Healthcare Operations Research and Management under Pandemics: a Review

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Abstract This literature review sought to identify the role of Operations Research and Management (OR&M) in the Healthcare Systems (HS) decision/policy making processes that have undergone a remarkable transformation when faced with pandemics, especially during the COVID-19 era. In this study, we investigate OR models and OM techniques that facilitate clinical decision-making with short- and long-term objectives for operational cost reductions and increase of social welfare from the HS's point of view and public policymaker's perspective, respectively. Here, our concern is investigating expensive and complex decisions to provide healthcare services during the outbreak of an infectious disease such as SARS,[a] Ebola, seasonal influenza and influenza pandemic,[b] COVID-19 pandemic, while available capacities are overwhelmed by the heavy influx of patients. The complexity of such tactical/operational decisions during pandemics may even turn their scope into triage decisions which may entail unknown future cost-trajectories. Based on the World Health Organization (WHO) guidelines, these decisions are categorized into *preparedness* and *response* plans to be performed before the declaration of a pandemic, in anticipation of such events and respectively, after its declaration to hedge its fatalities. We also highlight decision-making practices designed to allocate strategic investments for public-health policy-making purposes with conflicting and costly objectives to combat epidemics/pandemics at state- and national-level governments. Finally, we present future research directions in the pandemic context.

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[a]Severe Acute Respiratory Syndrome
[b]https://www.cdc.gov/flu/pandemic-resources/index.htm

1. Introduction

Since the early nineteenth century, several epidemics and pandemics have occurred with varying morbidity and fatality statistics. The "Spanish Influenza" was declared a global pandemic in August of 1918. The European countries faced the fatal wave of it in early summer, while the United States experienced it during fall. It caused 20-40 million losses of life worldwide (Taubenberger, 2006). In February of 2001, Foot-and-Mouth-Disease (FMD) started to spread in the United Kingdom targeting livestock animals (Grubman and Baxt, 2004). The FMD and its variants had detrimental economic consequences that almost struck everywhere around the globe, except New Zealand and North America. Asian flu, known as H2N2, with 1-4 million deaths during 1957-1958, and Hong Kong flu or H3N2 with 1-4 million fatalities worldwide during 1968-1969 WHO (2009) are two other pandemics from the past. The Severe Acute Respiratory Syndrome (SARS) was identified by the World Health Organization (WHO) as a fatal disease in the Spring of 2003. It infected 27 countries on all continents. As reported by Heymann and Rodier (2004), SARS and Avian influenza H5N1 are eventually contained by imposing rigorous controls after their outbreaks, although SARS still persists and turned into an endemic[1]. The influenza H1N1 (2009) pandemic claimed the lives of 151,700-575,400 individuals worldwide, as the report provided by the Center for Disease Control and Prevention (CDC) says[2].

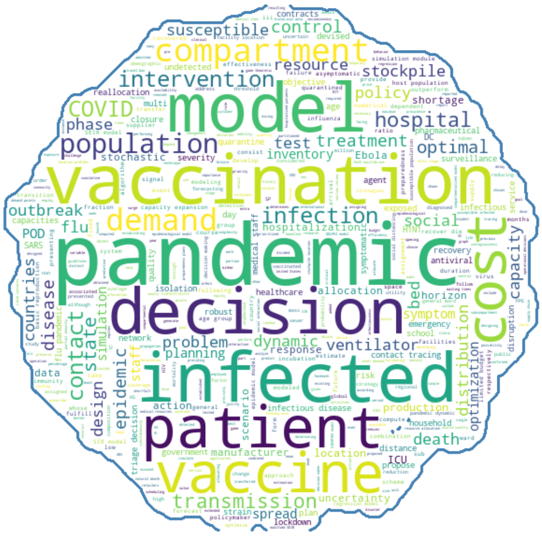

FIGURE 1. Word cloud

On March 11[th], 2020, the World Health Organization (WHO) declared the COVID-19 infection[3], caused by the SARS-CoV-

[1]A pandemic that is always present.

[2]https://www.cdc.gov/flu/pandemic-resources/2009-h1n1-pandemic.html
[3]https://www.cdc.gov/dotw/covid-19/index.html

2 virus, a global pandemic[4] only three months after the first confirmed cases[5]. For the rest of this review we recall that, an infectious[6] disease is called an *epidemic* when it can spread to many individuals in a community. It also can turn into a *pandemic* when it globally propagates in several countries[7].

Up to this date, more than 447.5 million confirmed COVID-19 cases and about 6 million deaths worldwide are reported[8]. In section §2, we represent epidemiological formulations devised in the past and recent models proposed for COVID-19, with which one can simulate pandemics' propagation.

The COVID-19 global outbreak imposed an immediate global life-threatening concern and a disruptive surge in demand for healthcare services. The overwhelming shortages and vulnerabilities in the core operations of the Healthcare Systems (HS), compounded by the heavy influx of patients, have motivated many innovative Operations Research and Management (OR&M) studies in the pandemic context.

To hedge the unprecedented uncertainties and disruptions in the healthcare service consumption and combat pandemics fatalities, there is a need for a national plan[9] (US-HSC, 2005) and global guidelines (WHO, 2009) to tackle such natural disasters. A new or frequently emerging epidemic with strain drifts (e.g., seasonal flu virus) entails more complexities to these plans in the execution time, which leads WHO to update them frequently (Holloway et al., 2014). These plans, in general, can be divided into *Preparedness* §3 and *Response* §4 plans.

The preparedness plans may be in the form of surveillance schemes combined with contact tracing to identify a new infectious disease, or trace a recurring epidemic. To trace epidemics, governments monitor reported syndromes to measure pandemic spread, severity, and transmission rate in order to estimate their outbreak risks. In preparedness phase, one can also envision the stockpiles of scarce medical items to tackle limited production capacities during recurring seasonal flu. Moreover, to anticipate seasonal flu outbreaks and their frequent drifts, the WHO decides the composition of vaccines by examining different strain combinations and potential production levels, see Fineberg (2014); Brandeau (2019) for preparedness and response plans for the flu of 2009 and anthrax.

In section §5, we proceed with a policy-centric perspective which notably increases the scope of plans to strategic *Policy-Driven* decisions at the governmental level to tackle a pandemic hardened by severe clinical and financial uncertainties. In such decision-making paradigms, the existing players' (e.g., pandemic, host population/public, individuals, pharmaceutical manufacturers, government, WHO, etc.) interacting decisions seek distinct or sometimes conflicting objectives. We investigate dealing with such challenges in both game-theoretic and mathematical programming frameworks. In the later, distinct decision model components such as objectives and constraints imposed by each player are mutually combined into a unified fashion. We note that the mathematical programming modeling approaches can barely provide a decision-making setting like the game-theory, in which several competing individuals affect each other's decisions and/or represent heterogeneous collective behaviors in the decentralized decision-making problems.

We have devoted section §6 to the best practices in healthcare supply chain during previous pandemics and natural disasters. Epidemics in general may impose striking disruptions/failures and their consecutive ripple effects across a supply chain network. These network failures are a common result of placing nonpharmaceutical interventions like curfew/lockdown, closure, or an imbalance between supply and demand during a pandemic. These restrictions may slow or stop raw-material transportation to production-plants. The latter consequences increase the production yield uncertainty for the downstream manufacturers. At the supply point, many manufacturing lines are capital-intensive; therefore, capacity expansions in the supply chain network under a severe shock may not be the first viable option. At the demand points, however, a pandemic may cause both increased and decreased demands for various goods, thus resulting in lengthened or idle services, including transportation operations.

We outline the future research avenues in OR&M applications in the pandemic context in section §7.

Remark 1. *In this remark, we present the theme of this review and targeted audiences. The main purpose of this review is not to compare the performance of OR&M mathematical formulations devised to cope with pandemics and adapted solution methodologies therein with each other, although we report all major and notable contributions.*

Here, we rather address and highlight issues, challenges, and a collection of decision/priority making processes faced by policymakers in the planning, organizing, and delivery of healthcare services to public in the epidemics/pandemics era that led OR&M community to come up with such optimization approaches Brandeau et al. (2005).

A word cloud of keywords used in this review is shown in Figure 1.

2. Epidemic Models

In this section, we review the epidemiological models that are developed to imitate the propagation of infectious diseases through the host population. The epidemic models enable the decision-maker to characterize the spread of the disease by quantifying its components and statistics, such as the number of the susceptible and infected individuals, death cases, transmission rate and contagiousness, etc., within the population. The healthcare policymaker can then forecast the pandemic's out-of-sample behavior and accordingly, the capacities and supplies to be provided to avoid future shortages.

Here, we first introduce the *compartmental* models in which the host population is divided into a set of distinct compartments, where each compartment exclusively represents individuals with an identical clinical status (e.g., compartments of susceptible, infected, or recovered individuals.). In this modeling category, during each time step, a constant number of individuals leave their current compartment for another. These transfers between compartments and their corresponding rates determine the size of each compartment at each time-step and overall dynamics through time. These changes in the

[4] https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

[5] COVID-19 (2020) is the sixth international concern after the H1N1 influenza pandemic (2009), twice Ebola outbreaks in Africa (2014 and 2018), the polio epidemic (2014), and Zika (2015).

[6] When the virus or other causes of an infectious disease may move from one host to another using a transmission mode.

[7] On March 12th 2020, more than 120 countries report 44279 cases totally, see https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200312-sitrep-52-covid-19.pdf

[8] https://www.nytimes.com/interactive/2021/world/covid-cases.html

[8] The background figure for our word cloud is the virus causing the COVID-19, see https://www.cdc.gov/dotw/covid-19/index.html

[9] Homeland Security Council (HSC)

size of compartments are mainly captured by differential or integral equations, see §2.1.

We then investigate network models in section §2.2. In a network, each node represents a unique individual in the host population. Each edge between two nodes implies the probability of a social contact with another individual, because of living in the same household, attending the same school, workplace, or random contacts in public gatherings. To each edge, a time-dependent contagiousness probability is also assigned.

The compartmental and network models represent two distinct sampling approaches of the host population. In compartmentalized models, individuals within each compartment are sampled identically[10] when are being transferred between two compartments. However, in the network models, the social behavior, contact and transmission rates, and other demographic specifications are uniquely defined for each individual, in a heterogeneous fashion. At the end of this section, we also present miscellaneous models in §2.3. The interested reader may see Pan et al. (2021) and Choisy et al. (2007) for a thorough exposition of various mathematical models proposed for infectious diseases and the related solution methods.

2.1 The Compartmentalized Models: SIR, SEIR, and Their Variants

The first compartmentalized model, called SIR (detailed in what follows), and its variants are introduced in three seminal papers by Kermack and McKendrick (1927, 1932, 1933). In the SIR model (Kermack and McKendrick, 1927), a host population is partitioned into three compartments (i) individuals *Susceptible* to infectious disease shown by S, (ii) currently *Infected* individuals denoted by I, and (iii) patients *Removed* due to death or *Recovered* represented by R. In this model, each susceptible individual meet other individuals (including infected patients) according to a constant contact rate. During a social contact with an infected individual, the infectious disease may be transmitted to the susceptible individual with the contagiousness rate[11]. When infected, susceptible individuals leave S to I with the transmission rate. In Kermack and McKendrick (1927), infected individuals will be transferred to the R due to recovery[12] or death at the same rates. It is worth noting that the SIR model in Kermack and McKendrick (1927) is suitable for epidemics in which the recovered individuals will obtain full-immunity so they will remain in R, once recovered.

In Kermack and McKendrick (1932), however, the authors assume that the infected population may be removed with distinct recovery and death rates. In this model, those recovered only obtain partial immunity (López and Rodo, 2021) and will regain susceptibility status through time. The infected individuals may also return to S due to false test results.

In many epidemic models, the infectious disease may also represent an *Exposed (E)* stage or incubation period, thus partitioning the host population into four compartments, called $SEIR$. During the incubation period, the transmitted infection represents a latency period during which, the individual is still asymptomatic and is not able to transmit infection. Therefore, an exposed person first leaves S to E.

There are several variations of the SIR and SEIR models in the literature[13] that are constructed by envisioning additional compartments in order to capture various clinical characterizations more exclusively [14] such as new birth, natural death (Carcione et al., 2020; López and Rodo, 2021), hospitalization/quarantine (Bertsimas et al., 2021a; Giordano et al., 2020), vaccination/partial immunity (López and Rodo, 2021; Ren et al., 2013; Bertsimas et al., 2021a), and social distancing (Mwalili et al., 2020). Other compartmental models rely on repartitioning the existing compartments based on the severity of symptoms, government interventions (Li et al., 2021; Gillis et al., 2021; Rădulescu et al., 2020), and disease subtypes, see Porco and Blower (1998) for an HIV epidemic model with two sub-types, the possibility of obtaining cross-immunity by vaccination, and natural deaths.

Carcione et al. (2020) present a different version of the SEIR model by accounting for new birth and natural death cases while distinct recovery- and death-rates are considered. New births will be added to S, and natural deaths will be heterogeneously reduced from all compartments. Mwalili et al. (2020) develop a new SEIR-P epidemic model for COVID-19. The proposed model represents some fundamental modifications to the SEIR model, like repartitioning I into asymptomatic and symptomatic subcompartments I_A, I_S (Rădulescu et al., 2020), the possibility of moving from E to S, and a Pathogens compartment P (Du et al., 2021). The latter compartment contains the virus produced by I_A and I_S subcompartments and its prevalence in the environment. Therefore, the individuals in S can be exposed to I_A, I_S, and P compartments.

To precisely model various infection rates, each corresponding to a specific type of social interaction in the host population, Chung and Chew (2021) divide the overall types of interactions into three sub-categories (i) fixed interactions (e.g., home, workplace, dormitories), (ii) temporary social gatherings, and (iii) random interactions in a crowd. Rădulescu et al. (2020) propose a modified-SEIR model with seven compartments and four age groups. The major difference is considering a fraction of exposed individuals in E who can also carry enough pathogens to infect susceptibles.

López and Rodo (2021) present a modified-SEIR model to investigate the spread of COVID-19 in Italy and Spain with new birth/natural death, hospitalization, and partial immunity. In this model, hospitalized individuals are assumed to be fully quarantined and unable to infect susceptibles. The approach employed to solve the dynamical system is based on an adjust-then-predict method (Bertsimas et al., 2021a), in which the time-dependent recovery/death rates are first fitted to historical data and then used in the test data for out-of-sample predictions. Gillis et al. (2021) consider a modified-SEIR model where I is repartitioned into three subcompartments, presenting pre-symptomatic, mild, and severe infection signs; three quarantine subcompartments and a hospitalization compartment are also added to the SEIR model. Then, each (sub)compartment is further divided by age and comorbidity indices. This model is used to measure the financial impact of interventions designed for Nova Scotia, Canada.

Lemos-Paião et al. (2020) propose a compartmental model with seven compartments, like incoming foreign travelers and the risk of infection (Barnett and Fleming, 2022), natural death, quarantine, and general ward/ICU hospitalizations, see Wood et al. (2020) for scenario modeling to mitigate ward/ICU capacity-dependent deaths. The main difference

[10] All individuals contained in the same compartment represent the exact replication of a single clinical status.

[11] It may be static or dynamic.

[12] When the immune system removes the infectious disease.

[13] https://docs.idmod.org/projects/emod-hiv/en/latest/model-seir.html

[14] And their associated dynamics to enter/leave a compartment from/to other compartments.

between previous models and this one is the possibility of being transferred between the general ward and ICU. In such cases, the patients admitted to ICU who do not develop severe symptoms can leave ICU for the general ward. Moreover, hospitalized patients in the general ward will leave to quarantine and then return to the S compartment due to recovery. Leung et al. (2021) use a modified-SEIR model to capture the dynamics of a Cholera outbreak in three different demographic populations: an urban city, a refugee camp, and an administrative complex with ten buildings. The Cholera infection can be transmitted through contact with infected individuals and the use of contaminated water. In this model, infected individuals may shed bacteria into the environment whether they are clinically asymptomatic or symptomatic. The prescription of a leaky vaccination with one or two doses reduces the susceptible population by providing partial immunity.

Watanabe and Matsuda (2022) address the deviation of actual infected COVID-19 patients from the confirm cases that is due to asymptotic cases in an extended $SEIR$ epidemic model with three types of infections (asymptomatic, presymptomatically infected, symptomatically infected) and isolations, called $SEIIIHHHR$ (no vaccine and specific medicine is modeled). The authors examine their proposed model under various levels of detection rates and compliances with isolation, with and without feedback on the latter. The numerical results explicitly determine detection rates with which healthcare capacity will be overwhelmed or result in an underestimation of death cases.

Bertsimas et al. (2021a) develop a new compartmental model for COVID-19, called DELPHI, that consists of the following compartments: susceptible S, exposed E, infected I, recovered R, deceased D, undetected, detected hospitalized, detected quarantined. Each one of these compartments is further decomposed into those individuals who either recover or die, shown by U^R, U^D, DH^R, DH^D, DQ^R and DQ^D, respectively. The hospitalized patients are partitioned into H^R and H^D as well. The diagnosed but undetected patients will generate two subcompartments, U^R, or U^D, which present the undetected individuals who will recover or die. The patients who have tested positive but have not been hospitalized yet will be posed in the self-quarantine compartments Q^R or Q^D. Then, an algorithm with descriptive, predictive, and prescriptive modules employs historical data and clinical results to train and test a regression model for forecasting compartments' size in the future.

Giordano et al. (2020) present an epidemic model in which the host population is partitioned based on the severity of clinical symptoms, being detected due to performing the COVID-19 test or being remained undetected. The SIDARTHE model considers eight compartments denoted by S for susceptible, I infected[15], D diagnosed[16], A ailing[17], R recognized[18], T threatened[19], H recovered, E extinct or dead. The clinical assumption made in the SIDARTHE model, which makes it different from the DELPHI model, is the possibility of being healed while being in I, D, A, R, or T compartment. However, in the DELPHI model, the hospitalized individuals admitted to ICU (severe symptoms) will be removed and cannot be healed. The second difference may lie in the fact that in the SIDARTHE model, an individual only with life-threatening clinical symptoms may be removed from E. However, in the DELPHI model, the undetected or quarantined patients can also be transferred to D too. The authors state that the SIDARTHE model approaches its equilibrium phase[20] whenever all I, D, A, R, and T compartments are empty, and apply control theory to justify that under a basic reproduction rate $R_0 < 1$ this condition happens.

2.2 Network Models

We devote this section to reviewing network models that are implemented in Agent-Based Simulation (ABS) modules to imitate epidemics. The ABS modules are developed to investigate the pandemics dynamic and efficiency of pharmaceutical and nonpharmaceutical interventions.

Dalgıç et al. (2017) address the significant advantages of the ABS models when compared to compartmentalized models in vaccine allocation strategies. First, a modified-SEIR model in which individuals are divided into five age groups is presented. Each individual whether susceptible, exposed, or infected has a vaccinated/unvaccinated label. Various age-based infection rates are considered, and these rates are independent of vaccination-status of each individual. The above compartmentalized model is then examined against FluTe[21], an open-source agent-based flu simulation code (Chao et al., 2010). For both approaches, MADS algorithm (Audet et al., 2021) is employed to perform a global search to assign vaccination priorities to various age-groups. The authors mention that while the ABS model in FluTe is computationally expensive, it results in a different vaccination strategy with respect to the compartmentalized model. The main difference between the ABS and compartmentalized models stems from the fact that under various transmission rates, the ABS model results in very different vaccination strategies. However, in the modified-SEIR model, the age-based vaccination policies remain unchanged when various pandemic scenarios are examined, implying to a major drawback in the compartmentalized models, see also Longini Jr. et al. (2005); Germann et al. (2006); Halloran et al. (2008); Wu et al. (2006) for employing stochastic simulation models for measuring the quality of various interventions such as (a) antiviral prophylaxis, (b) quarantine, (c) vaccination, (d) social mobility, (e) household quarantine, (f) isolation, (g) school closure, (h) community and workplace social distancing to contain flu pandemics under various infection rates and basic reproduction number assumptions, see Dorjee et al. (2013) for a thorough exposition of proposed simulation approaches for the flu pandemic.

To investigate the significance of mitigation strategies in the flu outbreaks, Das et al. (2008) design a large-scale comprehensive stochastic simulation framework which precisely mimics (i) the demographic- and community-based features such as the varying size of households based on census data, various businesses, schools, churches, shopping, and public centers, (ii) pandemic uncertainties in contact, transmission, mortality rates for each location, age, gender, health condition, and (iii) various daily activities for both weekdays and weekends. The devised simulation model is then tested for modeling a community of 1,100,000 inhabitants distributed in 400,000 households. The authors extensively examine several pharmaceutical and nonpharmaceutical interventions like (1) delay in declaring a pandemic due to a poor syndromic surveillance, (2) various definitions of high-risk groups for

[15] is asymptomatic or paucisymptomatic (i.e., below the threshold of detection by HS) and undetected
[16] asymptomatic infected or detected individuals
[17] symptomatic infected and undetected
[18] symptomatic infected and detected
[19] infected with life-threatening symptoms and detected
[20] The phase at which the pandemic will remain contained.
[21] https://www.cs.unm.edu/~dlchao/flute/

prioritizing hospitalization/vaccination[22] and their efficacies, and (3) a set of social distancing interventions, and (4) the length of isolation at hospitals. An MDP framework is devised to model the dynamic of a pandemic through time, and interventions taken to control it. In this setting, the state-space represents the pandemic's statistics, the level of available pharmaceutical interventions to be used in the following periods, the decision-space consists of various priority levels that could be assigned to each risk-group for vaccination, and the length of applying each intervention. We refer the interested reader to Aleman et al. (2011) for devising a simulation model to test the effects of complying with stay-at-home intervention on the number of infected individuals in Toronto with 5,000,000 population grouped in 1,800,000 households.

Lee et al. (2013) aim at resolving the operational challenges in the decentralized US health system to perform mass dispensing of pharmaceutical items during pandemics. To do so, a simulation-optimization routine, called RealOpt[23] (Lee et al., 2009) is developed. Mass dispensing for controlling a generic pandemic's propagation consists of the distribution of medical supplies through determining optimal dispensing facility locations, staffing, resource allocation, and household assignments to the opened facilities under a limited budget. The devised simulation performs two phases to optimize opening POD-facilities and in turn staffing them. Then, it assigns the households to the opened facilities by considering their distances. By opening each POD-facility, its inter-POD epidemiological dynamics capturing the social contacts within each POD facility will be augmented to a master outer-POD system that models the host-population epidemiological dynamic.

Rauner et al. (2005) address the HIV treatment challenges in the underdeveloped countries due to their insufficient medical and socioeconomic infrastructures. As reported, 70% of affected HIV/AIDS individuals live in Africa, and 90% of infections are transmitted from mother to child. To prevent mother-to-child HIV transmission, two policies are implemented in a discrete-event simulation module: (i) antiretroviral treatment using Nevirapine at the delivery time by accounting for the mother's infectiousness status, and (ii) bottle-feeding. In this simulation, the age, gender, disease state, treatment status, and disease propagation of the individuals are assumed to be targeted indicators to represent various subgroups in the host population. Overall, 27 scenarios for the combined interventions are envisioned for a 9-month duration. While the duration of using antiretroviral had a direct effect on preventing the infectiousness, the simulation justifies that the existing socioeconomic obstacles in the underdeveloped countries may turn the bottle-feeding treatment into a policy with counterproductive effects, see also Santos et al. (2012) for setting up a data envelopment analysis model to compare the efficiency of 52 countries in allocation of resources to prevent mother-to-child HIV transmission.

Mniszewski et al. (2008) employ the EpiSimS simulation model (Stroud et al., 2007) to examine the available pharmaceutical/nonpharmaceutical interventions such as antiviral stockpiles and school closures to control an upcoming H5N1 avian flu pandemic, while a strain-specific vaccine takes 3-8 months to be developed. Here, antiviral medications are prescribed for a ten-day course for each patient, and closure decisions are imposed for a 6-month duration. This simulation model imitates the population demographics in households, rooms, and other mixing spaces by considering a diverse set of social interactions. The numerical simulation justifies the effect of these interventions in delaying an avian flu outbreak and reducing its attack rate up to 1% below the baseline, although re-opening schools may result in the second wave of pandemic when full-immunity is not provided with vaccination.

2.3 Advanced Pandemic Models

In this part, we present compartmentalized epidemic models in which the stochastic processes of individuals' arrival rate at various compartments, and their contact rates are explicitly modeled.

Kaplan (1989) present a generalized epidemic model for the prevalence of HIV during risky sexes. The new arrivals (susceptible individuals) starting their risky sex-life increase the size of susceptible compartment when a generic vaccine only produces partial-immunity. Whenever an individual gets infected or his sex-life is finished without getting HIV, this size will be reduced. In the same fashion, an exposed individual leaves his compartment by the end of incubation time or sex-life. Similar to models presented in section §2.1, the infectiousness depends on contact rate multiplied by the infectivity of an infected individual. All primary compartments are repartitioned based on a set of predetermined rates of having risky sex, the length (or rate) of having risky sex-life, and the incubation rate of new arrivals. In this study, these rates may follow arbitrary distributions. The authors generate a set of scenarios based on the vaccine efficacy ratios using historical data. The simulation of scenarios indicates that even under an optimistic scenario, i.e., a full vaccine-efficiency, it takes at least fifteen years to eradicate AIDS from San Francisco.

Larson (2007) depict the heterogeneous contact rates and social interactions within a host population under an influenza pandemic by using a nonhomogeneous mixing model (see also Zaric (2002) for mixing models in epidemic networks). In the presented model, the susceptible and infected populations are repartitioned into several subcompartments each corresponding to a distinct contact rate[24], e.g., the individuals with low or high contact rates (the contact rates of a housekeeper and a student are assumed to be low and high, respectively.), while all rates follow Poisson processes. For each susceptible subpopulation, the probability that a susceptible becomes infected during a social contact with an infected individual can be computed by multiplying the contact rate of the susceptible person, probability of meeting an infected person, and infectivity of the infectious person, where the last two factors are independent of the social activity levels of any susceptible person. These contact-based probabilities are used to compute the reproduction number during each day and the overall severity of the flu pandemic. The presented model is extended to a generalized model with time-dependent contact rates. This models ensures that the contact rates proportionally tend to decrease when the size of susceptible population tends to decrease.

3. Preparedness Plans

In the WHO's classification of the pandemic propagation, the first three phases are (i) uncertain sources of infection and transmission rate, (ii) sustained transmission rate from human to human, and (iii) pandemic (WHO, 2009). Before the pandemic phase, the preparedness plans - with which one aims at identifying a new or declaring the start of a recurring pan-

[22] We consider these decisions as triage decisions.
[23] https://www.orau.gov/rsb/realopt/
[24] The set of distinct contact rates is predetermined.

demic - for mitigating the pandemic in the early stages and containing its first outbreak are of paramount importance, see Brandeau (2019) for the comprehensive preparedness and response plans in an anthrax pandemic.

The significant developments in global responses to pandemics in the past have helped the WHO to recalibrate its guidelines and evaluations of best practices in the preparedness plans. In this section, we review some of those best practices and the role of OR&M to combat infectious diseases before the pandemic phase. These areas are categorized as syndromic surveillance and contact tracing §3.1 and §3.2, stockpile location problem §3.3, vaccine composition and production planning §3.4.

3.1 Syndromic Surveillance: Statistical Methods, and Previous Experiences

3.1.1 Syndromic Surveillance

A pandemic can impose fundamental pressures on the host population, healthcare, and non-healthcare services. The role of healthcare systems is to provide the essential clinical services during pandemic, such as treatments, isolation, and vaccination for patients. Non-healthcare sectors simultaneously perform critical operations such as social, industrial, transportation and supply chain activities to preserve the functionality of the society for containing pandemic's impacts.

To better characterize an epidemic and its severity before it turns into a pandemic and disrupts the above-mentioned public services, the healthcare policymakers in each country or the WHO at the global level engage in *Syndromic Surveillance*. The syndromic surveillance aims at monitoring the real-time observations of disease syndromes that are being reported by patients arriving at hospitals, detected in laboratory tests, or mentioned in social media. The collected data will be grouped based on the symptoms and will be analyzed to determine the infection source(s) (animal, human, etc.), quantify the transmission rate, or basic reproduction number. It also helps to the design suitable social interventions by measuring the severity index of pandemic to further interrupt transmission chains, and to provide vital recommendations for international travelers (Barnett and Fleming, 2022) to curtail virus spread at the global level. Therefore, any country's failure to perform syndromic surveillance, provide adequate capacities to properly perform it, or carry out any other preparedness plan may easily threaten the globe with a pandemic (Heymann and Rodier, 2004).

The surveillance network consists of laboratory tests, tracking syndromes in the web[25,26] using data count, and change point analysis, see Siettos and Russo (2013) for constant and piecewise linear signals, Poisson regression, time-series, inter-event times, etc., and social media[27], see also Lawson and Kleinman (2005) for a comprehensive review of surveillance methodologies for disease detection, and Agapiou et al. (2021) for their applications in the COVID-19 era in Cyprus. These sources can be used to monitor the syndrome variations by detecting significant changes in the reported numbers or an unusual outbreak that leads to identifying a known or new emerging pandemic.

3.1.2 Statistical Methods To Declare A Pandemic

Sparks et al. (2010a) analyze patients' small arrival counts with symptoms of the Ross-River virus in New South Wales with day-to-day and intra-day nonstationary Poisson distributions for day-ahead planning, when standardizing forecast errors fails. A Poisson regression model, capturing daily patterns, weekly and seasonal cycles, and arrival lags, is designed to approximate the patient influx, see also Vicuña et al. (2021) for a quasi-Poisson regression model with distinct weekday and holiday covariates to predict COVID-19. To detect a potential outbreak, an adaptive Cumulative Sum (CUSUM) and Exponentially Weighted Moving Average (EWMA) statistics are introduced that can identify any unusual variation out of a predefined false-alarm threshold, see Costagliola (1994) for a definition of a cut-off point (i.e., a false-alarm threshold) in syndromic surveillance, Siettos and Russo (2013) for a comprehensive review of statistical-based methods for epidemic surveillance, and Sparks et al. (2010b) for extending surveillance plans in Sparks et al. (2010a) by modeling patient arrivals with negative binomial distribution counts.

Alternatively, Sparks et al. (2019, 2020) analyze the inter-detection times of patients with fever, head cold, and upset stomach syndromes, expressed in the social media. These arrival times or equivalently, their inter-arrival times are approximated by exponential, Gamma, and Weibull distributions. These surveillance plans extend plans proposed by Sparks et al. (2010a,b) by explicitly considering public and school holidays in the proposed regression models, see also Zwetsloot et al. (2021) for bivariate events modeling (HIV infection time and AIDS incubation time) of AIDS patients in Atlanta.

3.1.3 Previous Experiences to Combat New Epidemics

Based on Google search statistics and stock market reactions, Ru et al. (2021) present an empirical study of the 2003 SARS epidemic imprints in multiple countries to examine their response quality to COVID-19 and simultaneously population compliance with social distancing. The proposed regression model is fitted to the last two weeks of January 2020 in countries with SARS experiences, taking into account the number of detected cases and deaths. Then, a Cox proportional hazard model is developed to capture the effect of SARS imprints in the government's responses to COVID-19, considering the following covariates: SARS confirmed cases, COVID-19 confirmed cases, and their multiplication. The numerical results strongly validate a positive correlation between the number of SARS and COVID-19 cases. It has also shown that countries with fewer SARS imprints have responded to COVID-19 with lengthier delays and less social distancing compliance.

3.2 Contact Tracing

A healthcare policymaker performs contact tracing in pandemics to identify and break infection transmission chains. To do so, the close contacts of an infected individual should be identified, classified, and finally shortened based on a suitable scoring strategy for applying tests, isolation, or medical treatments. It is evident that the list should be shortened because the availability of contact tracing technology and available pharmaceutical and nonpharmaceutical interventions are restricted by a limited budget. Contact tracing approaches deal with determining the volume of close contacts and the strategy of prioritizing/shortening contacts to reduce its costs, see also Firth et al. (2020) for the effectiveness of tracing multiple contact layers, and the ineffectiveness of releasing close contacts of an infected individual from quarantine only with a

[25] https://www.healthmap.org/
[26] https://trends.google.com/trends/
[27] https://twitter.com/

negative COVID-19 test-result.

3.2.1 Policies and Limitations in Simulation

Armbruster and Brandeau (2007) investigate the design of an optimal budget assignment for contact tracing during a pandemic whose dynamic governed by a SIR model augmented with two additional compartments such as the traced individuals who are either susceptible or infected. First, a cyclic graph is established in which each individual is connected to her priority list of contacts. The transition rate can be computed by accounting the number of infected neighbors of each individual, and incoming international travelers (Barnett and Fleming, 2022) representing the endogenous and exogenous sources of infections. A discrete-event simulation model prescribes the treatment to an infected individual when she is detected by a positive test-result, and then transfers her to the recovery compartment. Next, the simulation module chooses a contact tracing policy e.g., contact scoring (scores are derived by counting the number of visits and social engagements of each close contact with the detected patient) to identify and then shorten the primary contact list of the confirmed case. A fixed cost is associated with each tracing action taken from shortened list by entailing the technology for tracing and test prescription costs. Finally, the simulation examines various tracing strategies to reduce the total treatment/contact tracing costs and number of new infections. Ubaru et al. (2020) employ time-dependent contact-tracing graphs to optimize performing both infection and recovery tests. In this model, the authors take simultaneously into account the spread of virus from contaminated surfaces and infected individuals. To impose quarantine and hedge the spread of the SARS-CoV-2 virus, Bicher et al. (2020) model both contact and location tracings in a Monte Carlo simulation framework. First, the contact list of each infected individual is extended by considering age, sex, and visited places such as households, workplaces, schools, or leisure places. To examine the efficacy of interventions, three baseline scenarios are constructed by taking into account for population compliance, and their leisure-time and social contact reductions. Then, the effects of imposing quarantine and closure are compared with these baseline policies. In this model, contact tracing ensures that as soon as an individual is detected, all her primary contacts will be informed and will be quarantined for 14 days. Moreover, location tracing enforces a temporary-closure of a workplace or school whenever a confirmed case reported, see also Yu and Hua (2021) for applying contact tracing for enforcing isolation and quarantine to control COVID-19 at Wuhan, and Maxmen (2020) for successful stories of surveillance, isolation, test, and quarantine policies. Pokharel et al. (2021) design an ABS module to compare manual vs. bulletin contact-tracings. In the former, any individual who was in a social contact with a detected individual (with a positive test whether categorized as asymptomatic or symptomatic) within a specific radius will be listed in the primary close contacts. The latter focuses on the locations visited by an infected person and contacting the individuals who were present at that location at the same time. The experiments performed on the SEIR model show comparable results for both types of tracing. However, by applying the bulletin contact-tracing one can take the following advantages such as being less resource intensive, easier to implement, and offering a wide range of privacy options.

3.2.2 Data-Driven Propagation

To handle pandemic propagation uncertainties, an alternative approach to restrictive epidemiological models is a data-driven propagation model. By using electronic Healthcare Reimbursement Claims (eHRCs) in the United States' HS, Zhang et al. (2019) propose a unified data-driven surveillance and contact tracing approach to break the transmission chains of flu. In the eHRC system, the patients' locational granularity only refers to their zip codes. Therefore, the authors first transform eHRCs to dynamic propagation logs, in which it is specified how many individuals are infected by COVID-19 in each zip code at each time step[28]. Then, these propagation logs are combined with contact networks of visits between different zip codes. Since several individuals live in each zip code, to extract actual visits of infected individuals, one must consider various cascades, each representing the selection of a specific individual as an actual infected person who may spread the virus with a known probability. The authors set up an optimization framework to optimally select a set of optimal cascades under a limited budget, thus deriving an optimal contact tracing strategy to reduce flu transmission rate.

3.3 Stockpiles for Vaccine and Antiviral Drugs

To reduce the spread of recurring infectious diseases or even new epidemics, the WHO strongly recommends establishing stockpiles of vaccines, antivirals, PPEs, ventilators, and other pharmaceuticals to all nations, aligned with the WHO's preparedness plans. In this part, we elaborate on the research studies that investigate optimal stockpile locations and optimal inventory levels at them. Here, we review a diverse set of problems as stockpile assignment at the international level (Sun et al., 2009), joint stockpile levels at several hospitals (DeLaurentis et al., 2008, 2009; Adida et al., 2011), stockpile levels for reserved customers (Harrington Jr. and Hsu, 2010), and a comparison between central and local stockpile designs (Huang et al., 2017).

3.3.1 Stockpiles: International Level, Hospitals and Central vs. Local Locations

Sun et al. (2009) model a selfish assignment of antiviral stockpiles at the international level during a pandemic event as a two-period game-theoretic setting. It is assumed that the source country, where the pandemic started does not keep any stockpile. Antiviral drugs have two main benefits: reducing the susceptibility of individuals to infection, and the infectiousness of infected individuals. In this operational policy, when transmission rates between different countries are low, all countries selfishly assign their drug stockpile only to themselves or the source country. If a central coordinator like the WHO tends to reduce the global effects of the pandemic, the decisions obtained by the Nash equilibrium assign the reserved stockpiles of each country to the source country as much as possible. DeLaurentis et al. (2008, 2009) studied determining the optimal stockpile levels at a set of hospitals that aim to share their antiviral inventories in preparedness for flu pandemics. The proposed game-theoretic model takes into the account the antiviral purchasing- and holding-costs, and penalties when the incoming demands remain unmet. In this setup, an excessive stochastic demand can be redistributed to those hospitals that are not participating in responding to the underlying pandemic. The authors show that the best response of each hospital is a piece-wise linear convex function

[28] Somehow increasing locational granularity to zip codes and then performing patient arrival counts, see §3.1.2

of its inventory-level and can be computed only when discontinuity points of its slope (the gradient of response function) change their sign. The Nash equilibrium is numerically obtained when the best response functions of two hospitals intersect.

Adida et al. (2011) compare a game-theoretic approach with a centralized set up to tackle optimizing the joint-stockpile levels of medical items entailing holding/shortage costs at several hospitals under stochastic aggregated demands, see DeLaurentis et al. (2008, 2009) for the disaggregated-demand version of this problem. It is assumed that the aggregated demands are associated with predefined regions and their stochasticity is explicitly modeled by a set of scenarios. To promote the design of stockpiles at hospitals, one must assume that the marginal holding cost is less than the marginal shortage cost. In the game-theoretic setting, when these hospitals are ordered based on the ratio of their holding to their shortage costs, at Nash equilibrium, only the hospital with the smallest ratio can hold inventory. In the centralized version, the decision-maker seeks to coordinate optimal stockpile levels for minimizing the total costs. In this setting, however, the authors suggest ordering hospitals based on their holding costs, with which Nash equilibrium implies that only the hospital with the lowest holding cost establishes the stockpile. Huang et al. (2017) propose a unified forecasting and optimization scheme to solve the mechanical-ventilator stockpile location-inventory problem during a flu pandemic in the US. Using a multivariate Gaussian distribution, the forecasting scheme employs a linear regression setup to estimate flu-related hospitalizations to predict the ventilator's demands at the county level in multiple periods. Once the regional ventilator demands are derived for three pandemic severity scenarios (i.e., mild, moderate, and severe), the optimization framework tackles the stockpile location and inventory problem, in which mechanical ventilators will be stored at central or regional stockpiles. The numerical results conducted on the CDC historical data for a flu epidemic in Texas recommend establishing local stockpiles rather than central inventories. This is due to the highly correlated regional demands and higher-quality services guaranteed with local stockpiles, mostly stemming from the reallocation distances and corresponding delays.

3.3.2 Manufacturer Stockpiles for Reserved Contracts

Harrington Jr. and Hsu (2010) investigate establishing reserved antiviral stockpiles at the manufacturing locations being envisioned based on pre-pandemic contracts with individuals. Such contracts enforce providing antivirals in a 24-48h time-window during a flu outbreak in the United States. In this inventory management problem, such contracts incur an extra reservation fee, but proportionally much less than the antiviral's price, and bind manufacturers to fulfill them with the highest priority compared with pandemic-time purchases. Therefore, the individuals with these contracts always will be served with the reserved inventory. The authors justify that without these contracts, manufacturers may proportionally increase their inventory levels only if the pandemic-time prices can be relatively increased with respect to pre-pandemic prices. Further results show that holding inventory does not make any notable advantages from the manufacturers' perspective when the expected profit and holding costs are close[29], while with a relatively low holding-cost, the optimal inventory level is the stockpiles' full-capacity.

[29] implying to a negligible marginal profit

3.4 Vaccine Composition and Production Planning

In this part, we review vaccine strain selection at international and country levels in sections §3.4.1 and §3.4.2. We first note that each year, the WHO starts planning for vaccine composition several months before the start of flu pandemic season, while the length of planning in the United States is about seven weeks.

To recall related studies, we first discuss some comparisons without accounting for the planning level. Özaltın et al. (2011); Cho (2010) only consider the current vaccine cross-effectiveness when facing future flu variants, however, Wu et al. (2005) also investigate the effects of previous epidemics, vaccinations, and immunities in terms of history to design new vaccines. Özaltın et al. (2018) investigate the vaccine design problem when the manufacturer aims at optimizing multiple competing objectives other than vaccine efficacy.

3.4.1 The WHO Plans and Objectives

Özaltın et al. (2011) investigate the flu-shot design and production of multiple strain combinations at the WHO for a multi-period planning horizon. The goal of the WHO is to improve its surveillance and decision-making process to hedge vaccine shortages and its cost during the flu season. In the proposed multi-stage stochastic program under demand uncrtainty for vaccination, the flu shots are designed by selecting the following three strains H3N2, H1N1, and an influenza B virus[30], that can also provide cross-effectiveness. For example, an individual vaccinated with H3N2 also obtains partial immunity against H1N1. Considering the existing cross-effectiveness, the goal is to maximize the expected utility of the vaccine coverage to treat all three flu types by choosing the best strain-combinations. In this setting, the flu season occurs at the final stage, while all previous stages are the manufacturing periods. A Dantzig-Wolfe decomposition technique is developed by establishing a master problem to construct the flu-shots strain composition decisions. The subproblem in turn evaluates strain composition decisions against production yield uncertainty and cross-effectiveness. To perform the numerical experiment, several instances with up to 512 scenarios are generated by considering low, moderate, and high attack rates for a maximum six-week time-horizon. The numerical experiments validate the benefits of flu shots when the attack rate is high. Wu et al. (2005) examine the optimal policy of repeated vaccinations for the WHO to control flu epidemics with Normal drifts in consecutive periods in a stochastic dynamic programming framework. In the first policy, a vaccine will be composed based on the expected upcoming strains. In the second policy, the history of vaccines and previous epidemic strains, called antigenic history, i.e., one considers the cross-reactive antibodies released in the past that decrease the effect of repeated vaccination in the next epidemic is used for vaccine selection. Each strain is mapped to Euclidean space for evaluating the spatial quantity of the immune system to determine the pre- and post-vaccine states, and the effect of a conditional drift on the immune system as a post-epidemic state. By precisely defining the underlying immune state-space, one can compute Markovian transitions between various states of the immune system. The objective is to maximize the minimum cross-reactivity of the new vaccine against the current immune state. A history-clipping approximation scheme is devised to reduce the size of stored history to only one period. This heuristic approach significantly

[30] https://www.cdc.gov/flu/prevent/vaccine-selection.htm

improves the computational complexity by resulting in near-optimal repeated vaccination-policies.

3.4.2 Vaccine Compositions in the United States

In the United States, every year, an advisory committee decides the seasonal flu composition during one of their consecutive meetings. The committee chooses one of these two options (i) the cross-effectiveness of previous vaccines against the new strain is sufficient, or (ii) defer the vaccine composition decision until the next meeting when new information is observed. The required information to make this decision evolves over time and will be updated when a new strain is detected, or an epidemic is declared. The latter reason and a lengthy period of 4-5 years for capacity expansion result in stochastic production yields. Moreover, the flow of information is a random process, and it depends on the syndromic surveillance performance. Therefore, once new information is observed, the committee can update its belief about the new strain and its prevalence severity. Cho (2010) construct an optimal dynamic policy that precisely quantifies the value of real-time information. This approach alternatively evaluates the future cost of choosing a wrong strain in vaccine composition. Such an optimal policy weighs the myopic choices against dynamic actions. The myopic policies in vaccine composition refer to producing the previous year's vaccine. Such policies lead to minimum production yield uncertainties, however, they are less effective whenever a new strain propagates. On the other hand, taking dynamic actions implies making here-and-now decisions that increase the risk of choosing the wrong strain. Nonetheless, this gives the vaccine manufacturers enough time to fulfill forecasted demands. The optimal production plan maximizes social welfare, although it neither presents symmetric characteristics in making static or dynamic decisions, nor monotonicity. The authors show that retaining or updating a strain may change production yields by more than ten million doses with four hundred million extra welfare expenditures during the early periods. However, when production is depleting rapidly, both retaining and updating policies result in the same production levels and welfare costs. Finally, optimal timing decisions validate a strain updating decision no later than 2-3 weeks after retaining previous strains. Özaltın et al. (2018) model the flu vaccine composition and production problem in a multistage stochastic bilevel program. In this bilevel formulation, the vaccine design committee, representing the leader in a bilevel optimization program, seeks the optimal strain selection to maximize the expected vaccine efficacy while the manufacturer, as the follower, aims at maximizing its expected profit under yield uncertainty. There are two categories of flu, i.e., A and B, each containing two different strains. The manufacturer produces trivalent and quadrivalent shots. In this setting, the committee first chooses the vaccine design and its timing, while the manufacturer selects production yields and remaining capacities, which are the result of delays in decision-making timing. The authors apply Dantzig-Wolfe decomposition by taking the leader and follower problems as master and subproblems. The numerical experiment performed during the 2014-2015 flu season in the United States justifies that the selection of strains with the least prevalence and drift should be carried out earlier.

4. Response Plans

As mentioned in Heymann and Rodier (2004), each country's failure in the executing preparedness and response plans may turn an epidemic into a pandemic, lengthen a pandemic outbreak, generate recurrent waves, or turn it into an endemic. Based on the WHO's guidelines (WHO, 2009), an infectious disease in its third phase is already in the pandemic phase and outbreak aftermath that requires a global coalition of the public, states, and countries to prescribe an aligned response plan to reduce and hedge its damages to the individuals' life, work, and economy.

These response decisions can be envisioned and then executed locally in the hospital wards (Fogerty et al., 2021) or within a state/province/country (Bertsimas et al., 2020; Mehrotra et al., 2020; Basciftci et al., 2023; Ramachandran et al., 2020). We start with intervention decisions taken by governments to contain pandemics after its third phase in section §4.1. In section §4.2, we recall studies in which pandemics are taken into account of schools and universities day-to-day planning.

Furthermore, these response actions can be taken to optimize the production and supply/inventory/reallocation of pharmaceutical items such as antibiotics, test-kits, and vaccines (Özaltın et al., 2011; Liu and Zhang, 2016; Du et al., 2021; Basciftci et al., 2023; Thul and Powell, 2021) in section §4.3, ventilators in section §4.4.1, allocation of ICU beds in section §4.4.2, bed capacity estimation in section §4.4.3, and medical staff planning and allocation (Bienstock and Zenteno, 2015; Georgiadis and Georgiadis, 2021; Gao et al., 2021) in section §4.4.4.

4.1 Interventions

In general, $\mathscr{R}_0$[31], the exposure or contagiousness rates vary considerably in different populations with demographic and sociobehavioral differences (Delamater et al., 2019), depending on the individuals' age, sex, type of contact, job, workplace, etc. To precisely capture the crucial effects of these factors in the spread of disease, researchers model them as social interactions. The healthcare policymakers can then examine imposing interventions such as the mandatory lockdown, travel bans, face-mask, etc., by either removing or restating the possibility of each social interaction in compartmental models §2.1, or simulation frameworks §2.2 for evaluating their response quality to contain pandemics (Chung and Chew, 2021; Rădulescu et al., 2020), or how their combinations can be optimized under a limited budget to provide a reasonable threshold of protection for the host population (Gillis et al., 2021).

4.1.1 Modeling Social Dynamics

To decompose the transition of susceptible individuals to I compartment, Chung and Chew (2021) exploit three types of time-dependent, but age-independent social interactions[32] using adjacency matrices with overlapping multiplex network topologies. The authors simulate these interactions to investigate the effect of different types of social interaction on the

[31] $\mathscr{R}_0$ is the most important parameter in epidemic modeling, whose value determines whether an infectious disease may turn into an epidemic (> 1) or not (< 1). The basic reproduction ratio $\mathscr{R}_0$ is an epidemiological metric to quantify the contagiousness or transmissibility of infection from infectious individuals during an outbreak. The biological, social contacts and environmental factors may have effects on $\mathscr{R}_0$, but three main indicators to describe this quantity are the duration of contagiousness, the likelihood of transmitting the disease to a susceptible during a contact, and the contact rate for an infected individual (Delamater et al., 2019).

[32] Including household, dormitory, and job interactions that are assumed high-frequency deterministic contacts, temporary social gatherings as the second type are considered low-frequency deterministic contacts, and the crowd network as the third type provide low-frequency uncertain contacts.

size of I. To simulate the infection circuit breaking in Singapore, 85% of social contacts in workplaces (the remaining 15% represent essential workers), and 95% of visits between households are removed, although social dynamics within each household remain unchanged. Rădulescu et al. (2020) simulate social dynamics in transmitting the COVID-19 infection by defining an age-based time-dependent mobility matrix to resemble mobility and trips between various locations in a generic college town. A set of predefined exposure rates based on visited locations and age groups is defined. In this way, each exposure rate corresponds to a specific type of social contacts to fully capture their individual and collective effects on the transmission of infection. In this setting, visiting a doctor is considered as a low-risk activity, while attending school or workplace imposes moderate risk to each individual. A hypothetical college town with 1000 individuals and two initial infections is modeled to perform the numerical experiments. The authors numerically validate that the closure of restaurants, bars, and entertainment venues had negligible effects, and were localized to those age groups involved when one enforces these closures separately. It is also shown that community contamination mainly took place during public gatherings and ceremonies. Li et al. (2021) define a time-dependent multiplicative exposure rate for COVID-19 transmission applied in the DELPHI model (Bertsimas et al., 2021a). In this approach, the government intervention and its effects are defined through an *arctangent* function providing three successive options such as no taken action, full closures, and their diminishing effects. These interventions can be depicted by the *arctangent*'s successive concave, convex, and flat graph behaviors.

4.1.2 The Closures, Travel-Ban and Isolation

Gillis et al. (2021) investigate the effect of weekly interventions such as closure, isolation, and travel-ban policies in an integrated epidemiological-optimization framework. The policy-maker selects a severity-level for each intervention per week that explicitly controls the dynamics of the epidemiological model. For instance, each severity level of travel-ban fixes the exposure rate to a specific value in the host population. These nonpharmaceutical interventions are chosen to minimize the total cumulative number of infections using a limited budget in Nova Scotia, Canada.

4.1.3 Isolation, Ring and Mass Vaccinations

Ren et al. (2013) consider various control strategies to minimize the fatalities from both disease and vaccination in a smallpox pandemic, governed by the SIR model dynamic. The nonpharmaceutical and pharmaceutical interventions tested by Ren et al. (2013) are the isolation, ring vaccination[33], and mass vaccination. One using the stronger intervention can reduce the basic reproduction number monotonically; for example, the ring vaccination also implies enforcing isolation. In the same fashion, the mass vaccination implies enforcing isolation and the prescription of ring vaccination. The baseline is set to the total number of fatalities under no control strategy. The authors compute the closed forms for the total number of fatalities under these three vaccination policies and compare them with the baseline policy separately. They also obtain the ranges associated to the SIR parameters under which a policy outperforms the other policies in the form of resulting in fewer fatalities, see also Kress (2005) for the effect of social mixing to control the propagation of smallpox.

[33] Vaccination of close contacts of infected individuals.

4.1.4 Closures and Priority-Based Vaccination

Deng et al. (2013) investigate the quality of triage and intervention decisions like prioritized vaccination schedules for high-risk groups or closure of cinemas, restaurants, and bars to prevent the spread of a synthetic pandemic in Portland, Oregon, where more than 1,600,000 individuals visit 250,000 locations. Each person can only visit a set of predefined places according to a preference probability distribution, and may get infected at any location, whether vaccinated or not, but with different rates. The population also represent compensatory behavior implying that if the first preferred location is closed, the individual will visit the location with the second highest desirability. The authors restrict the problem to 100 individuals and their 195 preferred locations, and design a greedy and an alternative exact algorithm to solve the restricted problem.

4.1.5 The Effects of Lockdown in Pandemic

Kaplan (2020) estimate the ICU-bed shortages in Connecticut during the COVID-19 pandemic when the infected individuals are decomposed by their infection durations corresponding to distinct transmission intensity-functions for each class of infection duration. In this approach, the arrival of infected individuals is modeled as known Poisson processes, providing an instantaneous intensity-function per transmission rate. In such a way, the cumulative number of infected individuals is computed by this collection of duration-specific infection intensity-functions. At each time, the cumulative number of infected individuals who can transmit the pathogen with various infection durations including incubation time is computed. Then, its multiplication to the susceptible population results in an instantaneous intensity function of the newly infected individuals. To reduce the instantaneous transmission rates, the volume of the susceptible population for the lockdown period, and the volume of new infections, the authors suggest imposing the following interventions respectively, the isolation/hospitalization of infected individuals, lockdown, and social distancing. The authors validate that the lockdown has only temporary effects as resetting the initial conditions for the susceptible population and shifting pandemic peaks forward through the time-horizon.

4.2 Pandemic in Universities and Colleges

Proano (2016) address the challenges the Rochester Institute of Technology (RIT) faced during the H1N1 flu pandemic, as the first global pandemic of the 21st century in the Spring of 2009. Considering the uncertainty in the severity of the H1N1 flu, part of these challenges were operational issues like matching the supply and demand for vaccines[34], and the lack of integrated vaccine registration to collect historical data from RIT faculty, student, and staff groups who have already received vaccination outside of the campus. The aim of this study was to investigate what would be the optimal vaccine doses to provide full immunity within the RIT community. Moreover, what decisions must be taken to avoid class disruptions and suspensions that incur extra costs to the students and RIT itself, or food-logistic decisions for the quarantined students? The authors conclude that the pandemic's uncertainties or "lethality and infectiousness" have direct influence on all RIT preparedness plans, therefore neglecting them will result in major disruptions in RIT's general activities.

[34] RIT ordered 13,000 doses but received 6,000, although 70 million purchased H1N1 flu vaccines remained unused in the United States.

Barnhart et al. (2021) investigate the in-person and online course scheduling problem with scarce resources in the COVID-19 era. The goal is to increase the number of students who can take multiple courses without any conflicts, while the mandatory social distancing policies reduce MIT's effective class capacities. This scheduling problem includes faculty assignments, term planning, course timetabling, room assignment, and course enrollment. Each in-person course will be constructed using 30-min lessons and will be distributed based on the availability of these time blocks during working days, while following the precedence constraints of prerequisites, and avoiding concurrent assignments. To tackle intractable instances whose complexity stems from the profusion of decision variables, various greedy procedures are designed. These schemes perform the following consecutive steps (i) restrict the course start-times to the beginning of time blocks, (ii) break the joint room-and-time selection decisions into a two-step procedure considering the online-course replacements to preserve the feasibility of schedules, and (iii) run the symmetry-breaking aggregations for the subgroup of students, presenting the same required courses.

4.3 Vaccine, Test-Kits, and Antiviral Allocation

In this section, we address the research conducted on the allocation of vaccine, test-kits, and antiviral by considering triage decision making §4.3.1, the tradeoff between prevention and treatment §4.3.2, advanced uncertainty modeling techniques §4.3.3, designing vaccination centers §4.3.4, and one vs. two dose coverage §4.3.5.

4.3.1 Triage Decisions: Resource Scarcity, Optimality, and Age Dependency

Cao and Huang (2012) investigate the tradeoff between lifesaving decision-making efficiency and ethical issues for allocating scarce pharmaceutical resources. A discrete-event simulation framework is developed to examine the following triage decisions: first come first served, random, most serious first, and least serious first. Overall, seven combinations of experiments are conducted demonstrating that when the scarcity of medical resources is high, the least serious first outperforms all other policies. The authors note that the least serious first triage-decision results in some ethical issues. However, when the level of pharmaceutical resource scarcity is low, there is no major difference between these four policies.

Ayer et al. (2019) analyze optimal triage decisions to prioritize providing expensive treatment for the Hepatitis C epidemic in the US prisons, where the prevalence is ten times more than outside prisons. A compartmental model with 14 compartments is established to capture five degrees of fibrosis severities for the inmates and new prisoners before and after prescribing treatments, which respectively represent passive and active transitions. This problem is classified as a limited-resource allocation with prioritization among multiple agents and is formulated as a weakly coupled MDP. The reward function in this formulation considers the prerelease accumulated quality-adjusted life-years (QALYs) of each patient, whether they are treated in prison or not. An optimal policy designed to extract the optimal indexing triage decisions to prioritize inmates and then choose to either apply the expensive and limited treatment or not. The authors address the sub-optimality of previously designed triage decisions when made only based on inmates' liver clinical status. They show that due to disease transmission between prisoners, prescribing treatment to inmates with longer sentences is more beneficial. As mentioned earlier, making allocation decisions in a pandemic may turn into triage decisions when the underlying resources are scarce. Lee et al. (2015) develop a combined pandemic-queuing optimization framework to derive an optimal prioritized H1N1 flu vaccination coverage at the Point of Dispensing (POD) for high-risk individuals to minimize the total attack rate[35]. In a prioritized vaccination policy, a high-risk group or a portion of it receives the vaccine before other groups. Each POD consists of several queues presenting the main waiting line outside each POD that will be divided into multiple sub-queues leading to several vaccination booths. Three compartmentalized models are considered to separately represent the population at PODs by individuals waiting outside of PODs, those waiting inside PODs, and individuals whose vaccination fails to create immunity. The authors numerically showed that a threshold-based prioritized vaccination strategy for high-risk individuals outperforms both a myopic non-prioritized policy and a fully prioritized strategy in reducing the attack rate. Furthermore, the devised solution framework significantly outperformed the available ABS modules in terms of computational complexity when the authors tackled the state of Georgia with more than nine million population. Bertsimas et al. (2020) present an optimization framework to reduce the death toll by allocating the COVID-19 vaccines subject to resolving real-time tradeoffs between pandemic dynamics and risk levels mapped to each age group in the United States. In this model, the dynamic of the COVID-19 pandemic is governed by the DELPHI epidemiological model proposed by Li et al. (2021). The NYT[36], the US census[37], and CDC[38] data, and the governmental policies and their responses are simultaneously used to tune and update the model's parameters and estimate the risk levels for various age groups successively. The proposed DELPHI-V-OPT algorithm repeatedly simulates vaccination proposals obtained by the original DELPHI model. Then, the infected population will be fixed during the optimization phase to determine the optimal vaccination allocation decisions.

4.3.2 Prevention vs. Treatment

To optimally allocate the limited budget for prevention and treatment interventions envisioned for HIV patients, Coşgun and Büyüktahtakın (2018) transform the traditional compartmentalized epidemic model SIAR[39] to a nonstationary Markov Decision Process (MDP). In this application, the policymaker is equipped with a set of intervention mixtures placed in action space that can be prescribed to individuals in S, I, and A. Each compartment is further repartitioned into two subcompartments representing individuals who either received a mixed intervention or did not. The state of the dynamical system at each time step determines the size of these three compartments and their sub-partitions. An ADP framework is designed to solve the dynamical system over a time period of six years, considering a limited budget for applying these interventions. The authors justify the resource allocation decisions for preventing actions rather than treatments. We refer the interested reader to Alistar et al. (2014) for addressing such a tradeoff in the allocation of scarce HIV resources in a multi-population model with distinct transmis-

[35] The ratio of newly infected individuals over susceptible populations during each period.

[36] https://www.nytimes.com/interactive/2021/us/covid-cases.html

[37] https://www.census.gov/data/tables/time-series/demo/popest/2010s-counties-detail.html

[38] https://www.cdc.gov/coronavirus/2019-ncov/science/forecasting/forecasting-us.html

[39] A: individuals diagnosed with AIDS.

sion modes to reduce its reproduction number, Brandeau and Zaric (2009) for investigating on the optimal amount of a limited expenditure that must be spent in HIV prevention programs, and Lasry et al. (2011) for the allocation of CDC prevention resources.

4.3.3 Advance Propagation Uncertainties: Distributional Constraints, and Belief

The most common approach to model uncertainty in a pandemic is to represent them as a set of scenarios[40]. Here, we highlight new modeling approaches applied in the recently published literature on the distributional constraints (Basciftci et al., 2023), and the use of belief on epidemic propagation (Du et al., 2021).

Basciftci et al. (2023) analyze the design of medical distribution centers (DCs) at various zones, each comprising several states in the United States, to distribute test-kits and vaccines at the demand points presenting spatiotemporal stochastic demands. The authors examined the SP and DRO paradigms against deterministic solutions to minimize unmet demands. In such a way, designing/selecting demand points to fulfill the stochastic demands can be assumed as the first-stage decisions. In this problem, the uncertainty may result in both excesses and shortages. Therefore, when a demand point is selected the inventory and backlog decisions are taken as recourse actions. These DCs can also be transformed into stockpiles when they can keep inventory for future demand periods. To represent demand stochasticity, the SP setup employs the Monte Carlo sampling scheme, while in the DRO paradigm, the distributional uncertainty is implicitly taken into account by imposing various moment constraints. The numerical results demonstrate that the DRO approach significantly outperforms SP and deterministic counterparts in reducing unmet demands.

Du et al. (2021) study the optimal allocation of pharmaceutical interventions like oral vaccines and antibiotics in a rolling horizon Approximate Dynamic Programming (ADP) setting to alter Cholera's spatial transmission through multiple communities. During each time epoch, a set of observations from infected individuals are combined with a single-period forecast of compartment I, first, to determine the size/distribution of the SIRB[41] compartments, and then, to approximate the state of Cholera propagation in the next period. In the optimization phase, the allocation decisions are determined for the next period using an estimation of state-variables in the future.

Thul and Powell (2021) model the stockpile location problem to distribute the COVID-19 test-kits and vaccines under uncertain demands, stochastic propagation parameters in the SIR model, and beliefs about the efficiency of test results and vaccines. The authors develop an ADP framework to tackle the problem. A two-step learning and vaccination scheme embedded in a parameterized rolling horizon look-ahead policy is devised to optimize vaccine-stockpile locations. First, the learning phase observes the environments, i.e., the size of compartments in the SIR model as the current belief, which further provides a forecast of infected individuals for the next period. Then, a Bayesian process combines one-period forecasts and test samples drawn from population into an updated belief for estimating the number of infected individuals in the following periods. The updated belief is then employed in the vaccination decision-making phase. This look-ahead vaccine policy outperforms other myopic policies by one percent, and can serve half a million more vaccinated individuals.

4.3.4 Designing Vaccination Centers

Tanner et al. (2008) tackle generating the optimal vaccination coverage for various household sizes in the SP framework. In this problem, the sources of uncertainty are the contact rate, number of susceptible or infected individuals, and efficacy of vaccination. The optimal vaccination policies are obtained such that the reproduction number remains less than one. Since the vaccination can be expensive and its availability is not unlimited, the chance constraints are employed to bound the percentage of families whose reproduction number leads to a disease-free equilibrium. To solve the underlying CCP for real size instances, the commercial solvers are employed, see also (Tanner and Ntaimo, 2010).

Dasaklis et al. (2017) highlight the role of an emergency supply chain for controlling the smallpox outbreak when pharmaceutical items and vaccines must be supplied from several emergency stockpiles to multiple regions and then to the point of dispensing (POD) to provide full immunity. In the underlying epidemiological model, the susceptible individuals are divided into those who either can or cannot be vaccinated due to medical reasons. Infected individuals with severe symptoms will be moved to the death compartment. Also, infected individuals can receive vaccination during preliminary stages of disease. The authors develop an integrated epidemiological-optimization model to maximize vaccine coverage and minimize the shortage of medical items at the PODs during the outbreak.

Yin and Büyüktahtakın (2022) formulate a multi-stage risk-averse vaccination-logistics model for the Ebola pandemic in Democratic Republic of Congo. In this approach, ring vaccination can be only performed at Ebola Treatment Centers (ETCs). It should be noted that establishing these centers at multiple regions is strongly constrained by available bed capacity and budget. The fluctuation in transmission rate between infected individuals and their close contacts is represented by a set of scenarios. The proposed model determines the optimal location of ETCs in addition to the optimal vaccination strategy tailored to each region in each time period to minimize the expected number of infected individuals[42], deaths and its conditional value at risk during the time horizon. The problem is solved in its extensive form with 32 scenarios and five periods.

Bertsimas et al. (2021b) present a predictive-prescriptive framework to optimize the effectiveness of the vaccination sites in the overall vaccine allocation. The authors take into account for various population centers, distances to vaccination centers and age-risk classes in the United States. The predictive model employs the DELPHI module (Bertsimas et al., 2020) to improve the time-dependent allocations of vaccination for various age-ranges. This module takes the dynamics of COVID-19, vaccine effectiveness budget, and zonal demographic information as input. The result of predictive module is used as an input itself for the related vaccination-facility location problem, in which one minimizes the death toll, number of exposed individuals, and distances to be traveled between vaccination centers and metropolitan areas. The coordinate descent algorithm is employed to tackle the bilinearity and nonconvexity in the location-allocation problem. To re-

[40] https://www.reuters.com/business/healthcare-pharmaceuticals/who-lays-out-plan-emerge-emergency-phase-pandemic-2022-03-30/

[41] B is the compartment representing the contamination

[42] And the close-contacts compartment.

duce average distances traveled[43] from remote communities to vaccination centers and resolve the vaccine assignment disparity issues in the United States, Bravo et al. (2022) model the COVID-19 vaccination facility-location problem by considering 58,000[44] vaccination centers as a large-scale MIP. The authors report a 62% reduction in average traveled distances. The key observation is that the location of vaccine centers are more critical than their capacity, specially when reducing disparity matters.

Zhang et al. (2022) tackle the mass COVID-19 vaccination scheduling of healthcare workers with an exact logic-based benders decomposition approach and a metaheuristic solution algorithm. In this study, opening vaccination centers entails a fixed cost, see Bravo et al. (2022) for vaccination centers with no fixed costs. The aim is to schedule healthcare workers in batch formats for vaccination at vaccination centers. A vaccination center may assign an appointment to a group or reject scheduling a batch. The proposed decision framework seeks the optimal opening of a set of vaccination sites to allocate time slots to accepted batches. The objective is to minimize the opening costs, traveled distances between scheduled batches of healthcare workers and vaccination sites, appointment rejection costs, and vaccination tardiness costs.

4.3.5 One vs. Two Dose Coverage

Matrajt et al. (2021) analyze single- and two-dose vaccination policies for 16 age groups in the state of Washington. Each dose of vaccination may provide three types of partial protection to each vaccinee: (i) reduction in the probability of getting infected when exposed to an infected person, (ii) reduction in the chance of developing symptoms, and (iii) reduction in the transmission rate of an infected individual. These 16 age-groups are integrated into a set of five vaccination ranges. To examine vaccination policies with various number of doses, MADS, a derivative-free blackbox optimization algorithm (Audet et al., 2021) performs a global search over all feasible vaccine allocations to these five groups. The compartmentalized model then approximates the effect of each allocation on future compartment sizes to compute a desired objective. Five objective functions to minimize (1) the cumulative number of infections, (2) symptomatic infections, (3) deaths, (4) maximum number of ICU hospitalizations, and (5) non-ICU hospitalizations are separately examined at each feasible allocation. In various settings, including low, moderate, and high transmission rates, the vaccine supplies for single and double doses are tested, considering the limitations of supplying the second dose vaccination for those who received only the first dose. The authors justify that using a single-dose vaccine with high efficacy may reduce the mortality rate by 22%. However, two-dose vaccination outperforms the single-dose when the host population is facing an infectious virus with high transmission rate.

4.4 The Allocation of Medical Resources and Personnel

As an infectious disease propagates through the host population and transforms from a few cases to an epidemic, the preparedness plans will be replaced by response guidelines/decisions when shortages in medical resources and staff emerge; then, triage decisions taken for individuals will be replaced by triage decisions for a group of individuals, city, or state when capacity depletions, shortages and disruptions frequently occur in healthcare systems.

[43]Without fixed cost of establishing the site.
[44]https://www.vaccines.gov/

In this section, we review research studies that address how scarce medical resources, stored at national/regional stockpiles or hospital inventories can be efficiently redistributed in an equitable plan at the time of public-health emergencies (see Melman et al. (2021) for a simulation framework to allocating scare hospital resources during the COVID-19 pandemic).

Recent pandemics such as the flu and COVID-19 often attack the respiratory system, imposing a need for mechanical ventilators for ill patients. Since these ventilators are of importance for other patients too, shortfalls in the allocation of ventilators can be easily envisioned (Mehrotra et al., 2020). All studies reviewed in section §4.4.1 investigate ventilator allocation at the state level, except Zaza et al. (2016) who propose a decision support system for the allocation of ventilators at the hospital level. In the context of medical resource allocation problems, hospital beds are accounted as scarce resources for admitting distinct patients with various ranges of health issues. Due to these differences, bed capacities mostly can not be shared between various wards of a hospital, see Ouyang et al. (2020) for an allocation of beds in the general ward and ICU. In section §4.4.2, we review research studies that investigate bed allocation to control Ebola (Büyüktahtakın et al., 2018; Yin and Büyüktahtakın, 2021; Long et al., 2018), seasonal flu (Liu et al., 2020), or COVID-19 (Abdin et al., 2021). Yin and Büyüktahtakın (2021); Abdin et al. (2021) address the equity in the bed allocation problem.

In section §4.4.3, we recall the statistical forecasting applications for bed allocation in hospitals.

4.4.1 Ventilator Allocation

Zaza et al. (2016) investigate reallocating ventilators at the hospital level, while the availability of space and experienced staff are of paramount importance. The authors present a conceptual model which considers a hierarchy for determining demands from the finest to the highest locational granularity including patients, hospitals, states, and federal levels. To reduce the disparity, a decision-making setting is devised to allocate/reallocate ventilators based on each state's population, the availability of experienced staff to utilize extra ventilators, and the patients' clinical statuses.

Mehrotra et al. (2020) propose a stochastic multi-period supply chain model for allocating ventilators to combat COVID-19 in the United States. In the United States, the FEMA[45] keeps an initial stockpile and also produces mechanical ventilators. As demand for ventilators varies with time and location, both shortfalls and excesses can be observed. The decisions to be made at FEMA consist of determining ventilator reallocation decisions to/from each state during each time-period to retrieve shortfalls and excesses. A state-dependent risk-averse parameter adjusts these reallocation decisions to make reallocating ventilators ethically more permissible. The FEMA's ultimate goal is to minimize the expected shortfalls of mechanical ventilators during a multi-period time-horizon. The multi-period stochastic model is solved in its extensive form.

Blanco et al. (2020) propose a robust reallocation model to redistribute the time-varying shortfalls/excesses of ventilators and other medical resources at the demand points in a hub-and-spoke model in Spain[46]. Various robust objectives such as (i) minimizing the maximum unmet demand observed over

[45]Federal Emergency Management Agency
[46]With paths from the highest level, i.e., country, to a finer tier like regions, provinces, and cities while only consecutive tiers are connected to each other.

periods or (ii) over the whole time-horizon are designed to derive conservative decisions leading to the least unavailability of medical items. The authors also construct a minimax regret objective function, with which the decision-maker seeks a redistribution plan with the least total deviation from scenario-based plans. A two-phase matheuristic algorithm first splits the overall time horizon into single-period subproblems to be solved efficiently, and then integrates the successive solutions to construct a complete redeployment of medical resources.

Bertsimas et al. (2021a) devise a predictive-prescriptive framework for ventilator reallocation in the United States. In the predictive phase, using the DELPHI model, one can predict new infections and then estimate the corresponding ventilator demands for the next period. In the prescriptive module, an assignment framework determines the optimal reallocation decisions to fulfill such demands. To do so, the availability of ventilators from previous period determines the excess and shortfall points and accordingly the reallocation decisions and their quantities.

Yin et al. (2021) investigate obtaining the optimal ventilator allocations when the size of untested-asymptomatic infected compartment and time-dependent transmission rates are uncertain parameters. In this setting, the face-mask, social distancing, and lockdown can be imposed to contain COVID-19. The underlying problem is modeled as a multi-stage risk-averse Stochastic Programming (SP) to reduce the total number of infected individuals and death cases, see also Yin and Büyüktahtakın (2022) for the same optimization framework for the vaccine allocation problem. The uncertainty in the actual number of untested-asymptomatic infected individuals is approximated by discretizing Normal distributions to construct a set of discrete scenarios. To shorten the optimality gap and the running time, the authors develop various lower/upper bounding schemes based on single-region restricted problems. Ho et al. (2019) propose a dynamic resource allocation scheme to provide non-stationary policies that impose prevention, screening, and treatment interventions to maximize QALYs. The authors devise a static roll-out policy to compute an approximated expected QALYs from the current state of health of a the sub-population to the end of time horizon. A backward scheme engages this static and approximated policy to generate a dynamic sequential multi-intervention policy.

4.4.2 Hospital Bed Allocation, Capacity Estimation, and Expansions

Büyüktahtakın et al. (2018) propose an epidemic-logistic optimization model in which one establish treatment centers with predefined bed capacities to provide treatment and control the spread of Ebola in multiple regions. The Ebola's compartmentalized dynamic is extended by repartitioning each compartment into regions, where the migration of susceptible/infected individuals from/to the surrounding regions is considered. The migration to other regions, epidemiological dynamics, budget, and capacity constraints mutually govern the spread of the Ebola virus and the associated facility location subproblems. We note that more than two billion dollars as a loan is given to three countries in Africa, which in general represents the severity of a potential Ebola pandemic and correspondingly the monetary value of the treatments. The numerical results conducted on the 2014-2015 outbreak in Guinea, Liberia, and Sierra Leone show a strong evidence of a significant reduction in the total number of deaths and infected individuals when the necessary budget is assigned for setting up the ETCs.

Yin and Büyüktahtakın (2021) sought equity in the distribution of the ETCs and their bed capacities to control Ebola in Guinea, Sierra Leone, and Liberia of West Africa in a multi-stage SP framework under stochastic transmission rate. The prevalence of Ebola can be in two ways, (i) person to person or (ii) touching an Ebola patient dead-body before the funeral. To characterize the uncertainty in the transmission rate of Ebola, its lower and upper bounds are used to generate propagation scenarios for an 8-stage time-horizon. First, the authors justify the value of stochastic solutions in minimizing the infected population and death cases under generated scenarios. The number of infected individuals and ETC bed capacities are defined as the target equity measures over multiple regions. To preserve equity, the mean-absolute deviation measure restricts the deviation between the region-based fraction of the infected individuals and the region-based proportional population to a predefined value. Surprisingly, when no equity constraint is enforced newly infected individual/funeral cases tend to decrease.

Abdin et al. (2021) establish a nonlinear program to examine the effect of testing and assigning treatment capacities at hospitals to better control COVID-19 and simultaneously derive equity over three major metropolitan regions in France. This novel pandemic model including the asymptomatic, mildly symptomatic, and severe symptomatic compartments for infected individuals is constructed to precisely imitate the COVID-19 dynamics. These compartments are further repartitioned into individuals whose infection is either confiremed so they are in isolation or not. The COVID-19 tests will be performed only on individuals who do not show severe symptoms. The individuals with severe symptoms will be admitted to hospitals. The decisions are how one can optimally: assign COVID-19 test capacities to individuals with asymptomatic or mild symptoms, and design new test capacities at various regions, while inter-regional mobilities and demographic correlations are taken into account. To preserve equity between regions, the Gini deviation measure to compute the weighted[47] deviation of allocated resources between regions is employed in the objective function. As expected, the treatment resources are mostly allocated to more populated metropolitan areas, except in the cases in which the incoming mobility flow to these regions was more, see also Birge et al. (2022) for the importance of mixing populations. To validate designing new test capacities, it is shown that performing COVID-19 tests can delay the admission-capacity depletion at hospitals by 2.5 months.

Liu et al. (2020) prescribe the optimal design of distant general wards in a minimax optimization setting to control the seasonal flu by providing treatment or isolation. A hospitalization compartment and a partially infectious compartment are added to the SEIR model. Both opening and closing of these temporary wards that provide hospitalization incur fixed costs. These wards are necessary to perform treatments at a unit variable cost for the infected or hospitalized patients. The maximum unsatisfied demand among all regions and periods is minimized to precisely simulate the H1N1 low mortality rate. The model is validated by conducting numerical experiments on the 2009 H1N1 pandemic in China by changing the intervention start-dates and measuring its effects on the number of isolated wards. Finally, it is numerically shown that a two-month delay in building these wards will results in a very steep increase in the necessary general wards from few

[47] based on the importance of regions

thousand to more than 100,000, highlighting how insufficient capacities may turn an infectious disease into an epidemic.

Long et al. (2018) compare four policies to plan for distributing medical interventions e.g., assigning ETU beds to patients for controlling[48] Ebola in highly dispersed sub-populations in West Africa. In this problem, distance-based mixing contacts[49] and behavior dampening[50] are taken into the account of the SIR model. In the first policy, these resources are allocated based on the cumulative number of infected individuals per region. The second policy works as follows: a sorting scheme first computes an upper bound on $\mathscr{R}_0$ per region by maximizing input/output mixing ratios to/from each region and asymptotic dampening. Then, pharmaceutical resources will be deployed according to the quantity of these upper-bounds until they get exhausted. The third policy refers to a one-step myopic policy with which one can estimate the parameters of the SIR model and apply forecasted demands to allocate medical resources in a predictive-perspective fashion. In the last approach, the authors model the problem as a finite-horizon ADP in which, the state-space variables are the compartments' size in the SIR model and action space includes all eligible bed assignments to regions. Surprisingly, the one-step myopic policy outperforms all other three algorithms.

4.4.3 Bed Capacity Estimation and Expansions

To address an increase in mortality rate of the non-ARIs patient, Gutierrez and Rubli (2021) examine hospital bed capacity expansion and patient reallocation by estimating the patient composition at wards and inflow shocks to hospitals' occupancy due to acute respiratory infections (ARIs) caused by the 2009 H1N1 pandemic. A regression model is devised to simulate the existing correlation between the number of ARI-patients admissions, the death rate of the non-ARI patients, the number of deaths, and their weekly effects. Only the local effects of the outbreak collected at the surrounding hospitals will be used in the regression model. By estimating the non-ARI patients' mortality rates, a policymaker can make precise triage, patient reallocation, or capacity expansion decisions to redirect patient congestion to reduce the mortality rate among all admitted patients.

Yang et al. (2021) provide probabilistic forecasts in the form of confidence intervals for bed demands for ARI and ICU patients at several hospitals, being prepared for the second wave of COVID-19 at the county level in California. To perform forecasting, the historical data for bed demands and a point forecast for the total regional hospitalizations are in hand. To estimate ward-specific forecast intervals, the authors equivalently aimed to predict the fractions of regional hospitalizations entering into these two wards. A probabilistic guarantee for the point estimate of quantities of interest is obtained by performing a simulation technique that generates Poisson hospitalization-arrivals, and bootstrapping the simulation results.

For predicting the bed occupancy of confirmed and suspected COVID-19 cases in ICUs and general wards, Heins et al. (2022) propose a forecasting model for three locational granularities such as local, regional, and the Free State of Bavaria. In this setting, the confirmed cases have a deterministic LOS[51] in isolation, but the uncertainty stems from those suspected cases, i.e., undiagnosed (Gao et al., 2021), who must stay until a positive test result is obtained. The later uncertainty significantly distorts the required bed capacity at hospitals. In a multi-step regression scheme, bed occupancy is estimated based on the historical cumulative occupancies, regressed newly infected patients, and ratio of newly infected patients who will be hospitalized subtracted by patients who stayed their regressed LOS.

4.4.4 Medical-Staff Allocation

Bienstock and Zenteno (2015) investigate the effectiveness of a robust optimization framework to preserve adequate staff levels at multiple Emergency Departments (EDs) during lockdown periods of a flu pandemic (the interested reader can see Saghafian et al. (2022) for the effect of hospitals closures amid the COVID-19 pandemic). A modified-SEIR model with nonhomogeneous transmission rates, and social contacts following Poisson distributions in both host population and EDs workforce is established to capture the flu dynamic. In this approach, the uncertainty set is contagiousness probability which is modeled as an interval. A robust multi-period ED schedule consists of staff-level decisions that entail the minimum total staff costs, when the worst contagiousness-probability is governing the propagation of the flu pandemic. To tackle the infinite-dimensional RO formulation, the authors propose a decomposition approach. At each iteration, when a staffing schedule represents an under-priced[52] staffing whose total costs does not correspond to the maximum regret over the contagiousness interval, a cutting plane removes such a staffing solution. Beeler et al. (2016) analyze the effect of staffing at the mass flu immunization clinics on the vaccination volume, patients' waiting time, operating costs, and flu transmission inside these clinics in Toronto. A mass-vaccination clinic consists of the following sections: an outdoor waiting line, indoor waiting line, registration, H1N1 flu assessment counter, vaccination, and recovery wards where, at each section, only one patient can be served. Except for the flu assessment section, the reneging and bulking are assumed in order to model realistic bounds on the waiting times and queue lengths, while considering various family batch sizes. The authors represent the uncertainty in the spread of flu, throughput, and operational costs by one baseline scenario and several hypothetical scenarios in an ABS package. The simulation setting numerically validates the marginal benefits of adding staff to these clinics to reduce transmission rate, see also Mondschein et al. (2022) for investigating the waiting times inside and outside of the voting centers during pandemic. When patient satisfaction is of paramount importance, Gao et al. (2021) prescribe a robust optimization technique to tackle an imbalance between the demand and supply of medical staff in the presence of data contamination during the COVID-19 pandemic. The authors highlight that demand uncertainty stems from the uncertainty in undiagnosed patients who are categorized into two groups: patients with either mild or severe symptoms. Data contamination occurs when staff demands in collected data are too small or too large, caused by personal preferences or highly volatile operating conditions. By observing the imbalance between demand and supply, the authors first label the underlying hospitals with constant shortages or surpluses, and balance points in their medical staff. Based on these labels, each region entails a distinct utility function, estimating the staff transfers from supply points to demand points. The utility function will be max-

[48] Reducing transmission from infected to susceptible

[49] Individuals from different sub-regions may have contact with susceptible individuals in other regions

[50] Reduction in transmission rate, when individuals greatly restrict their social visits during an outbreak.

[51] Length of stay.

[52] entailing an incorrect estimation of the future costs.

imized over all scenarios in the SP setting. To produce robust solutions that are less sensitive to outlier demands, the authors develop two robust-optimization models based on the median and weighted median of the number of undiagnosed patients.

5. Optimal Decisions for Policymakers

In this section, we review research studies in which one investigates the process of allocating scarce governmental resources or deriving prioritized public-health policies to cope with pandemics. These decision- or priority-making processes strive for a high level of research attainments, not only for all monetary and non-monetary expanses these decisions entail, but also how they can be better translated into the life-saving triage decisions. The competing players (the pandemic, WHO, governments, states, public, media, etc.) in the pandemic, their interactions, and the lack of a blueprint of the pandemic's severity may easily hinder general welfare, from policymaker's perspective. Game theory is the fundamental mathematical setup to make decisions for a group of players who may not seek the same objectives, and their individual and conflicting interests turn the decision making into a competing environment (Fudenberg and Tirole, 1991).

Whether the problem fits in the game theory setting or mathematical programming, both settings lead to insights describing the life-saving policies with major contributions of OR&M applications in this field for policymaking purposes. We categorize these studies first based on their decision types/usages in the pandemic, and then who the players are.

5.1 The Pandemic Signals

In this part, we review optimal policies to generate alerts with specific qualities to inform other players. The pandemic signals in the consecutive periods between the WHO and a member government (Alizamir et al., 2020), or to reduce economic/welfare expenditures in a game between government and public (de Véricourt et al., 2021).

Alizamir et al. (2020) design a Bayesian persuasion game in which a sender agent, here, the WHO generates various (in terms of quality and accuracy, e.g., high or low probable signals) signals by predicting recurring pandemics or natural disasters to inform a receiver agent to earn reputation through a history of sequential events. On the other hand, the signal receiver, in anticipation of future events[53] may take an early action (i.e., before observing the disaster event or experiencing a disease outbreak declared by a signal) as an intervention to mitigate future excessive costs. It is assumed that pandemics entail fixed costs to both sender and receiver players. In this setting, the sender's signal is in the form of a probability distribution capturing the occurrence of an outbreak or pandemic. The authors provide closed-form optimal policies for both parties in this game. Surprisingly, the sender's optimal strategy implies that she will downplay/exaggerate the risk of disaster occurrences when her reputation is improving/deteriorating.

de Véricourt et al. (2021) propose a game-theoretic approach to investigate how government may inform the public about a pandemic to reduce its effects on the economy and healthcare systems. In this setting, each individual independently decides whether to comply with social distancing or not. In this setup, both being infected[54] and staying at home entail their associated costs and economic expenditures. The government's information policy is in the form of a probability distribution i.e., a set of distinct messages representing the support set, and a set of probabilities associated to these messages. Each message corresponds to a predefined severity of the pandemic. Given the fact that the pandemic's severity is accounted as private information, four policies are defined to treat it: full disclosure, no disclosure, exaggerate, or downplay[55]. Each person in the society updates her belief about the severity of the pandemic when she receives the government's message and then decides either to comply or not by employing the updated belief. The optimal individual choices at the equilibrium is a threshold-based policy on their compliance costs. Here, the government's cost function is defined by a convex combination of health and economic burdens entailed by a pandemic, but prioritized based on government's preferences. The optimal policies for a government will be (i) full disclosure when its preferences are balanced, (ii) exaggerating the risk when healthcare cost matters, and (iii) downplaying the risk when economic burdens of social distancing are high.

5.2 Robust Surveillance Policies

Tang et al. (2021) investigate devising a robust surveillance strategy for monitoring the occurrence of pandemics in a zero-sum game. This game is defined over a network of individuals. While policymaker tends to reduce the cost of performing tests to detect a pandemic and its extent, pandemics are interested in creating large outbreaks. To infect the host population, the pandemic must choose a set of agents to be initially infected. The policymaker independently chooses (or maybe not) a set of agents to monitor (syndromic surveillance §3.1.1), perform tests and detect any potential infectious disease. Both strategies are represented by probability distributions. In such representation, each point in the discrete support distribution represent a group of agents from the host population. The success for the pandemic means increasing the number of infected individuals before being detected and hedged by imposed interventions. Accordingly, the success for the policymaker is to prevent the pandemic to reach a high prevalence resulted by infecting many agents.

The uncertainty lies in the imperfect knowledge of the uncertain transmission probability in each contact that is implicitly modeled as an interval. In this setting, the underlying pandemic propagating as a diffusion process seeks two conflicting objectives: in the same time it plans to create a large outbreak, and simultaneously it wants to remain undetected. A pair of primal-dual linear programs, respectively representing policymaker and disease problems, approximate the Nash equilibrium by choosing agents to be tested and infected successively that eventually results in an optimal utility for both players.

5.3 Designing Intervention Policies

In this section, we review the role and quality of interventions in distant communities (Brandeau et al., 2003), centralized and decentralized interventions (Brandeau et al., 2003; Biswas and Alfandari, 2022), the tradeoff between imposing closure and the amount of resulted unemployment of non-teleworkable subpopulation (Birge et al., 2022), individual social distancing (Kordonis et al., 2022), and competing for limited resources at international levels to perform interventions (Salarpour and Nagurney, 2021).

[53] Follow independently a Bernoulli distribution

[54] Due to not complying with social distancing and the size of the infected population.

[55] Bounded from above and below, respectively

Brandeau et al. (2003) investigate the optimal pharmaceutical and nonpharmaceutical resource allocations to control an infectious disease in multiple distant populations. These resources will be translated into governmental interventions and their corresponding severities. The policymaker chooses each intervention and its level of performance which fixes the transmission rate at a desired level. This in turn changes the pandemic dynamic. Each level of resources to fix that transmission level entails its distinct fixed and variable costs. The decisions are determining the optimal investments or equivalently optimal infection transmission rates for each population to minimize the total number of infected individuals in all regions by the end of the time horizon, under a limited budget. Several analytical results on the convexity and concavity[56] of infected individuals' graph are presented that relates the infected population with the magnitude of the reproduction ratio and transmission rate.

Biswas and Alfandari (2022) also optimize sequential nonpharmaceutical intervention decisions such as lockdown and curfew periods in both centralized (national-level decisions) and decentralized (region-based decisions), to control the spread of COVID-19 in 13 regions in France. Imposing these interventions aims aiming at minimizing the infected and death cases. A wide variety of interventions including self-isolation, travel bans, school closures, public gathering bans, lockdown and their combinations can be enforced to control the spread of COVID-19 when propagating under a modified-SIR model equipped with hospitalization. As in Brandeau et al. (2003), the available interventions are constrained by a limited budget for execution. Different intervention levels fix transmission rate to distinct levels that will reduce the number of infected individuals accordingly. The numerical results show that the severity of interventions will be reduced over time. Furthermore, the flexibility of decentralized decisions results in up to 20% fewer infected individuals.

Leveraging pre-pandemic phone mobility data, Birge et al. (2022) establish an optimization framework to control the COVID-19 pandemic in multiple neighborhoods of New York City (NYC) by restricting economic activities in predefined regions. To present various levels of mobility, each neighborhood is divided into three sub-groups corresponding to teleworkable, nonteleworkable, and unemployed individuals. Each individual can travel to other neighborhoods due to work or leisure, while the associated durations are given beforehand (e.g., big data of pre-pandemic time)[57]. Then, each susceptible person in this modified-SEIR model can be infected when visiting other neighborhoods. The decisions to make are determining the optimal allowable economic activities or equivalently closure interventions in each region. This corresponds to the fraction of work and leisure durations in that regions. Therefore, the fraction of region-based economic restrictions maps the size of mixing populations who are visiting each region, whether for working as a nonteleworkable person or having leisure time. It is worth noting that although the goal is to reduce infected and exposed individuals by increasing closures, unemployment will tend to increase which entails extra economic costs. The numerical experiments show resuming nonteleworkable jobs up to 42.4%.

Kordonis et al. (2022) investigate optimal social distancing strategies of infinitely many players grouped by a finite number of asymmetric infection cost functions. For each player, a probability distribution determines her clinical status in a separate SIR model, where social distancing as an available intervention may reduce the number of infected players. A cost function comprising the cost of getting the infection, and taking social distancing actions in ordinary visits or public places is associated with each player. The authors propose a piecewise constant action function during each period of time horizon to characterize optimal policies. Further, it is shown that these optimal policies are of threshold type during the time horizon. In the decentralized version, a person with a high infection cost function must impose a more severe social distancing action on herself. Finally, the variational inequalities are used to validate the existence of the Nash equilibrium.

A stochastic generalized Nash equilibrium is introduced by Salarpour and Nagurney (2021) to model the problem governments are facing when competing to provide N95 masks and ventilators in the COVID-19 era. In a two-stage SPR setting proposed to resemble the preparedness and response plans, each government may take two sets of decisions before and after the declaration of a pandemic, respectively. A Nash equilibrium is then a point composed of the supply storage and purchasing quantities before and after declaring pandemic. At equilibrium it is evident that storage and purchase decisions must entail the least expected unmet demands and procurement costs as a disutility function for all countries, see also Nagurney (2021).

5.4 Vaccination and Test Production Policies

In this section, we elaborate on research studies on the cost-sharing and payback strategies (Chick et al., 2008), a menu of contracts for unverifiable production promises (Chick et al., 2017), optimal subsidies (Yamin and Gavious, 2013), international levels (Mamani et al., 2013), production yield (Arifoğlu et al., 2012; Arifoğlu and Tang, 2022), and multi-phase vaccination (Yarmand et al., 2014).

Chick et al. (2008) investigate the manufacturing contracts for flu-vaccine production to fulfill the government's orders in both game-theoretic and centralized SC frameworks, when players or decision-maker are faced with various uncertainties in the pandemic propagation. The government seeks the minimization of the expected infected population and the manufacturer production yield, while the manufacturer aims to minimize the expected manufacturing costs. Both manufacturer production and government ordering problems are modeled as newsvendor models. It is shown that the necessary condition with which the coordinated system outperforms the game-theoretic formulation is establishing production/order contracts that are cost-beneficial for both government and manufacturers such that prescribing vaccination monotonically reduces the infection. Furthermore, under cost-sharing and payback contracts where the government pays a fraction of production costs, both the game-theoretic and coordinated settings result in the same pair of order-production contracts, enabling manufacturers to mitigate the excess production risks.

In a game-theoretic setup, Chick et al. (2017) study the flu vaccination contracts between a government and vaccine manufacturers facing probabilistic production yield and other uncertain factors. Such uncertainties mostly lead to a two-stage production process, including a late production period. The price of fulfilling production shortfalls deferred to the late production period is higher due to extra administration fees, production/unit effort costs and moral hazards. The underly-

[56] In general, the curvature.

[57] After the pandemic, teleworkable, and unemployed individuals only visit other neighborhoods during leisure time.

ing problem is analyzed in two settings whether manufacturers' productivity factors are assumed to be private i.e., it is unverifiable information from the government's perspective, or alternatively, are public information. In the setting where uncertain factors are public information, both selfish and coordinated productions are examined. For the latter, it is shown that mutual profits in wholesale contracts can be obtained only if there is no extra administration penalty for delayed productions. When manufacturers' production factors are unverifiable, the government may establish an optimal contract design problem to minimize the expected costs by setting up a menu of transfer payment functions tailored for each level of productivity. Interestingly, this menu of contracts imposes manufacturers to either select contracts that match their actual production efforts, or reveal their unknown production levels to the government.

Yamin and Gavious (2013) assess the effect of paying subsidies in designing vaccination policies in a game between the healthcare policymaker seeking the maximization of vaccine coverage, and the social planner interested in increasing social welfare. In this game, individual decisions in the host population are negligible whenever the probability distribution of vaccination compliance for all individuals is the same. In this setting, the social planner interest is to pay subsidies that will determine vaccine compliance and coverage in the host population. Both vaccination and not-getting vaccinated, that probably leads to getting infected, entail their associated utility/disutility costs. Given the probability distribution of getting infected under SIR dynamics, the authors present the closed form for compliance probability at the Nash equilibrium, whether the policymaker pays subsidy or not. The optimal strategy turned out to be the higher subsidies for flu with lower severity and low-risk age groups to preserve vaccination for the high-risk group ranging from 6-month-old children to four years of age.

Mamani et al. (2013) investigate the optimal vaccination policies of several countries during a pandemic started from a source country. Two types of prevalence are considered (i) a star-shaped network where the flu only spreads from the source country to the other countries, and (ii) a complete graph model in which, the flu spreads from any country to another. The authors examine three types of setups to derive optimal vaccination policies: (i) a game-theoretic setting, where each country minimizes its total costs (vaccination costs and welfare benefits) (ii) a centralized system to minimize the total costs entailed to all countries, and (iii) coordinating contracts in which the source country receives a subsidy from other countries for performing vaccination. When the cost of vaccination for a fraction of population is more than its benefits, the best response solution is strictly less than one, implying the unavailability of vaccine for all risk groups in the first and second approaches, see also Perez-Tirse and Gross (1992) for a detailed exposition of flu vaccine pharmaceutical and socioeconomic costs. It is shown that coordinating contracts reduce the centralized system costs in both prevalence models because of the reduction in the total number of infections.

Arifoğlu et al. (2012) investigate a game between a manufacturer and a host population under production yield uncertainty and selfishness of individuals who seek for extra doses. Such selfishness leads to vaccine shortfalls for high-risk groups. Here, a high-risk group is determined by a disutility threshold i.e., when the total cost of not getting vaccinated including the cost for drugs, subsidies, lost wages, or death of an infected individual is higher than a predefined threshold. In this setting, searching for a vaccine as well as receiving it impose their related and distinct costs, whenever there is a chance to obtain a dose for the individual searching for it. In this setup, the probability of getting infected is based on the vaccinated fraction of the population[58]. The authors first present the optimal vaccinated fraction and the number of infected individuals at the Nash equilibrium using a threshold-based policy that can be characterized by the level of infection disutilities. At equilibrium, each individual compares her individual infection disutility function against the overall expected disutility costs of searching for vaccine doses to determine her chance for receiving a vaccine. Arifoğlu and Tang (2022) prescribe a two-sided incentive program to resolve mismatches between supply and demand of flu vaccine in an imperfect vaccine setting, where both vaccinated and unvaccinated individuals may transmit the infection. In this centralized incentive program, the timing is as follows: the social planner offers a transfer payment menu along the wholesale price to the manufacturer that will determine manufacturer's production level; then the policymaker offers incentives for vaccination; and finally, each individual decides to seek for vaccine or not. Both offered incentives are based on the manufacturer's production level. It is worth mentioning that the fraction of vaccinated individuals in the decentralized setting may be fairly higher than in the two-sided incentive program, which leads to more expected profit for the manufacturer. Thus, from the manufacturer's point of view, even receiving the transfer payments in an incentive program may not lead in her favor. To retrieve this situation, the policymaker may derive an interval of fixed payments, under which the expected profit of the manufacturer in the incentive program is higher than the decentralized version, thus enticing both manufacturer and individuals to behave socially optimal.

While mass vaccination of a large population is the most effective way to control an epidemic in its early stages, even for seasonal influenza, insufficient vaccine doses and stockpile capacity limits are the main reasons to decrease the viability of a mass vaccination in action. Yarmand et al. (2014) tackle the above issue by modeling a two-phase vaccination plan for multiple regions with a two-stage SP constrained by a limited budget. In this approach, each region should be vaccinated at a minimum level, while the second phase of vaccination only assigned to those regions where the first vaccination phase has not completely controlled the disease yet. The authors numerically verify that the optimal vaccine coverage during the first phase in North Carolina has resulted in large monetary savings, a moderate attack rate, and coverage equity between various counties.

6. Healthcare Supply Chain Management under Pandemics

The COVID-19 pandemic has drastically restrained the healthcare supply chain and its main components. The high demand for medical items and staff, pharmaceutical ingredients, ventilators, etc., have disclosed its key vulnerabilities[59], which further led to a fierce competition to buy pharmaceutical supplies and rising prices[60].

[58] Hazard is the minimum portion of individuals whose vaccination imposes zero probability of getting infected to the host population.

[59] Ramachandran et al. (2020) state the fact that the best estimation of the number of ventilators in the United States is based on a 2010 survey and there are 15 states with > 50% deficit in ICU beds.

[60] https://www.mcknights.com/news/analysis-ppe-costs-increase-over-1000-during-covid-19-crisis/

In a supply chain network facing frequent disruptions and shortages with ripple effects throughout its network, making strategic decisions such as building new hospitals, roads/railroads, fleet of vehicles, airplanes, cargo ships, manufacturers or even manufacturing lines are not the first viable corrective actions, yet are considered extremely expensive ones. Furthermore, the viability[61] of such decisions cannot be precisely measured and justified over a long time horizon; e.g., post COVID-19 stockpiles of unused ventilators[62]. However, tactical or operational corrective decisions are cheaper and can be taken quickly after SC network failures. We may refer the interested reader to the following examples: constructing temporary camps, temporarily transforming stadiums and schools into vaccination centers, appointing General Motors and Ford manufacturers to build new ventilators[63], relocating extra ventilators between states at FEMA, reusing PPEs like masks, producing PPEs at Ford and Honeywell companies, restricting toilet papers each person can buy at retail stores, and many more.

But the question still remains; What can we do beforehand? One way to account for these failures and disruptions in SC networks before they happen is to consider planning for reserve personnel and capacities, multi-usage spaces, and other contingency protocols. Taking preparedness actions before natural disasters happen also incur its own relative complexity at the time of making strategic decisions as discussed above, which may profoundly depend on the size and length of disruptions, frequency of facing failures, correctly pricing the extra design, fortification and capacity[62] in anticipation of disruptions.

In this section, we review the previous studies in which, redesigning healthcare supply chain networks under pandemic or other natural disasters to secure robustness and resilience are addressed.

6.1 Facility Location Problem

Cui et al. (2010) propose a nonlinear reliability and reserved facility location design under disruption risks in natural disasters, where customers must be reassigned to other facilities when the designated facility is no longer available to fulfill its service. The layered SC network in this paper works as follows: the demand will be served from the second-layer facility only if the first-layer facility has already failed to fulfill the customers' demand due to disruptions or disasters, e.g., hurricanes. In this setting, each customer may also receive its demand from a set of DCs. Once all these DCs failed, an adhoc warehouse will fulfill customers' demand. Therefore, both the set of DCs to be assigned to and the governing distribution of receiving the total demand from them should be determined simultaneously. In such a way, the expected design costs turn into a nonlinear term which is tackled by a linearization technique. A customized Lagrangian relaxation algorithm is designed to tackle the problem at hand.

Liu et al. (2021) tackle the facility location problem to supply emergency medical items, test-kits, and vaccination to control the COVID-19 pandemic, equipped with capacity expansions to fulfill increasing demands. At each demand point, a fraction of stochastic demand as a predetermined service level must be satisfied with certainty. In the objective function, one minimizes the total unmet demands, facility design costs, and capacity expansions. A two-step solution framework is devised to seek near-optimal solutions. First, the optimal location of facilities and their initial capacities are determined such that the expected demands at given service levels are satisfied. Once the initial capacities are set, a dynamic allocation policy assigns capacity expansion decisions while only enlarging capacity is allowed. The original two-stage SPR is approximated by its sample average approximation counterpart and formulated.

Liu and Zhang (2016) establish a joint SC supply chain design model to design temporary, coupled with an SEIR epidemic model. The supply chain incorporates a network comprising hospitals, distributors, and pharmaceutical manufacturers. In addition to hospital resource allocation and vaccine transportation, the authors also include the inventory management of medical supplies in the proposed decision framework. The proposed approach incorporates the following phases: forecasting, planning, execution, and adjustment. The forecasting step attempts to predict the infected population to be treated at hospitals in the next cycle busing the SEIR epidemic model. In the planning phase, a mixed-integer programming model is formulated that determines the number of hospitals to be open, vaccine inventory management at distribution sites, and the distribution of the vaccines in the network. Since forecasted values of the infected population may be different from the actual observations, the execution of the planning phase may result in both shortages and surpluses. These shortages, surpluses, and actual values can be taken into account to further adjust the SEIR model's parameters and repeat the forecasting phase.

Villicaña-Cervantes and Ibarra-Rojas (2022) investigate the mobile test-labs locations problem to serve several demand centroids, each representing a point of service. Each person can move and choose her point of service from a predefined centroids. Due to considering these movements, an accessibility measure is computed to determine those locations than can serve each individual. To each mobile test-lab are associated the lower and upper bounds for the radius it can operates. The authors then model the problem in a MILP and design a heuristic to solve it where, the commercial solvers are unable to the underlying problems computational complexity, see also Risanger et al. (2021) for selecting pharmacies to ensure access for testing purposes.

6.2 Multiple Order Options

To preserve the resilience, agility, and viability of PPEs, N95 Masks, Gloves, and Gowns supplies in healthcare SCs facing the COVID-19 pandemic, Ash (2021); Ash et al. (2022) present a three-echelon (sourcing, warehouse, and hospitals) model with competing strategies to fulfill such protective items in a multi-period horizon. To better simulate real-life instances, the long and short-term decisions, multiple types of suppliers including long-term contracts, one-time purchases at the open market, and federal emergency stockpiles with fixed and quantity-based costs are envisioned. The objective is to simultaneously minimize the maximum unmet demand and operational costs under demand, supply, and price uncertainties. The RO, SP, and DRO approaches combined with an ϵ-constraint approach[64] are examined to study the structure of long and short-term decisions. The DRO model commonly selects long-term contracts as insurance against excessive short-

[61] the lack of precise pricing for them.

[62] https://www.washingtonpost.com/business/2020/08/18/ventilators-coronavirus-stockpile/

[63] https://www.vox.com/recode/2020/4/10/21209709/tesla-gm-ford-ventilators-coronavirus

[64] The ϵ-constraint approach first optimizes one objective and then optimizes the second objective while the first one is set to the first objective value.

term decisions.

Paul et al. (2022) propose a chance-constrained programming (CCP) model to address major disruptions with multidimensional impacts caused by COVID-19 in major services of the commercial SC companies. The authors first consider a traditional single-item three-echelon supply chain model with a set of suppliers, manufacturing plants, and retailers. The initial plans change to recovery plans when disruptions happen, especially when both social distancing and lockdown reduce the production capacity at suppliers and increase the demands by staying at home. The authors address these disruptions by associating extra costs to both reduced/increased productions as well as acquiring supplies from emergency suppliers. To tackle demand uncertainty at the retailer level, the appropriate chance constraints are imposed to enforce a predetermined confidence level at the regular and emergency suppliers to provide raw materials. An enhanced multi-operator differential evolution algorithm is devised to tackle the problem.

6.3 Inventory Levels, Transportation, and Plans with Confidence Intervals

A four-echelon daily COVID-19 vaccination planning SC problem is modeled by Georgiadis and Georgiadis (2021) in a MILP formulation to determine the optimal transportation/inventory decisions, daily vaccination plans, and medical staff assignments. The inventory levels at central hubs and vaccination centers, perishability of vaccines in refrigerators, the fleet of trucks, and their transportation costs are aptly considered.

Hovav and Tsadikovich (2015) present a multi-period three-echelon SC model in a MILP formulation for production, distribution, and administration of flu vaccines in Israel. The SC network is comprised of (i) manufacturers with weekly production and deliveries to distribution centers (DCs); (ii) DCs that receive vaccines, store, package and then deliver them to clinics; and (iii) clinics that receive the delivery from DCs, store vaccines, and perform the vaccination. The cost function consists of manufacturer DC selection fixed costs, delivery costs to DCs, inventory holding costs at DCs, delivery to clinics, inventory, and administration costs of each vaccine at clinics.

Bala et al. (2021) model the PPEs donor-recipient matching problem in a classic transportation problem to minimize the traveled distances per unit of PPE. The median was 214.3 miles during the COVID-19 pandemic in the United States. To balance surge demands which are typically larger than supplies, a fill rate at each recipient site is defined which measures the ratio of supply to demand. The transportation complexity for small donors is resolved by precluding multiple orders.

Alcock et al. (2022) develop an online application, Shield-Net[65], to match surge requests for face shields in the United States. The problem is formulated as a transportation problem by considering new suppliers in the market, the request's emergency level, size and type, supplier production capacity and location. A transportation problem to minimize the weighted traveled distances and unmet demand is established. During six months, Shield-Net generated 390 request-supplier matches, and a volume of 50,000 face shields, equivalent to 65% successful matches delivered.

[65] http://shield-net.org

6.4 Supply/Demand Redistribution at Hospitals

Parker et al. (2020) propose various optimization models for demand/resource redistributing and load balancing at multiple hospitals. The capacity expansion decisions are envisioned when patient overflow occurs. The authors first present an optimization framework for minimizing surge capacity expansions that also allows transferring non-admitted patients to other hospitals when the hospital's capacity is depleted. This model is further extended to specific groups of patients who require specific bed types. A load balancing formulation is also established to minimize the total absolute load deviations at the hospitals from the average system load to reduce stress at individual hospitals. An optimal resource reallocation model to transfer PPEs and nurses is also proposed.

Rottkemper et al. (2011) investigate a very similar problem, the reallocation of resources, where overlapping disasters may happen to harden an ongoing humanitarian intervention. A central depot must fulfill the unmet demands at the regional depots by sending a limited number of shipments. To tackle demand uncertainty during a 14-day period, penalizing the unmet demand is considered.

6.5 Food Distribution under Multi-Layer Network

Ekici et al. (2014) set up a capacitated multi-period food facility location and transportation problem for an influenza pandemic, spreading according to a modified-SEIR model. An ABS module is devised to model the underlying pandemic with rational compliance and voluntary quarantine, under a fixed reproduction number. The simulation model estimates the number of individuals who need food. The supply chain network consists of four echelons comprising the food-supply warehouses, major facilities, POD, and demand points. To tackle the real-size instances, the authors developed a heuristic solution framework, with which in the first phase the model attempts to satisfy the aggregated demand to make major openings. Then, the disaggregated demand is used to complete the design and flow decisions. Jia et al. (2022) devise a predictive-prescriptive framework for food delivery in local restaurants under rapid market nuances during COVID-19 in Nuevo Leon, Mexico, with a population of 5,000,000. To deal with such steep nuances in food demands, these restaurants may employ the third-party online services to add food delivery when by default, restaurants only can serve customers in a no-contact pickup. To capture highly volatile food demand, first, the SIR model is employed to forecast infected individuals. Finally, the authors develop a two-stage SP model to make partnership and fleet management decisions, consecutively.

7. Future Research and Conclusions

In this part, we elaborate research avenues that can be taken into account for further investigation on the OR&M applications in the pandemic context.

7.1 Surveillance, Signals and Pandemic Statistics

In a recent development at the WHO, the number of deaths due to COVID-19 and its aftermath between January 2020 and December 2021 is estimated to be about 14.91 million[66], see also Ludden et al. (2022) for the excess death cases categorized by sex and age-groups. The overwhelmed capacities prevent the recovery of patient waiting-lists for providing

[66] https://twitter.com/WHO/status/1522195970825535488

elective treatments Wood (2022). The number of infected individuals, hospitalized, quarantined and deaths are vital factors for the WHO and each country, especially in the early stages of the pandemic. These statistics, if correctly analyzed, represent the severity of a pandemic that accordingly determines the quality of pandemic signals, response plans and interventions for the healthcare policymakers. There are studies that investigate the role of the WHO signals at the time of the pandemic to governments.

Future studies can also investigate how in a dynamic-multi period-setting, the member countries may pass their pandemic signals back to the WHO, so the WHO can modify its signals and improve its resource and information management. The member countries' signals evidently consist of their pandemic statistics and current capacities to tackle pandemic. These signals will be sent to the WHO to receive potential subsidies in the form of loans, vaccines and the priority in receiving it, specialists, private guidelines, etc. These subsidies may be further assigned to better perform contact tracing in these countries. At the WHO level, high-quality signals received from member countries lead to better resource management decisions.

7.2 Stockpiles

Localizing versus centralizing stockpiles is already investigated by researchers who justify localization because of a higher efficiency when the ventilators are redistributed over shorter distances. Also, the ventilator shortages during the COVID-19 era led to its redistribution at FEMA, although when its outbreaks got contained many ventilator stockpiles are remained unused[62].

In general, one can study the role of a structured multi-layer network of stockpiles throughout a country, comprising of localized and/or centralized stockpiles with various capacities in disaster/pandemic management. It also can be examined whether such layered structures improve the redistribution of the pharmaceutical and non-pharmaceutical items in the magnitude that can avoid unused ventilator productions or not.

7.3 Vaccine

We devoted this part for research opportunities related to the vaccine composition, production, and assignment decisions, see also Dai and Song (2021).

7.3.1 Vaccine Composition/Production Challenges

There is an evident relation between the type of virus creating a pandemic and how its vaccine as the most effective tool for containing a pandemic should be produced. For flu vaccination, chicken eggs are being used since 1930s[67] with 82% overall contribution[68]. On the other hand, COVID-19 can not be replicated inside eggs. Moreover, an Avian Influenza, e.g., the H5H1 pandemic, may deplete egg stockpiles. It takes 12-18 months to refill an inventory enough to cope with a seasonal flu in the United States. Hence, the preparedness plans like stockpiles of eggs may not be an ultimate answer to produce vaccines for all types of virus that generate respiratory infections. Therefore, there is a need to develop alternative preparedness plans such as (i) non-egg based vaccines, and (ii) stockpile of multi-purpose vaccine prototypes ready before a pandemic starts.

What is the role of OR here? One can devise powerful tools that can thoroughly quantify the risk of not producing a vaccine until a satisfactory level of knowledge from the ongoing pandemic is obtained. To quantify such risk, one can precisely measure the spread of a pandemic, its fatalities, and associated costs during a six-to-eight month production period for a new vaccine to take production or stockpile design decisions to provide access for previous vaccines. Since the latter can be estimated by considering various levels of pandemic uncertainties, the policymaker may prepare her plans for non-pharmaceutical and pharmaceutical interventions to hedge the estimated risks and corresponding fatalities, infected individuals, hospitalizations in both ICU and general wards. Various stochastic optimization frameworks can be examined which model various risk-averse objectives and specific constraints.

7.3.2 Vaccine Assignment Based on Triage Decisions

When a vaccine is produced, its assignments matters, and due to its limited production capacity during the production period it can turn into a triage decision. In section §4.3.1, we reviewed the role of triage decisions when expensive scarce resources must be assigned to control a pandemic. These triage decisions were based on the scarcity of resources, problem-specific, and more importantly, were taken based on demographic specifications such as age, epidemic-specific risks (refer to the definition of risk groups in each pandemic[69]; for example, during the H1N1 flu pandemic, younger individuals and children were the first risk group, while in the COVID-19 older adults were more threatened), sex, location-dependent reproduction numbers, etc.

To design vaccination policies one must first consider demographic specifications and clustering[70] of the individuals in the host population based on their age, sex, predefined health risk-indices to be replicated by the employed simulation module. Then, by examining various vaccination policies and priorities in such simulation frameworks, one can evaluate the vaccination coverage and then score the obtained immunity in the alternating scenarios of a pandemic's propagation for various risk groups. Finally, when triage assignments are fixed by policymakers at the strategic level, operational decisions can be taken to determine the assignment of vaccines in states/provinces, cities, its scheduling, and other resource/vendor management challenges, respectively.

7.3.3 Vaccine Emergency Suppliers

Those countries that do not produce vaccine during epidemic/pandemic events must envision multiple layers of suppliers (Cui et al., 2010). In 1976, Canada was not able to provide flu vaccine from Canadian vaccine manufacturers that were banned to import supply from the United States due to a mass vaccination policy at the time in the United States[71]. This event led to the import the emergency supplies from Australia and eventually vaccine manufacturing contracts with shareholders of Canadian vaccine factories to ensure adequate vaccine production capacities in Canada in the early 1980s and afterwards.

This commonly concerns underdeveloped countries with a lower financial power when the peak demand for scarce med-

[67] https://www.cnn.com/2020/03/27/health/chicken-egg-flu-vaccine-intl-hnk-scli/index.html

[68] https://www.cdc.gov/flu/prevent/vaxsupply.htm

[69] https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON376

[70] including the number of clusters and structure of members that mutually result in a priority list of risk group in decreasing order

[71] https://archive.macleans.ca/article/1976/5/17/the-politics-of-swine-flu

ical resources increases their price up to 1,000%[72]. For example, during COVID-19, rich countries by paying excessive prices got on the top of waiting lines to receive the COVID-19 vaccine sooner[73].

In this part, we highlight two review studies (Salarpour and Nagurney, 2021; Harrington Jr. and Hsu, 2010) that can be used to retrieve the situation for underdeveloped countries in their vaccine purchases. First, we promote studies such as Salarpour and Nagurney (2021) who develop a specialized formulation for policymakers at the international level when competing with each other for scarce medical resources. The game-theoretic setting proposed by Salarpour and Nagurney (2021) decomposes the purchase decisions at each country into those envisioned as part of the preparedness plans, and those will be taken after the pandemic declaration during the response period including the outbreak and its aftermath. What could make a change in these two sets of decisions for each government is how the medical resources are priced before and after a pandemic declaration[74]. Future research may investigate price uncertainties in such settings and using other stochastic optimization frameworks to better tackle highly volatile demands and prices in pandemics.

In the second study, Harrington Jr. and Hsu (2010) propose reserved stockpiles for flu when customers can protect their early[75] purchases from the stockpile by paying a reasonable extra holding price. These manufacturer-customer contracts will enforce manufacturers to keep enough inventory of antivirals to fulfill demands for these customers in 24-48 hours. The same subsidy or binding strategies can be employed by underdeveloped countries to make contracts with vaccine manufacturers in advance to reserve vaccine supplies at a specific time in a pandemic. These settings may help policymakers in underdeveloped countries to make better strategic decisions such as how to invest a limited budget optimally or make alliances with other countries e.g., COVAX[76] for discounted prices, although COVAX struggled in both predicting highly volatile prices by paying almost five times more for each vaccine, and fulfilling vaccine demands[77].

7.4 Interventions

Whether interventions are of non-pharmaceutical type such as imposing school closure, lockdown, quarantine, travel and public gathering bans, or of pharmaceutical type such as providing vaccines, test-kits, or antiviral medicines, there is a limited budget and accordingly a specific time-horizon to perform them. To derive the optimal decisions for when, where, and which one of these interventions should be imposed, and to derive the best response from the population, the first step is to simulate the host population and its demographic diversity at its finest granularity, while considering computational complexities. The existing demographic diversities in a host population include but are not limited to the age, sex, ethnicity (e.g., for various responses to pandemics and pharmaceutical interventions), businesses, public places, organizations especially emergency departments, schools, restaurants, bars, shopping malls, and modeling social dynamics within private and public places to be replicated as much as possible based on the most recent census and mobility data. This gives us a precise mapping or imitation of social contacts, visits, and interactions by which an infectious disease spreads. Then, the pandemic spread and the quality of necessary interventions can be promptly modeled for various scenarios.

There are success stories from the past such as Das et al. (2008) and Aleman et al. (2011) in developing such simulation modules for large cities. The propagation and severity of COVID-19 may truly replicate a benchmark instance to design, develop, and recalibrate new simulation tools to forecast the dynamic of future epidemics and pandemics, their secondary waves, and the efficiency of interventions in every country.

7.5 Modeling Pandemic Uncertainty

As mentioned earlier in the section §4.3.3, the majority of research studies that investigate pandemics under uncertainty in its dynamics employ scenarios or predictive analytics. In this review, we have highlighted three research studies that tackle the pandemic's uncertainty with more modern concepts/contexts such as DRO framework and belief in POMDP.

In general, for an infectious disease that includes an incubation period, the precision in counting the number of new infected individuals and those who are in incubation periods may be difficult to estimate. In fact, the length of incubation time which is inherently a stochastic parameter itself somehow gives us a lower bound of latency to be able to observe the new infections. These observations evidently are not even close to perfect due to the size of a generic host population and the limited number of test-kits. Therefore, these parameters distribution, or better called stochastic models remain uncertain.

There are many rooms for future research in this area including examining the quality of these new modeling setups versus traditional methods, or changing the portion of test-kits in voluntary and mandatory tests.

7.6 Supply Chain

The lessons learned from the recent COVID-19 pandemic and the disruptions it imposed on the supply chains of various commodities are too many, but we recall some of them here in their broadest picture. There are three sources of uncertainties in a supply chain network, supply, demand, and flow and inventory of goods. Most companies rely on single suppliers from a single location which significantly limits responses to disruptions in pandemics. Furthermore, supply chain managers mostly have no knowledge of the secondary layers of suppliers, raw material warehouses, manufacturers, transportation modes, and beyond who have the main role in preserving the inventory level at the first layer suppliers. This lack of a twin digitized supply chain network[78] leads to a distorted flow of information for SC managers in the first place. It then results in an excessive uncertainty in the lead-times and a slow flow of goods from suppliers to their down-streams. Therefore, a partnership in terms of contracts or reserved capacities with a set of different suppliers located in the various regions may potentially prevent network failures when there is a reduced chance of disaster/pandemic ripple effects at all alternative suppliers, see Cui et al. (2010). In fact, placing partnerships with a diverse group of suppliers promotes resilience

[72] https://www.bloomberg.com/news/newsletters/2021-03-17/hard-hit-countries-face-big-vaccine-bills

[73] https://www.oxfam.ca/news/vaccine-monopolies-make-cost-of-vaccinating-the-world-against-covid-at-least-5-times-more-expensive-than-it-could-be/

[74] https://www.cbsnews.com/news/amazon-coronavirus-face-mask-price-gouging-shortages/

[75] before a pandemic declaration or the start of the recurring flu season.

[76] https://www.who.int/docs/default-source/coronaviruse/covax-facility-explainer.pdf

[77] https://www.theguardian.com/world/2021/aug/11/covid-19-vaccines-the-contracts-prices-and-profits

[78] in which all components of the network with their operational capacities and current functionality states are transparently mapped for all stakeholders

in SCN by opening up the possibility of external suppliers.

There are many research studies on distorted information about demand leading to bullwhip effects (Lee et al., 2000; Leng and Parlar, 2009). Pandemics represent highly volatile demands in medical items, cleaning goods, foods, etc., due to their recurrent waves and seasonality, and in general, time-dependent behavior. A fully-digitized and integrated supply chain equipped with powerful forecasting tools may hedge distorted information at upstream echelons.

In the middle stream, mostly inventory management and transportation decisions are of paramount importance. Supply chain inventory strategies usually aim at cost minimization and efficiency. These inventory policies focus on optimal inventory levels in a normal situation which can not be enough responsive during pandemics. Safety buffers, dynamic inventory management, and temporary capacity expansions can be studied as efficient alternatives when facing pandemics. On the other hand, transportation decisions are affected by pandemics because of medical examinations and regulations. For instance, two drivers are not allowed to use the same truck or a driver must pass the COVID-19 test to start a shift. These disruptions can be corrected with extended shifts (already carried out during COVID-19), although alternative operational plans can be envisioned in the future.

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