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A Systematic review on disease 'x'

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ABSTRACT

As the coronavirus era continues to plague civilization, there is a "unknown" danger lingering deep in the mountains, miles away from a town, waiting to cause the "next pandemic" in some corner of the world. The enigmatic name assigned to the very significant danger posed to human health by unknown viruses is Disease X. Disease X, alongside recognized killers such as SARS and Ebola, is on a short list of pathogens perceived to be a high priority for study by the World Health Organization. It's "Disease X" and this disease's X-factor is that anything about it is mysterious. Technically, it is not a "disease" but is a field of research for scientists exploring the possibilities of the next pandemic. Disease X is certainly not a new disorder, but a possible illness that has yet to be found. Disease X is a placeholder name that was adopted in February 2018 by the World Health Organization (WHO). It is not a threat currently identified, but a hypothetical illness that might arise and spark an outbreak/epidemic/pandemic in the future. The latest analysis is being carried out in order to examine the evidence available on disease X.

Keywords: Disease X, WHO, Pandemic, SARS.

INTRODUCTION

Scientists have uncovered at least about 200 viruses believed to cause illness in humans after the first animal-to-human outbreak, yellow fever, was recognized in 1901. New types of viruses are being found at a rate of three to four each year, according to studies by Mark Woolhouse, professor of infectious disease epidemiology at the University of Edinburgh. Most of them are derived from plants. The increasing number of new viruses is primarily the consequence of ecosystem degradation and trade in animals, experts claim. Where bigger species are wiped out, animals such

as rodents, bats, and insects survive as their natural environments vanish. They are able to live with human beings and are also accused of being the carriers that can introduce human beings new diseases. Past Ebola outbreaks have been related by scientists to serious human incursions into the rainforest. In a 2017 report, researchers used satellite evidence to establish that between 2001 and 2014, 25 of the 27 Ebola outbreaks located along the rainforest biome margins in Central and West Africa started in areas that had undergone deforestation about two years ago. They added that in areas where human population density was high and where the virus had ideal conditions, zoonotic

Ebola outbreaks appeared, but that the relative importance of forest destruction is partly independent of these causes.

An region greater than the scale of Bangladesh was cut down in the Congo River Basin rainforest in the first 14 years of the 21st century. The United Nations has warned that if the present patterns in deforestation and population increase persist, the rainforest in the region could have vanished entirely by the end of the century. As it occurs, in new and sometimes disastrous ways, animals and the diseases they bear will collide with humans. It doesn't need to be like this. A multidisciplinary community of scientists located around the U.S., China, Kenya and Brazil has projected that a \$30 billion annual global investment in rainforest security, halting animal trafficking and agricultural ventures will be sufficient to cover the expense of avoiding potential pandemics.

The group said that investing \$9.6 billion a year on global forest conservation programmes, published in the journal *Science*, could lead to a 40 percent decline in global deforestation in areas with the greatest risk of virus spillover. This may entail encouraging the people living in the woods and making their living, and preventing extensive deforestation and the commercialization of the trade in animals. A parallel initiative in Brazil led between 2005 and 2012 to a 70 percent decrease in deforestation, the scientists said. Although \$30 billion a year might sound like a lot, analysts contend that the investment will pay for itself quickly. According to Harvard economists David Cutler and Larry Summers, the former US Treasury Secretary, the coronavirus pandemic would cost the United States alone an extra \$16 trillion over the next 10 years. The IMF forecasts that, according to pre-pandemic predictions, the pandemic will cost \$28 trillion in lost production worldwide between 2020 and 2025. For now, "Disease X" is imaginary, according to WHO, an epidemic that experts and public health practitioners fear may lead to severe illnesses around the world if and when it happens. "X" stands for unpredictable. Disease X reflects on the latest review [1].

DISEASE X

Disease X reflects the understanding that a significant worldwide outbreak may be caused by human disease caused by a pathogen currently

unknown. The R&D Roadmap expressly aims to make early cross-cutting planning for R&D that is also applicable to an undefined "Disease X" [2]. Disease X is a replacement name that was introduced by the World Health Organisation (WHO) in February 2018 to reflect a potential, unknown pathogen that may spark a potential outbreak on their shortlist of priority diseases blueprint. To ensure that their preparation was sufficiently scalable to respond to an unexpected pathogen, the WHO adopted the placeholder name (e.g. broader vaccines and manufacturing facilities). Anthony Fauci, Director of the US National Institute of Allergy and Infectious Diseases, said that the idea of Disease X will enable WHO projects to concentrate their research efforts on whole groups of viruses (e.g. flaviviruses) rather than only specific strains (e.g. zika virus), thus enhancing the capacity of WHO to respond to unexpected strains. In 2020, it was speculated that COVID-19, caused by the SARS-CoV-2 virus strain, fulfilled the criteria for becoming the first Disease X, even within some of the WHO's own professional advisors. [3-9].

HISTORY

Jeremy Farrar, Chair of the WHO Science Advisory Group on R&D Blueprint [10] In May 2015, in pandemic preparations prior to the COVID-19 pandemic, the WHO was asked by member organisations to develop a 'R&D Blueprint for Action to Deter Epidemics' to produce proposals that would minimise the time gap between the detection of viral outbreaks and the clearance of vaccines/treatments, to stop the use of vaccines/treatments [11]"The emphasis was on the most extreme emerging infectious diseases (EIDs) for which few preventive measures were available. [11, 12] The WHO assembled a group of global experts, the "R&D Blueprint Scientific Advisory Group," [13] to draw up a shortlist of less than ten "priority blueprint diseases" [6, 7, 11]

The shortlist of less than 10 EIDs has been revised regularly since 2015 and has continuously included commonly recognised names such as Ebola, Zika and SARS (e.g. cause of large-scale infections) and more geographically specific names such as Lassa fever, Marburg virus, Rift Valley fever, and Nipah virus. [7] In February 2018, the WHO added Disease X to the Geneva'2018 R&D

Roadmap' conference [14] The placeholder of Disease X recognized the possibility for a possible outbreak that could be triggered by an unpredictable pathogen and asked the WHO to ensure that its preparation and capabilities were versatile enough to respond to such an occurrence by its inclusion. [15, 16]

"The WHO said at the 2018 announcement of the updated shortlist of priority blueprint diseases: "Disease X represents the understanding that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease." [17] John-Arne Røttingen, of the Special Advisory Group on R&D Blueprint,[9] said: "History tells us that the next major outbreak is likely to be something that we will be. We want to see the creation of 'plug and play' solutions that can function with any or a broad variety of diseases; systems that will allow us to build countermeasures at speed." [8, 12] US expert Anthony Fauci said: "WHO agrees that it must 'roll swiftly' and this includes developing platform technology," and that WHO would have to investigate entire classes of viruses to develop such platforms, highlighting". [9]

ADOPTION

"Wise in terms of communicating risk"wise in terms of risk communication,"panic and complacency are the hallmarks of the world's response to infectious diseases, with complacency currently in the ascendance"panic and complacency are the hallmarks of the response of the world to infectious diseases, with complacency currently in the ascendancy."Might seem like an uncool move designed to incite panic"might seem like an uncool move designed to incite panic,"get it on people's radars"might seem like an uncool move designed to incite panic [19]

"It may sound like science fiction, but Disease X is something we must prepare for," Richard Hatchett of the Coalition for Epidemic Preparedness Innovations (CEPI) wrote, recalling that after the progress in containing the 2014 Western African Ebola virus epidemic, disease strains had returned in 2018. [20] In February 2019, CEPI announced US\$ 34 million in support to the German-based CureVa [21]

Parallels were drawn with the activities of the United States Agency for International

Development (USAID) and its PREDICT programme, which was intended to serve as an early warning pandemic device, by sourcing and researching animal viruses, including "hot spots" of contact between animals and humans.[22]. In September 2019, The Daily Telegraph reported on how Public Health England (PHE) had launched it'sow [23].

In New York in October 2019, the WHO Health Emergencies Initiative implemented a "Disease X dummy run" to predict a global Disease X pandemic in order to help plan and exchange ideas and insights for combating such an eventuality for its 150 partners from diverse global health organizations and public health systems.[24, 25] A paper entitled 'Disease X: speeding the production of medical countermeasures for the next pandemic' was published in March 2020 by The Lancet Infectious Diseases, which extended the concept to include Pathogen X (the pathogen contributing to Disease X) and identified areas of product development and international cooperation that will help fight any potential Disease X.[26] In April 2020, The D [27]

ZOONOTIC VIRUSES

The WHO said it could come from several outlets citing haemorrhagic fevers and the more recent non-polio enterovirus involving the addition of Disease X in 2018. "It's a natural process and it is vital that we are aware and prepare. It is probably the greatest risk"It's a natural process and we need to be conscious and prepared. It is probably the greatest risk. Professor Marion Koopmans, WHO special advisor, also noted that the pace at which zoonotic diseases emerged was accelerating, saying: "The intensity of animal and human contact is becoming much greater as the world develops. This makes it more likely new diseases will emerge but also modern travel and trade make it much more likely they will spread" [28]

H7N9 (2018)

In 2018, some international health officials (but not the WHO or the R&D Blueprint group) compared a recent strain of the H7N9 'bird flu' virus, with a 38 percent mortality rate, to a possible Epidemic X.[29, 30] China does not exchange samples of the new H7N9 strain. They finally got

the epidemic under control, however, and the urgency dissipated [31]

COVID-19 (2019–present)

Marion Koopmans, Part of the WHO Special Advisory Committee on R&D Blueprint From the start of the COVID-19 pandemic, experts speculated on whether COVID-19 matched the criterion for disease X.(32)(33) At the beginning of February 2020, Chinese virologist Shi Zhengli of the Wuhan Institute of Virology wrote that coronavirus was the first disease X. Later that month, in the scientific journal *Cell*, Marion Koopmans, Head of Virus Research at the Erasmus University Medical Center in Rotterdam, and a member of the WHO Special Advisory Committee on R&D Blueprint, [34] wrote, "Whether it will be contained or not, this outbreak is rapidly becoming the first true pandemic challenge that fits the disease X category""In a nutshell, Covid-19 is Disease X"Covid-19 is Disease X in a nutshell.

SYNTHETIC VIRUSES / BIOWEAPONS

The media reported that a possible Disease X might be intentionally developed as a biological weapon at the 2018 unveiling of the revised shortlist of blueprint priority diseases [37]. In 2018, WHO R&D Blueprint Special Advisor Group member Røttingen was asked about the possibility of Disease X to come from the ability of gene-editing technologies to produce synthetic viruses (e.g. the 2017 synt virus) Røttingen said it was unlikely that a potential biological virus or bio-weapon will be the cause of Disease X. He acknowledged, however, the severity of such an occurrence, adding, "Synthetic biology allows for the creation of deadly new viruses. It is also the case that where you have a new disease there is no resistance in the population and that means it can spread fast"

Bacterial infection

Public Health England (PHE) announced in that bacteria's enhanced antibiotic tolerance, including 'last-resort' antibiotics such as carbapenems and colistin, might also transform into a possible Disease X, mentioning as an illustration the antibiotic resistance in gonorrhoea. [38] Prof. Tamfum said that this current infection could be more fateful than Ebola and Covid-19. Since doing

round in world media, his comment raises some concerns whether this "Disease X" is just a news disease. But, by now, you already know the answer. Prof. Tamfum also warned that many more zoonotic diseases could occur in the future, especially those that are spread from animals to humans. He said the viruses had all jumped from animals to humans, including pneumonia, rabies, and yellow fever. Such "occurrences are common and could lead to epidemics and pandemics in the future" he said. Since yellow fever, the first animal-to-human outbreak, was reported in 1901, scientists have uncovered at least about 200 viruses that can cause disease in humans, according to CNN. The increasing number of new viruses, experts believe, is primarily the result of ecological degradation and trade in biodiversity, the CNN article said. Nobody knew about the nature of such a virus until there was an Ebola epidemic in 2004 in South Africa, and then everybody was unprepared for it. It was an infectious plague that came into the universe and murdered a lot of people.

The introduction of "Disease X" in its priority list has supported the WHO—and countries around the world—to identify and make whatever preparations they can for diseases from unknown causes. In 2018, John-Arne Rottingen, chief executive of the Norwegian Science Council and a technical adviser to the WHO committee, told *The Telegraph*, "History tells us that the next major outbreak is likely to be something we have not seen before." It might sound strange to add a 'X', but the idea is to ensure that we train and schedule flexibly in terms of vaccines and diagnostic testing, "We want to see 'plug and play' platforms developed which will work for any, or a wide number of diseases; systems that will allow us to create countermeasures at speed,"Rottingen said. "Disease X"Disease X".As the ecosystem and human habitats change there is always the risk of disease jumping from animals to humans. A It's natural process and it is vital that we are aware and prepare. It is probably the greatest risk."As the ecosystem and human habitats change, there is always the risk of disease jumping from animals to humans... It's a natural process and we need to be aware and prepared. It's probably the greatest risk. Previously, Dr. Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases, said, "As experience has taught us more often than not the thing that is gonna hit us is

something that we did not anticipate...Just the way we didn't anticipate Zika, we didn't think there would be an Ebola that would hit cities."

STRATEGY TO FIGHT FUTURE PANDEMIC

"Professor Jean-Jacques Muyembe-Tamfum said, "If a pathogen spreads from Africa, it will take time to spread across the world... So, if this virus is discovered early—as in my institution here—there will be an incentive for Europe [and the rest of the world] to establish new methods to fight these new pathogens." At the time of Ebola, and in the coronavirus era as well, this was said. And, one such way of educating the planet for even greater pandemics that could possibly cause even longer lockdowns than humanity has already undergone is the concept associated with "Disease X" [39].

CONCLUSION

A significant number of possible future killer pathogens exist, and the tools allocated for detecting and reacting to them are woefully insufficient. In an attempt to brace for the next pandemic, the World Health Organisation (WHO) has developed the Research and Development (R&D) Blueprint, a global roadmap for pandemic response. A list of established priority diseases and a roadmap action plan for each of them are provided in the R&D Blueprint. The R&D Roadmap list contains diseases that, due to their ability to cause pandemics, pose a major public health danger as well as the lack of appropriate countermeasures against these diseases. MERS,

SARS, Ebola, Nipah and many other toxic infectious diseases are included. The WHO used this blueprint early in the Covid-19 pandemic to devise a fast pandemic response strategy; Covid-19 was later added to the list of blueprints.

"The list of blueprints also contains the ominously called "Disease X". Disease X, according to the WHO, reflects the understanding that a significant foreign outbreak may be caused by an unknown pathogen causing human disease. Disease X is a placeholder term for any amount of potential pandemic infectious diseases in the future. A modern coronavirus or a virus similar to the filovirus that causes Ebola may be the cause of the next pandemic. It could be due to a virus like the Nipah virus that we are already acquainted with in India. An entirely new virus or a frequent pandemic pathogen such as the influenza virus may be present. Screening, detection, separation, and characterization of Disease X present in wildlife populations should be the next step after managing the Disease X outbreak. To determine the likelihood of potential epidemics, both in vitro and in vivo experiments (using appropriate animal models) should be performed. Disease X currently lacks approved antiviral drugs or vaccines against SARS-CoV, MERS-CoV, and SARS-CoV-2. Development in the production of antiviral drugs and vaccines against many other infectious diseases, however, would help to evolve appropriate therapeutic agents in a limited period of time against Disease X. Before then, to deter this emerging epidemic from being a pandemic, we must focus solely on multiple control and preventive steps.

REFERENCES

- [1]. <https://edition.cnn.com/2020/12/22/africa/drc-forest-new-virus-intl/index.html>. Retrieved on 2021.
- [2]. <https://www.who.int/activities/prioritizing-diseases-for-research-and-development-in-emergency-contexts>. Retrieved on 2021.
- [3]. Daszak, Peter, "We Knew Disease X Was Coming. It's Here Now". The New York Times. Retrieved 2020.
- [4]. Gale, Jason. "Coronavirus May Be 'Disease X' Health Experts Warned About". Bloomberg News. Retrieved 2020.
- [5]. Shi, Zhengli; Jiang, Shibo, "The First Disease X is caused by a Highly Transmissible Acute Respiratory Syndrome Coronavirus". *Virologica Sinica*. 35(3), 2020, 63–265. Doi:10.1007/s12250-020-00206-5. PMC 7091198. PMID 32060789.
- [6]. "List of Blueprint priority diseases". World Health Organization. Retrieved 2020.
- [7]. Editorial. "What is Disease X?", *Economist*. Retrieved. By listing Disease X, an undetermined disease, the WHO is acknowledging that outbreaks do not always come from an identified source and that, as it admits, "A serious international epidemic could be caused by a pathogen currently unknown to cause human disease".

- [8]. Barns, Tom. "World Health Organization fears new 'Disease X' could cause a global pandemic". The Independent. Retrieved 2020.
- [9]. Scutti, Susan. "World Health Organization gets ready for 'Disease X'". CNN News. Retrieved 2020.
- [10]. "R&D Blueprint - Scientific Advisory Group members". World Health Organization. Retrieved 2020.
- [11]. World Health Organization Annual review of diseases prioritized under the Research and Development Blueprint (PDF) (Report). Geneva, Switzerland. p. 17. Retrieved 2020.
- [12]. Nuki, Paul; Shaikh, Alanna. "Scientists put on alert for deadly new pathogen – 'Disease X'". Daily Telegraph. Retrieved 2018.
- [13]. "R&D Blueprint". World Health Organization. Retrieved 2020.
- [14]. Shaikh, Alanna; Nuki, Paul. "What is 'Disease X', the mystery killer keeping scientists awake?". The Daily Telegraph. ISSN 0307-1235. Retrieved 2020.
- [15]. Lee, Bruce Y. "Disease X is what may Become the Biggest Infectious Threat to our World". Forbes. Retrieved 2018.
- [16]. "WHO | List of Blueprint priority diseases". WHO. Retrieved 2020.
- [17]. Whittam Smith, Andreas. "One hundred years on from the Spanish Flu, we are facing another major pandemic". The Independent. Retrieved 2020.
- [18]. Gulland, Anne. "Panic and complacency: how the world reacts to disease outbreaks". The Daily Telegraph. Retrieved 2020.
- [19]. Miller, Korin. "Disease X Might Cause The Next Big Global Epidemic". Women's Health. Retrieved 2020.
- [20]. Hatchett, Richard. "It might sound like science fiction, but Disease X is something we must prepare for". Daily Telegraph. Retrieved 2020.
- [21]. Gouglas, Dimitrios; Christodoulou, Mario; Plotkin, Stanley A.; Hatchett, Richard. "CEPI: Driving Progress towards Epidemic Preparedness And Response". *Epidemiologic Reviews*. 41(1), 2019, 28–33. Doi:10.1093/epirev/mxz012. PMC 7108492. PMID 31673694.
- [22]. Shute, Joe. "Virus hunters: Meet the scientists searching for Disease X". Daily Telegraph. Retrieved 2020.
- [23]. Gulland, Anne. "Revealed: Public Health England 'hot on the trail' of Disease X". Daily Telegraph. Retrieved 2020.
- [24]. Alexander, Harriet. "Disease X dummy run: World health experts prepare for a deadly pandemic and its fallout". Daily Telegraph. Retrieved 2020.
- [25]. Hamblin, James, "The Curve Is Not Flat Enough". The Atlantic. Retrieved 2020.
- [26]. Simpson, Shmona; Kaufmann, Michael C.; Glozman, Vitaly; Chakrabarti, Ajoy. "Disease X: accelerating the development of medical countermeasures for the next pandemic". *The Lancet Infectious Diseases*. 20 (5), 2020, e108–e115. doi:10.1016/S1473-3099(20)30123-7. PMC 7158580. PMID 32197097.
- [27]. Knapton, Sarah. "Drug created to fight 'Disease X' over 10 years ago will be tested in battle against coronavirus". The Daily Telegraph. Retrieved 2020.
- [28]. Cousins, Sophie. "WHO hedges its bets: the next global pandemic could be disease X". *The BMJ*. 361: k2015. doi:10.1136/bmj.k2015. ISSN 0959-8138. PMID 29748222. S2CID 13668695. Retrieved 2020.
- [29]. Gulland, Anne. "Deadly Chinese poultry flu could be 'disease X' that sparks worldwide pandemic". Daily Telegraph. Retrieved 2020.
- [30]. Andrew, Scottie. "What is Disease X? Deadly Bird Flu Virus Could Be Next Pandemic". Newsweek. Retrieved 2020.
- [31]. Majid, Aisha. "Disease X: China ignores UK request to share samples of flu virus with pandemic potential". Daily Telegraph. Retrieved 2010.
- [32]. Gulland, Anne (2020-01-09). "Have Chinese researchers uncovered the new disease X?". The Daily Telegraph. ISSN 0307-1235. Retrieved 2020.
- [33]. McKie, Robin. "Coronavirus: the huge unknowns". The Guardian. This hope now looks forlorn with the sudden emergence of the respiratory disease Covid-19, which has rapidly acquired most of the characteristic of a Disease X. Retrieved 2020
- [34]. "R&D Blueprint: Marion Koopmans (Biography)". World Health Organization. Retrieved 20 March 2020.
- [35]. Mercer, David, "Coronavirus outbreak could be feared 'Disease X', says World Health Organisation adviser". Sky News. Retrieved 2020.

- [36]. Aaro, David. "What is Disease X?". Fox News. Retrieved 2020.
- [37]. Cousins, Sophie. "WHO hedges its bets: the next global pandemic could be disease X". BMJ. 361: k2015. doi:10.1136/bmj.k2015. ISSN 0959-8138, 2018. PMID 29748222. S2CID 13668695.
- [38]. Campbell, Denis. "Bacteria developing new ways to resist antibiotics, doctors warn". The Guardian. Retrieved 2020.
- [39]. <https://www.indiatoday.in/science/story/what-is-disease-x-why-everyone-talking-about-it-1758875-2021-01-14>. Retrieved on 2020.

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