“**Principles and Standards for Benefit-Cost Analysis of Public Health Preparedness and Pandemic Mitigation Programs**”

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Abstract

The primary goal of this paper is to outline a set of principles and standards (P&S) to be used in benefit-cost analyses of public policies and programs for public health preparedness and pandemic mitigation (PHP/PM). These policies include the stockpiling and distribution of vaccines or antiviral drugs, disease surveillance networks, social distancing measures such as school closures, and quarantines or border closures. I focus primarily on pandemic influenza in the U.S. context, though the P&S suggested here could apply to BCAs of other epidemics or pandemics in other settings. Because cost-effectiveness analysis has been more widely used in the health sector, I briefly compare it with the benefit-cost approach. I then discuss several specific issues that arise in the economic analysis of PHP/PM programs, surveying the existing literature and professional standards in each to arrive at suggested P&S. These include: modeling the macroeconomic impacts of pandemic outbreaks; modeling the effects on households of school closure policies; uncertainty; discounting; disparate impacts and equity; valuing mortality risk; and health externalities. A supplementary appendix provides a literature review on economic analysis of policies and programs for PHP/PM.

1. INTRODUCTION

In the spring of 2009, the world saw the outbreak of a new strain of influenza virus (H1N1). Although earlier interest had been focused on the possibility of strains of avian (H5N1) influenza coming from Asia, the H1N1 strain had jumped carriers from pigs to humans, and was first detected in Mexico. Known as H1N1 or “swine flu”, it quickly spread around the world.

The WHO declared the outbreak a Phase 6 pandemic (the highest alert level[1]) on June 11, 2009. As of late February 2010, H1N1 caused 16,200 deaths in 213 countries[2]. The U.S. Centers for Disease Control estimates that there were 41 million – 84 million cases in the U.S., 183,000 – 378,000 hospitalizations, and 8,330 – 17,160 deaths attributable to H1N1[3]. Nevertheless, the disease has been milder than initially feared (i.e. a low case fatality rate), and during much of 2009 attention among citizens and public officials was focused intensely on preparations for the pandemic.

There are a number of policies and programs that can be implemented in both the private and public sector at the local, state and federal level to either contain the spread of epidemic or pandemic[4] influenza or mitigate its effects once it is already widespread. These containment and mitigation strategies have been studied extensively in the public health and epidemiology literature, often with state-of-the-art mathematical modeling approaches, to find "optimal" strategies. These analysts typically had a clear objective in mind when defining optimality: reduce the number of cases or deaths.

Many of these policies, however, imply large costs and benefits outside the health sector. For example, school closures are thought by many epidemiologists to be effective at slowing the spread of a pandemic or at least reducing peak caseloads, and are widely used. They may impose few costs on the healthcare system, but may involve large costs to families. Parents may need to miss work or arrange alternative childcare. These effects may differ by socioeconomic status (i.e. one-adult vs. two-adult households, availability of paid leave policies). On the other hand, the benefits of containment and mitigation programs (i.e. avoiding widespread morbidity and mortality by controlling the disease) may have very large macroeconomic effects which have only recently begun to motivate careful research. These types of economic costs and benefits have not been widely incorporated into existing economic analyses.

In addition to identifying the proper mix of policies to contain pandemic influenza (or any other infectious disease with the potential for rapid spread), an important economic and ethical question concerns the optimal level of public

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[1] http://www.who.int/csr/disease/avian_influenza/phase/en/index.html

[2] "Pandemic H1N1 2009, Update 89". http://www.who.int/csr/don/2010_02_26/en/index.html

[3] http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm#Table

[4] I will generally use the term "pandemic" throughout the paper, although epidemic and pandemic are not synonymous. A pandemic is an epidemic that "occurs over a very wide area (several countries or continents) and usually affects a large proportion of the population" (US CDC). An endemic infectious disease is one that is present on a regular basis in an area, such as seasonal influenza in the U.S., or malaria in sub-Saharan Africa.

sector investment. How do we evaluate expensive investments in systems and stockpiles to prevent low-probability but extreme-outcome events?

Here is one illustration. The influenza pandemic of 1918 killed many young, healthy adults because of an over-reaction of the healthy immune system known as a "cytokine storm". Patients died of pneumonia when their lungs filled with fluid. Had these patients had access to ventilators, however, most would have survived. A ventilator is therefore arguably the best insurance policy against preventing influenza deaths. At an extreme, should hospitals therefore stock one ventilator for each American? Should they stockpile ventilators using the expected mortality rate (for example, if the overall mortality rate for the 1918 pandemic influenza was 4 per 1000, stock 4 ventilators per 1000 people)? There were estimated to be approximately 105,000 ventilators in US hospitals in 2006, of which 100,000 are in use during a normal flu season. The Strategic National Stockpile stores an additional 4,000 – 5,000 ventilators, but the National Pandemic plan calls for 742,500 in a worst case scenario (approximately 1 for every 410 Americans). A ventilator costs approximately $30,000, however, and neither hospitals nor local or federal governments are willing to buy and store excess ventilators. They would also need to ensure adequate staff capacity to operate them. "We only have a certain amount of money to spend on preparedness," said Thomas W. Skinner, a spokesman for the federal Centers for Disease Control and Prevention in Atlanta. "We can't invest strictly in respirators."[5]

Two economic frameworks that could be used for these types of questions are cost-effectiveness analysis (CEA) and benefit-cost analysis (BCA). The CEA approach is more widely used in the health field, although BCA may prove a more useful tool for some types of questions, as I discuss below. Like any methodology, however, a lack of standardization about common assumptions and techniques in both CEA and BCA may lead to different policy recommendations. The main goal of this paper is, therefore, to begin a discussion of a set of principles and standards to be used in benefit-cost analyses of public health preparedness and pandemic mitigation policies. It is meant to be suggestive, not definitive. Neither is it meant to suggest that analysis should be <u>completely</u> standardized in parameter assumptions or in approach. Good analysis will always require good judgment, particularly in determining the appropriate scale of research given the scale of the question and the time and financial resources available for the study.

The audience for the paper is assumed to be practitioners and economic analysts (benefit-cost and cost-effectiveness) at research institutions as well as

[5] "Hospitals Short on Ventilators if Bird Flu Hits", New York Times, March 12, 2006 (http://www.nytimes.com/2006/03/12/national/12vent.html)

various local, state and federal agencies charged either directly or indirectly with protecting health and minimizing the economic disruption of a major infectious disease outbreak. My focus is primarily on policies and strategies in the context of the United States.

In the remainder of this section, I define more comprehensively the types of problems and policies intended under the rubric "public health preparedness and pandemic mitigation" (which I abbreviate throughout as "PHP/PM") and briefly describe previous influenza pandemics. Section 2 provides a brief conceptual comparison between the CEA and BCA. [A review of existing economic evaluations of PHP/PM programs, both CEA and BCA, is provided in Appendix A.] Section 3 discusses a specific set of empirical issues that may arise in conducting a BCA in this area. Section 4 concludes.

<u>What diseases and interventions?</u>

The types of infectious diseases that could become widespread in the United States and cause significant economic damage might include pandemic influenza, Severe Acute Respiratory Syndrome (SARS), antibiotic-resistant tuberculosis (Tb), MRSA (Methicillin Resistant Staphylococcus Aureus) or other antibiotic-resistant bacteria, smallpox, and hepatitis, as well as others. The types of preparedness and response policies and interventions will vary by disease; the disease focus in this paper is primarily on pandemic influenza in order to maintain tractability for such a broad topic and because it has received the most attention among health analysts and modelers.

The paper is limited to the economic analysis of public (rather than private) policies, programs and investments to prevent the spread of an infectious disease and mitigate the disease's effects once it becomes widespread. Table 1 lists these interventions in three broad categories of preparation, containment and mitigation. Although some of these programs will have spillover benefits to other national security threats such as bioterrorism (eg. contingency planning, emergency drills, etc), I do not address bioterrorism specifically[6].

What public sector agencies might be doing such analyses? The public health system in the U.S. is highly decentralized, with much of the funding, monitoring and surveillance, and policy responses such as school closures

[6] For more on the economics of terrorism and homeland security, see the CREATE program (create.usc.edu), or Richardson et al (2007). In addition, the journal Medical Decision-Making recently published a special issue discussing bioterrorism, see Vol. 29, No. 4, July-August 2009. Finally, the Institute of Medicine commissioned an expert panel evaluating the costs and benefits of its BioWatch program, as well as "enhanced national surveillance through hospitals" (described in more detail below). See: http://www8.nationalacademies.org/cp/ProjectView.aspx?key=HSPX-H-08-03-A

occurring at the local (i.e. county, city) and state levels. Nevertheless, federal agencies like the Centers for Disease Control (CDC) and Health and Human Services (HHS) play important roles in providing information, setting recommendations and guidelines for local public health agencies, and aggregating monitoring information. They also provide some funding to support monitoring. The Department of Homeland Security also has a limited role in a federal monitoring system called BioWatch, initiated in response to the anthrax attacks in the fall of 2001. The BioWatch program has deployed a series of outdoor air samplers in 30 major cities with the aim of rapid detection and characterization of aerosolized biological threats. All levels of government have the legal authority to enforce quarantines of patients, and the federal government theoretically has the power to close national borders and halt airline travel in the event of a pandemic.

Table 1. Programs, interventions and investments in PHP/PM

PREPARE (*before an outbreak*)	**CONTAIN** (*prevent a disease from entering a geographical region*)	**MITIGATE** (*slow the spread of the disease within a geographical region, reduce morbidity and mortality from the disease*)

• **Stockpiling antiviral medicines** (e.g. oseltamivir, zanamivir, amantadine, rimantadine) which can be used prophylactically or as treatment
• **Stockpiling low-efficacy vaccines** (until vaccines more targeted to the specific agent can be manufactured).
• **Disease surveillance networks** (state or county health depts) and information technology systems to share information (nationally or internationally)
• **Emergency preparedness plan formation** and **drills**[7].
• **Programs targeted at changing prevention behavior** (e.g. handwashing, improved infection control procedures in hospitals)
	• **Close borders to people**
	• **Close borders to goods** (trade restrictions)
	• **Ground airplane travel**
	• **Quarantine existing cases** (requires adequate surveillance capacity)
		• **Production and distribution of targeted high-efficacy vaccines** (lead times generally estimated to be 6-9 months after first appearance of disease, though highly uncertain). Could be distributed to target groups (frontline responders, close contacts of existing cases), or to the entire population.
		• **Antiviral distribution**. Could be used to treat all or a fraction of existing cases, or distributed prophylactically to target groups (frontline responders, close contacts of existing cases), or to the entire population.
		• **Social distancing policies[8],** such as:
		  • *School closures*
		  • *Ban on public gatherings* (sporting events, parades, etc)
		  • *Mandatory closure of some types of private businesses* (movie theaters, restaurants)
		  • *General recommendations to avoid contact, stay home* [9]

[7] For detailed plans for state and local governments on measures: http://www.pandemicflu.gov/

[8] All of the policies listed occurred during the 1918 influenza pandemic in the U.S.: see Hatchett et al. 2007

[9] There is also some concern that a strong recommendation for social distancing measures may lead to a breakdown in social cohesion. When families and communities must rely on each other for care during outbreaks (especially if the health infrastructure is overwhelmed), government recommendations to avoid the sick could be problematic (Middaugh 2008).

Historic pandemics

Because much of the existing economic analysis on PHP/PM deals with pandemic influenza planning, a brief introduction on the history of influenza pandemics may be helpful in understanding some of the key assumptions of these studies described later in the paper.

There have been three large influenza pandemics in modern times. The worst, and most well-known, is the 1918 influenza pandemic (Barry 2004). A mild "heralding" wave was noted in the American Midwest in the spring of 1918, although it received little attention at the time (James and Sargent 2006)[10]. In the fall of 1918, the virus returned in a more lethal form, sickening approximately 20-25% of North Americans and spreading worldwide. The virus was unusual in that it disproportionately killed predominately young, healthy adults from pneumonia (rather than the young, old and infirm), and that it spread very rapidly. In any given location, approximately 80% of cases occurred within one month. Excess mortality was estimated to be 4.1 per 1000 (0.4%) in the U.S., but between 8 and 55 per 1000 worldwide because of much higher mortality rates in poor countries like India (total mortality from the epidemic has been estimated at between 15 and 100 million deaths).

The two other pandemics occurred in 1957 and 1968. Both were much milder than the 1918 pandemic. Although the 1957 pandemic is believed to have sickened a higher percentage of people (35% vs. 25% in 1918), excess mortality was an order of magnitude lower (0.4 per 1000 in the US and 0.7 per 1000 globally). As with normal seasonal influenza, the deaths were concentrated in the very young and very old. The 1968 pandemic was milder still, with an excess mortality rate in the US of 0.2 per 1000.

2. COMPARING BENEFIT-COST AND COST-EFFECTIVENESS

There are a number of texts devoted to the theoretical underpinnings and practical implementation of both benefit-cost analysis (Zerbe 2008, Boardman et al. 2005) and cost-effectiveness/cost-utility analysis (Gold et al. 1996,Drummond et al. 1997, IOM 2006, Haddix et al. 2003). What follows is an introduction for readers who may be less familiar with one or both methodologies.

Cost-effectiveness

Cost-effectiveness analysis (CEA) seeks to achieve a given health objective at lowest cost. This health objective may be narrowly defined. For

[10] This section draws heavily from James and Sargent (2006), pgs 5 -16.

example, a CEA analyst may evaluate the cost of three different blood pressure medications in relation to their clinical effectiveness at reducing blood pressure (the health objective). (When all three medications have equal clinic effectiveness, the analysis would become a cost-minimization exercise). CEA is more useful, however, for comparing broader sets of health policies or interventions to inform health-sector budget allocation decisions. For example, if the health objective is defined more broadly as preventing mortality, several different types of programs within the health sector (i.e. R&D into new cancer-fighting drugs, expanded vaccination, public health education programs to reduce smoking) can be compared by their cost per life saved. Though conceptually straightforward, accurately determining the direct health care costs of various policies or interventions is by no means simple (see Lipscomb et al. 2009 for a recent review). The analytical perspective for CEA is typically either at the health system perspective (only costs incurred or avoided by the health-care provider are included) or the social perspective, which includes also includes costs borne by patients and society.

Because programs often have effects on both mortality (quantity of life) and morbidity (quality of life), CEA researchers developed measures in the 1970's that combine the two effects. The Quality-Adjusted Life Year (QALY) approach is the most common. To combine the effects of a program on morbidity and mortality, an analyst first calculates the incremental effect of the program compared to a status quo option in terms of extension of life and reduction in the amount of time spent in disability, pain, etc. The analyst then weights time spent in the disabled condition with a QALY weight which is equal to one for perfect health and zero for death. This time can then be added to life years lost to premature death to calculate QALYs gained from the program.

QALY weights, the subject to hundreds of studies, are generally elicited from the general population (not experts) using a variety of techniques[11]. The most common and theoretically uncontroversial (among CEA analysts) is the standard gamble approach. Respondents are described some condition or illness that involves pain or disability (i.e. a kidney disease that requires weekly dialysis). They are then asked to choose between two alternatives. In the first alternative, there is a treatment option for the kidney disease which will return the respondent to "perfect health" for their remaining t years of life with probability p, or will result in instant death with probability (1-p). In the second alternative, respondents will live with the kidney disease for the remaining t years of their lives. The probability is varied until a respondent is indifferent between these two alternatives, and the resulting probability is the QALY weight for that kidney

[11] Researchers interested in conducting or evaluating a study eliciting QALY weights should consult IOM (2006) for best practices in these survey techniques.

disease. Again, weights near zero indicate that living with the condition is almost as bad as death, and indeed negative weights are possible for conditions considered worse than death. Because of the elicitation approach, QALY weights are based on von Neumann-Morgenstern expected utilities, so this approach has also been called cost-utility analysis. These utilities, however, are cardinal (intervals are meaningful) and not tied in any way to how respondents might trade income for health improvements or risk reductions. These should not be confused with the ordinal utilities (only ordering is possible, and is sufficient) used by welfare economists.

A second type of weight used to combine morbidity and mortality effects is the Disability-Adjusted Life Year (DALY). The DALY approach was initiated by the World Health Organization and is more commonly used in the context of developing countries. It is different from a QALY in several respects. First, DALY weights are coded on a scale of zero as perfect health and one as death, exactly the opposite of the QALY scale. The effect of interest is therefore DALYs avoided, rather than QALYs gained. Second, DALY weights have been constructed from a process of expert elicitation rather than a survey-based approach from the general population. Third, DALYs as originally proposed weight effects by when the morbidity occurred in life. These age-weights are lowest for the young and the old, and peak at middle age when people are most productive (Murray and Lopez 1996). These age weights have proved controversial, however, and have not been commonly applied in recent CEA studies using the DALY approach (Jamison et al. 2006).

Health policymakers are advised to invest more health resources in programs with lower cost-effectiveness ratios ($ per lives saved, QALY gained, or DALY avoided) and less in programs with higher cost-effectiveness ratios. There are not, however, generally clear guidelines for when a program has such poor cost-effectiveness that it should not be undertaken at all. Is a health program with a cost-effectiveness of $5,000,000 per life saved worth undertaking? CEA can tell us to prefer a program with a ratio of $4m per life saved, but if this program has the lowest cost-effectiveness ratio it cannot be used to justify whether that program is worth doing. There are reference values that are widely used in CEA, although they are not grounded in welfare theory. Using a definition first suggested in the World Bank's 1993 *Investing in Health* report, interventions are often considered "very cost effective" if the ratio of cost per DALY avoided is less than per-capita GDP. An intervention is "cost effective" if the ratio is less than three times per-capita GDP. In Britain, the National Health Service will generally not cover interventions which have cost-effectiveness ratios higher than £20,000 - £30,000 per QALY gained[12].

[12] See: http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenesstheqaly.jsp

It also cannot tell us how this program might compare with a road-upgrading project which is expected to save lives but also save driver's time and improve transport efficiency. In this sense, CEA can be thought of achieving technical efficiency in spending resources that have been budgeted to the health sector by higher level decision-makers (Drummond et al. 1997). In this framework, these decision-makers (i.e. Congress, Parliament, etc) make implicit decisions about sectoral allocations.

Benefit-cost analysis

Benefit-cost analysis, on the other hand, can be used to answer these types of questions of allocative efficiency. Unlike CEA, the BCA framework is firmly grounded in welfare economics (in addition to the BCA texts cited above, see also Just et al. 2004). As such, it relies on several basic tenets which are normative in nature. First, social welfare is derived from the welfare (utilities) of the individuals that make up that society. Second, those individuals are the best judges of their own welfare (i.e. consumer sovereignty). Finally, a program which would make at least one person better off but make no one else worse off (a so-called Pareto improvement) is welfare-enhancing and should be implemented. In practice, because such improvements are nearly impossible to find, welfare economists rely on the potential Pareto test (the Kaldor-Hicks criteria): if the winners from a policy could fully compensate the losers and still be better off, the policy is welfare-enhancing. This framework focuses of increasing efficiency, and takes the existing income distribution as given. Like CEA, it does not explicitly consider equity effects, although this has been, and continues to be, the subject of debate among welfare economists and BCA analysts.

To assess potential Pareto improvements, a full BCA places shadow prices on all positive and negative impacts of a policy or program. In other words, a health BCA requires monetizing all health impacts by determining consumers' willingness to trade income (or wealth) for the health improvements or a reduction in mortality risk. Although these shadow prices are often unavailable and frequently controversial, they have the advantage of allowing economic comparisons with programs or policies outside the health sector. Willingness-to-pay is then summed over the affected population[13] to calculate total social benefits. The proper decision rule is to select projects with the highest net benefits: total social benefits less total social costs[14]. There will, of course, be

[13] In other words, which groups have "standing" in the analysis. This will generally hinge on the purview of the agency conducting the analysis (i.e. state vs. federal).

[14] It is well-known that benefit-cost ratios can be misleading because 1) the placement of categories of benefits in the numerator versus the denominator can change b/c ratios and 2) ratios can hide differences in the scale of projects, potentially favoring many smaller projects

categories of benefits or costs which are difficult or impossible to monetize. These should be presented alongside BCA results; BCA is intended to be a decision-making aide rather than the sole normative criterion for evaluating a policy or program.

Shadow values can be elicited using four types of approaches: a human capital approach, cost-of-illness, revealed preference, and stated preference. The human capital approach uses changes in the productive capacity of individuals with changes in health state as the measure of economic welfare. For example, if a 35 year old is expected to earn $1.5 million over the remainder of her life, a program that would prevent her death at age 35 would increase economic welfare by $1.5 million. This approach, however, is not consistent with the underlying theory of BCA in that it does provide information on individuals' WTP for risk reductions or health improvements (Drummond et al. 1997, Freeman 1999). Although commonly used in wrongful death suits in the court system, the human capital approach is uncommon in modern BCAs.

Cost-of-illness (COI) captures both the financial and economic costs of being ill. COI estimates are available for a number of illnesses in a number of populations, and provide an uncontroversial measure of the economic benefits of avoiding an illness. Public COI refers to the cost incurred by the public sector health system in treating an illness, such as staff salaries, publicly-provided treatments, capital costs of facilities, etc. Private COI measures financial and economic costs incurred by patients (i.e. lost work days, cost of medicines not covered by the public system, etc). In a BCA framework, *ex ante* COI (COI weighted by the probability of falling ill) can be compared with the costs of reducing the illness. From a health care provider perspective, the analysis may focus only on public COI avoided. A social perspective would include private COI avoided as well.

Avoided COI is also sometimes netted out of the numerator of cost-effectiveness ratios, although this may double-count benefits by placing one element of the monetized value of reducing illness in the numerator as well as the non-monetized QALY or DALY measure in the denominator[15]. The main problem with COI estimates in the BCA framework is that they do not capture the value of reductions in mortality risk. Treatment costs for a fatal illness are likely to underestimate ex ante willingness-to-pay to reduce mortality risk.

(each of which has a high b/c ratio but provides small net benefits in absolute terms) rather than larger projects with lower b/c ratios but higher net benefits in absolute terms. Internal rates of return, or the discount rate which equalizes benefits and costs, is also not a reliable decision criterion from the perspective of welfare economics.

[15] As noted earlier, QALY and DALY measures already include morbidity. This will not be double-counting if respondents were carefully told to exclude these potential costs of illness during the elicitation process for QALY weights, as is recommended by Gold et al (1996).

The third approach – revealed preference - relies on observing consumer behavior in markets related to health improvements. The most important application of the revealed preference approach in health is valuing changes in mortality risk through labor markets. By observing wages and fatality risks in a large number of jobs in the labor market, economists can deduce the wage premium that workers in less risky occupations forego to avoid the higher mortality risk (or the additional wages demanded by those who chose the riskier occupation). This willingness-to-pay for mortality risk reduction can then be used as the shadow price in a health BCA of a policy or program that would reduce the risk of death (see Viscusi and Aldy 2003 for a comprehensive review). Because risk changes are often presented as the number of deaths prevented, analysts often need to value these aggregate risk changes. If among a large group of people average willingness-to-pay to avoid a 1 in 100,000 risk of dying from a particular cause is $45, then the average willingness-to-pay to reduce one death among the group would be ($45 /0.00001), or $4.5 million. This value has unfortunately been termed the "value of a statistical life" (VSL), a label which draws ire from the general public, obscures the economic relationship of interest (WTP for small risk changes), and belies the large heterogeneity in these preferences depending on both individuals and contexts. A related concept is the "value of a statistical life year" (VSLY), or a VSL estimate which reflects remaining life expectancy by dividing the VSL by the discounted expected number of life years remaining (Robinson 2007). This approach assumes that VSLs are proportional to remaining life expectancy, an assumption not grounded in theory and which has not been borne out by empirical studies (Aldy and Viscusi 2007,Krupnick 2007,Viscusi 2010).

The fourth approach to valuing health outcomes is stated preference (SP). Researchers use either contingent valuation or stated choice methodologies to present respondents with a hypothetical product that would reduce their risk of dying, treat a condition, or prevent an illness. Respondents are asked if they would be willing to purchase the product at a given price. Prices are randomly chosen from a range of prices that allow the analyst to construct a bid curve (the percent of respondents purchasing the product by price). The area under this curve represents average willingness-to-pay for the health impact of interest. For mortality risk reductions, the WTP can be used to estimate the VSL.

Because of the hypothetical nature of the exercise, these SP techniques have been subject to two decades of close scrutiny and testing, much of it in the environmental and transport literatures. Although hypothetical biases in SP studies remain a threat and many poorly conceived and executed SP studies routinely appear, the technique has gained acceptance in federal government economic analysis and increasingly among economists. There are now a number of documents that provide guidance on how to conduct high-quality stated preference studies (Arrow et al. 1993, US EPA 2008, OMB 2003). Analysts using shadow prices from SP studies should consult these references for criteria to evaluate the quality of the underlying research. Researchers experienced in SP methods know these recommendations and criteria well (i.e. scope tests, high-quality survey administration, extensive focus group and pre-testing, "cheap talk" scripts etc). On the positive side, the hypothetical nature of SP provides a larger scope for valuing morbidity changes than revealed preference approaches. They may also capture categories of benefits in morbidity changes that are not captured in COI measures (e.g. fear, dread, suffering)[16].

Existing principles and standards

There are a number of well-known sources for principles and standards in both cost-effectiveness and benefit-cost analyses. In the U.S., the federal government is required to assess the benefits and costs of all major federal regulations[17]. The Office of Management and Budget is responsible for reviewing these benefit-cost assessments, and its Circular A-4 *Regulatory Analysis* (most recently updated in 2003) serves as a source of both analytical requirements and more general preferred practices. Most of the federal regulations examined under the requirements of Exec. Order 12866 have been environmental rules (Robinson 2010). As such, the Environmental Protection Agency, responsible for many of these rules, publishes its own guidance, *Guidelines for Preparing Economic Analyses*. First published in 2000, the EPA is in the process of updating these guidelines, and circulated a draft revised document in 2008. There are to my knowledge no guidelines specifically related to BCA in health care or public health preparedness, though the discussion of analytical framework, methods for deriving shadow prices, discounting, etc. in Circular A-4 and EPA (2008) would be an appropriate place to begin. I will reference these throughout the next section discussing individual analytical challenges for PHP/PM. Canada, the UK, and the

[16] There are a number of forthcoming papers on valuation of both morbidity as well as mortality risks from a large, representative web panel of Americans. The research group was headed by Trudy Cameron and J.R. DeShazo; for more information, see http://www.uoregon.edu/~cameron

[17] This requirement began with President Reagan's Executive Order 12291 (1981), and was updated under Presidents Clinton in 1993 (Exec.Order 12866) and G.W.Bush in 2002 and 2007 (Exec. Orders 13258 and 13422). Exec. Order 12866 requires an assessment of benefits and costs of any regulation expected to "have an annual effect on the economy of $100 million or more or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, of State, local or tribal governments or communities".

European Union have also developed regulatory impact analyses in recent years similar in approach to those used in the U.S. (for more details see Robinson 2010).

Cost-effectiveness analysis also has a well-developed set of principles and guidelines specifically in health-related applications because of its widespread use. The most commonly-cited is Gold et al (1996), a report from a U.S. Public Health Service-appointed expert panel on "Cost-Effectiveness and Health in Medicine". Other sources include the World Health Organization's CHOICE framework[18], the United Kingdom's National Institute for Clinical Excellence (NICE)[19], Weinstein et al (2003), the guidelines for submissions to the British Medical Journal (Drummond and Jefferson 1996), the Institute of Medicine's report on valuing health for regulatory CEA (2006), and the standards used in the compilation of cost-effectiveness studies in the recent Disease Control Priorities project (DCP2, outlined in Musgrove and Fox-Rushby (2006). OMB Circular A-4 also discusses CEA for major regulations, largely echoing recommendations from the Gold et al expert panel and explicitly stating a preference for BCA where possible. Since my focus here is on BCA, a complete discussion of these guidelines for CEA is beyond the scope of this paper.

3. SPECIFIC ISSUES

Modeling macroeconomic impacts

Perhaps the most important element missing from many existing economic evaluations of PHP/PM is the potential for effects outside the health sector, including large-scale macroeconomic effects. Beutels et al (2008) argue that "traditional health economic analysis is ill-equipped to estimate the cost-effectiveness and cost-benefit of interventions that aim at controlling and/or preventing public health emergencies of international concern (such as pandemic influenza)....Since traditional economic forms of evaluation are being used to inform decisions about controlling and preparing for these emergencies, they do not appear to be fit for the purpose." How might we adapt them to fit the purpose? I begin this section with a review of the existing literature on the macroeconomic impacts of pandemic influenza and the effects of school closure policies on households. I then offer some suggestions for how and when these types of effects should be included in BCAs.

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[18] See http://www.who.int/choice/en/

[19] See http://www.nice.org.uk/. Cost-effectiveness analysis is used extensively to support decision-making in the UK's National Health Service.

Existing literature

Several studies have attempted to document the macroeconomic consequences of infectious disease outbreaks, namely pandemic influenza. These studies do not attempt an economic evaluation of specific policies or programs, but seek to understand the various linkages between a pandemic and the wider economy using theory, models and historical evidence. These linkages could include: a decline in the size of the labor force due to illness and death, a reduction in household income as a result of missed work, a reduction in consumer demand for products and services that require more social contact, and a re-evaluation of investment risk, particularly with regards to price inflation (McKibbin and Sidorenko 2006). Several government reports and non-academic outlets have discussed these possible macroeconomic effects of influenza (CBO 2006, Langton 2008[20]), or the effect of the SARS in 2002-2003 (Conference Board of Canada 2003). Langton (2008), from the U.S. Congressional Research Service, analyzes possible trade disruptions due to an avian flu pandemic. Disruptions could include banning imported goods from infected regions, *de facto* bans or boycotts due to health concerns, or supply-side constraints from exporting countries. The study considers the potential impact of import restrictions from countries with confirmed avian flu cases from January 2004 to January 2008. Of those countries, imports from China, which account for 15% of total US imports, would have the largest potential impact on the US economy. Overall the effect on the macro economy would depend on the severity of the outbreak, the duration of the outbreak, and the number of countries affected.

Several studies have attempted to model these effects for a future pandemic (see Table 2). All of the studies take case attack rates and mortality rates from historical pandemics as various case scenarios, typically using the 1957 and 1968 pandemics as more moderate cases, and the 1918 pandemic as the worst case (McKibbin and Sidorenko (2006) and CBO(2006) use mortality rates double that of 1918 as their worst case). With the exception of Bloom et al (2005), the studies have predominantly been conducted by authors in developed countries with a focus on developed-country economies, although several make predictions about effects in developing countries.

The studies use a variety of modeling approaches, although none uses a full computable general equilibrium (CGE) model. McKibben & Sidorenko use a multi-sector structural model called G-Cubed, Jonung and Roeger (2006) use a QUEST model, Keogh-Brown *et al* (2009) use a structural model. James and Sargent estimate individual morbidity, mortality and absenteeism impacts separately based on historical data from 1918, 1957 and 1968. They also differ in

[20] See also The Economist, May 2, 2009 "Flu and the global economy: the butcher's bill"

several key assumptions about the level of absenteeism due to workplace-avoidance policies or school closures, and the degree to which demand shocks "bounce back" after the pandemic ends. A full discussion of the macroeconomic modeling approaches taken is beyond the scope of this paper.

Table 2. Studies of macroeconomic effects of pandemic influenza

Study	**Primary Country**	**Key scenario character-istics**	**Total Pandemic Year GDP effects**	**Decomposition of GDP effects**	
				Absenteeism from mortality, illness and workplace avoidance	**Remaining Indirect GDP effect**
James and Sargent 2006 (1)	Canada	1918 mortality (0.44 %), base case	Canada: **-0.4 to -0.9**%; similar impacts in other advanced economies and in emerging economies	-0.6%	-0.4%
James and Sargent 2006 (2)	Canada	1918 mortality (0.44 %), with workplace avoidance absenteeism	Canada: **-0.4 to -1.1%**; similar impacts in other advanced economies and in emerging economies	-0.7%	-0.4%
James and Sargent 2006 (3)	Canada	1957 mortality (0.04 %)	Canada: **-0.1 to -0.3%**; similar impacts in other advanced economies and in emerging economies	-0.3%	-0.1%
CBO 2006 (1)	US	Mortality double that of 1918 (0.75%)	US: **-5%**	-3.0%	-2.0%
CBO 2006 (2)	US	1957 mortality (0.03%)	US: **-1.5%**	-1.0%	-0.5%
Kennedy et al. 2006	Australia	Mortality half that of 1918 (0.2%)	Australia: **-9.3%**	-1.5%	-7.8%
McKibbin and Sidorenko 2006 (1)	Global	Mortality double that of 1918 in advanced economies	US **-5.5%**; Canada **-5.7%**; Japan **-15.8%**; Europe **-8.0%**; Singapore **-21.7%**; Phillipines **-37.8%**; LDCs **-12.2%**	-0.6%	-0.1%

Study	Primary Country	Key scenario character-istics	Total Pandemic Year GDP effects	Decomposition of GDP effects	
				Absenteeism from mortality, illness and workplace avoidance	**Remaining Indirect GDP effect**
McKibbin and Sidorenko 2006 (2)	Global	1918 mortality	US **-3.0%**; Canada **-3.1%**; Japan **-8.4%**; Europe **-4.3%**; Singapore **-11.2%**; Phillipines **-19.3%**; LDCs **-6.3%**	-0.7%	-0.8%
McKibbin and Sidorenko 2006 (3)	Global	1957 mortality	US **-1.4%**; Canada **-1.5%**; Japan **-3.3%**; Europe **-1.9%**; Singapore **-4.4%**; Phillipines **-7.3%**; LDCs **-2.4%**	-0.8%	-2.3%
McKibbin and Sidorenko 2006 (4)	Global	1968 mortality	US **-0.6%**; Canada **-0.7%**; Japan **-1.0%**; Europe **-0.7%**; Singapore **-0.9%**; Phillipines **-1.5%**; LDCs **-0.69%**	-1.0%	-4.7%
Bloom et al. 2005	Asia	Mortality double that of 1957 (0.1%)	Asia**: -2.6% to -6.8%**	-0.3%	-6.5%
Jonung and Roeger 2006	EU	Same as CBO (1) (0.75%)	EU: **-1.6%**	-1.1%	-0.5%

Notes: Adapted largely from James and Sargent (2006). "LDC" = less developed countries.

For 1918-like scenarios, estimates for the drop in GDP during the pandemic year range widely. James and Sargent's estimates range from 0.4 to 0.9% in Canada specifically, though they believe the effects would be representative of other "advanced economies". McKibben & Sidorenko predict a drop of roughly 3% in the US and Canada (and much higher in Asia and developing countries) for a 1918-like pandemic and mortality rate. Kennedy et al (2006) predict the largest effects: for mortality rates half as high as 1918, they predict a fall in GDP of 9.3% for Australia. As points of reference, real GDP fell by roughly 30% from 1929 to 1933 in the United States[21]. In two more recent

[21] Based in chained 2000 dollars, Bureau of Economic Analysis (http://www.bea.gov/national/index.htm#gdp), accessed June 2009.

recessions, U.S. GDP fell 1.9% from 1981 to 1982, and 0.2% from 1990 to 1991 (though these annual figures mask larger quarterly changes). The recession in 2008-2009 is currently estimated to have shrunk US GDP by 6.3% in the fourth quarter of 2008 and 5.5% in the first quarter of 2009.

James and Sargent further break out the component of GDP effects caused by absenteeism due to avoidance behavior (e.g. school closures, workplace avoidance, home care for ill family members) and mortality. Mortality in these models is not valued using a VSL calculation, but rather than the macroeconomic effect of losing workers in the economy. On average, these comprise roughly half of the total GDP effects across the various countries and models studied.

As can be seen from Table 2, however, there is not a consensus on how large the impacts might be, depending largely on assumptions about how households' economic behavior (purchasing, travel, workplace avoidance) may change in reaction to a pandemic. Estimates of the costs of a 1918-like pandemic flu for the US range from 0.4% to 5.5% of GDP (see Table 2). If current US GDP is approximately $14.1 trillion[22], the range of costs implied is $56B to $775B (approximately the same size as the economic stimulus package passed in the US in 2009). The results of a BCA that includes general equilibrium effects will clearly be extremely sensitive to distribution chosen for this parameter.

However, most of the data on what types of behaviors the public would undertake is based on historical analyses with sparse data or assumptions with little empirical support. Using a survey-based approach, Sadique et al (2007) asked residents in 5 European countries and 2 Asian countries what types of behavioral modifications they might make under one of two scenarios for a pandemic influenza outbreak. Nearly three-quarters of respondents said that they would avoid public transportation, avoid places of entertainment, and restrict their shopping to the essentials. Similarly, a survey by Balicer *et al* (2006) found that approximately half of public health workers in the U.S. said they would avoid work in the wake of a pandemic.

School closure

Similarly, relatively little is known about the economic and social impact of school closure (or "class dismissal" policies). This is of particular relevance because school closures policies are thought by some to be an effective policy for slowing the spread of outbreaks for many infectious diseases, although this is still the subject of debate among epidemiologists (Cauchemez et al. 2009 provide an excellent introduction to this issue, including a discussion of the epidemiological evidence, the social/economic impacts, and practical issues of school closure

[22] First quarter of 2009, in current dollars. Accessed from Bureau of Economic Analysis, June 2009

policies). They were widely used in the H1N1 pandemic.

Sadique et al (2008) use a large nationally-representative survey data from the UK to estimate the percentage of working adults with dependent children who may need to stay home to care for children in the event of a school closure. They estimate that 16% of the UK workforce would be primary caregivers, although this may be lower if parents find other informal care arrangements (friends, neighbors, etc.). The effect may also differ by sector, with workers in the healthcare and education sectors more likely to be a primary caregiver for a child than workers in other sectors. Because of this, school closure policies may have important effects on the capacity of the health care system to deal with large patient loads if health care workers are forced to miss work because of school closures. Using average sector-specific wage data, they estimate the cost of this absenteeism to be on the order of £0.2bn (BP) to £1.2bn per week, or 0.2% to 1% of British GDP for a closure lasting for the duration of a 12-week pandemic wave. They note that although these costs "might appear to be large, the benefits of the policy in terms of cases and deaths might be acceptable….only a fully economic analysis can shed light on whether such a policy should be adopted."

Similarly, Blendon et al (2008) surveyed 1697 American adults about prospective behaviors during an influenza pandemic. Among the subset of respondents with at least one school-aged child and one employed adult in the household, 86% reported that they could arrange care so that one adult could continue to work. Interestingly, though, they found that among the low-income (<$25,000 per year) subset of this group, 93% said they would have serious financial difficulties if they had to stay home because of a school closure lasting 3 months, compared to 64% of higher income (>$75,000) respondents.

Effler et al (2010) surveyed retrospectively 233 households affected by a H1N1-related closure of 3 schools in Perth, Australia in June 2009. Parents were advised to place their children under "home quarantine". Nearly half of parents (45%) of asymptomatic children reported taking at least one day off work to care for their child (range 1-5 days, median 3 days). Thirty-five percent said that they made special childcare arrangements for at least one day as a result of the closure (median of 2 days). One-third of parents thought the closure was inappropriate, while half thought it appropriate. In addition, they found that 74% of students reported going outside the home for sporting events, shopping, or outdoor recreation during the school closure period, despite the recommendation to avoid public gatherings. Parents of children with more outside activities more likely to think the school closure was inappropriate. The survey did not solicit information about wages or income, and did not attempt to identify whether the effect on households differed by socioeconomic status.

In contrast, Johnson et al (2008) found relatively modest impacts on 220 families from a one-week school closure due to an influenza B outbreak in a rural county in North Carolina. Although one-quarter of adults reporting missing work during that period, most were absent because of their own illness or to treat a sick child. The only respondents who missed work solely due to the school closure were school employees. Three-quarters of respondents said that someone was regularly available to provide childcare, and although 10% said they needed to make special childcare arrangements, only 2 respondents (1%) reported spending extra money. The closure was widely supported by parents, with 91% feeling the closure was appropriate. The authors note, however, that the rural county may not be representative as schools frequently close for large winter storms and parents may be more prepared with alternative arrangements. They also note that the county has a smaller-share of single-parent households than the national average.

Existing guidance and P&S

When should BCAs for PHP/PM incorporate larger-scale macroeconomic effects? There is little existing guidance on whether BCA models should use partial or general equilibrium frameworks. (All existing CEA guidance assumes a partial equilibrium framework by definition, since only effects within the health sector are included). OMB (2003) does not discuss when general equilibrium frameworks might be advisable, let alone required. EPA's draft 2008 guidance suggests that a general equilibrium framework may be more appropriate when it is clear that an environmental rule will affect many markets, although it does not provide exact guidance on when a GE framework would be required, nor how a GE model should be constructed.

The structural models described above are time-consuming to build and run, and the expertise needed is likely beyond that available to many government agencies charged with economic analysis. In addition, the errors arising from such models are likely to swamp any of the uncertainty in other parts of the analysis. Clearly, analyses should be proportionate to their scale of their analytical goals and available resources. A state health department conducing a BCA of a antiviral stockpiling program will probably not need, nor have the resources, to model the general equilibrium effects on the benefits side in their state, let alone nationwide. A full GE model may be a more appropriate investment for a federal analysis of a very expensive national-level program (such as stockpiling respirators, for example, or recommending nationwide school closure guidelines).

Incorporating macroeconomic effects may also be more important for BCAs of infectious disease outbreaks which appear suddenly and spread very quickly, producing a shock to the system. For diseases that spread more slowly like MRSA, drug-resistant tuberculosis, etc it seems more likely that individuals and economies would adapt over time (assuming relatively low attack rates – there are certainly large macroeconomic effects on countries with very high prevalence rates of disease such as malaria, HIV/AIDS, or tuberculosis).

For CEA, approaches like the one taken by Sander et al (2009) are a useful first step towards consideration of non-health impacts. As described in the appendix, Sander *et al* include as costs the estimate of work days lost as a result of child illness (for parents) and school closure policies (to teachers, staff, and parents). They also include travel and time costs of vaccination and antiviral treatment. Because the authors estimate a CEA model, they need not model the more difficult benefits side of the equation, but rather find the policies (or combination of policies) which have the lowest cost per QALY gained. Beutels et al (2008) also suggest ways that constrained treatment capacity (which would lead to longer waits for care for patients) could be translated into QALYs in a cost-effectiveness approach.

For BCAs, it may be prudent at this point to include best estimates of macro-level impacts on the cost side in a partial equilibrium framework but stop short of full-scale GE models for the benefits side. Decision-makers can examine these results, which provide a more complete picture of the costs of PHP/PM programs, alongside the emerging estimates of the potential GDP effects from pandemics described above. An alternative would be to model the range of impacts in the literature in a probabilistic sensitivity analysis, though as noted before the error in these estimates will almost surely drive the distribution of net benefits. Given the number of recent working papers in this area, as well as the attention brought by the H1N1 pandemic and the possibility of an H5N1 pandemic, this line of research may expand dramatically. If better estimates become available and GE models become easier to implement, these P&S would need to be adapted.

Uncertainty

The treatment of uncertainty will be central to any economic evaluation of PHP/PM programs because so many parameters[23] are not known with a high degree of certainty. First and foremost, the probability of a pandemic occurring[24] as well as its severity is highly uncertain.

[23] I address principally parameter uncertainty here, although it is important for analysts to also acknowledge and test for model uncertainty. Since most of this type of uncertainty comes in the approach for modeling epidemiological effects, I defer to the existing standards for CEA (Gold et al 1996, Weinstein et al 2003), as well as a recent paper specifically targeted at modeling disaster responses (Brandeau et al. 2003).

[24] One interesting source for these probabilities may be "prediction markets" – see Philip Polgreen's presentation at the October 7, 2009 session on pandemics at Resources for the Future (www.rff.org).

Existing guidelines and texts in both BCA and CEA stress the importance of addressing uncertainty (OMB 2003, Gold et al 1996, Boardman et al 2003, Drummond et al. 1997). This may take the form of univariate sensitivity analysis, where key uncertain parameters are varied in the analysis *ceteris paribus*, often in an attempt to identify "break-even" values where net benefits are equal to zero or where C/E ratios are equal to "cost effective" or "very cost effective" levels[25]. All six PHP/PM studies reviewed included a univariate sensitivity analysis.

Probabilistic approaches like Monte Carlo analysis are increasingly common in many fields as the availability of software and computing power has made conducting them fairly simple (Weinstein et al. 2003,Krupnick et al. 2006, Caulkins 2002). They are now required by OMB (2003) for regulations expected to have an economic impact of $1 billion or more. Monte Carlo techniques allow the analyst to allow several uncertain parameters to vary simultaneously and construct a range of possible outputs (e.g. net benefit measures). Specifically, the analyst defines a distribution of plausible values for each uncertain parameter. Parameters can be correlated. These distributions can be elicited from experts using Delphi methods (see Morgan and Henrion 1990), or can be estimated from existing literature. The Monte Carlo model then randomly draws from this distribution for each uncertain parameter and calculates the net benefits that would result from the "draw." It repeats this process many times (e.g., 10,000), each time generating a net benefit estimate. The result is a distribution of net benefits estimates, which can then be described probabilistically. OMB recommends reporting both measures of central tendency from this distribution (median net benefits and expected value (mean)) as well as 95% confidence intervals. Results can also be presented as the probability of observing positive net benefits. Four of six PHP/PM papers reviewed used Monte Carlo simulation approaches.

For preparedness programs, the probability of an infectious outbreak is perhaps the most important uncertain parameter, and an obvious but critical standard in any economic evaluation of preparedness programs is to vary the probability of an outbreak occurring in a sensitivity analyses framework (as Balicer et al. 2005 do). For the sake of transparency, this should include a univariate sensitivity analysis (probability of pandemic alone) in addition to any multivariate Monte Carlo simulations. Although historical data will continue to provide the best guide to the probability of a new outbreak, globalization has dramatically changed the ease and speed with which new diseases can be spread throughout the world (as modeled by Colizza et al. 2007). Furthermore, for some diseases in some countries the impact of a changing climate may also be an

[25] As discussed above, these cutoffs are fairly arbitrary and not grounded in what consumers might or might not be willing to pay for the health effects of interest.

important factor in the probability of an outbreak. A useful form of sensitivity analysis for the probability of attack might be a break-even analysis. Policy-makers can then use this information in making decisions about how much precaution to take.

For containment and mitigation programs like quarantines, border closures, and social distancing policies, however, the analyst is concerned with identifying the optimal policies given that the pandemic is occurring. Thus the probability of a pandemic occurring is unimportant. Rather, the uncertain parameters which are likely to be of the most importance are the characteristics of the pandemic (transmissibility and attack rate, mortality rate), the characteristics of the intervention (e.g. how much will a school closure slow transmission[26]), and the macroeconomic consequences of containment and mitigation programs, especially social distancing measures. Because of the large number of uncertain parameters, these types of programs would probably be best suited for multivariate, probabilistic Monte Carlo analysis.

The challenge, as others have noted (Caulkins 2002), is communicating probabilistic results to policymakers. One approach is to design models with accessible user-interfaces so that policymakers can personally run various scenarios with different assumptions. For a more in-depth discussion of approaches for presenting probabilistic information to policymakers and to the public, see Morgan and Henrion (1990) and Krupnick (2006).

Discounting

The issue of discounting, or how to adjust the value of benefits or costs that occur in the future to be commensurate with benefits and costs in the current period, will be important in many types of BCAs for PHP/PM. On the benefits side, for pandemics that have fairly short case durations and few long-term associated disabilities (like influenza), the choice of a discount rate will primarily affect the valuation of avoiding premature deaths. In other words, if most patients are sick for a few weeks and recover completely, there are few health effects occurring in future years to be discounted. On the other hand, some types of programs may involve costs in the current period but benefits occurring (with some probability) in future years. Preparedness training programs and the stockpiling of antiviral drugs or low-efficacy vaccines with relatively long shelf lives[27] are two examples. For many other types of programs, however, discount

[26] Annex 1 of the recent WHO guidance (WHO 2009) provides the most up-to-date information on assumptions that analysts should make about these first two categories of uncertain parameters.

[27] The shelf life for oseltamivir (Tamiflu) is 5 years (Siddiqui and Edmunds 2008)

rates may have little impact on net benefits. For example, mitigation or containment programs (e.g. social distancing programs like school closures, travel cessations, high-efficacy vaccine research and deployment) would have most benefits and costs occurring within a small time frame.

Because of its key role, the choice of an appropriate social discount rate has long been the subject of considerable discussion in the literature (Portney and Weyant 1999) and in benefit-cost texts (Zerbe and Dively 1994; Boardman et al. 2005; Brent 1996). An approach using the shadow price of capital (SPC) has the most theoretical appeal, but requires knowledge of how projects are financed (in order to estimate the fraction of benefits and costs measured as increments to consumption versus private sector investment) and estimates of the shadow price of capital, as well as the more common assumptions about the marginal social rate of time preference and marginal rate of return on investments.

The predominant analytical approach remains constant exponential discounting[28]. One alternative to this approach is hyperbolic discounting, which tends to make benefits or costs in the near future somewhat less important and those in the distant future more important (they are discounted less heavily). There is behavioral evidence that hyperbolic discounting may capture time preferences more accurately. In addition, much of the debate over constant exponential versus hyperbolic discounting has centered around analyses of policies, programs or investments with inter-generational equity concerns, chief among them climate change (see Portney and Weyant 1999). This may be less of a concern for PHP/PM programs, which have timeframes where both costs and benefits occur within a generation.

The OMB, in both Circular A-4 and A-94, provide clear guidance. In addition to undiscounted benefits and costs, results should be presented using two real discount rates. A rate of 7% represents the rate of return to private capital, while a 3% rate represents the consumption rate of interest[29]. Both OMB (2003) and EPA (2008) discuss discounting in the presence of intergenerational concerns. OMB recommends using a positive rate lower than 3% in sensitivity analysis when rules have "important intergenerational benefits and costs". EPA (2008) recommends using a schedule of discount factors based on a stochastic "random walk" (Newell and Pizer 2003) for programs with time horizons longer than 50 years. OMB recommends lower rates (based on the marginal rate of return on investments) for cost-effectiveness analyses (these were 0.9% for a 3-year time

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[28] Constant exponential discounting applies a discount weight to benefits or costs occurring in time t of the form $w_t = 1 / (1+r)^t$, where r is the discount rate. Hyperbolic discount weights are of the form $w_t=(1+\alpha t)^{-r/\alpha}$

[29] Circular A-94 does permit an analyst to use the SPC approach with "OMB concurrence".

horizon to 2.7% for a 30-year time horizon[30] as of December 2008).

There is considerable agreement in the health evaluation field to use a real discount rate of 3%, and this rate has been codified in several cost-effectiveness guidelines (Gold et al. 1996, Musgrove and Fox-Rushby 2006)[31]. This rate is applied to both discounting of health states (i.e. comparing life years saved in 1 year versus those saved in 10 years) as well as financial outlays in the current and future periods. (Many studies do not adjust specifically for inflation in future direct health care costs, implicitly assuming that health costs will rise in parallel with overall price inflation; an assumption that seems unwarranted in the U.S.[32]). This consensus is largely reflected in the PHP/PM evaluations in the Appendix. Five of six studies (both CEA and BCA) use a base case discount rate of 3% (the sixth uses a base case of 3.5%). Only two studies varied the discount rate in a sensitivity analysis. Siddiqui and Edmunds (2008) use a discount rate of 6% as an upper bound, and Nichol (2001) uses 5%.

To maintain consistency with the bulk of the health economic literature and because it is also consistent with existing OMB guidance, analysts should continue to present results using a real discount rate of 3%. All studies should also present results using a 7% rate, or whatever rate is currently recommended by OMB. Where the choice of discount rate has a substantial impact on results, analysts should avoid presenting the 3% rate as the "base case" value but rather both sets of results as equally plausible. In all cases, however, the discount rate should be varied in a sensitivity analysis. Results should also be presented in undiscounted form, which may be especially useful to policymakers given the uncertainty in the timing and magnitude of a pandemic.

Disparate impacts and equity

Pandemics may have disparate impacts within the U.S. population. These disparities may occur because some groups could be more or less susceptible to infection (age, health status, prior infection, occupation) or to have more severe

[30] http://www.whitehouse.gov/omb/circulars_a094_a94_appx-c/

[31] It is interesting to note that Gold (1996, pg. 159) recommend that "costs and health effects should be discounted to present value at a rate consistent with the shadow-price-of-capital (SPC) approach to evaluating public investments" and recommend a 3% real discount rate, in practice most studies seem to have adopted the latter recommendation but not the former.

[32] The cost of health care has in fact increased considerably faster than overall price inflation in the U.S. (inflation-adjusted health spending has taken an increasingly larger share of GDP). See: Chernew et al. 2003. It is certainly possible to use only the health-care components of the CPI to correct for this.

cases that end in death. There is a considerable amount of research on these types of impacts, and epidemiologists often focus their efforts on identifying and giving preferential treatment to these high-risk groups. Among groups which are similar in these characteristics, however, disparate disease impacts could also occur by socioeconomic status if a) lower-income groups have more difficulty accessing the healthcare system, b) low-income communities are targeted less by public health departments both in disease surveillance and in mitigation, and c) low-income groups are less able to cope with school closures or other social distancing programs because they may hold hourly-wage jobs with less-generous (or no) leave policies. Although plausible, there is little existing evidence of disparate health impacts of pandemic infectious disease outbreaks by socioeconomic status in the U.S[33]. This type of research would be useful, and the H1N1 pandemic may have provided an opportunity to evaluate prevalence rates controlling for socioeconomic factors.

Just as evidence of disparate age or health impacts are important to tailoring epidemiological responses, disparate impacts by income might imply different approaches to a benefit-cost analysis. In other words, should we treat programs that reduces illness and death in an economically-disadvantaged group differently? Even without disparate impacts, applying "distributional" or "equity" weights to groups by income may affect the results of a BCA. The use of distributional weights in economic analysis to accomplish equity goals has been widely discussed in standard benefit-cost texts (Zerbe and Dively 1994; Sugden and Williams 1978,Brent 1996,Boardman et al. 2005), but has rarely been implemented in practice. Economists for several decades have generally agreed that analyses should focus on increasing economic efficiency (using a potential Pareto criterion) and take the existing income distribution as given. According to Pearce (1997), " the procedure for integrating efficiency and equity into project appraisal fell largely into disuse, partly because it was not always easy to see the scientific basis for the equity weights[34], but partly because using projects to correct for fundamental inequities in income distribution is the wrong way to deal

[33] Differences between rich and poor countries, however, are more clear (Bloom and Canning 2006). In addition to vast differences in public health infrastructure and other private and public health investments, resource-poor countries may not have access to limited supplies of antivirals and vaccines in the event of an outbreak. This is an important ethical consideration raised in the WHO's recent guidance on pandemic influenza planning (WHO 2009). In practice, it seems unlikely that a global-level economic analysis of mitigation programs like stockpiling would be carried out, as there is currently no centralized purchasing mechanism large enough to accomplish the task nor institutional rules about how limited supplies would be distributed.

[34] Several authors have attempted to back-calculate the distributional weights implied by various government policies such as progressive income taxation or railroad closures in the UK (see Brent 1996 and Boardman et al. 2005).

with inequality." Although OMB (2003) recommends providing "a separate description of distributional effects (i.e. how both benefits and costs are distributed among sub-populations of particular concern)", it does not recommend explicitly applying equity weights. For more recent approaches to incorporating equity into economic analysis without using equity weights, interested readers should consult Adler (2008) and Graham (2008).

Similarly, cost-effectiveness analysis has generally avoided the use of distributional weights. Gold et al (1996, pg. 24) discuss distributional equity noting that the "assumption that all QALYs are valued equally may lead to some ethically unsettling distributional implications", though the guidelines do not recommend the use of distributional weights. As noted earlier, however, there has been some use of age weights in the calculation of DALYs (Murray et al. 2000), where health improvements or prevented deaths are weighted more heavily for working-age adults.

Of the economic evaluations of PHP/PM programs I reviewed, several used epidemiological models to separate populations by age, gender and occupation (principally to identify high-risk occupations like front line health workers). Unsurprisingly, none attempted to quantify impacts by socioeconomic status, and thus did not attempt to explicitly weight outcomes.

I will leave suggested principles & standards on this topic to another paper in this project examining methods for incorporating distributional equity (Loomis and Gonzalez-Caban 2010). As noted earlier, however, research on whether pandemics impact socioeconomic groups within the U.S. differently would be helpful. If such impacts occurred, it would be important to separately report benefits and costs for various groups as OMB (2003) suggests.

<u>Valuing mortality risk</u>

As described in section 2, a key distinction between CEA and BCA is the monetization of health impacts. For many health programs, how the analyst values changes in mortality risk will be a key decision. This will also be true for many or most pandemics like influenza or SARS which do not have long-lasting morbidity effects in many patients but do cause a number of premature deaths.

There has been an extensive discussion in both the economic and policy-analysis literature on the proper approach for valuing mortality risk changes, largely in response to environmental regulations in the U.S. like the Clean Air Act. Readers who come from backgrounds where CEA predominates may be unfamiliar with this large literature, and with the fact that the concept of mortality risk valuation is now well-established in regulatory BCAs. As described above, the two sources for establishing WTP for risk reduction that are theoretically-consistent with the BCA framework are revealed preference (typically wage hedonic studies or safety product studies) and stated preference (contingent valuation or stated choice). The US EPA has convened several expert panels to review this literature[35], and Robinson (2007) reviews estimates used in government regulation. There have also been two recent contingent valuation studies which examined WTP for mortality risk reduction in the context of pandemics. Gyrd-Hansen et al (2008) examined WTP for a course of the antiviral drug Tamiflu in Norway, and Liu et al (2005) examined WTP for a hypothetical vaccine against the SARS virus in Taiwan.

The most important continuing source of debate in the profession is the whether to use "differentiated" VSLs for different population sub-groups (e.g. by age, income, health status, or voluntariness of risk) or for different rule-making settings (e.g. cancer vs pandemics)[36]. This is an important debate in the context of pandemic planning and mitigation because of the differential impacts likely to be observed by age, health status, and risk. Although representative of preferences found in a number of revealed and stated preference studies, differentiation has proven controversial. An attempt by EPA to an age-adjusted VSL estimate in 2003 was characterized by the media as a "senior death discount", triggering a public backlash. The proposal was subsequently dropped by the EPA. OMB (2003) does not recommend using differentiated VSL estimates, and provides a range of VSL estimates from $1 million to $10 million while not endorsing a specific value. The EPA (2008) continues to recommend using a central estimate of $7.3 million per life saved (in 2009$), while recommending analysts note the limitations inherent in using a single estimate and presenting the distribution of impacts by age or risk category if possible. As noted above, the EPA has also convened a Science Advisory Board panel which is expected to take up this topic further.

Of the four PHP/PM benefit-cost studies reviewed, three use the human-capital approach to value mortality risk reductions, and one does not attempt a monetization at all[37]. None of the studies use estimates of individual WTP for risk reductions (e.g. a value-of-statistical (VSL) calculation).

In summary, there is a large amount of evidence suggesting that it is

[35] The most recent Science Advisory Board panel on VSL was convened in Sept. 2009. See: http://yosemite.epa.gov/sab/sabproduct.nsf/Meetings/34D7008FAD7FA8AD8525750400712AEB/?OpenDocument

[36] For an introduction to this topic, see Viscusi (2010) and Robinson (2009). Aldy and Viscusi (2007) summarize the evidence for heterogeneous WTP for risk reductions from revealed preference studies, and Krupnick (2007) reviews the evidence from stated preference studies.

[37] The study is framed as a "lower bound" benefit-cost analysis, but given that estimates for WTP for mortality risk are widely available, omitting this category of benefits might lead one to question whether the study could be properly called a benefit-cost analysis.

possible to derive a welfare-theoretic measure of individuals' WTP for mortality risk reductions and the practice of incorporating these values into BCAs is now well-accepted in government practice in the U.S. and elsewhere. The question of what estimates to use, and whether there is sufficient evidence to justify the use of differentiated estimates, continues to evolve. Analysts should consult current guidance from the OMB. Because much of the research and policy decisions on VSLs involve environmental rules, analysts should also be sure to consult the EPA's most current estimates and recommended practices in this area. As EPA suggests, where analysts can quantify the impacts of a PHP/PM program by age, health status or risk, they should present this analysis in the BCA without necessarily applying differential values. When using a central estimate of WTP for mortality risk reduction, this parameter should clearly be included in a univariate sensitivity analysis (reporting a break-even VSL would be helpful) as well as any probabilistic Monte Carlo analysis.

Externalities

An externality occurs when a transaction imposes costs on (or provides benefits to) a party outside that transaction. These are sometimes called "spillover" effects, and represent a market failure. In public health, the presence of positive or negative externalities is one justification used for public provision of health services. There are several types of externalities that may be relevant to a BCA of PHP/PM and which should be included in the analysis where sufficient data exist and where appropriate to the scale of the analysis. These include the possibility of positive externalities from vaccination or antiviral treatment and negative externalities from increasing microbial resistance. A related point, though perhaps not technically an externality, is the question of scope of the analysis.

Vaccines against some types of diseases provide indirect protection[38]. As the vaccinated population increases, the remaining unvaccinated population enjoys a lower probability of infection (i.e. "herd immunity"). The policy response here is old and uncontroversial in theory (Pigou 1920): vaccines will be underprovided in the private market, and a Pigouvian subsidy is needed to equate marginal costs with marginal social benefits. The extent of the externality may justify public provision with no user fees, although free provision runs the risk of

[38] This externality will tend to be larger for diseases which depend primarily on human hosts, and smaller (or zero) for diseases that also have non-human hosts or can survive for long periods of time in the environment.

vaccinating a higher fraction of the population than is socially optimal (i.e. the disease can be eradicated with less than 100% coverage precisely because of herd immunity).

Although vaccines are often cited as a textbook example of a positive externality, relatively few economic evaluations of health interventions have included an analysis of the effect of vaccination externalities (some exceptions include Beutels et al. 2002; Brisson and Edmunds 2003; and Jeuland et al. 2009). There has been only one study to attempt to identify the socially-optimal vaccine subsidy with field data (Cook et al. 2008). Widespread treatment with antiviral drugs like Tamiflu may also produce positive externalities if they reduce virus loads in infected patients and thus shedding of the virus to others (analogous to the effect of widespread use of anti-retrovirals on HIV/AIDS prevalence).

To the extent that epidemiological data are available on the magnitude of indirect protection from either targeted vaccination[39] or provisions of antivirals, these should be incorporated into economic evaluations of such programs using either a static model (like Jeuland et al. 2009) or a stochastic, agent-based model (like the one used in Sander et al. 2009, although they did not model vaccination or treatment externalities).

A second externality is the potential for the infectious agent to involve resistance to antimicrobial treatment (Regoes and Bonhoeffer 2006). Building on earlier work by Stilianakis et al (1998), Alexander et al (2007) use a mathematical modeling approach to show the connection between various antiviral treatment strategies and the potential for the resistance emerging (although the paper attempts no economic analysis). It may be possible, however, to incorporate these externalities into either a CEA framework (perhaps as an indirect cost in the numerator) or a BCA framework. The best economic work to date on this resistance externality is on resistance to antibiotics (Laxminarayan 2002) and anti-malaria treatments (Laxminarayan et al. 2006). There is sufficient evidence for anti-microbial resistance for many diseases that analysts in most cases should make an attempt to incorporate this into their analysis, again either through a static model or stochastic agent-based models. These models should allow the effectiveness of a treatment to vary stochastically and negatively-correlated with the level of use of the treatment.

Finally, economic evaluation of containment strategies present a problem that, while not technically an externality, presents a similar problem. Areas with poor quality public health infrastructure (including monitoring or quarantine procedures) may allow a nascent outbreak to spread to areas which have invested heavily in preparation and monitoring. Barring drastic measures such as complete

[39] There is, at least, evidence of indirect protection for annual influenza vaccination (Reichert et al. 2001).

border closures, cessation of air travel, and trade restrictions (all of which carry extremely high costs), a more prepared region or country may be unable to contain the disease[40].

At the international level, the principle policy of interest may be in investments to strengthen public health systems in poor countries which may be the source of the initial outbreak (e.g. SARS, avian influenza, multidrug-resistant tuberculosis)[41]. A full social benefit-cost analysis of such an investment program, however, would be extremely difficult. There is little epidemiological research to provide support for the magnitude of the spillover effects, and finding appropriate shadow prices would be more analytically and ethically challenging still (for example, should different shadow prices for prevented deaths be used in different countries?). Furthermore, strengthening public health systems in poor countries would potentially create large social benefits in the country, which donor countries may value for humanitarian reasons beyond pandemic containment. Although perhaps a useful exercise for large donors in the health sector or multilateral agencies (WHO, World Bank), a national agency like the U.S. CDC would be unlikely to set their planning area for an analysis so wide.

Within the U.S., should an analysis of public health preparedness spending in one county or state incorporate the spillover benefits to a neighboring county or state? Ideally, the scope of analysis would be large enough to encompass all relevant benefits and costs of a program. Still, I am unaware of completed evaluations of the economic value of surveillance or monitoring systems, even at the federal level[42]. The value of information for planning responses may also be quite high. As suggested in Handel et al (2007), it is critical that, at an early stage of an outbreak, information on the transmission characteristics of the pathogen be determined and provided to disease modelers. This would allow them to evaluate the potential effectiveness of various control strategies. Again, though, the

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[40] Although several studies use stochastic models to evaluate the effectiveness of various containment strategies (Colizza et al. 2007 Cooper et al. 2006), I am unaware of any studies that have attempted a cost-effectiveness or benefit-cost analysis of these strategies.

[41] Another analogous policy would be to improve reporting of disease outbreaks and information-sharing, even if the public health systems themselves are not improved. China's delay in reporting early SARS is believed to have increased the scope of the SARS outbreak. See "Learning from SARS, China Vows Swift Flu Reporting", ABCNews, April 27, 2009

[42] There may, however, be such an analysis completed soon. Congress directed the National Academies to commission a study to "evaluate the effectiveness of BioWatch (described in Section 1), including a comparison of benefits and costs" as well as "the benefits and costs of an enhanced national surveillance system that relies on U.S. hospitals and the U.S. public health system". The expert committee has so far issued only a brief interim report. See: http://www.iom.edu/Reports/2009/Effectiveness-of-National-Biosurveillance-Systems-BioWatch-and-the-Public-Health-System-Interim-Report.aspx

epidemiological data seem to be lacking, and I am unaware of research examining whether county-level public health spending is correlated with the number of reported cases during a pandemic (i.e. how effective is local preparedness in practice?)[43]. Although crucial in identifying the optimal level of PHP spending at both the local and national levels, incorporating these effects would seem impractical at this stage.

CONCLUDING REMARKS

This paper has illustrated a number of issues that might arise in conducting economic analyses (namely BCA, though also CEA) of public health preparedness or pandemic mitigation programs. Some of these issues raised have been debated extensively elsewhere (e.g. the choice of a social discount rate, the importance of sensitivity analyses, the use of distributional weights). Some of the issues have received less attention in the economic evaluation literature (how to incorporate externalities, the scope of larger macroeconomic effects). The aim has been to begin a discussion of appropriate principles and standards on both types of issues.

When might benefit-cost analysis be preferred to cost-effectiveness analysis? The choice of methodologies can unfortunately be contentious, and may be driven by the academic training and peer groups of analysts more than underlying theoretical justifications. I humbly offer a few thoughts in conclusion.

As described above, many of the policies and programs for pandemic mitigation may have large economic costs outside the health sector. Proponents of CEA might argue that those additional indirect costs should simply be added to the numerator of the cost-effectiveness ratio; the objective would remain minimizing illness and death at lowest cost. This is the approach taken by Sander et al (2009). Considerations such as constrained health capacity could also be incorporated into the CEA framework as well (Beutels et al. 2008). When examining policies to prevent the spread of a pandemic that is underway (i.e. containment or mitigation strategies), it may well make the most sense to continue to use CEA to improve the technical efficiency with which health funds which have already been allocated should be spent.

There is, of course, no guarantee that a strategy with the lowest cost-effectiveness ratio would pass a benefit-cost test. That would require an understanding of how individuals value a QALY saved or DALY avoided; most importantly, it involves understanding how individuals value reductions in

[43] Bloom and Canning (2006) discuss the correlation between income and epidemics at the national level. One problem with a county-level analysis that would arise is measurement error – areas with lower levels of public health infrastructure might be less likely to detect and report cases.

mortality risk. However, given the likely magnitude of the macroeconomic costs of a pandemic (as discussed below, from 0.4% to 5% of U.S. GDP), it would appear *a priori* that many containment and mitigation interventions would likely pass a benefit-cost test. The risk of a costly policy mistake would seem low, though this is an empirical question. The risk remains: closing schools and workplaces for five weeks to slow a pandemic may well dramatically harm the economy in the short run.

Public health preparedness problems, however, may lend themselves more to BCA methods. Here the principle issue is not simply which policies or programs will "work" best, but what overall level of preparation society is willing to pay for. This can still be incorporated into a CEA framework, but the derivation of the QALY or DALY effect will depend very heavily on the assumed probability of a pandemic occurring. This probability will also drive the BCA analysis, but it may be more transparent to present these tradeoffs in a BCA framework. Returning to the ventilator example mentioned in the introduction, how many ventilators should the U.S. stockpile for pandemic influenza? Ventilators (and the health professionals trained to use them) will not slow the spread of a pandemic, but will greatly enhance the health system's ability to minimize deaths from influenza or other acute respiratory illnesses. They are, however, very costly. By using information on how individuals reveal or report trading income for reductions in mortality risk[44], it might be straightforward to identify the socially optimal level of ventilator (and staff) investments that would equate marginal costs and marginal benefits. A similar argument could be made for the optimal size of stockpiles of poorly-targeted vaccines or antivirals, though these calculations would be more complicated for several reasons[45], including the

[44] One issue that arises would be "benefits transfer", or the use of shadow prices derived in one application or setting to another. Many of the existing revealed preference studies of WTP for mortality risk reductions are from labor market studies where the mortality risks are of fatal on-the-job injuries. Many of the stated preference studies have been in the context of familiar conditions with long latency periods (i.e. cancer, diabetes, heart disease). Individuals may view reductions in the risk of dying from a sudden and widespread pandemic differently because of fear, dread, etc.

[45] Because the shelf life for oseltamivir (Tamiflu) is 5 years, optimal stockpiling policies are of particular economic interest (Siddiqui and Edmunds 2008). Although several of the evaluations described in the Appendix discuss stockpiling, only one uses them in an optimization framework. Rowthorn *et al* (2009) combine a epidemiologic model with an economic optimization approach to find the optimal strategy for allocating a fixed stockpile of antiviral drugs when outbreaks occur in two locations. Using an objective of minimizing the discounted sum of total infection in the two regions, they find that the seemingly-intuitive strategy of deploying the most resources to the area with the highest number of infected is in fact the worst possible strategy. They instead find that the optimal strategy is to treat the area with the highest number of susceptibles (and thus lowest number of infected) preferentially. The result is robust to several extensions and assumptions, although the authors note that further work combining

externality of indirect protection.

In either approach, however, analysts should first and foremost bear in mind that their economic evaluations should serve as useful decision-making aides for policymakers. They should also aim to make clear the tradeoffs that policymakers face in designing public policies and making investment decisions, especially when some of those tradeoffs may not be immediately apparent. I would echo Weinstein (2003) and Garrison (2003) that health economic analyses should first and foremost be transparent and reasonable.

REFERENCES

Adler, M. D. (2008). "Risk equity: a new proposal." Harvard Environmental Law Review **32**: 1-47.

Aldy, J. E. and W. K. Viscusi (2007). "Age Differences in the Value of Statistical Life: Revealed Preference Evidence." Rev Environ Econ Policy **1**(2): 241-260.

Alexander, M. E., C. S. Bowman, et al. (2007). "Emergence of drug resistance: implications for antiviral control of pandemic influenza." Proceedings of the Royal Society B: Biological Sciences **274**: 1675-1684.

Arrow, K., R. Solow, et al. (1993). "Report of the NOAA Panel on contingent valuation." Federal Register **58**(10): 4601-4614.

Balicer, R., M. Huerta, et al. (2005). "Cost-benefit of stockpiling drugs for influenza pandemic." Emerging Infectious Diseases **11**(8): 1280-1282.

Balicer, R. D., S. B. Omer, et al. (2006). "Local public health workers' perceptions toward responding to an influenza pandemic." BMC Public Health **6**(99).

Barry, J. M. (2004). The great influenza: The epic story of the deadliest plague in history, Viking.

Beutels, P., W. J. Edmunds, et al. (2002). "Economic evaluation of vaccination programmes: A consensus statement focusing on viral hepatitis." Pharmacoeconomics **20**(1): 1-7.

Beutels, P., W. J. Edmunds, et al. (2008). "Partially wrong? Partial equilibrium and the economic analysis of public health emergencies of international concern." Health Economics **17**: 1317-1322.

Blendon, R. J., L. M. Koonin, et al. (2008). "Public response to community mitigation measures for pandemic influenza." Emerging Infectious Diseases **14**: 778-786.

Bloom, D. E. and D. Canning (2006). Epidemics and economics. Program on Global Demography of Aging Boston.

Bloom, E., V. d. Wit, et al. (2005). Potential economic impact of an avian flu pandemic on Asia. Economics and Research Department Policy Brief. Manila, Asian Development Bank.

Boardman, A., D. H. Greenberg, et al. (2005). Cost-benefit analysis: concepts and practices. Upper Saddle River, NJ, Prentice Hall.

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economic optimization with epidemiological modeling is needed.

Brandeau, M. L., G. S. Zaric, et al. (2003). "Resource allocation for control of infectious diseases in multiple independent populations: beyond cost-effectiveness analysis." Journal of Health Economics **22**: 575-598.

Brent, R. J. (1996). Applied cost-benefit analysis. Lyme, US, Edward Elgar.

Brisson, M. and W. J. Edmunds (2003). "Economic evaluations of vaccination programs: The impact of herd immunity." Medical Decision Making **23**: 76-82.

Canada, C. B. o. (2003). The economic impact of SARS, Conference Board of Canada.

Cauchemez, S., N. M. Ferguson, et al. (2009). "Closure of schools during an influenza pandemic." The Lancet Infectious Diseases **9**(8): 473-481.

Caulkins, J. P. (2002). "Using models that incorporate uncertainty." Journal of Policy Analysis and Management **21**(3): 486-491.

Chernew, M. E., R. A. Hirth, et al. (2003). "Increased spending on health care: How much can the United States afford?" Health Affairs **22**(4): 15-25.

Colizza, V., A. Barrat, et al. (2007). "Modeling the worldwide spread of pandemic influenza: baseline case and containment interventions." PLoS Medicine **4**(1): e13.

Cook, J., M. Jeuland, et al. (2008). "Re-visiting socially-optimal vaccine subsidies: an empirical application in Kolkata, India." Journal of Policy Analysis and Management **in press**.

Cooper, B. S., R. J. Pitman, et al. (2006). "Delaying the international spread of pandemic influenza." PLoS Medicine **3**(6): 845-855.

Drummond, M. F. and T. Jefferson (1996). "Guidelines for authors and peer reviewers of economic submissions to the BMJ." British Medical Journal **313**: 275-283.

Drummond, M. F., B. O'Brien, et al. (1997). Methods for the economic evaluation of health care programmes, Oxford University Press.

Effler, P. V., D. Carcione, et al. (2010). "Household responses to pandemic (H1N1) 2009-related school closures, Perth Australia." Emerging Infectious Diseases **16**(2): 205-211.

Ferguson, N., D. A. T. Cummings, et al. (2006). "Strategies for mitigating an influenza pandemic." Nature **442**: 448-452.

Fowler, R. A., G. Sanders, et al. (2005). "Cost-effectiveness of defending against bioterrorism: A comparison of vaccination and antibiotic prophlyaxis against anthrax." Annals of Internal Medicine **142**(8): 601-611.

Freeman, A. M. (1999). The measurement of environmental and resource values: Theory and methods. Washington, DC, Resources for the Future.

Garrison, L. P. (2003). "The ISPOR Good Practice Modeling Principles: A sensible approach: be transparent, be reasonable." Value in Health **6**(1): 6-8.

Germann, T. C., K. Kadau, et al. (2006). "Mitigation strategies for pandemic influenza in the United States." PNAS **103**(15): 5935-5940.

Gold, M. R., J. E. Siegel, et al., Eds. (1996). Cost-effectiveness in health and medicine. New York, Oxford University Press.

Graham, J. D. (2008). "Saving lives through administrative law and economics." University of Pennsylvania Law Review **157**: 101-244.

Gyrd-Hansen, D., P. A. Halvorsen, et al. (2008). "Willingness-to-pay for a statistical life in the times of a pandemic." Health Economics **17**(1): 55-66.

Haddix, A. C., S. M. Teutsch, et al., Eds. (2003). Prevention effectiveness: A guide to decision analysis and economic valuation. New York, Oxford University Press.

Handel, A., I. M. L. Jr, et al. (2007). "What is the best control strategy for multiple infectious disease outbreaks?" Proceedings of the Royal Society B: Biological Sciences **274**: 833-837.

Hatchett, R. J., C. E. Mecher, et al. (2007). "Public health interventions and epidemic intensity during the 1918 influenza pandemic." PNAS **104**(18).

Institute of Medicine (IOM) (2006). Valuing health for regulatory cost-effectiveness analysis. Washington DC, National Academies Press.

James, S. and T. Sargent (2006). The economic impact of an influenza pandemic. Canadian Department of Finance Working Paper.

Jamison, D. T., J. G. Breman, et al., Eds. (2006). Disease control priorities in developing countries. Washington DC, The World Bank and Oxford University Press.

Jeuland, M., J. Clemens, et al. (2009). "Incorporating herd protection into cost-effectiveness calculations of new-generation oral cholera vaccines: a multi-site analysis." Value in Health **forthcoming**.

Johnson, A. J., Z. S. Moore, et al. (2008). "Household responses to school closure resulting from outbreak of influenza B, North Carolina." Emerging Infectious Diseases **14**(7): 1024-1030.

Jonung, L. and W. Roeger (2006). The macroeconomic effects of a pandemic in Europe - A model-based assessment. Economics Papers, European Commission Directorate-General for Economic and Financial Affairs.

Just, R. E., D. L. Hueth, et al. (2004). The welfare economics of public policy, Edward Elgar.

Kennedy, S., J. Thomson, et al. (2006). A primer on the macroeconomic effects of an influenza pandemic. Treasury Working Paper. Washington DC.

Keogh-Brown, M., S. Wren-Lewis, et al. (2009). The possible macroeconomic impact on the UK of an influenza pandemic. University of Oxford Department of Economics Discussion Paper Series. Oxford.

Krupnick, A. (2007). "Mortality-risk Valuation and Age: Stated Preference Evidence." Rev Environ Econ Policy **1**(2): 261-282.

Krupnick, A., R. Morgenstern, et al. (2006). Not a sure thing: Making regulatory choices under uncertainty. R. f. t. Future. Washington DC, Resources for the Future.

Langton, D. (2008). Avian flu pandemic: Potential impacts of trade disruptions. Washington DC, Congressional Research Service.

Laxminarayan, R. (2002). Battling resistance to antibiotics and pesticides: an economic approach. Washington DC, RFF Press.

Laxminarayan, R., M. Over, et al. (2006). "Will A Global Subsidy Of New Antimalarials Delay The Emergence Of Resistance And Save Lives?
10.1377/hlthaff.25.2.325." Health Aff. **25**(2): 325-336.

Lipscomb, J., K. R. Yabroff, et al. (2009). "Health Care Costing: Data, Methods, Current Applications." Medical Care **47**(7): S1-S6.

Liu, J.-T., J. K. Hammitt, et al. (2005). "Valuation of the risk of SARS in Taiwan." Health Economics **14**: 83-91.

Loomis, J. and A. Gonzalez-Caban (2010). How Two Non-Market Valuation Techniques

Can Improve Compliance with Environmental Justice Requirements: Three Case Studies Using Hedonic Property and Contingent Valuation Methods to Quantify the Distribution of Benefits by Ethnicity and Income. Benefit-Cost Analysis Center, University of Washington.

McKibbin, W. and A. Sidorenko (2006). Global macroeconomic consequences of pandemic influenza. Sydney, Australia, Lowy Institute for International Policy, Australian National University.

Meltzer, M., N. J. Cox, et al. (1999). "The economic impact of pandemic influenza in the United States: Priorities for intervention." Emerging Infectious Diseases **5**(5): 659-671.

Meltzer, M. I., K. M. Neuzil, et al. (2005). "An economic analysis of annual influenza vaccination of children." Vaccine **23**: 1004-1014.

Middaugh, J. P. (2008). "Pandemic influenza preparedness and community resiliency." Journal of the American Medical Association **299**(5): 566-568.

Morgan, M. G. and M. Henrion (1990). Uncertainty: A guide to dealing with uncertainty in quantitative risk and policy analysis. New York, NY, Cambridge University Press.

Murray, C. and A. D. Lopez, Eds. (1996). The global burden of disease: A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Global Burden of Disease and Injury Series. Cambridge, MA, Harvard University Press.

Murray, C. J. L., D. B. Evans, et al. (2000). "Development of WHO guidelines on generalized cost-effectiveness analysis." Health Economics **9**: 235-251.

Musgrove, P. and J. Fox-Rushby (2006). Cost-effectiveness analysis for priority setting. Disease Control Priorities in Developing Countries. D. T. Jamison, J. G. Breman, A. R. Meashamet al. Washington DC, The World Bank.

Newell, R. G. and W. A. Pizer (2003). "Discounting the distant future: how much do uncertain rates increase valuations?" Journal of Environmental Economics and Management **46**(1): 52-71.

Nichol, K. (2001). "Cost-benefit analysis of a strategy to vaccinate healthy working adults against influenza." Archives of Internal Medicine **161**: 749-759.

Nichol, K., K. P. Mallon, et al. (2003). "Cost benefit of influenza vaccination in healthy, working adults: an economic analysis based on the results of a clinical trial of trivalent live attenuated influenza virus vaccine." Vaccine **21**: 2207-2217.

Pearce, D. W. (1997). "Benefit-cost analysis, environment and health in the developed and developing world." Environment and Development Economics **2**(210-214).

Pigou, A. C. (1920). The economics of welfare.

Portney, P. R. and J. P. Weyant, Eds. (1999). Discounting and intergenerational equity. Washington DC, RFF Press.

Regoes, R. R. and S. Bonhoeffer (2006). "Emergence of drug-resistant influenza virus: population dynamical considerations." Science **312**(5772): 389-391.

Reichert, T. A., N. Sugaya, et al. (2001). "The Japanese experience with vaccinating schoolchildren against influenza." The New England Journal of Medicine **344**(12): 889-896.

Richardson, H. W., P. Gordon, et al., Eds. (2007). The economic costs and consequences

of terrorism. Northampton, MA, Edward Elgar.
Robinson, L. A. (2007). "How US Government Agencies Value Mortality Risk Reductions." Rev Environ Econ Policy **1**(2): 283-299.
Robinson, L. A. (2009). "Valuing lives, valuing risks and respecting preferences in regulatory analysis." Regulation and Governance **forthcoming**.
Robinson, L. A., Ed. (2010). Assessing regulatory costs and benefits. Encyclopedia of Environmental Health, Elsevier.
Rowthorn, R., R. Laxminarayan, et al. (2009). "Optimal control of epidemics in metapopulations." Journal of the Royal Society Interface.
Sadique, M. Z., E. J. Adams, et al. (2008). "Estimating the costs of school closure for mitigating an influenza epidemic." BMC Public Health **8**(135).
Sadique, M. Z., W. J. Edmunds, et al. (2007). "Precautionary behavior in response to perceived threat of pandemic influenza." Emerging Infectious Diseases **13**(9): 1307-1313.
Sander, B., A. Nizam, et al. (2009). "Economic evaluation of influenza pandemic mitigation strategies in the United States using a stochastic microsimulation transmission model." Value in Health **12**(2): 226-233.
Schmier, J., S. Li, et al. (2008). "Benefits and costs of immunizing children against influenza at school: An economic analysis based on a large-cluster controlled clinical trial." Health Affairs **27**(2): w96.
Siddiqui, M. R. and W. J. Edmunds (2008). "Cost-effectiveness of antiviral stockpiling and near-patient testing for potential influenza pandemic." Emerging Infectious Diseases **14**(2): 267-274.
Stilianakis, N., A. S. Perelson, et al. (1998). "Emergence of drug resistance during an influenza epidemic: Insights from a mathematical model." Journal of Infectious Diseases **177 (April)**: 863-873.
Sugden, R. and A. Williams (1978). The principles of practical cost-benefit analysis. New York, Oxford University Press.
U.S. Congressional Budget Office (CBO) (2006). A potential influenza pandemic: An update on possible macroeconomic effects and policy issues, Congressional Budget Office.
U.S. Environmental Protection Agency (EPA) (2008). Guidelines for Preparing Economic Analysis: External Review Draft. Washington DC, Environmental Protection Agency.
U.S. Office of Management and Budget (OMB) (2003). Circular A-4, Regulatory Analysis.
Viscusi, W. (2010). "The heterogeneity of the value of statistical life: Introduction and overview." Journal of Risk and Uncertainty **40**(1): 1-13.
Viscusi, W. K. and J. E. Aldy (2003). "The Value of a Statistical Life: A Critical Review of Market Estimates Throughout the World." Journal of Risk and Uncertainty **27**(1): 5-76.
Weinstein, M. C., B. O'Brien, et al. (2003). "Principles of good practice for decision analytic modeling in health-care evaluation: Report of the ISPOR Task Force on Good Research Practices - Modeling studies." Value in Health **6**(1): 9-17.
WHO (2009). Pandemic influenza preparedness and response: A WHO guidance

document. Geneva.
Zerbe, R. O. (2008). Benefit-cost analysis. Northhampton, MA, Edward Elgar.
Zerbe, R. O. and D. D. Dively (1994). Benefit-cost analysis in theory and practice. New York, Harper Collins College.

APPENDIX

Cost-effectiveness studies of public health preparedness

Sander *et al* (2009) examine the cost-effectiveness (dollars per QALY gained) of several interventions for mitigating an influenza pandemic (see Table 2 for a summary of this and other CEA studies on PHP/PM). They take a societal perspective of costs and benefits, and use a 6 month time horizon (the time assumed to be needed to develop a more effective vaccine). Although several earlier papers explored pandemic mitigation or containment strategies with a stochastic agent-based model (Cooper et al. 2006,Ferguson et al. 2006,Germann et al. 2006 Colizza et al. 2007), Sander et al are the first to use stochastic modeling in an *economic* evaluation. They compare 17 different combinations of: antiviral prophylaxis (TAP), targeted either at the households of identified cases (they assume 60% of symptomatic cases can be identified), or at all contact groups of identified cases; school closures; and pre-pandemic immunization with low-efficacy vaccines. Costs of the status quo (no mitigation strategy) included physician visits, hospitalizations, and use of antibiotics and over-the-counter drugs. Households with children under 12 are assumed to lose 2.5 days of work loss per week if the child is sick or if schools are closed. School closure programs also cause teachers and other school professionals to lose 5 days of work per week. These workdays lost were valued using a human-capital approach (average compensation plus fringe benefits for parents, average earnings for teachers separately). Travel and time costs were also included as costs. They also varied assumptions about the size of the stockpile of antiviral drugs (as a percentage of the population). They find that both fully-targeted antiviral treatment and pre-pandemic vaccination are cost-saving from a social perspective (i.e. the reduction in health care expenditures from the base case are greater than costs of intervention). Also, the full TAP strategy reduced the 54% of cases at the lowest cost to society or $127 per capita.

Fowler et al (2005) compare vaccination and antibiotic prophylaxis against a bioterrorist anthrax attack. They take a societal perspective, and examine three post-attack strategies (in addition to a baseline do-nothing strategy): vaccination alone, antibiotic prophylaxis alone, or a combination of the two. They include lost wages but not time or travel costs of vaccination or treatment. They find that, should an attack occur, a combination of vaccination and antibiotic prophylaxis is the most cost-effective strategy.

Siddiqui and Edmunds (2008) examined the cost-effectiveness of stockpiling anti-viral drugs in the UK. They use the baseline epidemiologic scenarios from the UK Department of Health's Pandemic Contingency plan, which assumed an attack rate of 25% over 1 wave lasting 15 weeks. They modeled a 1918 scenario with a case fatality rate of 2.3% and a 1957/1969 scenario with an overall case fatality rate of 0.3%. Using a static decision-analytic model, they find that stockpiling enough antivirals to treat the expected number of cases only would be cost-effective (by standards adopted for the UK's national health insurance system). A stockpiling program which also tested close contacts of index cases and treated those as well was much less cost-effective (and would not pass the threshold under any conditions if case fatality rates were as low as in 1957/69).

Table 2. Summary of cost-effectiveness/cost-utility studies related to public health preparedness and pandemic influenza

	Country	**Disease/ Problem**	**Interventions evaluated**	**Epidemiological model approach**	**Macroeconomic effects**	**Discounting**	**Sensitivity analysis**
Sander et al (2008)	US	Pandemic flu mitigation	Cost-effectiveness of 17 strategies - targeted antiviral prophylaxis (TAP) alone and in combination w/ school closures and prevaccination	Stochastic agent-based microsimulationmodel	Lost work days for parents of sick children and teachers (school closure) using average wage rates	3% for life years saved	Univariate sens. Analysis on: attack rate, basic reproduction number (R_o), resource use, school closure, mortality rates
Fowler *et al* (2005)	US	Anthrax bio-terrorism	Vaccination, antibiotic prophylaxis	Static, Decision-analytic model	Lost work days	3%	Univariate sens. analysis on probability of attack; multivariate Monte Carlo
Siddiqui & Edmunds (2008)	UK	Pandemic influenza	Stockpiling of antivirals (oseltamivir), enough to treat cases, or to treat cases and (tested) close contacts	Static, decision-analytic model	None (healthcare provider perspective)	3.5%, varied up to 6% in sens. analysis	Univariate sens. analysis (all params and charts for major params); multivariate Monte Carlo

Benefit-cost studies of PHP/PM

Table 3 summarizes the existing BCA studies on PHP/PM. Meltzer et al (1999) analyze the potential effects of a pandemic flu in the US. They estimate the economic costs of an outbreak, and evaluate the costs, benefits, and policy implications of several possible vaccine based interventions. Using a Monte Carlo simulation model, the authors estimate 89,000 to 207,000 deaths; 314,000 to 734,000 hospitalizations; 18 to 42 million outpatient visits; and 20 to 47 million additional illnesses. The overall impact to the US economy is estimated between \$71.3 to \$166.5 billion, not including disruptions to commerce and society. Loss of life accounted for approximately 83% of all economic losses. If the vaccine could be provided for \$21, the authors found that a program to vaccinate the entire US population would pass a benefit-cost test. If vaccination proved more expensive (\$62 per vaccinated person), a program targeting only high-risk populations would pass a BCA, but a mass (untargeted) program would not.

Balicer *et al* (2005) estimated the health-related impact of pandemic flu in Israel, calculated direct costs to the health system associated with those outcomes, and analyzed strategies for stockpiling antiviral drugs for a possible pandemic flu outbreak (including therapeutic use, long-term pre-exposure prophylaxis, and short-term post-exposure prophylaxis for close contacts of flu patients). Although the study took a social perspective and valued lost workdays (at US\$72 per day), it did not attempt to monetize the benefits of avoiding flu deaths. Even omitting this large category of economic benefits (the aim of the study was "to elicit minimum cost-benefit estimates"), the study found that current stockpiling of oseltamivir (Tamiflu) would pass a benefit-cost test if the probability of a pandemic occurring were greater than 1 in 80. Furthermore, stockpiling would be cost-saving to the health care sector (i.e. not counting work days lost) if the stockpile were only large enough to treat patients at high risk.

There have been a number of pharmacoeconomic studies on vaccination against seasonal, rather than pandemic, influenza. I will discuss one illustrative example only; interested readers can find more detail on studies of annual influenza vaccination of the elderly in Nichol (2003) and of schoolchildren in Meltzer et al (2005) and Schmier et al (2008). Nichol (2001) examined vaccination of healthy adults for seasonal influenza from a societal perspective. Costs of the intervention included the direct cost of vaccination (vaccine and administration), indirect costs from work absenteeism in order to be vaccinated, and direct and indirect costs from side effects of the vaccine. Benefits (which Nichol frames as "costs averted due to vaccination") include reduced medical care, reduced work absenteeism, reduced loss of life (valued using a human capital approach), and increased "work effectiveness"[46]. Net benefits were presented in the paper per vaccinated person rather than for the program as a whole. Using a probabilistic Monte Carlo framework, Nichol estimated that the 95% confidence interval of net benefits to patients from vaccination was ($32.97, -$2.18): vaccination was mostly likely cost-saving. Reductions in indirect costs (lost work days and reduced productivity) accounted for 78% of benefits. Nearly all of the pharmacoeconomic studies reviewed in Nichol (2003) find that vaccinating the elderly against seasonal influenza would be cost-effective or even cost-saving, and Meltzer et al (2005) and Schmier et al (2008) find similar results for vaccinating high-risk schoochildren.

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[46] Decreased work productivity was calculated by scaling down the average wages paid.

Table 3. Benefit-cost studies in public health preparedness

Author	Country	Disease/ Problem	Which interventions	How are lives valued	Macroeconomic effects	Discount-ing	Sensitivity analysis
Meltzer et al. 1999	US	Pandemic flu	Vaccination - targeted by age, risk, group	Human capital approach (~$1.0M for those under age 65, $65K for those over)	Lost work days only	3%	Multi-parameter sensitivity analysis and Monte Carlo simulation
Balicer et al. 2006	Israel	Pandemic flu	Stockpiling anti-viral drugs for 1) therapeutic use, 2) long-term preexposure prophlyaxis, 3) short-term post-exposure prophylaxis	Not included	Lost work days only; overall direct and indirect costs ~0.5% of Israeli GDP	3%	One-way sensitivity on the yearly probability of a pandemic
Nichol 2001	US	Seasonal influenza	Vaccination of healthy working adults	Human capital approach	Lost work days	3% base case, 5% for "worst-case scenario"	One-way sens. analysis on several parameters; Monte Carlo simulation