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THE HEALTH EFFECTS OF MANDATORY PRESCRIPTIONS

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The Health Effects of Mandatory Prescriptions

Sam Peltzman

It is a commonplace of life in the developed world that consumers are required to secure the advice and permission of a physician before they may consume certain drugs. It was not always so, and is not so today in large parts of the world. Others, notably Peter Temin (1979, 1980, 1983), have investigated the origin of the prescription requirement and some of its costs. I will focus on the benefits--specifically, the health benefits--of this requirement.

I begin with a brief summary of the relevant American history and a description of current regulatory practice in other countries. Then I outline how the regulation might be expected to affect drug consumption decisions and, through these, the health of consumers. The bulk of the paper is devoted to an empirical investigation of health effects of prescription requirements which uses both U.S. and international data. That investigation reveals, with some twists, little effect of these requirements on health.

I. The History of Compulsory Prescriptions

Prior to 1938 a U.S. consumer seeking any non-narcotic drug could buy it much as he buys, say, aspirin today--without the need to first obtain a prescription for the drug from a physician. The consumer could seek the advice of a physician and obtain a prescription which was to be filled by a pharmacist. But there was no legal requirement that he do so. That innovation dates from the way in which the Food and Drug Administration (FDA) chose to interpret the 1938 Food, Drug and Cosmetic Act, an interpretation which received formal statutory blessing in 1951.

The 1938 Act was, arguably, the most important piece of "consumer safety" legislation enacted up to that time. It was motivated by concern, partly

aroused by a contemporary scandal,¹ that drug consumers were being overexposed to drugs which were either intrinsically harmful or harmful when used improperly. The provisions that ultimately led to mandatory prescriptions tried to overcome this danger by increasing consumer information. (See Temin (1979) for a fuller treatment of what follows). Specifically, Sec. 502 requires every drug to bear "adequate directions for use" and warnings against "unsafe" uses on its label. Otherwise it would be deemed "misbranded" and banned from sale. The FDA was also permitted to exempt drugs from this labeling requirement where the requirement "is not necessary for the protection of the public health." On its face, the law seems intended to encourage more informed choice of drugs and dosages by the consumers who would be reading drug labels. There is no hint of any requirement that they get permission of a physician before buying the drug.

That requirement came about as a result of the way FDA interpreted the law. By the end of 1938, the FDA had ruled that:

- a) a drug labeled "Caution: to be used by or on the prescription of" a physician and sold on that basis was exempt from the labeling requirements of the Act.²
- b) certain (named) drugs were intrinsically unsafe and, therefore, misbranded if the "prescription only" legend did not appear on the label, and
- c) "all drugs which may be dangerous to health unless used under appropriate supervision" would be misbranded without the prescription warning.³

¹In which a drug was unintentionally dissolved in anti-freeze and sold, with fatal effect, as an oral solution.

²3 Federal Register 3168 (Dec. 28, 1938).

³Kleinfeld & Dunn (1949, pp. 561-3).

Thus a new category of drugs which could be sold only by prescription had been created. But how was it to be determined which drugs were so "dangerous to health" as to require a prescription?

The answer took a while. The 1938 FDA communications had named a few specific drugs but hinted that others should also require a prescription. Up to 1940, the FDA refused to be more specific and left "the responsibility for determining whether or not any particular drug is dangerous ... upon the manufacturer and distributor." The FDA eschewed any "intention of assuming this burden."⁴ But eventually it assumed it nonetheless. In response to "numerous requests from drug manufacturers, retail and wholesale drug associations, and others, for a list of drug products which [FDA] considers dangerous when sold otherwise than on prescription", FDA made its list of "examples" steadily longer until a fairly complete list of about 30 drug categories emerged in early 1941.⁵ A decade later the de facto assumption by FDA of the power to determine which drugs could be sold by prescription only was codified by the Durham Humphrey Amendments to the Food, Drug and Cosmetic Act.

Something like this American history could undoubtedly be told for much of the world, in that a substantially overlapping set of drugs are available only by prescription of a physician in many countries. But in other countries, including some with non-trivial drug consumption levels, the pre-1938 U.S. institutions still prevail. The statutes of these countries may prohibit non-prescription sales of certain drugs, but they are not enforced in day-to-day practice.

⁴Kleinfeld and Dunn, 1949, p. 634.

⁵Kleinfeld & Dunn, 1949, 713-14.

Since I wanted to exploit this international variety, I sought to determine, country-by-country, the de facto status of its drug retail system. I was unable to find this in any extant literature, so I conducted my own investigation. This consisted of interviews and correspondence with: drug manufacturers, trade associations, drug market research organizations and individuals who had worked in drug retailing in the relevant country. The question I posed to them was, essentially: "Could a consumer easily obtain, without prescription, a drug which is "prescription only" in the U.S.?" I also wanted to know whether the answer differed by type of drug. Because the question proved somewhat sensitive, I had to guarantee anonymity to secure many answers, and what follows is my summary of the consensus that emerged.

As a broad generalization, a foreign system resembles either the current American system or the pre-1938 American system. That is, either essentially the same drugs that are "prescription only" here are "prescription only" there or, with the possible exception of narcotics, most all of them are available without prescription. I found isolated examples of attempts to control specific categories (e.g., antibiotics) within generally permissive systems. But, for simplicity, I placed each country into a "Permissive" or "Restrictive" category; Table 1 shows the result. There is a clear connection between the degree of economic development and the stringency of regulation, and this creates obvious interpretive problems for my subsequent international comparison.

II. The Effect of Prescription Regulation on Health

It needs to be recalled that consumers were using doctor's prescriptions frequently before they became mandatory. Just how frequently is shown in Table 2. From the few scraps of available data, it appears that around 1/4 to

Table 1. Classification of Foreign Countries
by De Facto Status of Prescription
Requirements

<u>Restrictive ("Prescription Only" Requirements Enforced)</u>	<u>Permissive ("Prescription Only" Requirements Mainly not Enforced)</u>
--	--

A. North America & Europe

Canada	Austria	Greece
UK	Spain ¹	Yugoslavia ¹
Scandinavia	Portugal	
Ireland	Italy	
Benelux		
France		
Germany		
Switzerland		

B. Latin America

Argentina	Mexico	Peru
Uruguay	Central America	Venezuela
	Brasil	
	Chile	
	Colombia	
	Ecuador	
	Bolivia	

C. Asia/Africa/Middle East

Israel	Egypt	Phillipines
South Africa	Nigeria	Singapore
Japan	Bangladesh	Thailand
Australia	India	Taiwan
New Zealand	Pakistan	Hong Kong
	Sri Lanka	Korea
	Burma	
	Indonesia	
	Malaysia	

Source: Author's Survey

1. Government health services pay for drugs bought on prescription, but the same drugs are available without prescription. In Spain, circumvention of the health service is, I am told, uncommon, while in Yugoslavia this is common.

Table 2: Prescription Drug Sales as Percent of Drug Store Sales and Drug Purchases. Selected Years, 1929-1981

YEAR	Prescription Sales as Percent of		Total Drug Consumption
	Drug Store Sales From: Lilly Digest Sample (1)	Other Sources (2)	
1929	--	11.4%	31.8%
1937	12.8%	--	--
1939	11.8	10.7	27.3
1941	13.2	--	(29.9)
1943	13.4	--	(30.3)
1945	14.2	--	(31.7)
1948	18.8	14.6	40.2
1950	20.4	--	--
1955	27.3	--	--
1960	34.6	25.7	47.0
1965	40.9	30.6	57.9
1970	44.5	34.1	63.5
1975	48.6	42.2	70.5
1981	51.2	47.2	72.7

Source: Col. 1 Eli Lilly & Co. Lilly Digest, various years.

Col. 2: (a) 1929, 1939, 1948. U.S. Bureau of Census, Census of Business. (b) 1960-81: Prescription Sales estimated as difference between total consumer spending on drugs and retail sales of non-prescription drugs (both from Statistical Abstract of the U.S.). Drug store sales from Historical Statistics of the U.S. and Statistical Abstract.

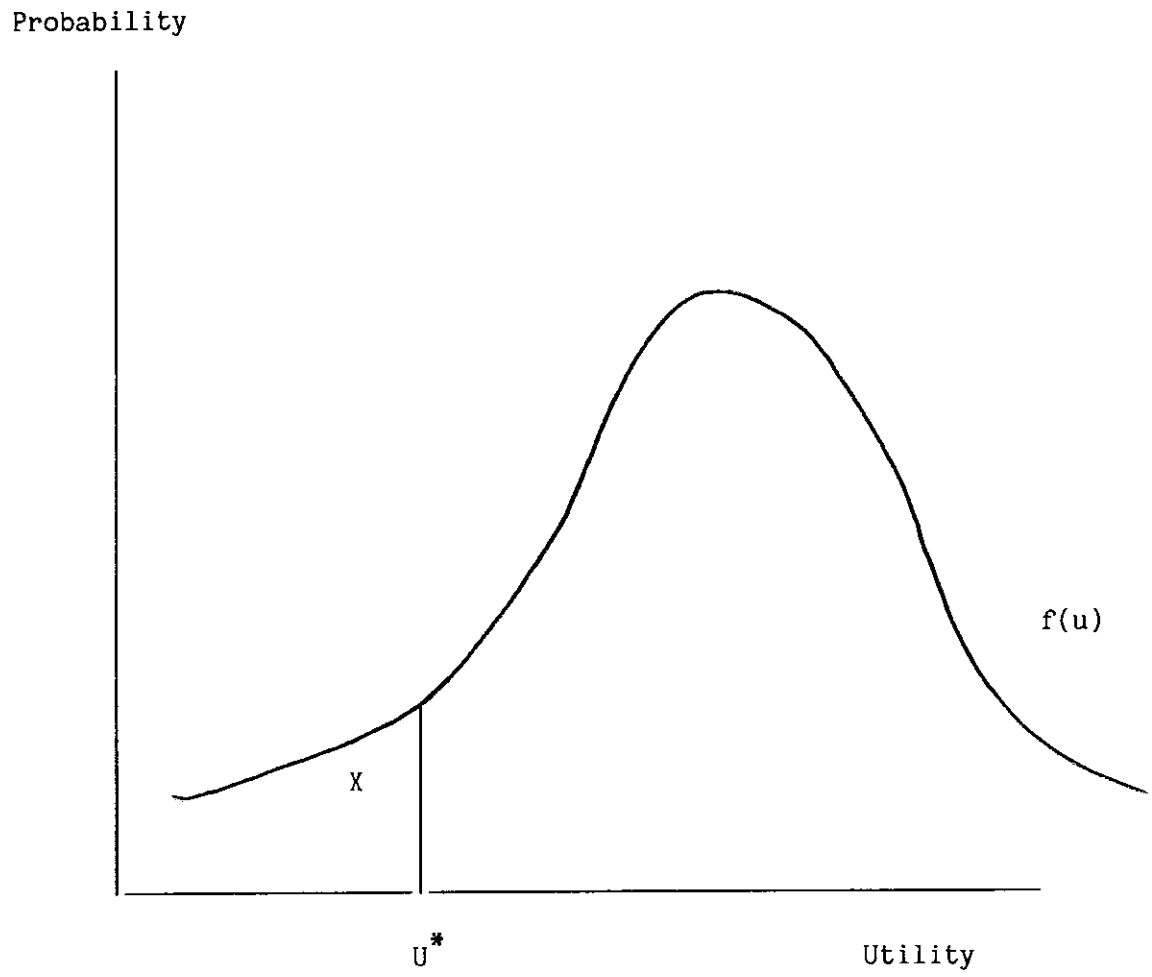
Col. 3: 1929, 37, 48: Prescription sales from Census of Business divided by total consumer spending on drugs (from Historical Statistics of the U.S. 1960-81. See col. 2. Figures in parentheses are interpolations based on changes in col. 1. The ratio of the 1939-48 change in col. 3 to the change in col. 1 is multiplied by the change from 1939 to the indicated year in col. 1.

1/3 of all drug purchases were made via prescription prior to 1939. This figure did not increase materially until the post WWII advent of antibiotics. Once it is understood that the absence of regulation does not imply the absence of prescriptions, the implications of regulation for consumer health are less clear than might be imagined.

To see this, consider the decision facing a consumer with some malady in an unregulated, voluntary prescription world. He can (1) do nothing and let nature take its course, (2) go to a drug store and select a drug himself, with whatever help he can glean from friends and druggist, or (3) pay a physician for advice on which drug to select (i.e. buy a drug on prescription, the simplifying assumption is that each doctor visit results in a prescription). Each alternative has associated with it a probability distribution of utility outcomes like $f(u)$ in figure 1: if the actual outcome falls below U^* , a dire consequence--death--occurs, and prospectively, the probability of this occurrence is X . The shape of the distribution, its location and the size of X differ according to the choice of treatment⁶ as does the consumer's expenditure on treatment. The consumer then buys the option which is, prospectively, most attractive. For an expected utility maximizer, this amounts to selecting the option with the highest Expected Net Utility (ENU) from the following list (where o = do nothing, n = non-prescription drug, p = prescription drug).

⁶In the pre-antibiotic era, X was probably larger for either the prescription or non-prescription drug options than for "do-nothing". Most drugs then were palliatives, but some carried a risk of poisoning.

Fig. 1.



(1) $ENU_o = EU_o$

(2) $ENU_n = EU_n - P_n$

(3) $ENU_p = EU_p - P_p - F$

Drugstore prices (P), doctor's fees (F) and expected gross utility (EU) are in common units. Thus, for those who select the P-option, $EU_p - EU_n > F$ (assuming for simplicity that $P_n = P_p$). As a general matter, it is plausible to assume that $EU_p \geq EU_n$ because F is presumably purchasing information on how to get "more" out of a drug (including how to avoid dangerous side effects) that can, in this unregulated world, be purchased under the n-option. The important point, however, is that $EU_p > EU_n$ does not imply $X_p < X_n$. Presumably, some drugs involving high X are frequently bought under the p-option precisely because the consumer seeks thereby to make X smaller. But the post-advice X can still exceed that of X_n .

Let's see, first, how regulation affects the consumer's choice and, then, how it affects his health. Regulation amounts to forcing drugs that would have been bought under the n-option into the p-option. Because $EU_n < EU_p$, both the n and p-options will now have lower expected utilities--ie. $EU_n^R < EU_n$ and $EU_p^R < EU_p$ (the R-superscript denotes Regulation). The first inequality reflects the smaller range of choice available under n. The second inequality reflects the lower EU of those drugs formerly bought under n, now put into p, compared to those formerly bought under p. Of course, the EU of those former n-drugs can increase when they are put into p--the doctor's advice on how to use the drug is presumably worth something. However, these drugs formerly were bought under n because $EU_p - EU_n < F$, while the inequality was reversed for those formerly bought under p. So some decrease of EU_p seems inevitable.

Because the attractiveness of both the n- and p-options decline relative to the o-option, the only clear a priori effect of regulation is a switch from "drugs" to "do-nothing." The implications for sales of n, sales of p and their shares of total drug sales are ambiguous. In particular, once account is taken of the sequence of decisions involved in some purchases, we cannot localize the effect of regulation to those drugs directly affected by it: those formerly bought under n, but now in the prescription only category. These are now clearly more costly--they require F--than drugs which remain in n or p. But this need not shift sales from n to p, because the expected net benefits of proceeding down the path of physican treatment has declined.

Table 3 has a simple illustration of this last point. It show the expected payoff (col. 5 and col. 8 - ignore col. 3 and col. 4 for the moment) of three hypothetical drugs, one of which--MEDIUM--is directly affected by regulation. To fix ideas, the example is rigged so that, if a single choice had to be made once-for-all, STRONG would be bought with a prescription in either regulatory regime. The example could be easily altered (e.g make the expected utility of MEDIUM 34 instead of 31) so that regulation diverts sales from MEDIUM to either STRONG or MILD. But, given consumer and physican uncertainty about the payoffs, single once-for-all choices do not exhaust the relevant possibilities. For example, suppose the consumer expects 31 utils from MEDIUM because (a) there is $\frac{1}{2}$ a chance it will yield 62 utils and $\frac{1}{2}$ a chance it will yield none and that (b) the utility of STRONG becomes clear (to both patient and physican) only if MEDIUM fails. Then the relevant decision is "do I take MEDIUM first?" Without regulation, the answer is "yes"--the expected net utility (the gross utility less drug prices and doctor's fees as shown in Table 3) of this course is

Table 3. Example of Effect of Regulation on Consumer Choice

DRUG	STATUS UNDER		Utility if		Expected Utility (5) = $\frac{1}{2}$ (3) + (4)*	Price of DRUG (6)	MD Fee (7)	Expected Net Utility (8) = (5)-(6)-(7)
	VOLUN- TARY (1)	REGU LATION** (2)	BAD (3)	GOOD (4)				
MILD	N	N	0	40	20	10	0	10
MEDIUM	N	--	-8	70	31	20	0	11
	--	P	-8	70	31	20	40	-29
STRONG	P	P	-16	200	92	40	40	12

N = Non-prescription, P = prescription

*BAD and GOOD are assumed equally likely.

**MEDIUM is moved into category-P by regulation, but MILD is left as a non-prescription drug. STRONG would be bought with a prescription without regulation; the utilities for this drug are conditional on a doctor's advice.

$$\begin{aligned} & \frac{1}{2}(\text{Net Utility if MEDIUM works}) = \frac{1}{2} \times (62-20) \\ + & \frac{1}{2}(\text{Net Utility if MEDIUM fails and STRONG works}) = \frac{1}{2}[(0 - 20) + (92 - 40 - 40)] \\ \text{or } & \frac{1}{2}(42) + \frac{1}{2}(-8) = +17 \end{aligned}$$

which is better than the +10 ENU of MILD. In this unregulated world $\frac{1}{2}$ the consumers with symptoms like this will eventually buy with prescription. But if MEDIUM now requires a prescription, the best strategy is to buy MILD, because the doctor's fee now has to be paid even if MEDIUM works. The calculation now is:

$$\begin{aligned} & \text{Expected Net Utility of Visiting a doctor} = \\ & \frac{1}{2} \times (\text{Net Utility if MEDIUM Works}) = \frac{1}{2}(62 - 20 - 40) \\ + & \frac{1}{2} \times (\text{Utility if MEDIUM fails and STRONG WORKS}) = \frac{1}{2}[(0 - 20 - 40) + (92 - 40)] \\ \text{or } & \frac{1}{2}(2) + \frac{1}{2}(-8) = -3 < +10 \text{ ENU of MILD.} \end{aligned}$$

The reduction of 20 expected utils reflects the probability ($\frac{1}{2}$) that the doctor's fee (40) will be wasted.

The example could be altered to, e.g., make the utility of MEDIUM higher when bought with a physician's advice without changing the general point: regulation decreases the net utility of buying some prescription as well as non-prescription drugs, and therefore has ambiguous implications for relative sales of the two. The potential empirical force of this point is illustrated in Table 2. Notice that the market share of prescription drugs did not jump after the onset of regulation. That occurred only after the advent of antibiotics and other major drug innovations in the late 1940s and 1950s.⁷

⁷Of course, the regulation may have been laxly enforced or enforced against drugs with a small volume of sales.

The effects of regulation on health, which is the paper's main concern, are subject to the same cross-currents as are sales. These are illustrated in cols. 3 and 4 of Table 3, where, for simplicity, the distribution in fig. 1 is collapsed to two states-of-the-world. Higher absolute utility losses in the "bad" state correspond to higher X - values in figure 1, and I assume that more potent drugs are also more dangerous. Regulation can improve health in two complementary ways: (1) Increase the probability or completeness of cure (the "good" state) or (2) decrease the probability or consequences of non-cure. To keep the discussion relevant to the empirical work, think of higher utility, in the good state as a higher probability of not dying from a life threatening illness and higher bad-state-disutility as a higher probability of dying from drug poisoning. We have already seen that regulation can lead to shifts to or from potent or mild drugs as well as from drugs to "do-nothing." Accordingly, the effect of regulation on health is ambiguous. Regulation could increase drug poisoning by shifting consumers to more potent drugs or it could increase deaths from treatable diseases by shifting consumers away from them. In this state of intellectual anarchy, I shall permit the data to tell us what the plausible effects of regulation have been.

III. Empirical Analysis

Prescription regulation can benefit a consumer by leading to improved health or by preventing further deterioration. At the extremes, this means curing life threatening illness or preventing death by drug poisoning. My analysis of the health effects of regulation is confined to these extremes, because the only relevant data are Vital Statistics; there are no data on, e.g., the extent of pain. Moreover, at the onset of American regulation, life saving drugs were essentially non-existent. The most important of these--the antibiotics--began coming onto the market in the late 1940s, and all of them

are "prescription only " drugs. So, the effects of technology and regulation on the life saving benefits from these drugs are inseparable. Accordingly my analysis of American data is confined to the effects of regulation on misuse of drugs as reflected in poisoning deaths. I broaden the inquiry later with International cross-section data.

A. American Time Series: 1900-1980

In recent years, 2000 to 3000 Americans have died annually from accidental poisoning by drugs. A roughly comparable number of suicides is attributed to drugs. As a hedge against the uncertainty of distinguishing accidental from suicidal poisoning, I shall analyze both. The most straightforward null-hypothesis about the effect of regulation is that there is less of both types of poisoning than otherwise: by interposing an expert between consumer and druggist, these extreme manifestations of ignorance (or recklessness) can be reduced. I test this hypothesis against time series of US. poisoning death rates.

(1) The Vital Statistics Data

Only in recent years have American Vital Statistics become sufficiently detailed to distinguish drug-related poisonings. The finest disaggregation available for my purposes, however, includes poisonings by solid and liquid substances other than drugs. Specifically the death rates I have to work with are:

AP = accidental poisoning by solid and liquid substances, except food,
and

SP = suicidal poisoning by solid and liquid substances

In recent years, these aggregates are dominated by drug-related deaths, which account for around 70 or 80 per cent of both AP and SP. Moreover, fragmentary data imply that drug related deaths also dominated these aggregates in the

pre-regulatory period.⁸ If the drugs of that day were less effective than today's, they were not obviously safer.⁹

Table 4 contains a summary of the time series I shall analyze. They are not the garden-variety time series characterized by simple trends. Instead, as is hinted by the table and shown more clearly later, all of them follow a very long cycle. They decline over the first 40 or 50 years of the period and then rise over the last 30 or 40. This long cycle is especially evident in the AP data: e.g. APH is higher in 1980 than 1900 and both are over twice the 1940 value. Another interesting wrinkle is that the recent increase in both AP and SP series terminates abruptly in the mid 1970s.

The preceding discussion treated drug poisonings as the occasional unwanted by product of optimizing decisions on drug consumption. That suggests a simple proportional relationship between poisoning and consumption: in terms of figure 1, for every 100 decisions to buy drugs, 100X will result in poisoning. Here I will embellish that treatment with only two variables in addition to regulation:

1. Long run improvements in education, permanent income, knowledge about drugs, etc. will presumably decrease X. I measure these by a simple time index.

⁸For 1937-40, Vital Statistics Special Reports gives a partial breakdown of SP and AP by the substance involved. The substances listed in this survey accounted for about 60 per cent of AP and 80 per cent of SP. By consulting pharmacopoeiae of the time, I was able to determine which of these substances were being used in the drugs then being sold. These drug-related substances accounted for 67 per cent of all classified AP and 83 per cent of the classified SP.

⁹The pre-miracle-drug armamentarium contained some dangerous compounds which are still widely used--e.g. barbiturates, salicylates. It also contained drugs made of dangerous substances, such as arsenic and mercury, which have been replaced by safer items.

Table 4
Accidental and Suicidal Poisoning
Deaths. 1900-1980¹

Symbol	Definition	Mean (S.D.)	Value in		
			1900	1940	1980
	<u>Accidental Poisoning Deaths from solid and liquid substances, except food</u>				
APR	1. per million population	15.4 (5.9)	29	10	15
APP	2. as percent of all accidental deaths	2.31% (.84)	4.4	1.4	3.2
APH	3. as percent of all accidental deaths in the home ²	3.99% (1.32)	5.5	2.5	6.4
	<u>Suicides by solid and liquid substances</u>				
SPR	1. per million	22.9 (12.2)	33	20	18
SPP	2. as percent of all suicides	17.57% (7.47)	29.0	14.0	14.4

Notes: Source Vital Statistics of the U.S..

1. Pre-1911 data included food poisoning in accidental poisonings. I adjusted these by multiplying each pre-1911 rate by the average 1911-20 ratio of (AP)/(AP + Food Poisoning rate).
2. Denominator excludes work and motor vehicle accidents.

2. Non-drug-related economic activity competes with drug-related risk. I measure such activity by per-capita GNP. If a (short-run) increase in GNP implies more risky activity per unit time (i.e. if "pure leisure" is less risky than production and consumption activity), then, ceteris paribus, APP and APH should decline. The implications for APR are not so clear,¹⁰ but I include the variable for completeness.

Thus, the statistical model to be estimated is thus simply

$$(4) \quad AP_ \text{ or } SP_ = F(DC, GNP, T, R)$$

where

DC = real drug consumption per capita

GNP = real GNP per capita

T = time index

R = regulation = 0 for all years to 1940, +1 thereafter (I allow two years for the effects of the 1938 law to take hold)

and the predicted partial partial derivatives are:

$$F_{DC} > 0, \quad F_{GNP} < 0 \text{ or?}, \quad F_T < 0 \text{ and } F_R?$$

Some attention needs to be paid to the precise form of F. For example, consider the following simple forms

$$(5) \quad APR = A + B \cdot DC + C \cdot T + \dots$$

$$(6) \quad \ln(APR) = a + b \cdot \ln(DC) + c \cdot T + \dots$$

The first implies $\frac{\partial APR}{\partial DC} = B$, while (6) implies $\frac{\partial APR}{\partial DC} = b \cdot \frac{APR}{DC}$.

The theory suggests the proportional relationship in (5) between DC and APR. But (5) also implies $\frac{\partial APR}{\partial T} = C$, while (6) gives $\frac{1}{APR} \frac{\partial APR}{\partial T} = C$.

¹⁰The non-drug-related activity could "complement" or "substitute" for drug consumption in its effects on APR. E.g., a rise in GNP may induce more care in use of drugs because the alternative cost of misuse has risen but the same increased value of time implies less time (care) per unit of drug consumption.

Arithmetic here leads us to prefer (6): any declining trend has to approach APR's lower bound of zero asymptotically, as (6) does, and we want to rule out negative APRs, which (5) does not. Of course, (5) and (6) can be permuted. We can depart from OLS and estimate (5) with an exponential trend, or we can estimate something like

$$(7) \quad \ln(\text{APR}) = a' + b' \cdot \text{DC} + C' \cdot T + \dots$$

in which case we have a "sensible" trend, no declining marginal danger of DC as in (6), but an awkward dependence of $\frac{\partial \text{APR}}{\partial \text{DC}}$ on the level of APR. The qualified implication of all this is that, if the simple theoretical connection between APR and DC is empirically important, forms like (5) or (7) should fit the data better than (6).

The test of this implication is summarized in Table 5. I compare the "fit" of pairs of various forms of (4). For each pair, the only difference is that the DC variable is entered linearly in one form and log-linearly in the other. The clear message of the table is that the linear DC variable "works" much better than the log version. Comparisons between columns (1) and (2) of Table 5 show how important the difference in "fit" is; reductions in sum-squared-errors of over half are common. In addition, columns (4) and (5) indicate that the time series of residuals from the linear DC regressions tend to be better behaved. These differences are not as pronounced for the SP regressions, where none of the OLS regressions succeed in ameliorating a severe residual autocorrelation.

Table 5 does not, of course, exhaust a catalog of functional forms from which a transformation of DC superior to the linear could emerge. The table does, however, imply that functional form is important and that the proportional DC effect implied by the theory does not do obvious violence to

Table 5. Goodness of Fit Measures. Linear and Log Drug Consumption Variables. OLS Regressions, 1900-80 DATA

Form of Other Variables:		Adjusted ¹ SSEx10 ³ when DC is:		Box-Cox d ²	Durbin-Watson when DC is	
DEPENDENT	GNP	LIN (1)	ln (2)	(3)	LIN (4)	ln (5)
1.	ln APR ln	787	3570	61.2	.92	.30
2.	APR LIN	1079	2760	38.0	1.41	.92
3.	ln APP ln	1216	4171	49.9	.86	.70
4.	APP LIN	1574	4267	40.4	1.13	.85
5.	ln APH ln	904	3768	57.8	1.07	.39
6.	APH LIN	929	4053	59.7	1.50	.74
7.	ln SPR ln	3186	5492	22.1	.25	.19
8.	SPR LIN	6436	8332	10.5	.22	.24
9.	ln SPC ln	1834	2396	10.8	.27	.30
10.	SPC LIN	3330	3014	4.0	.31	.45

Note: Each regression summarized above has a poisoning or suicide rate dependent variable in either linear (LIN) or log(ln) form. The independent variables are per capita drug consumption (DC) and per capita GNP in the indicated form plus a linear trend.

1. Cols. (1) and (2) give sums of squared errors from the OLS regression. If the dependent variable is linear, the SSE has been adjusted according to the procedure in Box and Cox (1964) to make it comparable to the SSE for the regression employing a log dependent variable.
2. Statistic for significance of difference between col. (1) and (2). It has chi-square distribution with d.f. = 1 and P(.05) = 3.8, P(.01) = 6.6. Accordingly all differences are significant, except line 10.

Sources: Mortality Rates: Vital Statistics of the U.S.

GNP: Historical Statistics of the U.S. and Statistical Abstract of the U.S.

DC: See Appendix

the data. Comparisons of pairs of rows in column (1) gives some further insights. The differences here are generally smaller than those between columns (1) and (2), but they imply a preference for a log-linear v. linear trend (the former invariably gives the lower sum squared error).¹¹

The detail of some regressions explaining Accidental poisoning deaths with linear DC terms is given in Table 6. The regressions are shown with and without a regulation dummy and with and without correction for residual autocorrelation, and they permit the following conclusions:

1. A simple process in which the effects of growing drug consumption pull against a declining trend seems adequate to explain most of the evolution of the accidental poisoning rate over the past 80 years. The coefficients of the DC and TIME variables always have extravagant t-ratios, and substantial (offsetting) effects. Figures 2 and 3 illustrate just how well the regression describe these data. The predicted values do not catch every wiggle in the data. However, they duplicate all of the main story: the long decline to the 1940s or 1950s, the subsequent rise and its termination after 1970.

2. Figures 2 and 3 show no obvious overprediction of poisoning deaths in the post-regulatory era. This hints at what the regression with a regulatory dummy confirm. In fact, the coefficients of that dummy are positive when they are significant. But the main conclusion is that accounting for regulation adds little to our ability to explain poisoning deaths.

3. Fluctuations of GNP around its trend seem to affect mainly the share of poisonings in total accidents. (The GNP coefficients are consistently significant in the APP and APH regressions). In particular, holding DC

¹¹Regressions like those on line 2, but with exponential, instead of linear, trend they gave roughly the same mean-square-error as the corresponding regression on line 1.

Per Million
←

Fig. 2 ACCIDENTAL POISONINGS, 1900-80, PER MILLION POP.
PREDICTED * ACTUAL VALUES

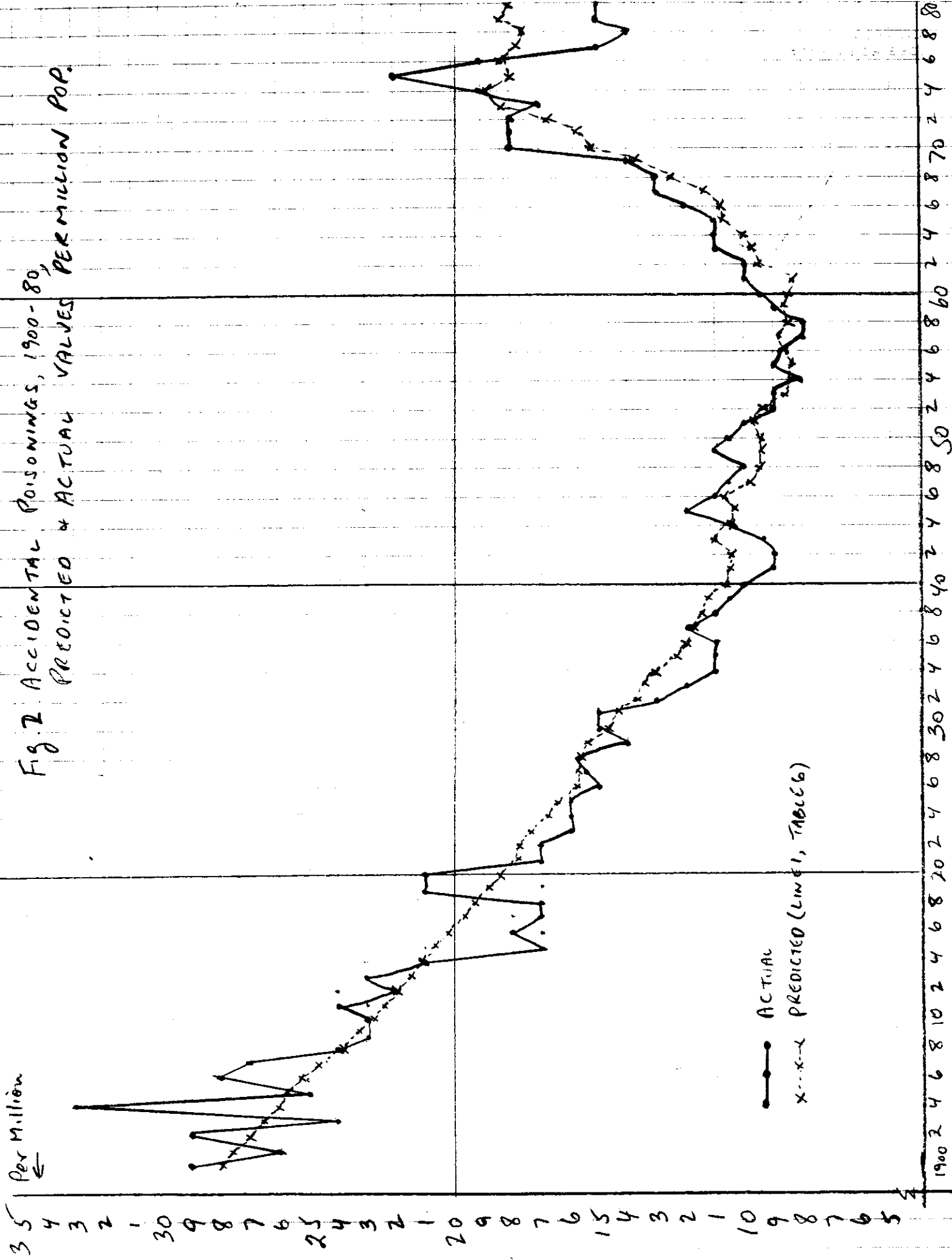


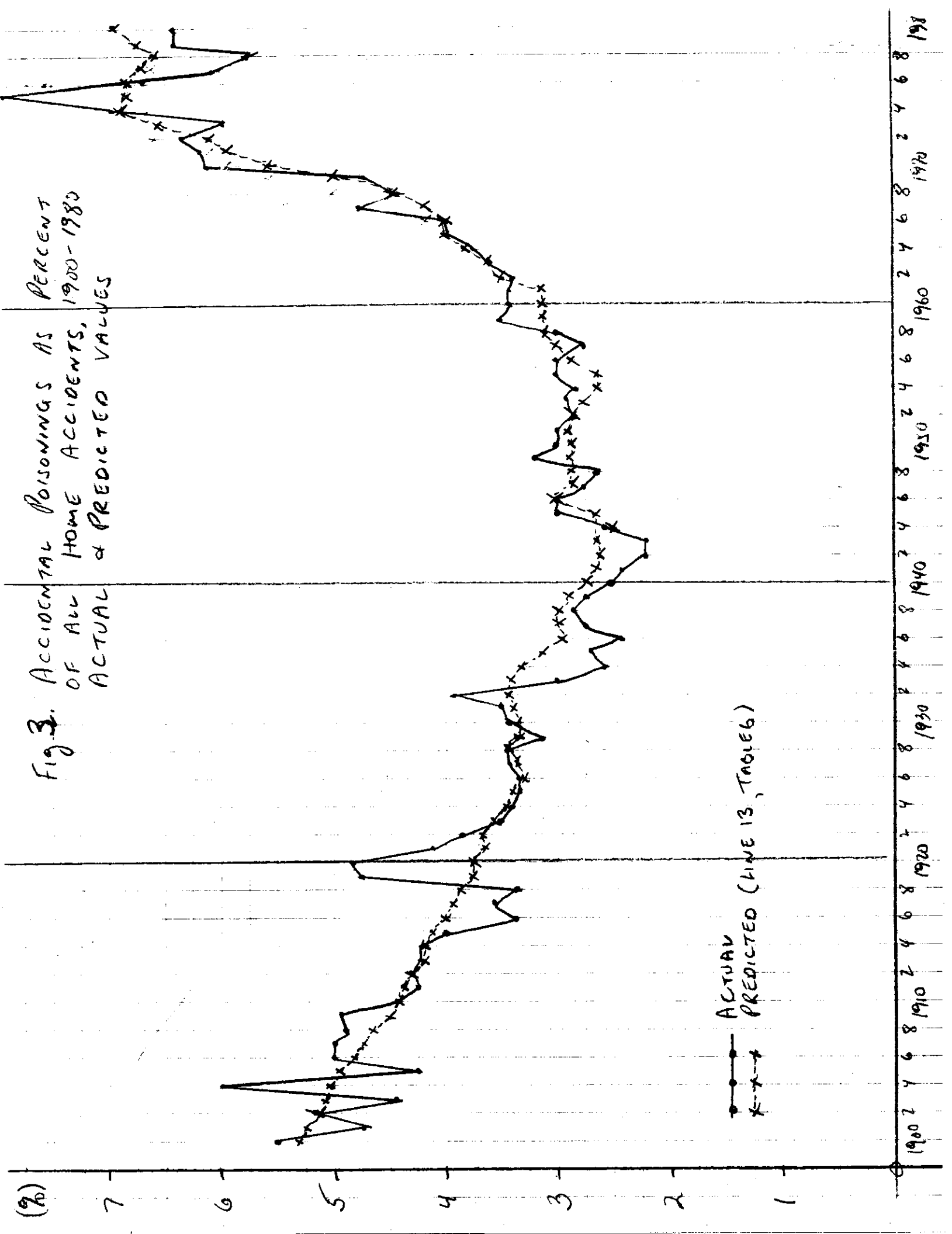
Table 6. Accidental Poisoning Regressions
1900-1980

Dependent Variable (See Table 4)	Type ¹ Estimate		Independent Variables and Coefficients								R ² (9)	S.E. (10)	DW (11)	ρ (12)	
	DC COEFF	T	GNP COEF	T	TIME COEF	T	REGULATION COEF	T							
Accidental Poisoning Deaths:			(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)					
per million population (APR)	1	0	.066	12.2	-.69	.6	-.49	19.0			.92	1.72	1.4	--	
	2	0	.076	14.5	-2.89	2.8	-.51	21.4	2.60	3.0	.93	1.62	1.6	--	
	3	G	.067	10.0	-1.10	.8	-.48	14.8			--	1.66	2.1	.28	
	4	G	.076	13.2	-2.80	2.6	-.50	18.1	2.42	2.6	--	1.59	2.0	.19	
ln APR	5	0	.004	22.1	-.08 ²	.7	-.03	16.6			.93	.101	.9	--	
	6	0	.004	20.6	-.03	.3	-.03	18.0	-.06	1.1	.93	.101	1.0	--	
	7	G	.004	13.2	-.13	.9	-.03	10.6			--	.087	2.0	.53	
	8	G	.004	13.2	-.16	1.5	-.03	11.1	-.05	0.6	--	.086	2.0	.55	
as percent of accidental deaths (APP)	9	0	.012	12.7	-.31	1.5	-.06	13.1			.87	.31	1.1	--	
	10	0	.014	15.4	-.70	3.8	-.07	15.9	.55	3.6	.89	.29	1.3	--	
	11	G	.014	9.6	-.63	2.3	-.06	8.0			--	.29	2.0	.46	
	12	G	.014	13.4	-.68	3.6	-.07	11.8	.49	2.6	--	.27	1.9	.33	
as percent accidental deaths in the home (APH)	13	0	.021	16.0	-.82	3.1	-.07	11.4			.90	.42	1.6	--	
	14	0	.021	15.8	-.86	3.3	-.08	12.4	.23	1.0	.90	.42	1.5	--	
	15	G	.021	13.6	-.93	2.9	-.07	9.1			--	.41	1.9	.22	
	16	G	.021	14.4	-.92	3.3	-.08	10.0	.24	.9	--	.40	1.9	.24	
Mean of Variable			\$145		\$2.19 x 10 ³										
S.D.			146		1.00										
Elasticity ⁵ at Mean of															
APR			.62		-.10	-.032 ³			+.169 ⁴						
ln APR			.58		-.08	-.030			-.060						
APP			.75		-.29	-.026			+.240						
APH			.76		-.45	-.018			+.057						

Notes:

1. OLS regressions are denoted "0". Those denoted "G" are corrected for first-order auto-correlation of residuals by GLS. The auto-correlation coefficient used to transform variables (ρ) is shown in column (12). Column (11) shows Durbin Watson statistic, for this sample size (n = 81), D.W. < 1.4 implies significant auto correlation at 1 percent.
2. ln GNP is used in this set of regressions.
3. Percent change per year.
4. (Approximate) percent effect of regulation.
5. Based on coefficients of first regression in each quadruplet.

Fig 3. ACCIDENTAL POISONINGS AS PERCENT OF ALL HOME ACCIDENTS, 1900-1980
ACTUAL & PREDICTED VALUES



constant, a rise in GNP implies an increase in the share of other forms of accident risk.

Table 7 and figure 4 show results for suicidal poisonings. They are similar to the accident results, but the simple model does not do nearly as well in explaining these data. It misses two major cycles in the early part of the century, and it lags by about a decade the upturn that starts in the late 1950s.¹² There does, however, remain a broadly accurate sketch of a history of long decline which terminates after 1940 and is unaffected by regulation.

The preceding data imply that, at least in the case of accidents, the same simple process has been generating poisoning deaths for most of the last century in spite of the regulatory changes and the enormous technological change that has occurred in this period. That implication can be scrutinized more rigorously than by imposing a fixed process on the data and noting its "good" fit, as we have done so far. To do so, I split the sample period into pre- and post-regulation halves, fit the model to each sub-period, and compared the fit to that of the fixed process. This is a rather rigorous test, because the underlying trends in the sub-periods are so different: it should be easy to "beat" a model with a fixed trend. Nevertheless, the fixed-trend model survives this test fairly well. This is shown in Table 8, which contains tests of the hypothesis that a common structure describes the two sub-periods. This hypothesis cannot consistently be rejected, and where it is

¹²The residual auto-correlation statistics in cols. (11) and (12) of Table 7 hint of the problem. Essentially, these say that the data are described by first-difference version of the model. And, indeed, the predicted value for the GLS regressions eliminated most of the unexplained movements in the suicidal poisoning series. But this mainly relabels our ignorance in that it consigns to to a "cumulation of random errors" category much of what is interesting about the data.

Table 7. Suicidal Poisoning Regressions. 1900-1980

Dependent Variable (See Table 4)	Type ¹ Estimate	Independent Variables and Coefficients								R ² (9)	S.E. (10)	D.W. (11)	ρ (12)	
		DC COEFF T (1) (2)		GNP COEF T (3) (4)		TIME COEF T (5) (6)		REGULATION COEF T (7) (8)						
Suicidal Poisoning deaths per Million (SPR)	1	0	.113	6.2	-7.43	2.0	-.708	8.1		.78	5.89	.2		
	2	0	.140	5.9	-13.02	2.7	-.739	8.4	5.99 1.7	.79	5.82	.2		
	3	G	.079	2.6	-8.14	2.7	-.405	2.1			2.66	1.8	.91	
	4	G	.077	2.5	-7.77	2.5	-.391	2.0	-1.38 .5		2.67	1.8	.91	
ln SPR	5	0	.004	11.2	-1.01 ²	4.6	-.019	5.3		.82	.203	.3		
	6	0	.004	9.4	-.927	3.1	-.019	5.2	-.054 .4	.82	.204	.2		
	7	G	.003	2.8	-.692	3.5	-.014	2.1			.097	1.8	.90	
	8	G	.003	2.8	-.646	3.2	-.013	2.0	-.095 .9		.097	1.7	.90	
(SPC) as percent of all suicides	9	0	.058	5.4	-.090	.04	-.541	10.7		.80	3.40	.3		
	10	0	.084	6.4	-5.72	2.1	-.572	11.7	6.03 3.1	.82	3.22	.4	--	
	11	G	.047	2.8	-.744	.4	-.449	4.6			1.81	2.2	.85	
	12	G	.050	3.0	-.890	.4	-.452	4.6	-.024 .01		1.80	2.2		
Elasticities ⁵	at Sample Means:													
		SPR	.72		-.71		-.031 ³		+.262 ⁴					
		ln SPR	.58		-1.01		-.019		-.054					
	SPC	.48		-.01		-.031		+.343						

See Notes to Table 6.

Fig. 4. Suicidal Poisoning Rate, 1900-80
ACTUAL + PREDICTED VALUES

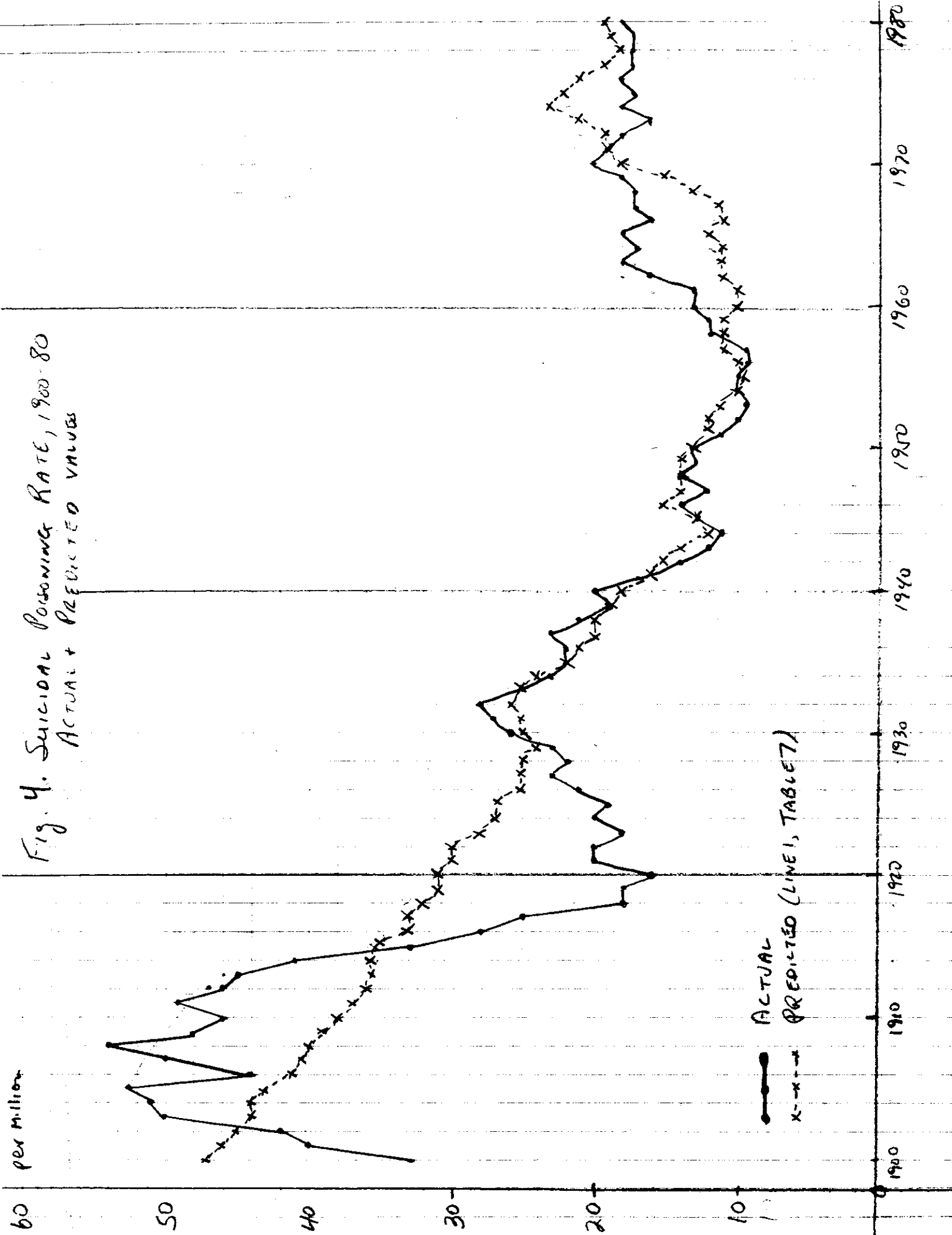


Table 8. Analysis of Covariance. Sub-period v. Full Period Regressions. Accidental and Suicidal Poisonings

Dependent Variable	Regression No. (Table 6 or 7)	Sum of Squared Errors		F ¹
		Restricted Model (Table 6 or 7) (1)	From Unrestricted Model (1900-1940) and 1941-80 subperiods) (2)	
APR	1	223.9	180.5	4.39
&n APR	5	.7869	.7316	1.38
APP	9	7.616	5.507	6.36
APH	13	13.418	11.905	2.32
SPR	1	2612	2152	4.41
&n SPR	5	3.186	2.911	1.72
SPC	9	88.95	47.65	15.82

Note: The restricted model is the one estimate in Table 6 or 7, i.e., a single regression is estimated for the whole 1900-1980 period. The unrestricted model allows coefficients in 1941-1980 to differ from those in 1900-1940, i.e., separate regressions (with the same set of variables) are estimated for each period. The restricted model has d.f. = 77, while d.f. = 73 for the unrestricted model. So F is

computed as: $\left(\frac{73}{4}\right) \left[\frac{\text{col.}(1) - \text{col.}(2)}{\text{col.}(2)} \right]$

1. F_{.01} = 3.6, F_{.05} = 2.5.

rejected the accompanying improvement in fit tends to modest--a reduction of no more than $\frac{1}{4}$ in unexplained variance. (The SPC regression is a clear exception to this).

If there are structural differences between the pre and post regulatory period, the most interesting, for present purposes, would be in the coefficient of DC. Table 9 tests the hypothesis that the marginal damage of a unit of drug consumption is the same after as before regulation. This is done two ways: 1) holding constant all other coefficients and 2) allowing the other coefficients to change between periods. Either way, the data fail to reject the hypothesis. Where they hint otherwise it is that the coefficient of DC increased after regulation. In short, the U.S. time series analysis reveals a simple, stable and strong relationship between drug consumption and accidental poisoning that goes back to the beginning of systematic collection of Vital Statistics data. This, and the similar, if less powerful, relationship between drug consumption and suicidal poisoning, may be the most interesting result of the analysis in that they illustrate a potentially fruitful way of studying epidemiological data. But my specific goal was to test hypotheses about prescription regulation, and the data fail to reject the hypothesis of no effect. Indeed, because prescription regulation virtually coincided with the panoply of safety regulation embedded in the 1938 Drug Act, my test inevitably fails to reject the hypotheses that the gamut of this regulation was ineffective. The main limitation of the test is that regulation is also virtually coincident with a technological explosion in pharmacology. One could argue that the post-regulation drug armamentarium was potentially more dangerous as well as more beneficial than that which preceded it. On this view, the stable epidemiological relationship which I have uncovered could be masking offsetting effects in which regulation is

Table 9. Tests for Change in Coefficient of Drug Consumption.
Accidental and Suicidal Poisoning Regressions.
1900-1940 and 1941-1980

Dependent Variable	Regression No. 1 (Table 6 or 7)	Change in Coefficient of DC			
		Other Coefficients Held Constant		Other Coefficients Permitted to Vary	
		Change (1)	t (2)	Change (3)	t (4)
APR	3, 4	+.009	.2	+.062	1.3
ln APR	7, 8	+.004	1.1	+.003	1.1
APP	11, 12	+.007	.7	-.004	.4
APH	15, 16	+.018	1.6	+.021	1.6
SPR	3, 4	--	--	-.130	.5
ln SPR	7, 8	--	--	+.0003	.03
SPC	11, 12	--	--	-.109	.7

Note: Columns (1) and (2) are from regressions on 1900-1980 data which include dummy variables for the intercept and slope of DC for 1941-80. The coefficient and t-ratios of the slope dummy are shown.

Columns (3) and (4) are from separate 1900-1940 and 1941-1980 regressions, and the difference of the two DC coefficients and its t-ratio are shown.

1. All data are derived from GLS regressions with connection for auto-correlation.

effectively suppressing the potential extra danger. For this reason, I examine in the next section more contemporary cross-section data from countries with diverse regulation, but with access to similar technology.

B. International Cross-Section: 1970-1980

This analysis focuses on a sample of 22 "middle income" countries, whose per capita GNP ranges from about 5 to 50 percent of the U.S. figure. All of the very richest and none the very poorest countries enforce prescription-only regulation. So these countries at the extremes of the world income distribution had to be excluded to obtain a sample with some independent variation of per capita income and the degree of regulation the countries.

I analyzed mortality data from the sample countries for effects of regulation, and the main, heavily qualified, conclusion is that the degree of regulation doesn't matter. Specifically, mortality from neither infectious diseases nor poisoning seems related to the degree of regulation. Before elaborating the basis for the conclusion and the qualifications, some background on international differences in health and their potential connection to drug consumption patterns is useful.

The small economics literature on cross-country mortality differences (see, e.g. Preston, 1975, 1979) finds that, as a broad generalization, only per capita GNP and literacy rates seem to "matter". Variables that might seem more directly related to the potential health of a population, like caloric intake or the density of doctors, are unrelated to mortality rates. In addition, there is substantial variance around the mortality-GNP relationship, and it is non-linear: the marginal effect of income essentially vanishes at developed country income levels. All this suggests that the subtleties of the effects of prescription regulation will surely be lost in broad measures of mortality. The search needs to be focused on specific types of mortality,

like poisoning deaths, where drug consumption patterns are more likely to matter. Apart from poisoning, infectious disease mortality offers the most promising potential example. For developed countries like the U.S., the connection between drugs and infectious disease mortality seems clear: for much of these populations the mortality risk from these diseases¹² was essentially eliminated after the introduction of antibiotics in the late 1940s. However, these diseases have not been eliminated in lower income countries. In my sample infectious disease mortality ranges from around 1 percent (roughly the U.S. figure) to around 25 percent of all deaths with a mean of about 8 percent. With so great a variation in the failure to realize the demonstrable potential of drugs, an inquiry into the role of regulation becomes at least potentially interesting.

Table 10 contains regressions describing infectious disease and poisoning mortality rates. The dependent variable is the rate for working age adults (age 20-64) standardized for differences in the age distribution within this group.¹³ By focusing on this group I hope to avoid special problems of childhood and geriatric diseases that may be only remotely connected to drug consumption patterns. The choice of independent variables is influenced by the empirical literature. They include per-capita GNP and a variable related to the distribution of income. The latter, median/mean income, is included in light of the non-linearity in the GNP-mortality relationship. If this non-linearity holds within a society, mortality and the variance of income should be negatively related--i.e., holding per capita GNP constant, a higher median

¹²A category which includes tuberculosis, syphilis, diphtheria, etc., but excludes viral diseases.

¹³The standardized rate is a weighted average of the rate for 20-49 year olds and the 50-64 year old rate, where the weights are the sample-average proportions in these age groups.

Table 10. Regressions of International Infectious Disease and Poisoning Mortality Rates. 20-64 Years Olds. 22 Middle Income Countries. 1970-80

Dependent Variable and Type of Regression	Coefficients/t-ratios					R ²	S.E. x 100 (p̂)
	GNP Per Capita (1)	Median Mean Income (2)	MD's Per Capita (3)	Time Period Dummy (4)	Regulation (5)		
A. Infectious Diseases							
1. 1970-75 Average	-.14 0.7	-1.09 1.8	-.64 2.6		-.30 1.1	.81	44.1
2. 1976-80, Average	-.36 2.0	-1.31 2.1	-.55 2.6		-.15 0.6	.83	44.1
3. 1970-85, 1976-80 Pooled, OLS	-.26 2.0	-1.21 2.9	-.58 3.8	-.13 1.2	-.22 1.2	.82	42.2
4. 1970-75, 1976-80 Pooled, GLS	-.35 2.3	-1.14 2.1	-.55 2.9	-2.50 2.2	-.19 0.8	--	20.7 (.87)
5. 1970-75, 1976-80 Pooled, GLS	-.54 3.5	-1.57 2.5		-4.57 5.7	-.40 1.5	--	20.9 (.90)
B. Poisoning							
1. 1970-75 Average	-.12 0.4	-1.94 2.5	+.27 0.9		+.53 1.5	.31	56.4
2. 1976-80 Average	-.19 0.8	-1.41 1.6	+.31 1.0		+.52 1.4	.23	61.6
3. 1970-75, 1976-80 Pooled, OLS	-.16 0.9	-1.68 3.1	+.30 1.5		.52 2.2	.26	56.1
4. 1970-75, 1976-80 Pooled, GLS	-.10 0.5	-1.70 2.3	+.26 1.0	-3.62 2.2	+.51 1.6	--	32.1 (.82)
5. 1970-75, 1976-80 Pooled, GLS	-.01 0.0	-1.50 2.1		-2.31 2.1	+.61 2.0	--	31.61 (.83)

Note: All variables, except dummies, are natural logs. Preliminary estimates revealed substantial heteroscedasticity in residuals in regressions with non-log dependent variables.

Mortality rates are annual averages for the 20-64 year old population (adjusted as described in fn. 13) for the two-subperiods 1970-75 and 1976-80. In a few cases, missing years were estimated by interpolation or extrapolation from a simple regression of the log of the rate on time. GNP and MD's per capita are estimates as of 1972 and 1978 for the 1970-76 and 1976-80 sub-periods respectively. The Regulation dummy is +1 if the country enforces prescription-only regulation, and the time period dummy is + 1 for the 1976-80 subperiod in regressions 3. - 5. which pool the two sub-samples.

The GLS regressions (4. and 5.) take account of the very strong correlation between residuals from 1970-75 and 1976-80 observations on the same country in pooled OLS regressions (which assume that successive observations on the same country are independent). The assumption underlying regressions 4 and 5 is that the residuals from country i in period t and $t - 1$ are related by

$$U_{i,t} = \rho U_{i,t-1} + e_{it},$$

where the e_{it} are serially independent. The estimate of ρ ($\hat{\rho}$) used to implement this assumption is the correlation coefficient between $U_{i,t}$ and $U_{i,t-1}$, and is shown in parentheses in col. (7). In every case, the transformation using $\hat{\rho}$ eliminated the serial dependence of residuals.

Sources of Variables:

Infectious Disease and Poisoning Mortality Rates: World Health Organization. World Health Statistics.

GNP per capita, and Physicians per capita: World Bank, World Development Indicators.

Median/Mean Income Ratio: Estimated as average of the 5th and 6th decile shares from income distributions in Jain (1975). Wherever possible a household income distribution for post-1970 data is used. Because of missing data, Greece and Portugal are assigned the value for Spain and Singapore is assigned the value for Hong Kong. The sample countries are (* = country enforces prescription-only regulation. See Table 1).

Latin America

*Argentina
Chile
Colombia
Ecuador
Mexico
Peru
*Puerto Rico
*Uruguay
Venezuela

Asia

Hong Kong
*Japan
Phillipines
Singapore
Thailand

Europe/Middle East

Greece
*Ireland
*Israel
*Italy
*Portugal
*Spain
Yugoslavia
Egypt

income should imply lower mortality.¹⁴ I also include the density of doctors, because preliminary work implied that, unlike other types of mortality, availability of doctors seems to affect infectious disease mortality. No other variable suggested by this literature seemed to consistently matter, including literacy,¹⁵ so I spare the reader a detailed discussion. No drug consumption variable appears in the poisoning regressions, though the U.S. time series results suggest that one belongs there. International drug consumption data are too sparse to permit replication of the U.S. time series. However, later I shall use some fragments of such data to shed light on the connection between drug consumption and both mortality and regulation.

I had enough data to estimate separate regressions for two subperiods in the 1970-80 decade (regressions 1. and 2. in each panel of Table 10). In addition, regressions (3.) for the pooled subperiods are shown, but their t-ratios are too generous, because the successive observations on a country are not independent. There are strong persistent "country-specific" elements in mortality rates. Accordingly, the reader should give more weight to the t-ratio in the GLS regressions (4. and 5.) which take account of these persistent elements. All the regressions confirm previous findings about the role of per capita income, but they show how especially important the distribution of income is. Median income is negatively related to mortality, but, holding the median constant, a higher mean (i.e. greater inequality) implies higher mortality (this is indicated by the consistently smaller absolute value of the coefficient in col. 1 than in col. 2).

¹⁴See Preston, 1975, pp. 241-43 for elaboration.

¹⁵And caloric intake and urbanization.

By scanning down column (5) of Table 10, the basis of my conclusion about the effects of regulation becomes apparent. The only coefficient on the regulation dummy which passes the conventional test for significant difference from zero (line B.5) implies an increase in poisoning deaths from regulation; this regression deletes the doctor density variable which seems unrelated to poisoning mortality. There is, however, one important hint that regulation may have benign effects. This is in regression A.5 which also deletes physician density. There is no "statistical" reason for doing this, in that all the preceding regressions imply that greater availability of doctors reduces mortality from infectious diseases. But I show later that the availability of doctors may be endogenous to regulation, in which case the regulation coefficient in A.5 would be summarizing both direct and indirect effects (i.e. those working through availability of physicians). Those with strong priors that regulation is ineffective will not want to revise them much based on the 1.5 t-ratio of the coefficient in A.5. But the magnitude of the coefficient is sufficiently large (it implies a 1/3 reduction in infectious disease mortality due to regulation) to encourage further inquiry. The same applies to the suggestively large positive coefficients in the poisoning regressions; they imply a regulation induced increase in poisoning deaths of approximately 70 percent.

Consider the following scenarios, both consistent with the hints in Table 10:

Scenario 1. A. has a malady and, only because he lives in a country enforcing prescription only regulation, is he induced to visit a doctor. The doctor prescribes, and A buys, drugs for such a malady more often (or in larger dosages or in greater strength) than otherwise. Because the doctor is wise and drugs are risky, A is saved from TB but dies of poisoning.

Scenario 2. Same as 1, except that, A spends no more, maybe less, on drugs when he must get a prescription than he otherwise would. The doctor's wisdom resides in steering A away from useless or inappropriate nostrums. A's health is the same as in 1., but his wealth is greater.

As pointed out earlier, these are not the only scenarios consistent with effective regulation. But both are consistent with a regulation-induced increase in the demand for physician services, and this is empirically plausible. Given this, I show that Scenario 2 is the more plausible--i.e., regulation does not seem to raise the aggregate demand for drugs.

Table 11 shows the basis for these conclusions. Most of the data underlying the Table comes from Kravis et al (1982), which is the only source I am aware of with internationally comparable drug consumption data at the requisite level of detail. All three regressions seem to trace demand functions. The first implies that the demand for physician services is raised considerably--about doubled--by regulation. The second regression shows no similar effect on the demand for drugs, but the third implies a shift in the composition of that demand toward the type of drugs commonly sold by prescription only in the U.S. The skimpy sample sizes and dubious quality of the data in Table 11 both caution against pushing these conclusions too far.¹⁶ This caveat aside, the general thrust of Tables 10 and 11 is that regulation raises the propensity of consumers to seek medical advice and that, as a result, they end up buying more potent drugs than otherwise.

¹⁶For example all the "quantity" figures for Table 11 are obtained essentially by deflating expenditures by a price index. This tends to bias the price coefficient toward -1, and calls into question whether I have really identified demand functions. Also, the ethical drug sales used in regression 3 are from surveys of pharmacies. In unregulated markets, some sales of such drugs are made outside pharmacies and pharmacies may not be reporting some non-prescription sales, since these are technically illegal. Accordingly the regulation coefficient in regression 3 is probably biased upward.

Table 11.
DEMAND FOR PHYSICIAN SERVICES AND DRUGS
16 MIDDLE INCOME COUNTRIES. 1975

DEPENDENT VARIABLE (PER CAPITA QUANTITIES)	COEFFICIENTS/t-RATIOS					S.E. x 100
	PRICE	GDP PER CAPITA	REGU- LATION	R ²		
1. PHYSICIAN SERVICES	-.56 4.9	1.18 4.4	.68 2.5	.92	31.8	
2. DRUGS	2.2	-.71 4.5	1.24	-0.04 0.1	.85 31.9	
3. ETHICAL DRUGS (9 COUNTRIES)	2.8	-.83 5.2	.68	.59 3.2	.96 18.8	

Note: All variables, except Regulation dummy (= +1 for countries enforcing prescriptions only regulation), are in natural logs. For regressions 1. and 2. data for GDP, physician services and drugs and their prices are from Kravis et. al (1982). They estimate indexes of per capita Quantities consumed for 151 goods and services and their price levels in national currency units per U.S. dollar. The price variable in the regression is this price divided by the aggregate price index in national currency units per dollar for all consumer goods. Their estimate of GDP is essentially an aggregate quantity index expressed in U.S. dollars; it is not the more conventional conversion of National currency GDP into dollars at market exchange rates.

The 16 countries in the sample are:

Brazil ¹	Yugoslavia	*Uruguay	Korea ¹
Columbia	Iran ¹	*Ireland	Malaysia ¹
Jamaica ¹	Syria ¹	*Italy	Phillipines
Mexico	*Japan	*Spain	Thailand

Regression 3 is based on data in Cullen (1983). He gives dollar sales of ethical drugs (i.e. drugs sold on a prescription-only basis in the U.S.) and price indexes (where New Zealand prices = 100) for 18 countries. I obtained quantities in U.S. dollars by dividing national sales by the national price index; this procedure tends to bias the coefficient of price in regression 3 toward -1. GDP per capita is from World Development Indicators. The regression is based on a 9 country middle income subsample of Cullen's data comprising *Argentina,² Brazil,¹ Colombia, Mexico, Peru, Venezuela, Phillipines, *Italy, *Spain

*Regulation dummy = +1

1. Country is not in sample for Table 10

2. Drug price index unavailable, value for Brazil is used.

The major problem with this conclusion lies in the implied causality-- from regulation to increased demand, for medical services. One could just as easily relabel "physician services" as "availability of doctors"¹⁷ and reverse the causation--i.e. argue that enforcement of prescription-only regulation is more feasible where there are many doctors. The first regression in Table 11 is consistent with this story, as it is with the "demand-shift" story.¹⁸ More generally, the cost of enforcing prescription-only regulation will tend to be lower, the more frequently consumers contact doctors, the greater the perceived value of medical advice, the more conveniently located doctors are, etc. So most anything that shifts the demand or supply of physician services and that is either not accounted for or measured badly will be correlated with the degree of enforcement of regulation. This possibility has to be heeded in interpreting the regressions in Table 10, and it tends to ask that more weight be given those regressions, like A.4, which include both physician density and regulation. This regression implies that the marginal effect of regulation on infectious disease mortality is indistinguishable from zero ($t = 0.8$).

In other words, holding the number of doctors constant, requiring a consumer to seek the advice of a doctor does not, apparently, lead to better informed consumption of e.g. antibiotics than otherwise. Thus, if regulation shifts the composition of drug demand toward "ethical" drugs, as Table 11

¹⁷The correlation between the Kravis et al. estimates of per capita physician service consumption and the density of doctors is +.97 for the sample in Table 11.

¹⁸Suppose there is no demand effect from regulation at all but that, as is almost certainly true, the price of physician services is being measured with error. Then if regulation depends on the availability of doctors, it will have a positive coefficient in a regression like the first one in Table 11. The reason is that the regulation variable will be correlated with the error from the imperfectly estimated demand and function.

suggests, it is apparently doing so for drugs other than antibiotics or for consumers with maladies other than life-threatening infections. Indeed, the strongest hint in the mortality data that regulation may be affecting drug consumption patterns comes in the poisoning regressions. These suggest ($t = 1.6$ in B.4) that, holding the number of doctors constant, regulation induces an increase of about 2/3 in poisoning deaths. And that would be consistent with a regulation-induced shift toward more powerful "ethical" drugs from weaker" over the counter" drugs.

To follow up all these hints requires data on drug consumption patterns which are not publicly available. In the epidemiological literature, I found only one bit of data potentially relevant to the issue of the information content of prescriptions. Hossain, Glass and Khan (1982) surveyed drug consumption patterns in rural Bangladesh, an area much poorer than any in my sample. They found that only 8 percent of drugs were purchased with a doctor's prescription,¹⁹ and that the share of antibiotics in total purchases was essentially the same (around 1/4) for these 8 percent as for the other 92 percent. The two groups are, of course, self-selected. So, it is too much to conclude that the propensity to buy antibiotics would be unaffected by enforcing prescription regulation. But this bit of data does suggest that even very poor consumers are not ignorant about the kind of drugs that require a doctor's advice in the developed world.

Some evidence that drug consumption and poisoning mortality are related in the middle income countries comes from combining some of the data in Tables 10 and 11. Only 10 of the 22 countries in the sample for Table 10 also show

¹⁹But only 5 percent were self-advised. The remaining 87 percent were prescribed by a variety of local advisers: pharmacists, clerks, medical students, village practitioners, etc.

up in the Kravis et al. sample for Table 11. For this subsample, the average residual for the poisoning mortality regressions (B.1 and B.2 in Table 10) is correlated $+0.64$ with income-adjusted drug consumption.²⁰ This is just significant at 5 percent, and tends to corroborate the link between drug consumption and poisoning mortality in the U.S. time series.

A similar correlation of drug consumption and infectious diseases mortality residual yields a significant negative coefficient of -0.71 . This is a somewhat surprising,²¹ but striking confirmation of the potential benefits of medical technology in reducing infectious disease mortality.

IV. Summary and Conclusions

I have tried to draw inferences about the health benefits of prescription regulation by analyzing mortality data. The kind of data available essentially dictated this research design. Accordingly, I have had either to ignore the less extreme health effects of this regulation, such as those manifested in the duration of illness and discomfort, or to assume that these are correlated with mortality. In addition, nothing like a controlled experiment on the effects of regulation is available. Historically, change in

²⁰The adjustment consists of deducting the income effect on drug consumption in line 1 of Table 11. This leaves, in effect, the residual plus a price effect. The adjustment is necessary because income affects both drug consumption and poisoning mortality (in opposite ways), and here I want to ask if countries with the same level of income but different drug consumption have different poisoning mortality. For this purpose, it is immaterial whether the difference in drug consumption is due to different drug prices or "other" factors, so I made no adjustment to consumption for price differences.

²¹High morbidity risks would raise the demand for drugs, so that, a priori, a positive correlation between mortality and drug consumption could not be ruled out. Also, the share of anti-infective drugs in the total varies widely across countries, roughly following infectious disease morbidity. The 25 percent share reported above for Bangladesh seems typical of less developed tropical areas and is on the order of twice that in developed countries (see Hossain, Glass and Khan, 1978). Thus, total drug consumption would appear to be a crude proxy at best for consumption of the relevant subset of drugs.

regulation has been accompanied by important change in drug technology. Internationally, a society's willingness to enforce regulation appears related to its wealth, literacy and the cost of access to professional medical advice. Thus, the usual caveat about the tentative character of results applies with special force here.

The main conclusion that emerges from my analyses of two types of data-- U.S. times series and International cross-sections--is that enforcement of prescription-only regulation does not significantly improve the health of drug consumers. This shows most clearly in poisoning mortality. Accidents (and suicides) related to drug consumption have been an important source of poisoning deaths in the U.S. both before and after the adoption of prescription-only regulation in the late 1930s. But the poisoning mortality risk from drug consumption appears unaffected by the regulation. In fact, the post-regulatory period is characterized by a dramatic reversal of a long decline in poisoning mortality. But this seems due mainly to accelerated growth in drug consumption; the process linking drug consumption and poisoning mortality seems unaffected by prescription regulation (or, more generally, by the whole panoply of safety regulation embodied in the 1938 Food and Drug Act). Indeed that process seems remarkably precise and stable over the whole of the twentieth century.

The "drug revolution" which began after WWII spawned drugs which can reduce mortality, especially from certain infectious diseases. Thus, if compulsory prescription regulation affects the information that consumers have about this technology it can affect mortality rates from these diseases. The only practical way to get at any such effect is via an international comparison of infectious disease mortality in groups of countries which do or do not enforce compulsory prescription regulation. My analysis of 1970-80

infectious disease mortality in middle-income countries indicates that higher per capita incomes, more doctors and less income inequality are each associated with lower mortality. I found no additional favorable effect from enforcement of compulsory prescription regulation; i.e. no evidence that consumers with a given income and access to doctors were better informed about the life saving potential of drugs in countries where a prescription is required for purchase of antibiotics. Fragmentary data on drug consumption tends to corroborate this: infectious disease mortality is negatively correlated with drug consumption, but drug consumption is uncorrelated with the degree of enforcement of prescription regulation. I did, however, find a potential indirect benefit of this regulation. Making prescriptions compulsory appears to raise the demand for (and equilibrium supply of) doctor's services, and I found that more doctors are associated with lower infectious disease mortality. Now, if doctors help cure infectious diseases by prescribing the appropriate antibiotic, how can a legal requirement for antibiotic prescriptions fail to help in the cure of these diseases? The implicit answer would be that a patient with such a disease and with a given income and price of doctor's services is no less likely to seek a doctor's advice if he can get antibiotics without a prescription. Apparently consumers are able to understand the value of a doctor's advice even if they are not required to seek it.

Finally, an international comparison of poisoning mortality corroborated what I found in the U.S. time series--no favorable effects of regulation and a positive correlation between poisoning mortality and drug consumption. In fact, if anything, poisoning mortality is higher than expected in countries which enforce prescription regulation. If this result holds up, it suggests that regulation does affect the pattern of drug purchases for those

less-than-life-threatening illnesses where a consumer might not otherwise seek the advice of a doctor. In these cases, the regulation seems to shift consumption toward more potent drugs. Again, international drug consumption data tend to corroborate this: while overall drug consumption seems unrelated to enforcement of regulation, the share of ethical drugs (i.e. those sold on a prescription-only basis in the U.S.) is higher where prescriptions are required for their purchase.²²

On the whole, the suggestive and, hopefully, improvable results in this paper do not support the view that mandatory prescription regulation plays a major role in helping consumers cope successfully with the complexities of pharmaceutical technology.

²²There is no paradox or perversity entailed by a safety regulation which leads to more risky consumption. See Peltzman, 1975 or Viscusi, 1984 for other examples.

Appendix

This describes the construction of the real drug consumption series used in the U.S. time series analysis. The following symbols are used (dates of availability in parenthesis; the \$ symbol denotes a nominal dollar series)

\$C = U.S. drug consumption expenditures (1929 on)

R = general symbol for a drug retail price index

BR = BLS Consumer Price Index for drugs (1935 on)

BTR = BLS all-items CPI (all relevant years)

\$Q = Value of U.S. drug production (Census of Manufacturers years: semi decadal 1899-1919, biennial 1919-37)

\$S = W. H. Shaw's (1947) estimate of the value of U.S. production of drugs, toileteries and household preparations (annually 1889-1933, 1935, 1937)

W = a wholesale price index for drugs

SW = Shaw's price index for \$S (see \$S)

BW = BLS wholesale price index for drugs (1935 on)

BTW = BLS all commodities WPI (all relevant years)

M = (Retail/Wholesale Price) of drugs, i.e. the retail "markup".

I use two alternative expressions for estimated real drug consumption expenditures

$$(1) \quad C = \frac{\$C}{R}$$

$$(2) \quad C = \frac{\$Q}{W} \times M$$

For 1935 on, I simply use BR to estimate (1). For 1929-35, \$C is available, but R must be estimated R. For pre-1929, only sporadic

estimates of \$Q are available, so gaps have to be filled in, and M and W have to be estimated to apply (2).¹ The estimates were made as follows:

\$Q: For 1899-1937 the following regression was estimated on annual rates of change between census years (standard error in parentheses)

$$\overset{0}{\$Q} = \text{constant} + .952 \overset{0}{\$S}, R^2 = .956,$$

$$\text{SEE} = 1.81\%, n = 13.$$

I then estimated annual values of $\overset{0}{\$Q}$ by plugging the annual value of $\overset{0}{\$S}$ into this regression and adjusting the constant so that the sum of the estimated $\overset{0}{\$Q}$ equalled the actual change between Census years. These estimates of $\overset{0}{\$Q}$ are then tacked onto the \$Q for the last Census year to interpolate the missing values.

W: SW, spliced to BW at 1935. (I experimented with an alternative, using BLS data on drug ingredients' prices; this yielded regression results essentially identical to those based on SW).

M: I used the 1929 value of ($\$/\Q)

Sources: \$C, BR, BTR, BW, BTW -- Historical Statistics of the U.S. and Statistical Abstract.

\$Q -- Census of Manufacturers

\$S, SW -- Shaw (1947).

¹Equation (2) holds only if (changes in) production = (changes in) consumption--i.e., if inventory changes, and foreign trade can be ignored. From Shaw's data for 1899-19, the latter seems reasonable: net exports accounted for only 2 to 4 percent of \$S.

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