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Chapter 7: Predictive models for early detection of diseases and managing public health crises

7.1. Introduction

In 2020, humankind was awakened to the harsh reality that, despite several initial successes in different fields of physical and life sciences, we are still not fully equipped to deal with biological and healthcare-related issues and are incredibly vulnerable to unforeseen events like the COVID crisis. Rapid developments have been made in many different areas related to disease predictions and applications; however, research and development in predictive models, especially in healthcare and medical decision-making, have not been satisfactory and are still in a premature stage. Because of all these reasons, we have been encouraged to explore further the application of new and innovative methods in predictive healthcare and illustrate many different areas related to that. This book is intended as a first step in this direction. Health is one of the most important aspects of an individual's life as well as of a society as a whole. Over the past several years, numerous research activities around the world have been undertaken in different areas related to the field of public health. Numerous predictive models have been developed as data mining tools that can be deployed to enhance the decision-making capability of individuals as well as of policymakers and authority figures in the healthcare field. Specific examples include predicting the epidemic of diabetes, cardiovascular diseases, chronic diseases, COVID-19, and even predicting the number of infections and deaths caused by COVID-19. These models can assist individuals as well as authority figures in the healthcare field in planning and executing the necessary tasks in the timely management of these diseases, thus reducing the number of hospital visits and admissions and the consequent medical expenditure associated with this disease. In addition to these distinct areas, predictive models have been used in several other distinct healthcare issues (Dilsizian & Siegel, 2014; Krittanawong et al., 2017; Lee et al., 2017).

During infectious disease outbreaks, the rapid dissemination of knowledge and a coordinated global response play a major role in mitigating their impact. Governments depend on reports from infected countries before they are affected by the infection. The speed and effectiveness of this response rely on the rapid sharing of reliable, secure, and high-quality information, as well as on public stockpiling of emergency supplies, which remain at low levels for prolonged times during the pandemics. The international media play a major role in relieving the panic of people by delivering high-quality information concerning the outbreaks to the public (Ristevski & Chen, 2018; Mehta et al., 2019).

Fig 7.1: Early Detection of Diseases and Managing Public Health Crises

7.1.1. Background and Significance

Infectious diseases significantly threaten human and animal health. Despite extensive research efforts and significant advances in chemistry, immunology, treatment protocols, and vaccine technology, emerging and re-emerging diseases still occur and can even spread rapidly across continents. Infectious diseases account for 25% of total deaths per year. The emergence and re-emergence of infections are caused by increasing population growth, an aggressive advance of urbanization, ecologic changes, impacts of the global economy, and growing travel and trade among economically integrative countries. The recent and ongoing outbreaks of global infectious threats initiated by newly emerged viruses, along with the re-emergences of infections, have provided a gloomy prediction for the future presence of these events. The control of these diseases is even problematic and hazardous for the world during the pandemic status.

7.2. Overview of Predictive Modeling

When distinctive patterns are found that might suggest the propensities of experiencing particular future socio-health states, or when the potential effects of certain modifiable variables of interest on the expected incidence embodied on the patterns for such socio-health states are uncovered, it is indeed predictive modeling, regardless of the methods utilized for that. Predictive modeling is an unusual term in the methodologies used within the social sciences, distinctively so when speaking about socio-health research. Hence, such researches have been referred to cluster detection studies, which nevertheless hold common elements to predictive modeling. Unlike many predictive models, cluster detection models tend to have a purely exploratory nature; that is, they do not propose a predefined model. Still, researchers using predictive modeling often rely solely on a testing methodology in order to validate the models, which is not totally devoid of exploration, because the testing methods provide information about the suitability of certain model specifications amongst the joint models considered. Unfortunately, technical restrictions typically pose major limitations to predictive modeling of rare event occurrences within the social sciences; particularly, small sample sizes on the estimating stage of the modeling. Combining the information from multiple data sets while accounting for the correlations among moderating effects enables a possible approach to handle the small size challenge; specifically, multiple occasions of the same social units.

An increased availability of cross-sectional micro-level data on large populations has facilitated research efforts to label and model predictive geo-social determinants for many socially relevant events, where motivating this type of researches is the longstanding concern in the socio-health area about descriptive studies finding extremely high relative incidence variations across space. In social epidemiology there is widespread recognition that identifying the determinants of health outcomes and the disparities in their distribution across social groups is critical for designing effective interventions. Descriptive studies assess the health-related burden of specific events, associating socio-health units with the socio-health events at hand.

7.2.1. Research design

Predictive modeling provides estimates for outcomes based on one or more self-contained statistical models that combine a set of predictors defined beforehand for every data point in the data. Predictive modeling rests on an assortment of explanatory and predicting models aimed at drawing predictions of a response from a range of predictor variables that help better explain the response variable. There are a number of assumptions underlying prediction model development: the use of prospective data, sample sizes that vary by prediction rule, an outcome that is clinically useful, the availability of historical data, the absence of modeling mapping transitions to predetermined endpoints, testing of rules on several populations, and the implementation of results in clinical practice modules. Predictive modeling operates through the formation of data into an event-derived model and through classical validation methods like cross-validation, splitting methods, bootstrap resampling, etc. Extensions of the aforementioned concepts are nomograms, neural networks, faithfully calibrated prediction rules under Bayesian concepts, etc., which have remained non commercially utilized, with the exception of neural networks and nomograms for some areas.

Health prediction uses a variety of modeling techniques borrowed from traditional econometric or health economic modeling tools. Examples include Bayesian and conventional econometric techniques such as weeks-dependent indirect demand equations, or time-dependent dynamic factor models. These, along with discriminant analyses and fuzzy models, can be used for estimating short-term health prediction studies. Genetic algorithms are now being used to assess decision thresholds to balance overall prediction risk for large epidemics with small probabilities of occurrence. These modeling techniques require access to abilities of epidemiologists, economists and health service managers, along with user access to cross-disciplinary modeling resources in identifying realistic sources of error such that usable probabilistic information can be disseminated.

7.3. Types of Predictive Models

Predictive analysis incorporates a diverse range of model types and methods. There are statistical methods that carry a long tradition of statistical tests associated with confirmatory statistical analysis. These methods have an important rationale in detecting if relationships exist and, in that case, to provide information about their nature, i.e. the nature of the dependence or correlation relationships, the direction of these relationships (positive or negative) and the way they relate to the random variable or the response sets. Predictive analysis goes a step further; not only seeks to understand relationships but to go a step further and infer more specific information, like the values of the random variable. This type of analysis is possible by setting for the user a predictive algorithm, usually a regression of one of the response variables on the one or several of the independent variables, which can be used with the explained model and when especially careful about generalization errors, used with the personalized model that is more ameliorative in terms of generalization errors. The major models for that purpose are linear regression and logistic regression. And several modifications of these models including regularized versions to incorporate the effect of having many variables or variable selection methods.

We also have machine learning and artificial intelligence methods that were developed during the last decades. They have become increasingly more popular. These data-driven methods, known for being able to treat a high number of explanatory variables, rely on algorithms that can replace statistical models and are known for their predictive power. These algorithms include k-nearest neighbor, decision trees, random forest, support vector machines, neural networks, generalized additive models or deep learning architectures.

It is possible to define the parametric approximation error using an information-theoretic model, but in practice, designers of statistical models use common sense assumptions that are driven by experience with similar past prediction problems. If these fit well, the prediction will be good; if they do not, the prediction may be terrible; but this is also true of most machine learning methods.

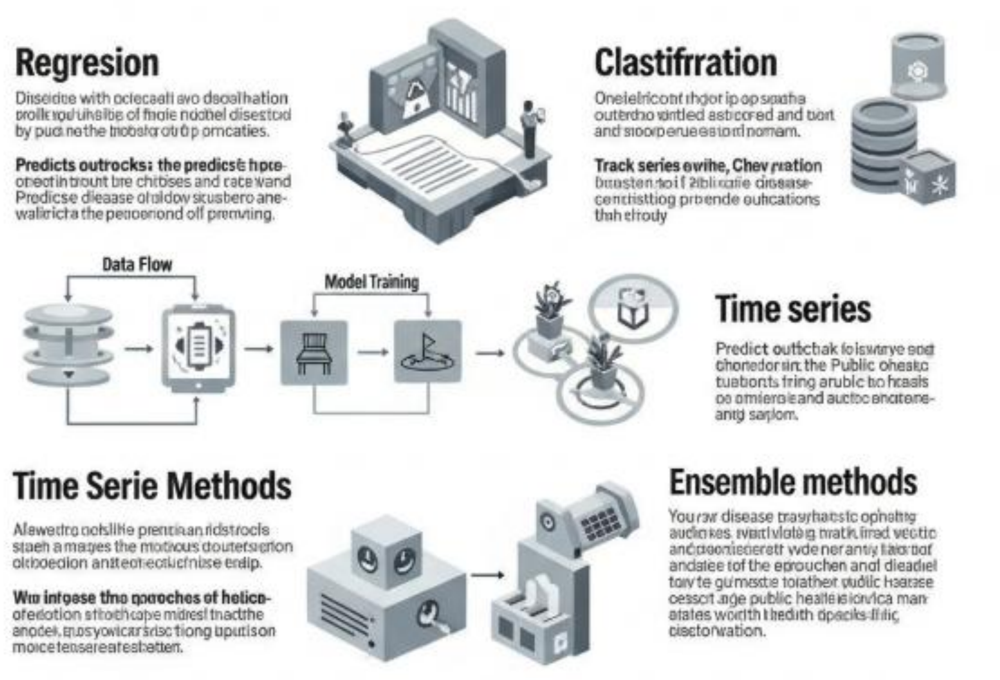

Fig 7.2: Types of Predictive Models

7.3.1. Statistical Models

The methods that take the observed data to discover the relationship between the predictor and the response variable are called statistical models. The term "statistical model" is used in a very narrow sense and is distinguished from "machine learning models" because the latter take no explicit encapsulated structure. The distinction becomes a bit vague because of the close kinship of the two paradigms. Most machine learning model methods make use of the available training data to make inferences about the underlying joint distribution generating the recognition. Such training, if it happens, becomes just a technical detail. In statistical methods, such inferences are central and unavoidable. A second technical distinction emerges from the different ways that the two methodological classes think about generalization, meaning how they think their algorithms can work successfully on data outside the training set.

Statistical methods typically formalize generalization by postulating some parametric model complexity that generalizes well from the data set used to set the parameters. The model typically has a small number of parameters, thus avoiding overfitting problems on the data set (but may underfit). Statistical models have to make specific assumptions about the problem at hand, usually about the distribution of the function, to be trained to properly encapsulate the similarity of the observed training input-output pairs to be successful elsewhere. The accuracy of a statistical model depends on the place of prior knowledge and how well these assumptions match the underlying task.

7.3.2. Machine Learning Models

Unlike traditional statistical approaches, which hinge on strict assumptions regarding the data, machine learning techniques are adaptable, demanding fewer a priori specifications. However, against this flexibility stands a plethora of learning architectures with diverging inductive biases. Therefore, it is imperative to judiciously select candidates for any supervised predictive task. From a make-or-buy standpoint, standard linear methods and classic generalized additive models may be considered entry-level products to out-of-the-box solutions, whose strong performance on benchmark datasets is indicative of the credibility of the results they produce; however, these results also need to be treated with due skepticism. Relating to the latter, offline validation remains essential for any machine learning model. None of the techniques being used will ever substitute the brain ability to embed the underlying signal in the proper configuration of the model complexity, which will, consequently, be informed by the dataset at hand.

Numerous studies have associated critical healthcare tasks with standard machine learning models. Logistic regression has been employed to predict chronic disease through instrumental variable analysis, to estimate the probability of hospitalization following radical prostatectomy and the need for readmission following liver transplantation, to model the choice of pediatric providers, or to jointly analyze individuals' cardiovascular risk scores and comorbidity patterns. Least squares, or support vector regression, have been applied to fingerprint the public health effect of smoking bans in restaurants and bars, or to predict length-of-stay following total hip arthroplasty. Also, linear and multi-class support vector machines have been exploited to predict which patients would accept participating in a tailored intervention to reduce alcohol use. Artificial neural networks have been used in forecasting breast cancer incidence rates or predicting bed utilization, heart transplant, or hospice utilization. Nonetheless, to the best of our knowledge, no comparative study has considered all mentioned algorithms for predictive tasks in Public Health.

7.4. Data Sources for Predictive Modeling

Understanding of a phenomenon and its description using prediction models require availability and accessibility of a wide range of appropriate data. This is valid for any field of research and predictive modelling is not an exception. Moreover, quality and quantity of data are directly linked to the accuracy and reliability of the obtained model and inference. Predictive modeling of infectious diseases needs a large-scale and multimodal set of data to ensure accuracy and reliability. Data sources are primarily determined by the type of organism and the disease. However, it is essential that the available data should cover representative and large geographic areas during an extended period of time, otherwise, the predictive capabilities of the models may not be of real use in a real-world scenario.

For related research, appropriate data can be mentioned as: Genomic and transcriptomic data, Metabolomic and proteomic data, Epidemiological data, Phylogenetic data, Climatic data, Environmental data, Social media data, Electromagnetic data, Mass spectrometry imaging data. A major source of epidemiological data comes from universities, public health institutes, or governments. Additional data, such as travel-related data, can also be found in some commercial airlines or in some initiatives. Genomic and transcriptomic data are retrieved from samples from field outbreaks and clinical cases or from publicly available bioinformatics databases. For modeling the transmission risk of zoonotic diseases, the adequate epidemiological data resources include: Disease outbreak reports, additional data sources. For modeling fungal respiratory infections, additional data sources were mentioned.

7.4.1. Epidemiological Data

Epidemiological data consist of individual-level records on diseases, environmental and host factors over time. These data are collected in different ways, usually through disease surveillance systems, clinical trials, or observational studies. The best known source of epidemiological data is at the population level, comprising counts of observed cases of disease and counts of the population at risk at a specified place and time. Collecting disease data at the population level is useful for identifying disease outbreaks, but does not provide individual-level information on other factors associated with increased risk of disease such as environmental factors, genetic predisposition, socio-economic status, and comorbidities. Individual-level data are necessary for developing predictive models that include these factors.

For infectious diseases, individual level data can often be obtained from the notification of infectious diseases or from observatory studies that are motivated by the infectious disease notification. Both of these sources can provide varying levels of additional information. A more complex source of epidemiological data consists of individual-level data for a large number of people, such as those provided by population-based health surveys. These include data on infectious and non-infectious diseases, demographics, comorbidities, socio-economic data, and behavioral and lifestyle factors. While there are very few surveys that include questionnaire data on infectious diseases, many others include data on non-infectious diseases. Such surveys are also used for linking population-based health records to genotype information for various diseases and traits. Disease and risk factor data from such surveys are usually collected cross-sectionally and are not suitable for predictive modeling purposes.

7.4.2. Genomic Data

The emergence of new pathogens has posed a challenge to public health agencies. In the past, scientific agencies have compiled genomic, phylogenetic, and epidemiological data to characterize novel pathogens in outbreaks. These efforts are crucially important, as the genomic data enable us to understand if a pathogen has an unusual rate of genetic change and if it is related to other pathogens that have caused disease but have not yet been identified. With the explosion of data available, it is now possible to rapidly bring together large amounts of phylogenetic and genomic data for many of the more important pathogens. Thanks to these data, new pathogens can be compared with known pathogens, and ongoing evolutionary changes in nucleotide, amino acid, and gene content can be identified for trend studies. In this section, we briefly outline the available data and the important role they play for public health agencies.

Since 1999, when the first complete prokaryotic genomes were sequenced, we have witnessed an explosion of genomic data for many pathogen species or groups. For many key pathogens in public health–related species, the available information includes sequencing data, annotations for gene function, phylogenomic data, protein signals, repeat regions, and transcriptome and RNAi data, as well as virulence gene databases and virulence prediction resources. Such genomic data are important for several reasons. If an outbreak strain is genetically related to a virulent strain from another location, we may be concerned that it is a new example of a strain that is capable of causing disease. If it is not, we must orient our control measures differently. From genomic data, it is also possible to analyze the evolutionary history of the pathogenicity locus, and its relationship with loci from other similar pathogen species, and to analyze if the new or outbreak strain differs significantly from its relatives from other locations and times.

7.5. Model Development Process

The model development process in predictive modeling can be complex and iterative. After the problem statement has been defined, the first task is to collect the data. This would depend on how the data might be defined from different disciplines under different conditions. The data can be from primary sources, where the investigators are required to develop the data collection process, or secondary sources, where relevant data can be utilized from existing repositories considering how the dataset matches with the problem statement. The development of models for disease detection and managing public health crises can use historical databases from the healthcare departments related to the occurrence of the specific disease or adverse events caused by the rationale of the development of the predictive model. The data could also include risk factor questionnaires, surveillance data, and data from biosensors. In the case of health emergencies, forecasting models can also use crowd-sourced data available in the public domain to develop predictive models for detecting public health emergencies critical to allocating community intervention resources.

Most of the data used in modeling processes are prone to variations and need preprocessing in the modeling stage. Preprocessing includes data organization, cleaning, and transformation. The preprocessing of data aims to ensure the data is available for modeling without detrimental effects on misinterpreting the outcomes. The preprocessing steps may also include de-identification, dimensionality reduction, and conversion of data types to reduce noise and avoid overfitting and underfitting the classification models or prediction models. The methodology should ensure balance in the dataset when population sizes across the output class are unequal to avoid biasing the model for classes with larger training samples. These preparatory techniques help in addressing the problems that could augment analytical bias and allow for selection bias that could change the nature of the data and add uncertainty to the estimation of the predictive model.

7.5.1. Data Collection

Data collection is pivotal in designing predictive models. Adequate and relevant data is essential to recognize the patterns specifying a condition. When sufficient data is not available, it leads to poor and unreliable model performance. Several data sources exist to collect data to monitor public health diseases. Population inquiries provide demographic and economic data on a periodic basis. If data on requirements relevant to disease prediction is collected, these inquiries can be beneficial. However, the data is only available at yearly intervals or longer. There are also a few low-sized surveys that collect data quickly but are not adequate for temporal disease prediction.

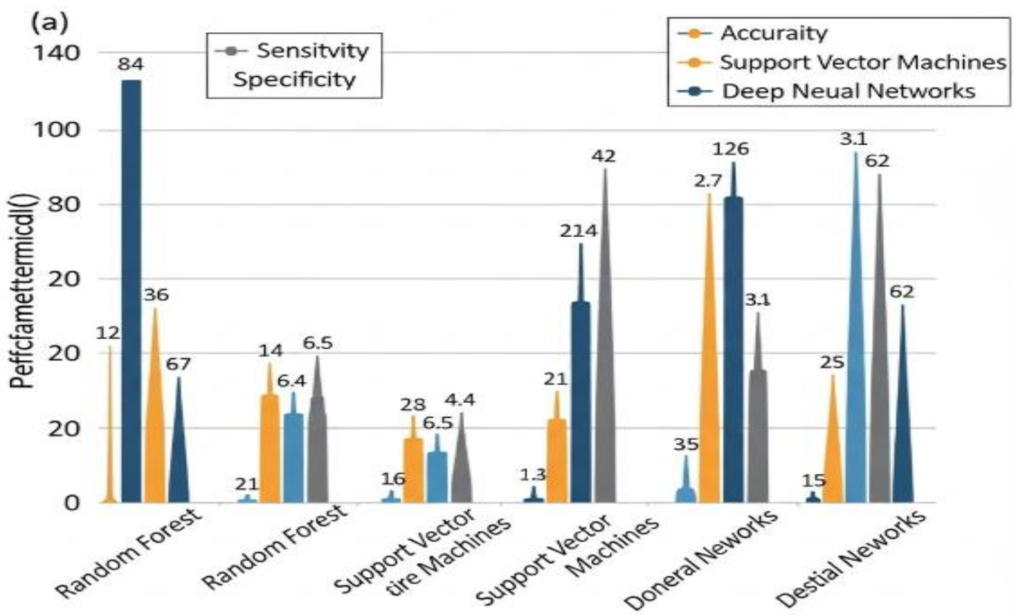

Fig : Predictive Models for Early Detection of Diseases and Managing Public Health Crises

In a majority of cases, hospitals, clinics, and emergency department visitations provide data for predictive modeling. Using routine data from monitoring systems to detect changes in health indicators could assist in targeting data collection of other variables more efficiently. Any widespread collection of health-related information on the target population from one of the disease monitoring systems will be exceptionally beneficial as it provides a wide temporal window of information and a shorter historical record. The drawback of this method, however, is that in order to consider a health outcome indicator as a predictor variable, it cannot be regularly included in the model and should definitely be publicly available.

7.5.2. Data Preprocessing

Preprocessing the data is one of the important but often neglected procedures in building models in the health domain. In the health domain, data is often not clean because they were collected from different health institutions, observers, and environments. Health records usually refer to many items, having different data types, such as numeric, categorical, free-text, dates, and times. Data usually has conditions such as missing values, outliers, and noisy data. All these conditions make the data unprepared for the model to learn efficiently and effectively. Preprocessing aims to eliminate as much as possible these conditions and prepare the data in a suitable format so that more meaningful and precise results can be provided by the model. By neglecting preprocessing, its consequences might lead to understanding incorrectly or misinterpreting the results given by the model. The models created would incorrectly represent humans' and animals' health, especially they could not be used again for further predictions.

Given these reasons, in this section we highlight the most frequently used data preprocessing techniques in the models presented in this study. The procedures described below should be used as guidelines, and the actual implementation should depend on the specific context of the data, and the experience of the data scientist. Health data frequently has values that are not available. Consequently, data needs to be either discarded or handled, so that they can be incorporated into the decision models. If only a few records in the data are missing values, then the records can be omitted, and the model is developed with the remaining data. In contrast, if a large number of records has missing values, this might produce a poorly developed model that cannot make good predictions from the health data. These missing values can be imputed using several techniques, such as replacing the missing values with the mean or median of the non-missing values in the attribute, replacing the missing value with the mode for the specific class attribute, or seeking the records that have similar attributes and identifying their similarity using distance formulas.

7.6. Applications of Predictive Models

In recent years, increasing efforts have been put into the development of predictive models for the early detection of health problems or risk situations. There is great interest in finding early signals that would alert public health authorities, allowing them to take quick preventive measures that would otherwise not be taken if using more traditional analysis methods. Predictive models have been used to predict an infection outbreak, usually the subject of prediction being a location or population group. Models in the biostatistics area have been used for this purpose, particularly those dealing with the analysis of time series of health-related data.

With predictive models, health authorities can take early actions that impact the growth of an epidemic, especially in the case of infectious diseases. These actions can be controlling the disease spread if it is virulent, such as the plague, or motivating vaccination of at-risk populations if they are subject to the development of detrimental consequences as a consequence of an infection, such as the case of hepatitis and pneumonia caused by viruses. The predictive models are based on prediction equations involving some relevant variables such as climatic variables, behavior patterns, demographic data, and economic factors, which, once known, help estimate the future trajectory of expected cases or mortality. There are examples of applied models predicting the incidence rate of diseases such as malaria, dengue, rabies, tuberculosis, and various types of influenza.

7.6.1. Disease Outbreak Prediction

The outbreak of communicable diseases tends to be spatially and temporally periodic. Their distribution and dynamic patterns are influenced by many socio-economic and environmental conditions. Therefore, accurately predicting their spatial-temporal patterns is beneficial to risk management. Moreover, accurate forecasting is helpful for vaccination programs, security companies, and local health authorities to carry out health education to prevent disease incidence. Indeed, early warning of disease outbreak is necessary for vaccine companies to prepare for the vaccines which could avoid the occurrence of possible epidemics. Health authorities and consequently the economy would also greatly benefit from accurate disease forecasting. Predictive models can provide an advance warning for the probability, type, timing, and likely location of an outbreak. It is essential for public health agencies to implement control and mitigation measures in a timely manner to avoid severe consequences.

Not many efforts have been taken to specifically evaluate predictive models that can reliably forecast human infectious diseases. Here, we review statistical predictive models and machine learning predictive models. Moreover, the accuracy of the prediction models is also compared. The performance of some prediction tools is summarized. The statistical predictive models include time series models. Regression models rely on virus data and covariates to develop a forecast. The classic regression models in operation include modeling cases and seroprevalence as functions of temperature, humidity, or other factors. Machine learning methods have recently gained great popularity across a variety of research domains. Decision trees in operation incorporate virus data and one or more covariates. Random forest and gradient boosting machines involve an ensemble of decision trees. Bioinformatics research relies on neural networks, hidden Markov models, and support vector machines. Many compare quite favorably against classical methods.

7.6.2. Resource Allocation in Health Crises

In response to health crises, there is a demand for accurate projections of the future progression of an epidemic. For a variety of reasons, this situation might be problematic. The timing of the first peak is normally not certain, and the height of the first peak is very uncertain unless it is far in the future. It is typical for many new infections to happen days during the week and fewer on weekends and holidays. If the tail of mortality representing deaths due to causes unrelated to the epidemic is too short, forecasts will tend to be negatively biased. Forecasts will tend to be positively biased if the tail is too long. Furthermore, most forecasting models are estimated on the historical record, which may be a poor guide for truly novel diseases. Many prior pandemics have exhibited exponentially increasing episodes of exponential growth of some duration, pre-picking the peak and size. The very nature of pandemics compels attention to multiple objectives in guiding policy.

While predictive research has made major pathways and conceptual advances, the requirements of timely forecasts in the middle of possible catastrophe imply some need for basic rapid R&D in theory and method. It is commendable that there are applied operational groups working to distill arguments from simulations. It might also be timely to assemble data on prior countrywide forecasts to inform about forecasting capabilities. In most countries recountings within each category of death provide private information about the cause of death, and its direction for prediction purposes. Usefulness of online panels for daily infection and vaccination counts within certain special categories about special group-focus guidance is being demonstrated family by family. Prior experience with pandemic preparedness plans has led to country-by-country differences in predicted mortality from new and re-developed pathogens.

7.7. Conclusion

The use of predictive models can be an essential resource for the healthcare system. Furthermore, several examples were observed where predictive models were able to differentiate predictive healthcare events before being expressed. Consequently, if knowledge about an important healthcare issue can be detected earlier than common practice, then predictions may provide additional and valuable knowledge to the public sector. It helps to allocate limited resources in a smarter way, facilitate additional focus on critical and pending deadlines, and support the public sector in achieving a more efficient use of the available resources to solve public health issues faster. The experience and competencies embedded in predictive models are remarkable, and should be made available to public actors. Predictive models may therefore function as a lighthouse for public actions, illuminating the path ahead. Based on these, a further reflection on handling predictive models can shed additional light on how to link private efforts with the unfolding of highly relevant issues in new ways.

If it is implicitly or explicitly decided that the predictive models should function in an explorative mode, it is anticipated that they will be used to revise plans and budgets dynamically during the next hospital admission based on how the situation, as recognized in the model, evolves during the execution process. This is the ideal use to cope with the complexity, uncertainty, and unforeseeable nature of modern public healthcare predictions, and may shift focus from detection and control of exceptions with postmortem consequences towards a more proactive search for proactive public action. Consequently, healthcare hospitalization predictions should be made available at the management level, with the clear understanding that knowledge about hospital admission forecasts becomes cumulative as new experience and historical data unfold, so that foresight can be improved along the way. All in all, the availability of predictive models can foster a proactive public healthcare policy.

7.7.1. Emerging Trends

Tele-health and telemedicine are starting to be used to provide enhanced services for patients that need specialized medical expertise that is not available in their geographic area. mHealth and the use of mobile health devices that include monitoring features are becoming more common in particular for patients with chronic diseases, as the ability to non-invasively and continuously monitor these patients can save the healthcare system a large amount of money, and greatly benefit individual patients as well. Behavior-influencing apps and goals are being widespread and being integrated into some of these platforms and services. Not only do these apps help patients become aware of their behavioral habits, they provide suggestions and techniques to patients to help reinforce and even help modify undesired or poor behavior. With the introduction of new mobile-connected devices, the sports fitness environment is undergoing a renaissance of new and improved comfort, performance, and monitoring features, enabled by technology and user-centric design. Together with the introduction of expert systems and powerful mobile apps that are able to non-invasively capture private user key behavioral indicators, the predictive health monitoring framework will be greatly enhanced and improved.

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