nonphysician sources for Compazine (9%), Diuril (11%), Valium (18%), and Darvon (22%).

Goldsworthy et al.[1] correctly noted a number of consequences of medication-sharing behaviors, to which we would add an additional consequence: pharmacoepidemiology studies of drug safety increasingly rely on exposure information drawn from computerized prescription or pharmacy records (often as part of HMO or claims data). Our earlier conclusion, now supported by the work of Goldsworthy et al., is therefore even more relevant today:

> [I]n addition to concern that [information from such sources] includes false positive 'exposures'—prescriptions issued or filled but not consumed—our findings suggest that these data sources may also include appreciable numbers of false negative exposures—drugs consumed but obtained from nonidentified sources.[3(p675)]

Appreciable exposure misclassification would have very serious consequences when it comes to using prescription data sources to identify adverse effects of medication exposures; any such efforts must take into consideration the extent to which studied medications are shared. ■

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GOLDSWORTHY RESPONDS

Mitchell's letter concerning our study raises an important public health issue related to prescription medication sharing that our study—focused as it was on direct effects on consumers—did not consider: the impact of such sharing on research and evaluation predicated upon prescription data sources. Mitchell is absolutely correct in asserting that there is considerable potential for consumer loaning and borrowing of prescription medication to affect the accuracy of traditional adverse effects reporting systems. We agree that efforts using these sources, whether for ongoing surveillance or as part of clinical trials, may need to take into consideration the potential underreporting of adverse effects that may be present when prescription medications are shared. ■

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INFLUENZA ANALYSIS SHOULD INCLUDE PNEUMONIA

Doshi[1] makes a number of interesting points, including a trenchant observation about the sharing of surveillance data collected under public auspices. Doshi's conclusion that "the next influenza pandemic may be far from a catastrophic event,"[1(p944)] may turn out to be true. However, the author's optimism is not supported by his analysis, which omits pneumonia.

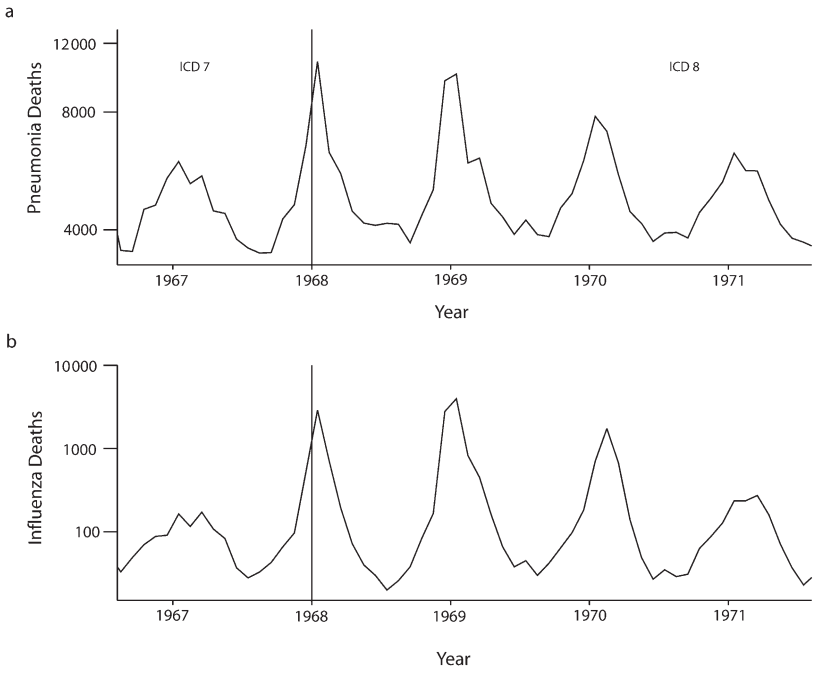
Doshi contends that the mortality consequences of influenza pandemics have been overstated. Epidemiologists, demographers, and vital statisticians analyze mortality from influenza and pneumonia combined as a single cause. This is because influenza kills through pneumonia and is coded as such on death certificates. Concern about "laboratory confirmation"[1(p939)] of influenza may be germane in the clinic, but vis-à-vis historical time series, it is nothing more than splitting hairs.

Influenza pandemics occur when new strains of influenza A virus emerge. Consider the most recent pandemic in 1968–1969, when H3N2 influenza emerged. Figure 1 shows time series data on mortality in the United States, from the multiple cause of death data files,[2] for 60 months encompassing the 1966–1967 to 1970–1971 flu seasons. It is easy to see that the 1968–1969 pandemic brought not just increases in influenza mortality, but also pneumonia mortality. The resemblance between the 2 panels is uncanny, but pneumonia kills more people. Looking at influenza deaths alone misses most of the story.

How much are influenza and noninfluenza pneumonia in lockstep? Figure 2 is a scatter plot of influenza deaths (x-axis) versus noninfluenza (viz., no explicit mention of influenza) pneumonia deaths (y-axis), on a log–log scale, with linear fit. The data are the same as those from the 60 months plotted in Figure 1. The linear fit is very strong ($R^2 = 0.89$). This could be dismissed as mechanical correlation, because both causes are cyclical and in phase. However, we see from Figure 1 that, even comparing only winter peaks, whenever influenza rises, so does pneumonia. This may be attributed to the 1968–1969 pandemic—but that's the point.

Some pneumonia is caused by respiratory syncytial virus, and others like it, but why does pneumonia mortality spike during influenza pandemics and covary so strikingly with influenza mortality? Is it plausible that respiratory syncytial virus becomes more deadly when new strains of influenza emerge? A more likely explanation is that many influenza deaths are being coded as pneumonia deaths. Thus, the usual practice of looking at pneumonia and influenza mortalities combined is wiser than looking at influenza mortality, *sensu stricto.*

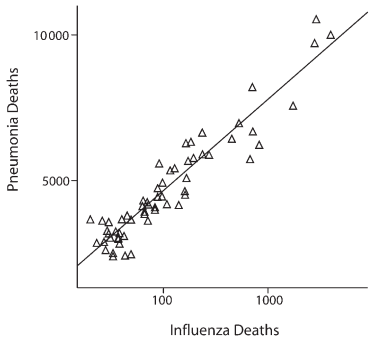
The 1977–1978 flu season serves as a closing vignette for Doshi. The 1977 reemergence of H1N1 was not a pandemic because it was not an antigenic shift. It was believed to have escaped from a laboratory and was identical to strains from 1950, and the world population 20 years and older was largely immune.[5] Doshi uses the occasional aberrant classification of 1977 to argue that there is no "a priori connection"[1(p944)] between pandemics and mortality. With the use of properly classified pandemics, the connection is an empirical one, not a priori. The connection is strong, and



Note. The vertical line marks the division between *International Classification of Diseases, 7th* and *8th Revisions*,[3,4] death classifications.
[a]Excludes deaths coded as influenza.

FIGURE 1—Monthly mortality time series for pneumonia (a) and influenza (b): United States, 1966–1967 through 1970–1971 influenza seasons.

Doshi's discussion of 1977 is the sort of sophistry that takes hold when standard practice is summarily set aside without good reason.



Note. 1 data point = 1 month. Both axes are logarithmic. The least-squares fit line is also shown; R^2 = 0.89.

FIGURE 2—Scatter plot of number of deaths from influenza and pneumonia: United States, 1966–1967 through 1970–1971 influenza seasons.

That pandemics are high-mortality events is fact, not, as Doshi states, a "false assumption."[1(p944)] To avoid such pitfalls, analysis of influenza time series should include pneumonia. ■

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DOSHI RESPONDS

In studies of influenza mortality, many researchers employ the combined category of recorded influenza and pneumonia deaths as their unit of analysis. Noymer suggests that my study[1] should have done the same. My objective was "to describe trends in historical influenza mortality data . . . and compare pandemic with nonpandemic influenza seasons."[1(p939)] Therefore, I "primarily considered the relative (rather than absolute) value of recorded influenza death rate statistics, which allowed me to compare 1 influenza season (or 1 month) with another."[1(p943)] Some may wonder whether influenza-classified deaths alone are a reliable category of analysis for these purposes. The evidence suggests that it is: first, death rates consistently increase in the winter and decrease in the summer, just as one would expect of influenza, a seasonal illness; second, the data trend downward over the 20th century, similar to that of most infectious diseases[2]; finally, other researchers have found influenza-certified deaths to be a good predictor of excess all-cause mortality.[3]

Noymer writes that "pandemics are high-mortality events," and points to the impact of the 1968–1969 pandemic on recorded pneumonia deaths. But the important question is whether the increases in pneumonia mortality during a pandemic are notable—and if so, to what extent is influenza the cause? Here, Noymer's figure (Figure 1) shows that the recorded pneumonia mortality impact during the 1968–1969 pandemic is almost indistinguishable from the nonpandemic season preceding it. Rather than weakening the strength of my conclusions, Noymer provides additional evidence to support my study's finding of similarity between pandemic and nonpandemic mortality.