in GDP. The coefficients of determination (R^2) in the plots are very high for low-income and lower-middle-income countries as compared to the upper-middle and high-income countries. In high-income countries, the change in GDP per capita has little influence on electricity consumption. In contrast, an increase in GDP per capita significantly amplifies electricity consumption in low-income and lower-middle-income countries, as previously reported[33]. This amplification in energy consumption may have resulted from the presence of suppressed demand.

The trends in per capita gross national income (GNI) and energy consumption for the period 1960–2013 of eighteen randomly selected countries from four World Bank economic classifications are illustrated in Fig. 4. In the high-income and upper-middle-income countries, the relationship between GNI per capita and electricity consumption per capita has a logarithmic progression, which denotes that when a country reaches a stable income level, the energy consumption becomes linear in characteristic (Fig. 4). In the case of developing contexts with lower middle and low income, the increase in GNI boosts the electricity consumption exponentially (Fig. 4), because GNI per capita augmentation influences the 'suppressed' demand by allowing more people to access electricity. Moreover, improved buying capacity enables consumers to buy and utilize more electronic products, resulting in exponential electricity consumption growth. After reaching a stable economic stage, the energy consumption growth slows steadily[34], despite the fact that the GDP can keep rising.

In developing economies, corruption influences policy decisions, including the procurement of megaprojects — often resulting in the selection of higher-cost options[35,36] that may benefit the decision-maker(s) to the detriment of the environment and economy. For example, after 2009, Bangladesh's increased dependence on volatile international energy markets for oil imports was due to the growth in for-profit, private sector oil-based generation plants operating during off-peak hours that resulted in greater macroeconomic risks[37]. The sub-optimal decision to increase oil-based electricity generation beyond peak generation capacity requirements has been reported as ad-hoc and short-sighted[37].

Evidence suggests that reduced corruption can result in a significant increase in GDP; for example, if Bangladesh can enhance its bureaucratic integrity and efficiency to the level of Uruguay its annual GDP growth would elevate by over half a percentage[35]. Figure 5 compares inflation with the Corruption Perceptions Index (CPI) of different nations. Countries with higher CPI scores are less corrupt and more developed and in most cases, have less inflation. In contrast, countries with higher levels of corruption tend to have higher inflation. The economic inflation rate is associated with the size of the national debt of a country. Energy projects are typically big and require significant investments. Loans from international financial organizations such as the World Bank, Asian Development Bank (ADB) and International Monetary Fund (IMF), and local and international banks, constitute a large proportion of energy investments in developing countries. Corruption has been reported in all life-cycle stages of energy projects, but most evidence on its existence and extent are reported for the tendering process[38], which directly increases the project cost and corresponding loan amount. The terms of these loans are typically longer (for example, decades) and interest rates are higher, due to the perceived risks of political instability and inflation — resulting in higher repayment cost and increased national debt. The consequences of increased pressures on public finance are the inevitable rise in personal and sometimes business tax rates, further increasing inflation. Another impact of a corruption-related increase in macroeconomic stress is the detrimental effect on social and economic development, as money intended for these sectors is often reallocated for debt repayment[37].

Comparatively low levels of corruption in developed countries have limited effects on energy projects and the economy. Modelling corruption is, therefore, a low priority. In contrast, energy project procurement, management and operation in developing countries are evidently corrupted with severe impacts on the economy[39]. Corruption and its effects on micro- and macroeconomic performance in all life cycle stages of energy planning should, therefore, be an integral part of any modelling effort in developing countries.

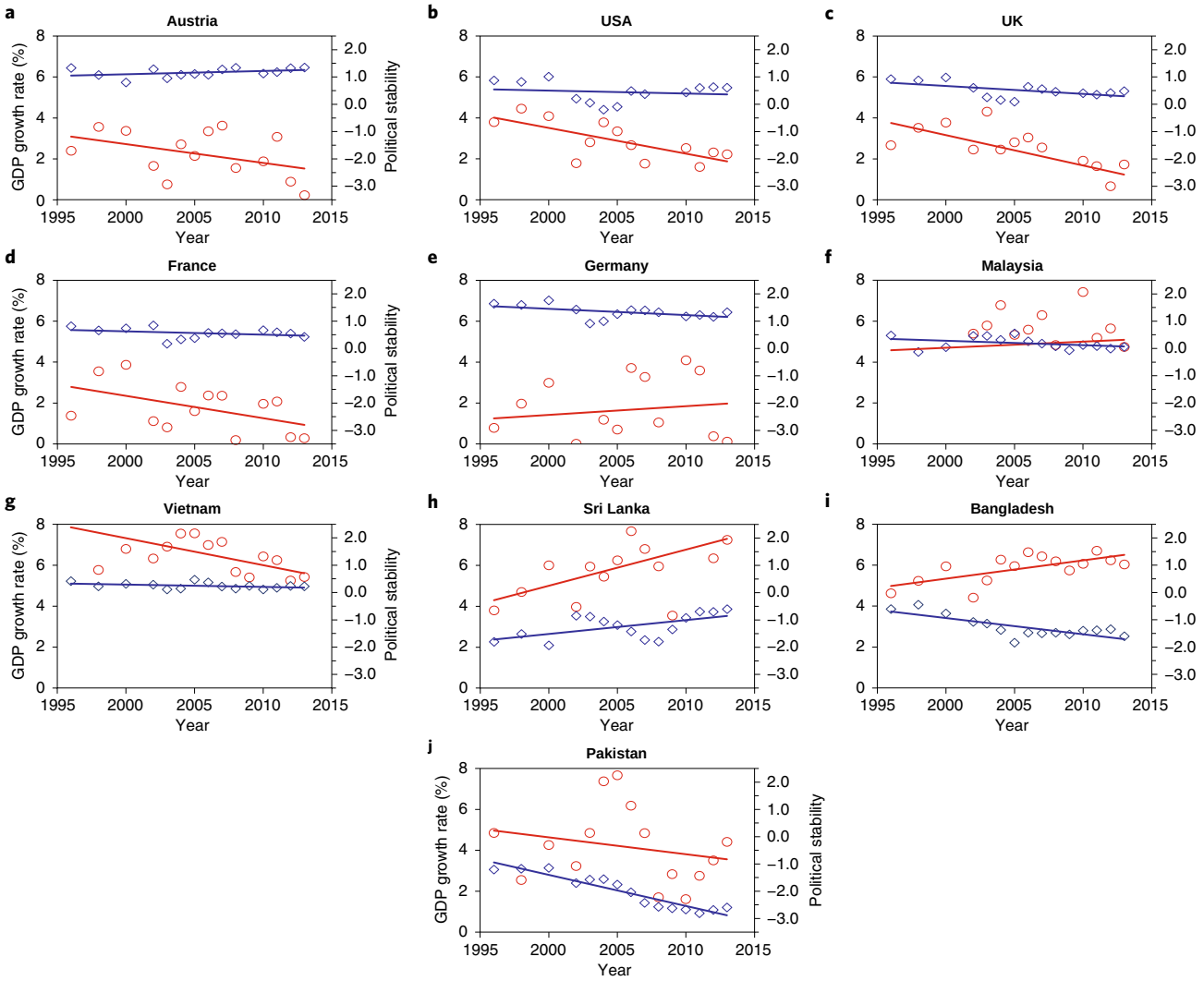

Fig. 2 | Trends in GDP growth and political stability. a–j, GDP growth and political stability scores are shown for developed (**a–e**) and developing (**f–j**) countries. Political stability (political stability and absence of violence/terrorism) and GDP growth are illustrated by hollow blue diamond and red circular shapes respectively. Straight lines represent the fitted regression line, visually depicting the trend in the data. Data is taken from refs [64,65].

Among the 34 reviewed EPMs, none addressed the implications of corruption on the energy economy. In addition to corruption, none of the reviewed models considered the effect of political instability on the economy, which was found to be prominent in developing contexts. Also, the influence of per-capita income change drives energy consumption differently in developing economies compared to in developed ones; it was found that this aspect was modelled less elaborately in the reviewed EPMs.

Data inadequacy. Estimation and projection quality in EPMs depends on data adequacy and accuracy, as historical trends determine the future projection. EPMs are mostly mathematical models in which data inadequacy can result in inaccurate estimation, or at least increase the uncertainty of prediction. Also, incomplete data records hinder the assessment of potential interrelations among the variables, rendering the EPM development process difficult. Data inadequacy is reportedly more pronounced in developing contexts than that of developed ones[40–42], in particular regarding the required level of disaggregation and resolution, as well as the provenance of data. Careful considerations should be given, especially in developing contexts, to the collection of quality-assured data. On the other hand, modelling approaches should be flexible enough to accommodate incomplete historical data up to an acceptable limit while compensating for the possible variations in temporal and spatial resolutions.

Climate change impact. Climate change is projected to disproportionately impact some developing countries (for example, Bangladesh, Philippines, Malawi and India) not only because of their development status and perceived shortcomings in adaptation capacity but also because of their inherent geographical and social vulnerabilities. Moreover, the global energy system is transitioning away from centralized generation and management to a more distributed, intermittent renewable energy and land-based system, where land and infrastructure resilience to natural hazards is becoming increasingly important, even for energy planning[43]. The impacts of climate change on the broader economy and environment require the consideration of region-specific and country-specific parameters for resilience, adaptation, mitigation, and development in EPMs. None of the EPMs reviewed considers the impacts of climate change. Even energy emissions models consider only energy-related emissions and may also consider their future evolution from decarbonization perspectives.

Energy versus land versus food considerations are also important. Land-based economic sectors are particularly vulnerable to

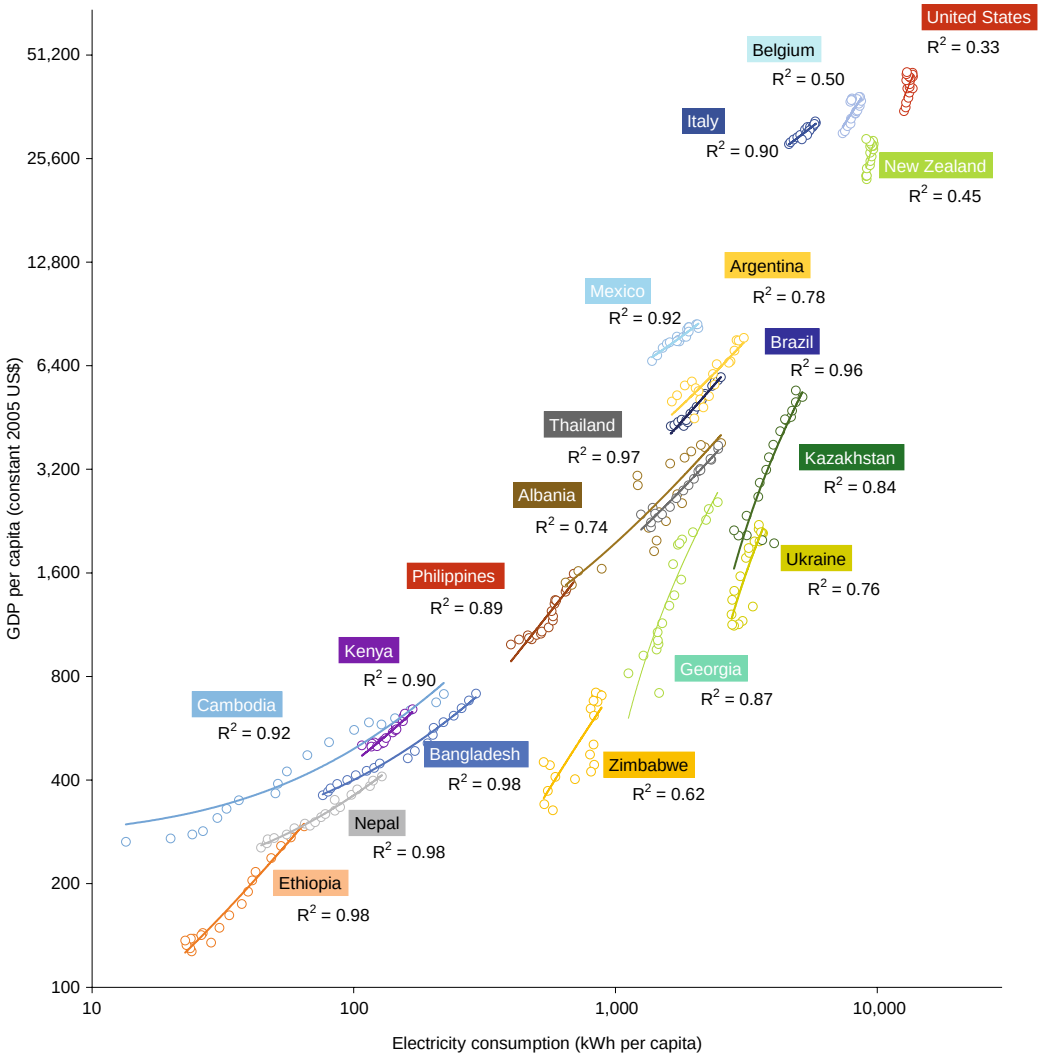

Fig. 3 | GDP per capita versus electricity consumption from 1995 to 2013. The R^2 values denote the coefficient of determination, which measures how close the data are to the fitted regression lines. Data taken from ref. [9].

sea-level rise, as well as natural disasters such as floods, tsunamis, and landslides due to increased precipitation, all of which are projected to occur with increased frequency. Developing countries are particularly vulnerable to these impacts because of their tropical and sub-tropical locations and geomorphology[44]. For projected sea-level rises of 45 and 100 cm, up to 15,600 and 30,000 km^2 of land area respectively will be permanently flooded in Bangladesh[45], corresponding to up to about one-fifth of the country's total land area. The production of rice, the staple food, will decrease from 236 to 96 kg per capita per year if the sea level rises by 32 cm by 2050, and 30 kg per capita per year if the rise is 88 cm by 2100 (ref. [46]). In the case of Maldives, the entire island country could drown if the sea level rises, as the highest point is only 2.4 m higher than sea level. Moreover, energy infrastructure in several countries is vulnerable to sea-level rise[47,48], as they are situated near the water resource, such as rivers and seas, for cooling purposes[49]. Direct impacts of climate change on energy systems are thus related to energy infrastructure resilience and energy production when vulnerable lands are used for energy crops.

As a matter of course, and in line with the theoretical discourse on stages of economic growth, the least developed and developing countries aim to become developing and developed respectively — representing a gradual shift in focus from agricultural towards more industrialized societies[50]. Industrial development is often manifested in the transformation of agrarian lands into industries and energy infrastructures in populated countries with severe shortages of buildable land — which affects food production. The situation is exacerbated when a significant share of arable land is allocated to energy crop production, leading to a conflict between the goals of energy and food securities — both of which are critical issues for developing countries with relatively large populations and modest land mass, such as Bangladesh. Of the 34 studied models, only BD2050 considered the effects of energy sector development (for example, land-based bioenergy) on food production[51]. Before BD2050's launch in 2015, the International Atomic Energy Agency's (IAEA) Wien Automatic System Planning package (WASP) was predominantly used for energy planning. WASP is essentially an optimum-solution finder for supply-side expansion and is mostly unsuitable for modeling land-based interactions. The increasing interactions between food, land and energy, therefore, need to be modeled and assessed holistically for informed decision-making.

Effects of extreme weather events also need to be considered. Extreme weather events are typically rare, yet climate change will make some of these events more likely to occur and more likely to be severe[52]. Slow-onset events such as heatwaves and unexpected low temperatures have a direct effect on comfort-related energy demand[53], in addition to the resulting increased mortality, especially among the elderly, children and the infirm. While effects

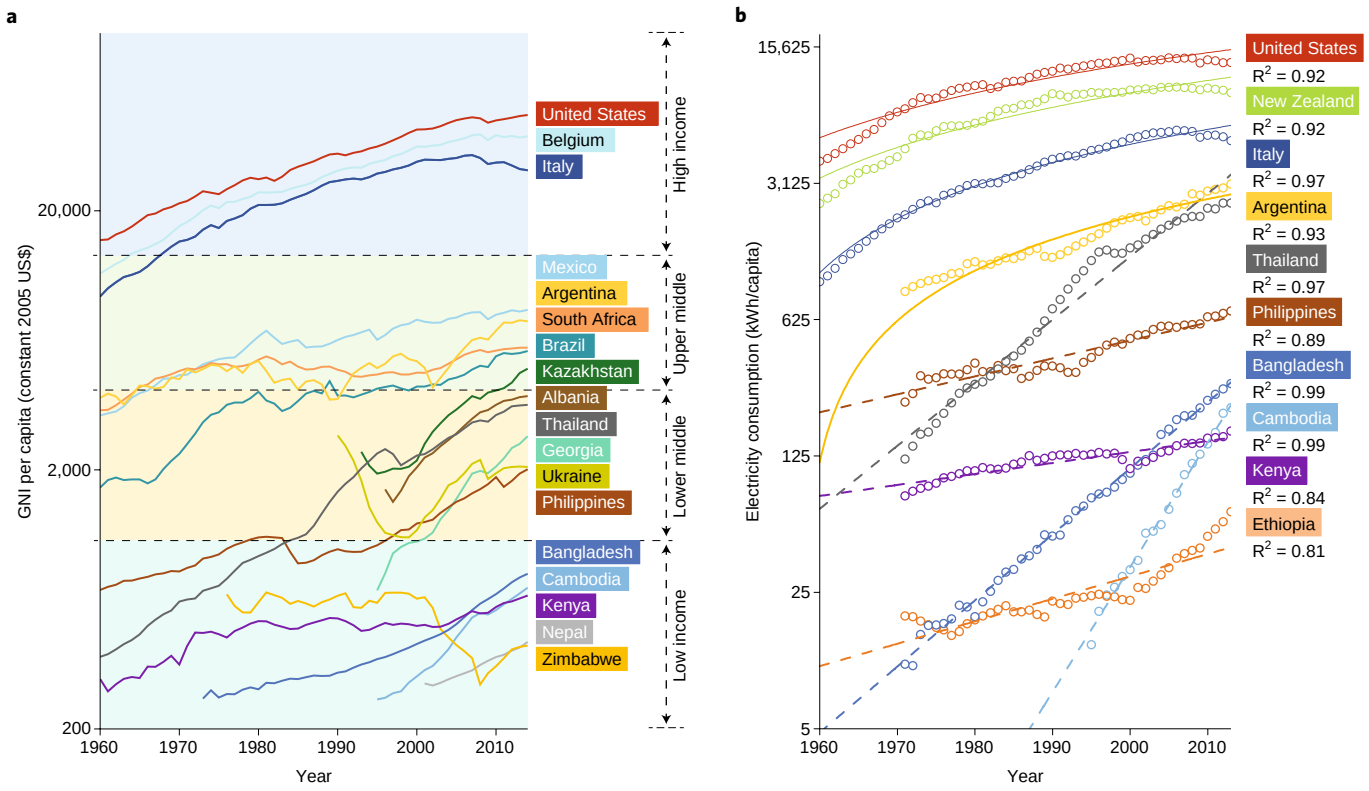

Fig. 4 | Growth trends across developed and developing countries. a, Growth in GNI per capita of different countries from 1960 to 2014. **b**, Growth trends in electricity consumption of different countries from 1960 to 2014. In **b**, trends in the data are visually depicted by fitted regression lines. The y-axis values are on a logarithmic scale, and the dashed and solid lines denote exponential and logarithmic progression of the data, respectively. The income group classification used here is that from the World Bank list of economies (July 2015): low income, US$1,045 or less; lower middle income, US$1,046–4,125; upper middle income, US$4,126–12,735; and high income, US$12,736 or more. Data taken from ref. [9].

such as these are common to both the developing and developed countries, the amplitude and duration of extreme events, as well as the inability to cope with their sudden onset, are often more pronounced in tropical and sub-tropical developing countries; for example, heatwaves in India and Pakistan in 2015 (ref. [54]). Air conditioning accounts for 28% of electricity consumption in the hottest months in Delhi, India[55]. Although India started its first energy-efficiency rating for air conditioning and labeling programme in 2006 (ref. [56]), aimed at reducing annual electricity demand by 27 TWh by 2020 (ref. [57]), a heatwave can escalate that demand[58]. Climate change impacts are seldom considered in EPMs probably because they originate in developed countries that have been shown to be less vulnerable than developing countries, where climate change can cause immense damages[59]. None of the reviewed EPMs considered the climate change impact. BD2050 only explored the implication of energy policies on food security. That does not necessarily explore the impact of climate change in Bangladesh. Energy demand projection and infrastructure resilience should, therefore, consider the probability of extreme weather events, especially in EPMs for developing countries.

Effects of poor characterization. Poor characterization of the energy system and its underlying socio-economic parameters can lead to inappropriate modeling of future energy and emissions scenarios in both developed and developing countries (Table 4). Inaccurate projections affect energy system planning and infrastructure development, especially in the long term. Furthermore, energy dynamics in developing countries are complicated because of the prevalence and different distribution of the following socio-economic and political parameters: political stability, energy-use characteristics of the extremely poor, the pervasiveness of small unregistered businesses, the presence of large informal sectors, corruption, and subsidies. Moreover, most of these aspects have seldom been addressed in a reasonable level of detail in the literature. The gap in knowledge is exacerbated by the limited availability of modeling expertise in developing countries. Complexities such as these make the energy models in developing countries more vulnerable to poor characterization compared to the energy models in developed countries.

Implications and considerations for EPMs

Although developing countries have lower per-capita GHG emissions than those of developed countries, there is an increasing trend in emissions since 1990. The rate of change is often higher than previously projected. For example, despite the energy system being mostly based on renewable energy (93.3% of the total in 2010), per capita, CO_2 emissions in Costa Rica increased by 78.6% between 1990 and 2011 (ref. [9]). Similarly, higher emissions growth rates can be found for United Nations Framework Convention on Climate Change (UNFCCC) non-Annex countries that did not have an emissions reduction target[9]. In contrast, most developed countries demonstrate a decreasing trend. CO_2 emissions from the middle-income nations already surpassed that of the high-income countries, as illustrated in Fig. 1d. Upper-middle-income nations are also about to exceed the emissions from high-income countries. Although India and China dominate in emissions growth at present, Brazil, India, Indonesia, China and South Africa are projected to eclipse global GHG emissions in 2050 (ref. [60]). According to the 2017 IEA World Energy Outlook[17], China will start to decrease CO_2 emissions from 2030 but will still emit 2.8 times more in 2040 than

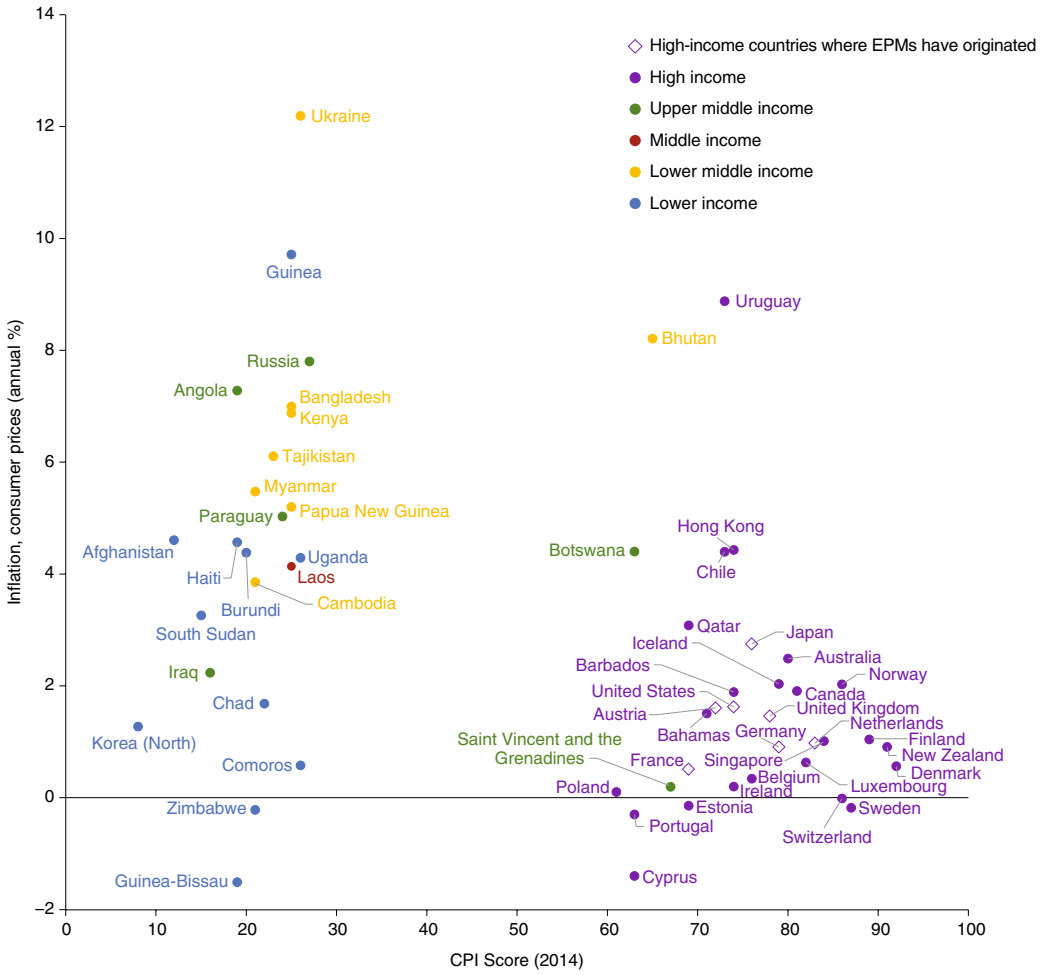

Fig. 5 | Comparison of corruption perceptions with inflation. Corruption Perceptions Index (CPI) 2014 versus inflation (2014) among the top and bottom 35 countries of the CPI list. High-income countries where EPMs have originated are illustrated by hollow purple diamond shapes. For detail, see Table 3. Data taken from refs [9,66].

in 2000. On the other hand, CO_2 emissions from advanced economies started to decline in 2014, and by 2040, they will emit 0.3 times less than in 2000. However, CO_2 emissions from the rest of the world will keep increasing gradually, and will collectively emit 2.4 times more CO_2 by 2040 than in 2000.

The current discourse on economic development is that along with Brazil, Russia, India, China and South Africa (BRICS), eleven further countries, known as N-11 countries — Bangladesh, Egypt, Indonesia, Iran, Mexico, Nigeria, Pakistan, the Philippines, Turkey, South Korea and Vietnam — have a high potential of becoming among the world's largest economies in the twenty-first century[61]. Projections of energy demand growth in smaller economies with more significant populations have mostly been inaccurate. For example, the 2010 Power Sector Master Plan (PSMP) projected that primary energy demand in Bangladesh in 2030 would be 616 TWh (ref. [62]), which was later revised up in the 2015 plan to 860 TWh in the 'business as usual' (BAU) scenario — a 40% increase in the projected amount within five years (ref. [63]). The updated projected demand can be ascribed to flawed assumptions of the probability of demand growth and the lack of the consideration of suppressed demand. Policies based on inaccurate projections are unlikely to be efficient and sustainable.

The treatment of the identified deficiencies in energy planning models needs to consider the local contexts in developing countries, both regarding integration with existing models and for the development of new ones. In cases where empirical relationships between deficient parameters and outcome variables are well established and accepted by the stakeholders, the decision on integration versus new EPM development will depend on the complexity of integration with the existing model and the potential for contribution in policy development and energy planning. On the other hand, not all deficiencies need to be accounted for in all model types. Table 5 provides an applicability matrix of the identified variables against model typologies.

A summary of potential considerations for the identified deficiencies for the development of or integration into future country-specific or region-specific localized EPMs follows.

Suppressed demand. Detailed relationships between the constituent variables of energy demand — such as the elasticity between income threshold and buying capacity and grid connectivity — need to be addressed in EPMs for developing contexts.

Dynamics between political stability and economic growth. Not all developing countries share similar political stability. If there exists an evident correlation between economic growth and political stability, it should ideally be explicitly modeled in the EPM. Where the relationship is not conclusive, further research needs to be conducted, even for implicit or proxy considerations.

Influence of corruption on the energy economy. The treatment of corruption in models should be context specific. Multiplier-based

Table 4 | Effect of poor characterizations of energy systems and economies of developing countries in energy planning models

Model typologies	Effect of poor characterizations
Mathematical procedures	
Regression, economic, simulations and accounting frameworks	Fragmented or inaccurate data and relations in the calculation can prompt incorrect results
Optimization	Calculated best solutions may be incorrect, because of the inadequate interpretation of economy and resources framework
Equilibrium	Overlooking the disequilibrium of business sectors and overestimating business sector impacts that prompt contorted results[21]
Modelling approaches	
Top-down model	Incorrect or incomplete linkage or data in model frameworks results in incorrectly computed outputs
Bottom-up model	Influenced by inappropriate or incomplete relations and information in the frameworks, leading to incorrect results
Hybrid model	Hybrid models could lead to inconclusive results due to inappropriate interrelations of different parts of the system with economic and scientific data

Table 5 | Applicability of suggested variables in existing EPMs

Variables	Types of models			
	Energy information systems	Energy demand–supply model	Energy economic model	Energy emissions model
Political stability		✓	✓	
Corruption			✓	
Suppressed demand	✓	✓	✓	✓
Climate change impacts		✓	✓	✓

modelling will be time and cost effective if a significant relationship exists between corruption and outcome indicators. In cases where the relationship is not apparent or cannot be mathematically formulated conveniently, underlying causes can be investigated further.

Data gathering, validation and sharing. A structured data gathering and sharing system can contribute to the enhanced accuracy of the EPMs, as well as the effectiveness of the resulting policies.

Climate change impacts on energy infrastructure and systems. Depending on the country-specific impacts of climate change on energy systems and infrastructure, its degree of incorporation in EPMs can be varied. If the projected climate change has a significant effect on future energy infrastructure and systems, it should be modelled explicitly, especially for land-based variables such as land use, distributed energy generation, food production and bioenergy. In most cases, the explicit modelling of climate-change impacts would require further investigations on the interactions between related variables.

Outlook

Distinct differences exist between the evolution of energy systems in developing and developed countries, as a response to varying social, technical, economic and environmental stimuli. Developed countries primarily aim to reduce climate-affecting GHG emissions while enhancing energy security. In contrast, developing countries are predominantly concerned with increasing access to conventional forms of energy through infrastructure expansion, which is often seen as a prerequisite for economic and social development. Despite the differences in overall policy goals, EPMs play a central role in energy sector development and transformation in both developing and developed countries. Current EPMs were mostly created in developed countries, often with the assumptions and biases of the country and region in which they were developed. Recognizing the importance of EPMs in shaping the energy future, our analysis of 34 EPMs revealed several important shortcomings for the developing context.

A key finding from our Review is the lack of consideration in the analysed EPMs of the unique socioeconomic characteristics in developing countries such as suppressed demand, corruption, and political instability. Disregarding suppressed energy demand can potentially underestimate total demand, rendering future planning inaccurate and ineffective, especially for long-horizon planning such as 2050 pathways. Corruption is a complex socio-economic factor and can increase capital and operation costs of energy projects and infrastructure in some developing countries, affecting sustainability. Also, the economy is sometimes linked with political instability, which on its own can affect energy infrastructure resilience.

Apart from the developing-context-specific socio-economic deficiencies in the current EPMs, climate change impact on land availability and food production is likely to alter the dynamics of energy–food–emissions interactions, especially in the highly populated developing countries. Increasing penetration of distributed energy resources and bioenergy goals require that EPMs should now consider land-based interactions between energy, food, and environment for future planning and development.

Country-specific trends in GHG emissions are also evolving. Collectively, middle-income and upper-income countries now emit more than high-income countries, and this has been the case since 2007. Emissions are increasing at a much faster rate in developing economies than previously projected. EPMs can play an essential role in setting emerging economies on a low-carbon pathway while enhancing access to energy. Most reviewed EPMs were initially intended for their country or region of origin in the developed world. Their later use in developing countries demonstrated their potential for informed decision-making on energy systems planning. However, the identified shortcomings in this Review suggest that the formulation of localized EPMs are essential not only for the countries concerned but also for a low-carbon pathway for the world.

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Competing interests

The authors declare no competing interests.

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