Is polypill a stroke of luck for cardiac patients?

Cardiovascular diseases (CVDs) account for around 18 million deaths every year, an estimated 31% of all deaths worldwide. Over 75% of deaths are in low- or middle-income countries, as they often lack access to integrated primary healthcare programmes for early screening and treatment of people with risk factors compared to those living in high-income countries. In India, nearly 30% of all deaths and 15% of morbidities are caused by CVDs. The most important behavioural risk factors for heart diseases and stroke include unhealthy diet, smoking, harmful alcohol consumption and sedentary lifestyle. The effects of these factors can be seen in individuals as high blood pressure, high blood sugar, high blood lipids, overweight and obesity. Although they are normal and treatable, they are generally undertreated. A large number of lives can be saved every year if more individuals with the above medical conditions get proper treatment. However, in most cases, the conditions go unnoticed for long as they usually cause no symptoms. Presently, as indicated by a study introduced at the American Heart Association's Scientific Sessions 2020, a polypill, with the addition of a daily portion of aspirin may reduce cardiovascular failure and stroke by up to 40%. The outcome is a feature of The International Polycap Study-3 (TIPS-3), a randomized, placebo-controlled trial to test the adequacy of a fixed-dosage blend treatment.

A polypill is a medication in pill structure that consolidates various dynamic drug fixings. The prefix 'poly' signifies 'various', alluding to the variety of medications in a given 'pill'. Giving individuals a pill containing numerous conventional medications that forestall coronary episodes was first proposed nearly 20 years back; however, advancement and adoption was restricted. For treating CVDs, a polypill combines three different blood pressure medications (atenolol, hydrochlorothiazide and ramipril) and a cholesterol-lowering statin medication simvastatin. Atenolol is used as a beta blocker for BP, hydrochlorothiazide is a diuretic while ramipril is an ACE inhibitor. Polypills can be used as such or with aspirin, a blood thinning medicine.

While numerous examinations have upheld a polypill procedure for auxiliary avoidance, little advancement has been made in its use globally. Also, despite having advertising endorsements in about 40 nations around the world, the use of CVD polypills is still restricted. Obstructions incorporate a doctor's poor knowledge, absence of proof on hard clinical results, and non-eligibility of government reimbursement. Another possible block for wider use of polypills is linked with worries that unfriendly impacts related to one of the polypill's parts could prompt its cessation and the deficiency of the multitude of other segments' advantages.

Regardless of huge clinical advancement in the prevention and treatment of CVDs, the utilization of crucial drugs is deficient in low- and middle-income nations. The use of 3–4 fundamental medications can essentially lessen mortality related to CVDs, particularly in auxiliary anticipation. The remaining blocks include low levels of investment by pharmaceutical companies, uncertainty related to intellectual property rights, and manufacturing and regulatory issues.

TIPS-3 involved about 5700 volunteers from nine countries, almost half of whom were provided by India. Male volunteers were 50 years of age or older and female 55 or older. All of them were moderately at risk for heart problems because of underlying conditions such as diabetes or high blood pressure. While the formulation of polypills may vary, those used in this study included 100 mg of atenolol, 25 mg of hydrochlorothiazide, 10 mg of ramipril and 40 mg of simvastatin or placebo per day, aspirin (75 mg) or placebo per day, and vitamin D or placebo monthly. The group was split into four and was invited to take one of the following each day: both polypill and aspirin, polypill alone, aspirin alone or a placebo. The researchers monitored them closely for nearly five years and discovered that combining a polypill with aspirin provided the best benefits. This reduced heart problems and deaths by 31% and people who continued to take the pill without interruption for about four years saw a 40% reduced risk of heart problems. The researchers also found that the polypill alone reduced risk of CVDs by 21%, compared to 14% in those who took aspirin alone. About 4.1% of those who took aspirin alone contracted heart disease, compared with 4.7% of those who took a placebo.

One of the reasons that high blood pressure and high cholesterol are not treated properly is that the medications prescribed to treat them are not taken reliably by the patients. It is likewise hard to make sure to take a few drugs or different dosages of prescriptions consistently as they can cause side effects, and can be costly as well. One potential method to improve the consistency of medications is to combine at least one or more of them in a single pill, or polypill. The benefits of this approach include: depending on the particular meds and portions, a polypill might be less expensive than taking several individual prescriptions; lower portions of each medicine might be required, conceivably decreasing the rate of bothering results; several low-portion medications can be more powerful than higher doses of one medication; fewer doses are simpler to recall, and fewer pills and lower portions of prescription may reduce the number of emergency clinic visits, blood tests and other observing measures.

As the potential benefits of a polypill are obvious, they may be offset by its disadvantages which include: taking various drugs, even at low dosages, may prompt higher paces of results and if such result comes, it could be difficult to know which of the medications in the polypill are dependable; when consolidated, medications may interact, causing serious issues like extreme or lack of potency, unfavourably susceptible responses, or joined results; some individuals just need a couple of prescriptions to treat a sickness, and polypills may give more than the perfect measure of a drug; polypills have fixed portions of a few meds, so it may not be conceivable to change the portion of one medicine without changing all of them. Though some people reported dizziness, muscle pain and indigestion, these problems were found to be minimal and also common among those who did not take the pill.

Scaling up a worldwide polypill system could add to the World Health Organization's (WHO's) objective of decreasing mortality from non-transmittable illnesses (counting CVDs) by 30% by 2030 of each a financially savvy

way, and would help accomplish the target of precaution drug inclusion at any rate 50% of the populace with indicative CVD. The World Heart Federation (WHF) could unite specialists from around the world to improve admittance to prescriptions for CVDs and specifically to help a polypill procedure for auxiliary avoidance of CVDs by leading support exercises, backing the consideration of the polypill on the WHO Essential Medicines List. They can be accomplished by taking part in correspondence endeavours and fitting them with other related activities; for example, the new Coalition for Access to NCD Medicine and Products.

It may well be assessed that if just 50% of individuals with either hypertension or diabetes are treated with a polypill, about 2–4 million unexpected deaths, heart failure and stroke could be forestalled on a yearly basis. This could be useful in ensuring the well-being of individuals who have less access to medical facilities. Later, polypills with more up-to-date statins could additionally diminish LDL cholesterol and blood pressure, and lessen the danger of CVDs by more than 50%. Polypill companies would also have to look for Controllers' endorsement to sell their pills in different nations, and those generic medication creators may group with large insurers to offer the treatment. Also, the purpose of giving out a polypill in financially weak networks may strike some as paternalistic. That worry should be weighed against the risks of proceeding with the current course, with extending well-being incompatibility among low and high-financial status networks. A system based on polypill may well benefit all networks, but it seems reasonable to start with networks where requirements and limitations may be more notable. Many people are open to down-to-earth ways to deal with improving their cardiovascular well-being, including the utilization of a polypill. At any rate, realization of the current preliminaries should stimulate the enormous use envisaged to contrast a methodology based on polypills and the best accessible options.

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MEETING REPORT

Modelling atmospheric–oceanic processes for weather and climate extremes*

A rapid increase in the frequency of extreme weather events has been seen over India in recent decades. Countries in Asia are witnessing increasing number of extreme weather events such as typhoons, cyclones and threats of exacerbating these events (due to warming climate) on mankind are looming large. The events like the recent floods over Kerala and Tamil Nadu, drought in Assam, extreme rainfall in Mumbai, etc. are causing huge damage to property and result in loss of lives. An important step in the short-term mitigation of weather extremes is that we should be able to reliably predict such events well in advance. The prediction of tropical weather is a challenge due to the inherent uncertainty of the atmosphere and especially the extremes due to gaps in the proper understanding of the processes involved.

With this vision in mind, an international workshop was organized in 2019 which brought together both academic and operational researchers from India and abroad to facilitate an understanding of the challenges in operational forecasts of extreme weather events with a focus on atmospheric–oceanic processes in the tropical climate, particularly in Asia.

The workshop received overwhelming response with around 100 submissions from several countries (Indonesia, Malaysia, Singapore, Bangladesh, Thailand, China, Saudi Arabia and Japan), especially from research students and early career scientists. There were 42 poster presentations and about 25 oral presentations.

M. Rajeevan (Secretary, Ministry of Earth Sciences, Government of India) in the inaugural address highlighted increasing occurrences of extreme weather and emphasized challenges in accurately predicting the same with further need to augment the research efforts in this direction. The first technical session on the first day of the workshop was based on challenges in operational forecasts of extreme weather events. U. C. Mohanty (IIT Bhubaneshwar), who was the keynote speaker of the session, presented an assessment of observations and predictions of extreme weather events over India, viz. tropical cyclones over the Bay of Bengal, severe thunderstorm and lightning. He mentioned that the Hurricane Weather Research and Forecasting (HWRF) model system has achieved significant improvement in track prediction, occurrence of thunderstorms over the Bay of Bengal's basin because of higher model resolution, improved physics, assimilation of satellite data, impact of Doppler radar reflectivity and radar position, and representation of large-scale synoptic conditions and other features.

Muhammad Firdaus Ammar Bin Abdullah (Malaysian Meteorological Department) presented a case study of an extreme rainfall event over Kuala Lumpur, Malaysia, which was analysed using Weather Research and Forecasting (WRF)-1 km model to study the impact of terrain in shaping the synoptic factors. He stressed upon the need for an enhanced systematic observation network in the region for improving the forecast of extreme events.

Aspects of seamless modelling system for weather/climate were elaborated by A. K. Mitra (NCMRWF, Noida). He discussed how NCMRWF aims to have a

*A report on an International Workshop on 'Modelling Atmospheric–Oceanic Processes for Weather and Climate Extremes', organized by the Centre for Atmospheric Sciences (CAS) of Indian Institute of Technology Delhi (IIT Delhi) in collaboration with the Asian Network on Climate Science and Technology (ANCST), during 28–29 March 2019. The workshop was hosted by IIT Delhi. MAPEX 2019 is a key activity of the Special Topic Group on 'Atmosphere–Ocean Interactions' of ANCST. The key sponsoring organizations from Government of India included MOES, SERB and DST.