REVIEW ARTICLE

Decoding the Future: Genomic Sequencing's Vital Role in Communicable Disease Prevention within Public Health Practice - A Scoping Review

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ABSTRACT

Precision public health using genomic sequencing is a new field that has gained interest from public health practitioners for prevention and control measures. This study aims to identify the various applications of genomic sequencing for the prevention of communicable diseases in public health practice. Articles containing relevant keywords were determined using a systematic search strategy applied in Medline, Scopus, and Springer electronic databases. Full text included in the study was retrieved and categorised. A total of 24 articles were included in the final review. The main themes regarding the application of genomic sequencing in the prevention of communicable disease that were found in the articles were describing transmission patterns, investigating outbreaks, diagnosing infection, developing and evaluating interventions including vaccines, outcomes response treatment, and monitoring antimicrobial resistance. In conclusion, genomic sequencing has the potential to enhance the prevention and control of communicable diseases globally.

Keywords
Precision, Public Health, Genomics, Communicable Disease, Implementation

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INTRODUCTION

Precision public health is a relatively new field of interest that incorporates the elements of precision medicine, for example, the use of genomics and phenomics, and big data analysis to predict health risks and outcomes, and to improve population health status. It can be defined as the application and combination of new and existing technologies, which more precisely describe and analyse individuals and their environment over the life course, to tailor preventive interventions for at-risk groups and improve the overall health of the population.[1] The integration of population-level characteristics, such as genetic, socio-behavioural, and environmental factors, into the three levels of preventive strategies will allow the public health practitioner to be able to provide the right intervention to the right population at the right time.[2]

The core of precision public health lies in its capacity to create more precise approaches for identifying complex risk factors and their impact on population health, tailored policies, and programs for health promotion and disease control.[3] Several authors have outlined that the application of genomics in the field of precision public health can be further divided into the use of human and pathogen genomics.[4,5] In view of the recent COVID-19 pandemic, there is a spike of interest in incorporating genomics in terms of the prevention and control of communicable disease, for example in elucidating the virulence properties of the microorganisms, and in predicting genetic risk to aid clinical risk prediction for identification of patients who are more likely to develop further severe symptoms.[5] This new approach complemented other public health measures like COVID-19 vaccination as evidence showed that vaccine literacy, fear, and hesitancy had varying effects on vaccination acceptance depending on the preferred vaccine type. [40]

The World Health Organization (WHO) defines genomics as the study of genetic or epigenetic sequence information in organisms, with the goal of understanding both the structure and function of these sequences and their associated biological products.[6] The area is multidisciplinary, utilising a variety of laboratory and bioinformatics tools and sequencing techniques such as genome editing approaches including

CRISPR/Cas9 technology, antimicrobial resistance (AMR) and virulence factor profiling. Genomic sequencing techniques have captured the attention of public health practitioners for their potential to enhance precision in preventing communicable diseases. However, there is a notable gap in integrating these techniques into field practices. The advancement of genomics can greatly support epidemiologic investigations of communicable diseases, offering valuable insights for informing public health prevention and control measures.[39] In response to the need to systematically explore the extensive literature on the application of genomics in communicable disease prevention, a scoping review was undertaken. The central research question guiding this review is: "How is genomics implemented for communicable disease prevention in public health practice?" Through this review, we aim to contribute to the understanding of the role of genomics in communicable disease prevention and lay the groundwork for future advancements in this critical intersection of genomics and public health.

MATERIALS AND METHODS

Scoping reviews have become an increasingly popular form of knowledge synthesis.[7] It is exploratory in nature and allows researchers to extract and understand key findings in literature pertaining to a specific research area. This approach is done systematically and may contribute to the identification of key concepts, research gaps, and evidence to inform practice, policies, and existing research.[8] To achieve the aims of this study, the enhanced methodological steps outlined in the Arksey and O'Malley framework were followed.[9] Based on the PICO framework recommended by the JBI Manual for Evidence Synthesis, key elements were identified to guide the search process which are: 'communicable disease' as the problem, 'genomics' as the intervention, 'public health practice' as the context, and 'prevention strategies' as the outcome.

Search Strategy and Study Selection

Prior to conducting a systematic search discussion was done between the team members and an initial limited search on the topic to identify relevant keywords. The keywords identified were adopted in the full search strategy. The search strategy ("infectious disease" OR communicable disease) AND ("human genomic research" OR genomic' OR genetic') AND prevention AND (public health OR community health) AND (implementation' OR application' OR uses) was conducted in Medline, Scopus, and Springer electronic databases, which provide adequate and efficient coverage for related literature. The search strategies done in Medline and Scopus were adjusted to include articles with keywords in the 'Abstract'. This was done to yield a more specific search result pertaining to the study conducted.

A set of inclusion and exclusion criteria was constructed based on the framework mentioned to select relevant studies to be included in the scoping review. The inclusion criteria are original quantitative studies, related to the prevention of communicable diseases by application of genomic sequencing, relating to public health practice, in the English language and published between the years 2010 and 2022 as the genomic study application in public health has shown much progress and advancement in the past 10 years. In contrast, the exclusion criteria are mixed methods and qualitative studies as well as non-original articles such as conference proceedings, perspectives, commentary, opinions, reports, systematic reviews, and meta-analyses. Other exclusion criteria are articles with no full-text access and those focusing on laboratory research.

Once all the search results were retrieved, two independent reviewers initially screened the title and abstract against the inclusion and exclusion criteria. Any disputes on the relevance of a study were discussed with the whole team and a collaborative decision would be made on its inclusion. Due to time constraints, a pilot test was not done to ensure congruency between the two reviewers, but team discussion was conducted in case of disputes.

Data Extraction and Data Charting Process

The full text of eligible studies was retrieved from electronic databases and was divided among five team members for data extraction and charting. The studies were categorised into six themes (Table I) of genomic implementation for communicable disease prevention as

described by Centres for Disease Control and Prevention (CDC), U.S Department of Health and Human Services.[10]

Table I: Themes of application of genomic sequencing.

No.	Themes
1.	Describing transmission patterns
2.	Investigating outbreaks
3.	Diagnosing Infection
4.	Developing and evaluating interventions including vaccines
5.	Outcomes response treatment
6.	Monitoring antimicrobial resistance

RESULTS

The search yielded 111 articles from Medline, 73 from SCOPUS, and 132 from Springer, resulting in 316 unique hits. Only 69 articles were included in the full-text assessment after rigorous selection screening, and finally, 24 articles were included in the review as shown in the PRISMA flow diagram (Figure 1). Included articles are listed in Table II with information on the author, origin country, year of publication, outcome of the study, and application themes.

There were 45 articles excluded from the final review due to several reasons. The reasons are as follows; 25 review articles, 6 laboratory-based studies, 4 not related to genomics, 3 studies related to animals, 3 not related to communicable diseases, 3 studies unable to locate full text, and 1 study was qualitative.

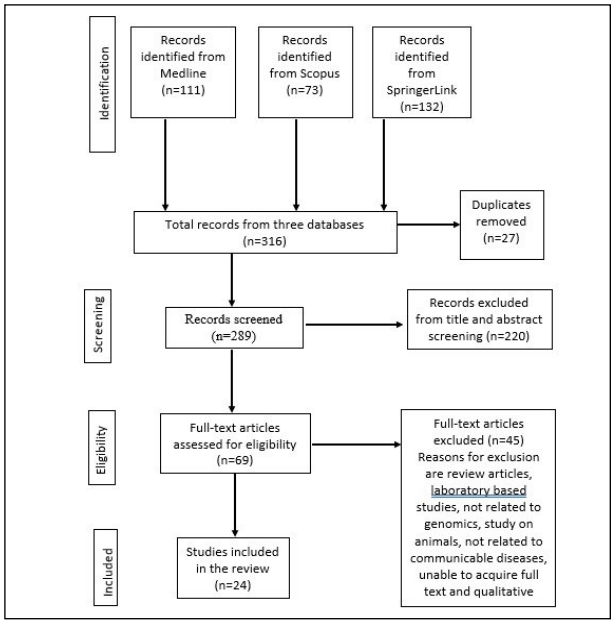

Figure 1: PRISMA flow chart illustrating the article selection process for this scoping review.

Table II: Author, origin country, year of publication, study outcome, and application genomic sequencing themes of included articles.

No.	Applications of genomic sequencing themes	Outcome	Country	Author/Year
1.	Describing transmission pattern	Prevention and control of Dengue	China	Li et al. (2022)
		Control of COVID-19	China	Qiu et al. (2022)
		Prevention and control of Tuberculosis	China	Chen et al. (2021)
		Control of COVID-19	Colombia	Ballesteros et al. (2021)
		Control of HCV among people who inject drugs (PWID)	USA	Hochstatter et al. (2021)
		Control and prevention of Sars Cov-2	Zimbabwe	Mashe et al. (2021)
		Surveillance of food-borne pathogens	Kenya	Hendriksen et al. (2019)
		Control of Hepatitis C Virus (HCV) among HIV-HCV coinfected clients	Australia	Bartlett et al. (2017)
2.	Investigating outbreaks	Prevention & control of HIV Cluster	USA	McCloskey & Poon (2017)
		Prevention of hospital-acquired Methicillin-resistant Staphylococcus epidermidis (HA-MRSE)	Sweden	Widerström et al (2016)
		Prevention of Human Adenovirus	China	Lu et al. (2014)
		Control of Pseudomonas aeruginosa infection or colonization	Switzerland	Catho et al. (2021)
		Prevention and control of COVID-19	Switzerland	Abbas et al. (2021)
		Prevention & control of Clostridium Perfringens	UK	Kiu et al. (2019)
		Prevention and control of HIV	China	Pan et al. (2018)
		Control and prevention of HIV cluster	USA	Wertheim et al. (2018)
		Control and prevention of HIV cluster	USA	Tookes et al. (2018)
		Control and prevention of measles outbreak	Congo	Scobie et al. (2015)
3.	Diagnosing Infection	Prevention and control of Hepatitis B Virus (HBV)	Cambodia	Ko et al. (2020)
4.	Developing and evaluating interventions including vaccines	Prevention of Human Papilloma Virus (HPV)	Congo	Boumba et al. (2014)
5.	Response treatments	Prevention of Human Immunodeficiency Virus (HIV)	Uganda	Birungi et al. (2015)
		Prevention of HIV	Sub-Saharan Africa	Sivay et al. (2021)
6.	Monitoring antimicrobial resistance	Prevention and control of Malaria	Africa, Asia, Ocenia, South America	Turkiewicz et al. (2020)
		Prevention and control of H1N1 influenza	Global	Janies et al. (2010)

Themes of Genomic Sequencing Applications

From our review, 24 articles included in the final review were categorized into six themes with various distribution according to implementation of genomics for prevention of communicable disease in public health practice[6]: transmission patterns (50%), investigating outbreaks (25%), diagnosing infection (4.2%), developing and evaluating interventions including vaccines (4.2%), outcomes response treatment (4.2%) and monitoring antimicrobial resistance (12.5%). Other themes not described in the articles are host susceptibility and long-term disease sequelae. Most of the past 5-years of articles elicited in this review apply genomics to describe disease transmission patterns and monitor antimicrobial resistance.

Describing Transmission Patterns

There are 12 articles mentioning genomics was used for describing transmission patterns of communicable diseases in their study. Three authors mentioned that genomics was applied in preventing and controlling COVID-19 or SARS-COV2 in their study.[11,12,13] As shown in Table II, two authors[14,15] applied genomics in preventing and control of HIV infection while another two authors[16,17] applied genomics in preventing and control of HCV infection. The other five authors[18,19,20,21] applied genomics in their study of the prevention and control of HA-MRSE, Human Adenovirus, TB, and dengue respectively.

Investigating Outbreaks

There are six articles mentioning genomics was used for investigating outbreaks of communicable disease in their study. Genomics was applied genomics into the investigation of outbreaks to prevent and control HIV outbreaks.[22,23] Other articles applied genomics in their study for the prevention and control of COVID-19, Pseudomonas aeruginosa, Clostridium Perfringens, and Measles outbreaks respectively.[24,25,26,27]

Diagnosing Infection

We found one study[33] describing the application of genomic sequencing in diagnosing infection in their study to prevent and control Hepatitis B Virus (HBV) infection. This study describes the method of dried blood spot which can be applied for resource-limited countries to be used in genomic sequencing to identify the HBV genotypes (B and C) and S gene mutation which are predominantly found in Cambodia and the border of Vietnam.

Developing and Evaluating Interventions, Including Vaccine

From our review, only one study describes the application of genomic sequencing in developing and evaluating interventions, including vaccines in preventing and controlling Human papillomavirus (HPV) infections.[28] In this study, it was described that HPV genotyping was used to identify the most common HPV genotype in the population which contributed to a high risk for cervical cancer and invasive cervical cancer. This technique may aid in the development of vaccinations based on the types and prevalence of HPV in order to give more effective interventions.

Response Treatment

Our review found that one study describing the application of genomic sequencing in measure of response to treatment in their study to prevent and control HIV infection[29]. The genomic sequencing was used to develop the phylogenetic trees in identifying the genetic link of seroconversion within the serodiscordant couples who did not receive the antiretroviral treatment (ART), couples who received ART during the study, and couples who received the ART during the enrollment of the study.[29]

Monitoring Antimicrobial Resistance

There are three articles mentioning genomics was used for monitoring antimicrobial resistance in their study. Three studies applied genomics to prevent and control HIV, H1N1, and Malaria infection respectively.[30,31,32]

DISCUSSIONS

Describing Transmission Patterns

In describing the transmission pattern of COVID-19, the SARS-CoV-2 virus sequence was used in study analysis to reveal the lineages circulating in Amazon[11]. Similar

findings were also found by a study[13] that used retrospective nasopharyngeal samples in Zimbabwe for whole genome sequencing to analyze the origins of imported SARS-CoV-2. Apart from origin, different COVID-19 variants showed different transmission patterns. Based on analysis using publicly available data from existing databases in ten countries, the highest R0 values were reported for the Omicron variant, followed by Delta, Alpha, Gamma, and Beta.[41] Interestingly, a study conducted in China that used the Susceptible, Exposure, Infected, and Remove (SEIR) model was able to predict the trend of the pandemic and evaluate different measures and implementation taken on the COVID-19[12].

Another infectious disease that has taken a lot of implementations from the benefits of genomic advancements is HIV infection. McCloskey and Poon in the USA developed a fundamentally new approach based on the Markov-modulated Poisson process (MMPP) using HIV-1 genetic clusters.[14] The researchers were able to predict the transmission rates which were significantly shorter compared to other methods. Tookes et al. on the other hand in their study were able to rapidly identify high -risk groups using risk networks.[15] Moreover, in his study, PWID all achieved viral suppression within 70 days of treatment.

A study about colonizing Healthcare-associated methicillin resistance *Staphylococcus Epidermidis* interestingly found that out of 65 samples taken from the patient, healthcare workers, and environment, only one sample originated from the community[18]. The study also explained that 88% of HA-MRSE are from nasal carrier genotypes. Adenovirus mutation was studied by a researcher[19], who discovered three primary strains of Adenovirus in Mainland China: the China strain, Taiwan strain, and Singapore strain; all shared hexagonic and fiber genetic properties. The researchers in the study also expressed concern about the potential emergence of new recombinant adenovirus strains due to the increasing speed of mutations over the past decades.

Another interesting study on the association of polymorphism and environmental factors among TB patients and their household contact found that 2 groups of MTB genotypes named IL-10 and IFN-γ expressed different infectious rates in different groups of people and different environments[20]. A global network of the DENV -1 population has been developed, allowing the researchers to identify 12 epidemic regions by their content and patterns.[21] This framework would help to control the outbreak of DENV 1 among emerging epidemic countries.

Investigating Outbreak

Researchers also found ways to use genomics while investigating outbreaks. HIV-1 genetic sequences can be used to infer transmission spread and its dynamic[23]. They found that previous growth dynamics were superior predictors of future transmission cluster growth that are most likely to give rise to new cases the following year. Almost similar finding that studied the transmission of HIV outbreak during Immunotherapy due to contamination[22].

In their study, rapid identification and implementation of effective control measures using knowledge of gene sequences helped to control the outbreak. In Switzerland, a widely covered genomic sequencing study was applied in a rehabilitation clinic to study the outbreak of SARS-CoV-2 among healthcare workers and patients.[24] The analysis showed the big cluster tree from the suspected index case and found the role of HCW in the transmission of SARS-CoV-2. Another healthcare setting that also used genomic sequencing to control the spread of infection found that Pseudomonas aeruginosa (Verona Integron-encoded Metallo-beta-lactamase) VIM was epidemiologically linked between clinical and environmental strains using whole genome sequencing (WGS).[25] This helps to eliminate the source and protects the vulnerable groups from contracting infections.

A phylogenomic analysis of gastroenteritis-associated Clostridium Perfringens in England and Wales spanning 5 years revealed the presence of clonal toxigenic strains involved in multiple outbreaks and widespread engagement of plasmids encoding enterotoxin (CPE).[26] In Africa, a WGS study in the People's Republic of Congo revealed the measles outbreak that happened was due to a

large number of unvaccinated children and not due to the introduction of the new strain. Aside from current evidence, there are uncertainties in genomic prediction due to the underappreciated heterogeneity of diseases' natural histories and varied disease penetrance driven by genetic, environmental, and other factors.[42]

Diagnosing Infection

Knowledge and understanding of genomic study help to diagnose infectious disease using a new approach. Several researchers studied the prevalence of Hepatitis B antigen (HBsAg) in Cambodia[33]. Instead of employing point-of-care methods, researchers opted for the use of dried blood spots (DBS) for transportation, which is a valuable alternative to point-of-care testing in resource-limited areas. Through genomic sequencing studies, they identified an S gene mutant of HBV and emphasized the need for effective strategies to prevent and control mother-to-child HBV transmission in Cambodia.

While genomic sequencing is crucial for diagnosing infections, several considerations must be weighed when deciding to implement these technologies in a laboratory setting. These include the high operational costs, the shortage of trained personnel, inadequate computational infrastructure in many facilities, limited reference microbial genomics databases, and the challenge of establishing efficient, accredited, and standardized bioinformatics protocols. Using sequencing in routine diagnostics also poses a risk, as it may lead to a loss of valuable knowledge in fundamental microbiology with the transition to sequencing[34]. Notwithstanding all of these issues, we cannot deny that sequencing applications will soon satisfy unmet diagnostic demands in clinical microbiology and show definite advantages to patients.

Developing and Evaluating Interventions, Including Vaccine

A study implemented a genomic study to identify strains of HPV in Congo[28]. Formalin-fixed paraffin-embedded (FFPE) was used for sampling before HPV DNA detection followed by genotyping. They found that the 4 main genotypes of HPV among 125 women with HGSL and ICC are HPV 16, 33, 18, and 31. With this knowledge, primary prevention using the current HPV vaccine could reduce the burden of cervical cancer in Congo. Nevertheless, the application of genomics in other important and new vaccine developments like COVID-19 and dengue vaccines was not elicited from the reviewed articles.

Response Treatment

Genomic research can help to evaluate the response to certain treatments including the response of Highly Active Antiretroviral for Prevention (HAARP)[29]. The use of antiretroviral therapy (ART) was not significantly associated with reducing the incidence of HIV infection among serodiscordant couples. Higher viral load and polygynous relationships were associated with an increased risk of seroconversion. A genomic study was applied in this study to find the link between the new infections and found that 11 out of 14 new infections are genetically linked, indicating that the infections were likely acquired from their respective partners. This information is important in assessing the effectiveness of antiretroviral therapy (ART) in preventing HIV transmission among serodiscordant couples.

However, the main challenges for genomic application especially in undeveloped and developing countries are the limited resources, disparities, and lack of expert assessment, which require robust evaluation before actual implementation for the population at large.[42]

Monitoring Antimicrobial Resistance

One study[30] applied genomic research to monitor HIV drug resistance in HIV infection prevention and control. With regards to H1N1, drug resistance of the virus was monitored to prevent and control H1N1 infections[31]. By understanding the genetic background of the pathogen, resistance to specific antimicrobial drugs can be monitored. In Africa, HIV genotyping was found to be able to detect major drug resistance mutations that help to determine their drug of choice[30].

Meanwhile, the evolution of resistance to oseltamivir in pandemic H1N1 could be due to point mutations in the neuraminidase or a reassortment event between seasonal

H1N1 and pandemic H1N1 viruses[31]. Genomic sequencing, despite its potential for preventing and controlling communicable diseases by monitoring antimicrobial resistance, faces challenges. Its adoption lags because genotypic testing is slower than phenotypic testing, and there is limited information about antimicrobial resistance mechanisms that impact function[34,35]. In addition, there is also lacking of international standards for genomic detection of antimicrobial resistance mechanisms making it difficult to compare between studies.[36] However, advancement in genomic sequencing has made the process more cost effective[37], encouraging more application of genomic sequencing in the prevention of communicable diseases.

LIMITATIONS

This study has limitations. As no meta-analysis was done, our study was unable to compare and comment on which genomic sequencing technique is statistically more effective in the prevention of communicable diseases. Besides that, the role of publication bias in this systematic review must be acknowledged as grey literature was not included. This study only included peer-reviewed original articles.

CONCLUSIONS AND RECOMMENDATION

This study illustrates the global potential of genomics in strengthening the prevention and control of communicable diseases. The study's findings can contribute to an improved understanding of genomics application in public health practice and policy planning, especially in disease prevention and control measures. Given that genomics is a relatively new field in precision public health, it is advisable to conduct a more focused review to gain a deeper understanding of specific applications of genomic sequencing techniques and methods for preventing communicable diseases in public health. This will facilitate better learning opportunities for future implementation endeavours. This review can be improved if the literature search was conducted on a wider variety of search engines and types of documents. We also recommend broadening the keywords used for literature searches by finding more synonymous words and reviewing the application of genomic sequencing in the prevention of specific diseases.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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