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DISSERTATION

Three Papers in International Health Policy

Modeling the Links Between Economics and Epidemiology

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Summary

Economic and epidemiological models should be connected such that resource allocation decisions in international health policy are based on realistic expectations of disease outcomes, and meet public finance criteria. However, epidemiological models which best capture uncertain real-world processes have been in the specialist domain and are usually not amenable for use by the informed social scientist or policymaker. As a result certain international health policy decisions have had uncertain bases and related economic analyses have been wildly imprecise. Desktop models can be constructed which closely match the dynamics of complex epidemiological simulations but are easily editable with new data such as: proven results from clinical trials or other laboratory testing on the efficacy of certain interventions, and indicative bounds from mathematical modeling for outcomes with or without interventions in a real-world setting.

Paper I establishes the benefits of linking epidemiological modeling with international health resource allocation decisions, reviewing the recent modeling literature on pandemic influenza control. The review indicates that outbreaks in resource-poor settings are controllable with moderate resource intensity and complexity of effort for viral strains of moderate infectiousness. However, very high resource allocations for preparedness in industrialized nations – at low geographic risk for the pandemic – are predicated on containment failure in countries at higher risk of outbreaks. Without assuming the infectiousness of a future flu virus, a redistribution of resources to the developing countries at primary risk reduces overall systemic risk of containment failure. The payoffs in terms of reduced global mortality and morbidity are higher with increased infectiousness.

The two other papers are associated with implementing the experimental desktop models for the context of India. *Paper II* first constructs a scenario-based non-epidemiological model of pandemic influenza introduction to, and subsequent spread within India under various assumptions. The model uses published data on attack rates in Asia during previous pandemics as well as seasonal influenza. The model exploits geographical risk variations across provinces of India as well as the provinces' demographics, transport networks, and rural-urban settings. The simulated epidemics achieve overall attack rates of 7-21% of the population, well below the 30% figure used in

economic analyses. A range of benefits is estimated for preventing introduction of the virus via the air network (as compared to the later, inevitable entry via land & sea), from 60,000-100,000 averted deaths and averted economic costs of US$400-710 million. Separately, a desktop spatial epidemiological model – EpiFlex – is exploited to analyze disease spread in New Delhi. The attack rates under a realistic metapopulation simulation are higher than using the average-based attack rates in the countrywide model. The EpiFlex results also indicate that superspreading, which resists conventional outbreak containment, might be a factor in the dense urban environments of India. Policy recommendations include the inclusion of a proactive air travel shutdown policy, with potential social benefits higher than total private costs.

Paper III re-estimates the estimates of people living with HIV/AIDS (PLWHA) in India by combining the available prevalence data from the latest sero-surveillance data as well as the National Family Health Survey (NFHS-3) of 2005-06. The estimated total prevalence after accounting for biases in 2008 is 0.4%, within the bounds of the recent official announcement of 0.36% for year 2007 (0.27%-0.47%). The related 2.41 million PLWHA confirms that the prevalence had been overestimated by 230% till 2007.

The paper continues to comprehensively analyze antiretroviral (ARV) policy in India, beginning with the estimation of total costs of utilization under public and private market rates for first-line ART. A cohort simulation is conducted using a desktop model of disease progress in the population without access to ARVs. Deaths and morbidities are measured, and the availability of opportunistic infection prophylaxis is accounted for. Separately, the same modeling framework is used to simulate disease progress in a cohort of 122,947 (based on those eligible to ARVs using WHO criteria from the 15% of those without any treatment currently). First-line combination ARV therapy based on non-nucleoside reverse transcriptase inhibitors (NNRTI) is administered to this cohort with different treatment variations, and treatment efficacy is simulated based on published clinical and observational data. Second-line protease inhibitor (PI) therapy is made available, and outcomes are revised.

Cost-effectiveness (CE) is estimated based on years of life saved compared to no treatment. The desktop model results confirm cost-effectiveness of both one and two lines ART compared to no treatment, and CE values are within bounds of a recent stochastic, individual-based simulation (Freedberg *et al.* 2007), as well as prior studies. Advantages of

the model – besides tractability and customizability – includes the inclusion of treatment failure and the ability to model physician decision to continue first-line treatment even on failure, a reality considered in India given the low availability of second-line treatment. Here, the model yields novel results: continuing first-line therapy till end of follow-up (the realistic treatment horizon) is cost-effective compared to ending first-line treatment at physician-determined treatment failure. Compared to Freedberg *et al*., PI-based second-line ART is not found cost-effective by WHO standards compared to NNRTI-based first-line therapy, at prevailing PI-combination drug costs.

Policy recommendations include expanding first-line ART coverage, which is cost-effective, and will avert many premature deaths and reduce severe morbidity. Increasing survival with second-line ART comes at higher cost. Co-trimoxazole prophylaxis in situations without ART is an interim necessity. Continuing, compared to stopping, first-line ART in the case of treatment failure is promising, as long viral resistance and transmission is monitored and curtailed.