Global Pharmaceutical Policy Model (GPPM)
Technical Appendix

Darius Lakdawalla
Dana Goldman
Pierre-Carl Michaud
Neeraj Sood
Robert Lempert
Ze Cong
Han de Vries
Italo Gutierrez

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1. General Structure of the Model

This document describes a microsimulation model used to simulate the effect of pharmaceutical regulation on health for the age 55+ population. The Global Pharmaceutical Policy Model (GPPM) models and tracks the evolution of future health and innovation under different policy regimes. It consists of a population health module and an innovation module. Each module is a set of dynamic interactions that link present health and innovation to their future values. For example, next year's health states depend on today's health states, and a set of random health shocks that vary with individuals' own risk-factors — e.g., their age, health behaviors, and current disease conditions. The innovation module links this year's stock of drugs to next year's, by allowing sales and profits from pharmaceutical sales to affect future innovation. Figure 1 outlines the mechanics of the model.

In a given year, say 2024, sample individuals may have diseases and/or disabilities that put them at risk of contracting new diseases and disabilities, or even dying, in 2025. Moreover, new drugs are introduced in 2024 that reduce some of these risks. We estimate a health transition model to simulate how population health will look in 2025, given the number of new drug introductions and existing health conditions. Finally, mortality will have shrunk the population in 2025, but the sample is "refreshed" by introducing those who were 54 in 2024, and who now age in to our target population. This forms the set of sample individuals for 2025. The same process is then repeated to obtain the population in 2026, and so on for subsequent years, until the final year of the simulation.

Theoretically, the current rate of innovation depends on future sales, which measure the profitability of current research effort. We assume it takes 10 years — from research inception to launch — for a pharmaceutical company to introduce a new drug. Moreover, we assume that drug companies have rational-expectations, in the sense that today's sales are used as a forecast for sales ten years in the future. Therefore, the number of new drugs today depends on sales (or market size) 10 years ago. The empirical economics literature provides us with an estimate of how innovation changes in response to changes in market size. For example, this elasticity is applied to the change in market size between 2014 and 2015 to estimate the change in the number of new drugs between 2024 and 2025.

The model is global in the sense that both Europe and the U.S. enter the model. Interactions arise because new drugs depend on total market size and are then available to both markets. Hence the effects of regulation in one market will have indirect effect on the other market.

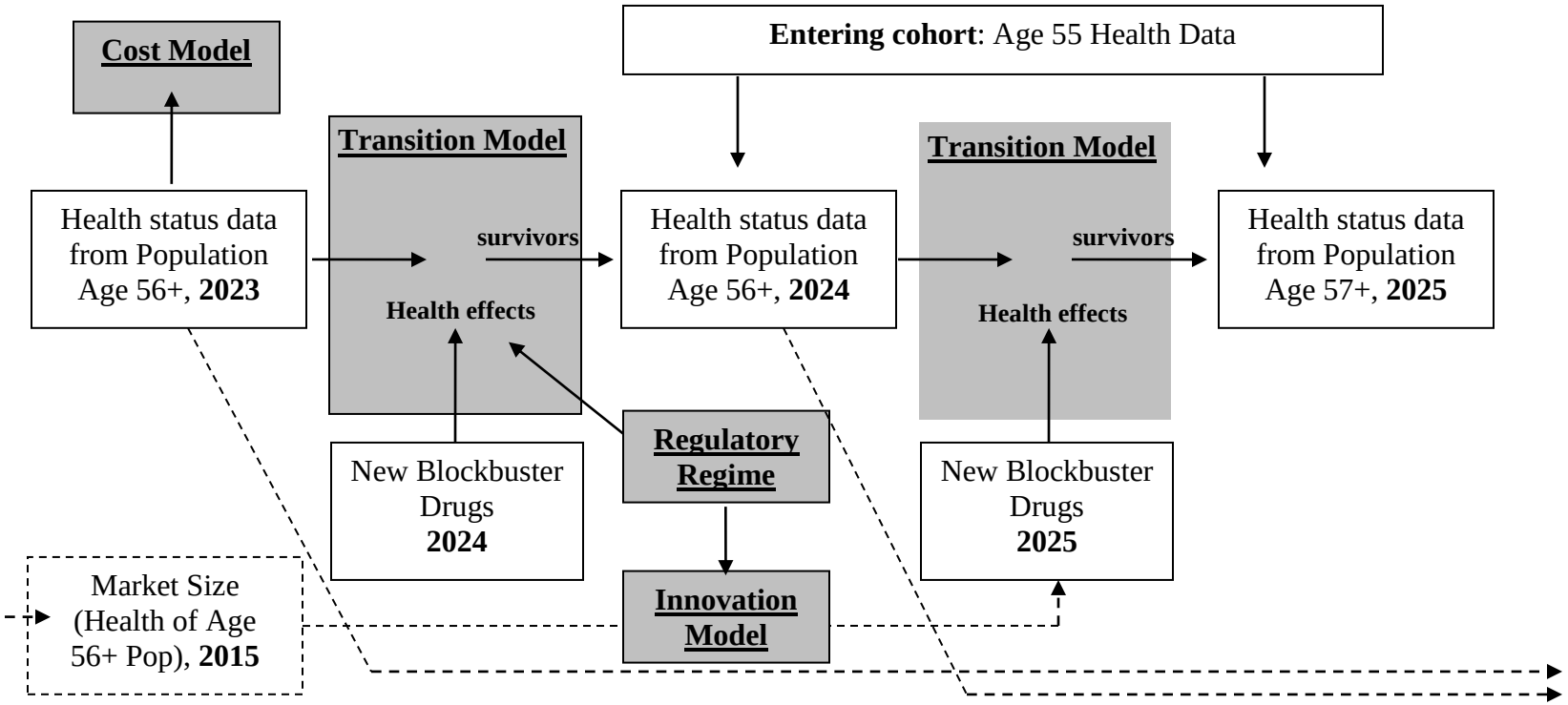
Regulation affects market size. Results from Sood et al. (2007) suggest that price controls leads to a 22.5% reduction in market size. Hence, this is the lever we use to simulate the effect of price controls as well as the effect of introducing co-pay subsidy. This is explained in more detail in Lakdawalla et al. (2007).

To measure cost and benefits across scenarios, we use life-years and medical expenditures. We translate life-years in dollar terms using a value of a statistical life estimate. For expenditures, we use cost regressions estimated on micro data.

The simulation are stochastic, because the arrival of new drugs is random, new diseases' arrival date is random as well. We discuss how this is implemented in the model. Furthermore, we also discuss how weights are used to reach population figures.

We present in turn details on each of these components. First, we explain how the transition model was estimated on HRS data and then adjusted for the European data. Second, how we constructed clinical effects of new drugs. We then discuss the process of innovation and how it relates to market size. Next we discuss how costs and benefits were calculated to evaluate each scenarios. Finally, we discuss how the stochastic components of the model are implemented and how we used sample weights throughout.

Figure 1.1 Mechanics of the GPPM



2. The Health Transition Model

We use the Health and Retirement Study, a nationally representative longitudinal study of the age 50+ population as our main source of data for the U.S.. We use the observed (reported) medical history of respondents to infer incidence rates as a function of prevailing health conditions, age and other socio-demographic characteristics (sex, race, risk factors such as obesity and smoking). The data from the Health and Retirement Study consists of longitudinal histories of disease incidence , recorded roughly every 2 years, from 1992 to 2002, along with information on baseline disease prevalence in 1992. Since incidence can only be recorded every two years, we use a discrete time hazard model.

The estimation of such model is complicated by three factors. First, the report of conditions is observed at irregular intervals (on average 24 months but varying from 18 to 30) and interview delay appears related to health conditions. Second, the presence of persistent unobserved heterogeneity (frailty) could contaminate the estimation of dynamic pathways or "feedback effects" across diseases. Finally, because the HRS samples from a population of respondents aged 50+, inference is complicated by the fact that spells are left-censored: some respondents are older than 50 at baseline and suffer from health conditions whose age of onset cannot be established.

Since we have a stock sample from the age 50+ population, each respondent goes through an individual-specific series of intervals. Hence, we have an unbalanced panel over the age range starting from 50 years old. Denote by j_{i0} the first age at which respondent i is observed and j_{iT_i} the last age when he is observed. Hence we observe incidence at ages $j_i = j_{i0},..., j_{iT_i}$. Record as $h_{i,j_i,m}$=1 if the individual has condition m as of age j_i. We assume the individual-specific component of the hazard can be decomposed in a time invariant and variant part. The time invariant part is composed of the effect of observed characteristics x_i and permanent unobserved characteristics specific to disease m , $\eta_{i,m}$. The time-varying part is the effect of previously diagnosed health conditions $h_{i,j_i-1,-m}$, (other than the condition m) on the hazard.[1] We assume an index of the form $z_{m,j_i} = x_i\beta_m + h_{i,j_i-1,-m}\gamma_m + \eta_{i,m}$. Hence, the latent component of the hazard is modeled as

$$\begin{aligned} &h^*_{i,j_i,m} = x_i\beta_m + h_{i,j_i-1,-m}\gamma_m + \eta_{i,m} + a_{m,j_i} + \varepsilon_{i,j_i,m}, \\ &m = 1,...,M,\ j_i = j_{i0},..., j_{iT_i},\ i = 1,...,N \end{aligned} \quad . \tag{2.1}$$

We approximate a_{m,j_i} with an age spline. After several specification checks, a node at age 75 appears to provide the best fit. This simplification is made for computational reasons since the joint estimation with unrestricted age fixed effects for each condition would imply a large number of parameters.

Diagnosis, conditional on being alive, is defined as

[1] With some abuse of notation, $j_i - 1$ denotes the previous age at which the respondent was observed.

$$h_{i,j_i,m} = \max(I(h^*_{i,j_i,m} > 0), h_{i,j_i-1,m}) \quad m = 1,...,M,\ j_i = j_{i0},...,j_{iT_i},\ i = 1,...,N \tag{2.2}$$

As mentioned in the text we consider 7 health conditions to which we add functional limitation (disability) and mortality. Each of these conditions is an absorbing state. The same assumption is made for ADL limitations, the measure of disability we use. The occurrence of mortality censors observation of diagnosis for other diseases in a current year. Mortality is recorded from exit interviews and tracks closely the life-table probabilities.

2.1 Interview Delays

As we already mentioned, time between interviews is not exactly 2 years. It can range from 18 months to 30 months. Hence, estimation is complicated by the fact that intervals are different for each respondent. More problematic is that delays in the time of interview appear related to age, serious health conditions and death (Adams et al., 2003). Hence a spurious correlation between elapsed time and incidence would be detected when in fact the correlation is due to delays in interviewing or finding out the status of respondents who will be later reported dead. To adjust hazard rates for this, we follow Adams et al. (2003) and include the logarithm of the number of months between interviews, $\log(s_{i,j_i})$ as a regressor.

2.2 Unobserved Heterogeneity

The term $\varepsilon_{i,j_i,m}$ is a time-varying shock specific to age j_i. We assume that this last shock is Type-1 extreme value distributed, and uncorrelated across diseases.[2] Unobserved difference η_{im} are persistent over time and are allowed to be correlated across diseases $m = 1,...,M$. However, to reduce the dimensionality of the heterogeneity distribution for computational reasons, we consider a nested specification. We assume that heterogeneity is perfectly correlated within nests of conditions but imperfectly correlated across nests. In particular, we assume that each of first 7 health conditions (heart disease, hypertension, stroke, lung disease, diabetes, cancer and mental illness) have a one-factor term $\eta_{im} = \tau_m \alpha_{iC}$ where τ_m is a disease specific factor-loading for the common individual term α_{iC}. We assume disability and mortality have their own specific heterogeneity term α_{iD} and α_{iM}. Together, we assume that the triplet $(\alpha_{iC}, \alpha_{iD}, \alpha_{iM})$ has some joint distribution that we will estimate. Hence, this vector is assumed imperfectly correlated. We use a discrete mass-point distribution with 2 points of support for each dimension (Heckman and Singer, 1984). This leads to $K=8$ potential combinations.

2.3 Likelihood and Initial Condition Problem

[2] The extreme value assumption is analogous to the proportional hazard assumption in continuous time.

The parameters $\theta_1 = (\{\beta_m, \gamma_m, \mu_m, \tau_m\}_{m=1}^{M}, F_\alpha)$, where F_α are the parameters of the discrete distribution, can be estimated by maximum likelihood. Given the extreme value distribution assumption on the time-varying unobservable (a consequence of the proportional hazard assumption), the joint probability of all time-intervals until failure, right-censoring or death conditional on the individual frailty is the product of Type-1 extreme value univariate probabilities. Since these sequences, conditional on unobserved heterogeneity, are also independent across diseases, the joint probability over all disease-specific sequences is simply the product of those probabilities.

For a given respondent with frailty $\alpha_i = (\alpha_{iC}, \alpha_{iD}, \alpha_{iM})$ observed from initial age j_{i0} to a last age j_{T_i}, the probability of the observed health history is (omitting the conditioning on covariates for notational simplicity)

$$l_i^{-0}(\theta; \alpha_i, h_{i,j_{i0}}) = \left[\prod_{m=1}^{M-1} \prod_{j=j_{i1}}^{j_{T_i}} P_{ij,m}(\theta; \alpha_i)^{(1-h_{ij-1,m})(1-h_{ij,M})} \right] \times \left[\prod_{j=j_{i1}}^{j_{T_i}} P_{ij,M}(\theta; \alpha_i) \right] \quad (2.3)$$

We make explicit the conditioning on $h_{i,j_{i0}} = (h_{i,j_{i0},0}, ..., h_{i,j_{i0},M})'$, we have no information on health prior to this age.

To obtain the likelihood of the parameters given the observables, it remains to integrate out unobserved heterogeneity. The complication is that $h_{i,j_{i0},-m}$, the initial condition in each hazard is not likely to be independent of the common unobserved heterogeneity term which needs to be integrated out. A solution is to model the conditional probability distribution $p(\alpha_i \mid h_{i,j_{i0}})$. Implementing this solution amounts to including initial prevalence of each condition at baseline each hazard. Therefore, this allows for permanent differences in the probability of a diagnosis based on baseline diagnosis on top of additional effects of diagnosis on the subsequent probability of a diagnosis. The likelihood contribution for one respondent's sequence is therefore given by

$$l_i(\theta; h_{i,j_{i0}}) = \sum_k p_k l_i(\theta; \alpha_k, h_{i,j_{i0}}) \quad (2.4)$$

where the p_k are probabilities for each combination of points of support α_k $k=1,...,K$.
The BFGS algorithm is used to maximize the log sum of likelihood contributions in equation (12) over the admissible parameter space.

2.4 Clinical Restrictions

Although statistically speaking, all elements of γ_m for all diseases should be unrestricted, it is likely that some of these estimates will reflect associations rather than causal effects because they help predict future incidence. Although we control for various risk factors, it is likely to that we do not observe some factors which are correlated with other diseases. In medical terms however, some of these effects might be ruled improbable and we use results from the medical literature to guide restrictions to impose on the elements of the γ_m.

We use a set of clinical restrictions proposed by Goldman et al. (2005) based on expert advice. It turns out that these restrictions are not rejected in a statistical sense one we include initial conditions and unobserved frailty.

Table 2.1 Clinical Restrictions

	hazard at (t)								
prevalence t-1	heart	blood pressure	stroke	lung disease	diabetes	cancer	mental	disability	mortality
heart			x				x	x	x
blood pressure	x		x				x	x	x
stroke							x	x	x
lung disease							x	x	x
diabetes	x	x	x				x	x	x
cancer			x				x	x	x
mental							x	x	x
disability							x	x	x

Notes: x denotes a parameter which is allowed to be estimated.

2.5 Descriptive Statistics and Estimation Results

For estimation, we construct an unbalanced panel from pooling all cohorts together. We delete spells if important information is missing (such as the prevalence of health conditions). Hence, in the final sample, a sequence can be terminated because of death, unknown exit from the survey (or non-response to key outcomes), or finally because of the end of the panel.

In each hazard, we include a set of baseline characteristics which capture the major risk factors for each condition. We consider education, race & ethnicity, marital status, gender and behaviors such as smoking and obesity. Finally, as discussed previously, we also include a measure of the duration between interviews in month. The average duration is close to 2 years. Table 2.2 gives descriptive statistics at first interview.

Table 2.2 Baseline Characteristics in Estimation Sample

Characteristics (at first interview)	N	mean	std. dev.	min	max
age in years	21302	64.1	11.2	50	103
less than high school		0.350	0.477	0	1
some college education		0.346	0.476	0	1
black		0.140	0.347	0	1
hispanic		0.068	0.251	0	1
married		0.703	0.457	0	1
male		0.431	0.495	0	1
ever smoked		0.591	0.492	0	1
obese (BMI>30)		0.210	0.407	0	1
duration between interviews (in months), averaged over all waves		23.4	2.8	1.8	30.9

Notes: All HRS Cohorts (HRS, AHEAD, CODA, War Babies)

Estimates of the hazard models are presented in Table 2.3. Estimates can be interpreted as the effect on the log hazard. To judge the fit of the model we perform a goodness-of-fit

exercise. To do that, we re-estimate the model on a sub-sample and keep part of the sample for evaluating the fit. We randomly select observations from the original HRS cohort with probability 0.5 and simulate outcomes for this cohort starting from observed 1992 outcomes. Table 2.4 gives the observed frequencies as well as the predicted ones. Predicted and observed frequencies are quite close to each other in 2002.

Table 2.3 Estimates with Heterogeneity and Clinical Restrictions

	Heart disease	Blood pressure	Stroke	Lung disease	Diabetes	Cancer	Mental	Disability	Mortality
prevalence t-1	pe	pe	pe	pe	pe	pe	pe	pe	pe
heart			-0.212 *				0.037	-0.160 *	0.599 **
blood pressure	0.033		0.042				0.169 *	-0.115	0.426 **
stroke							-0.172	0.240 *	0.864 **
lung disease							-0.225	0.185	1.152 **
diabetes	0.062	0.346 **	0.043				-0.422 **	-0.086	0.634 **
cancer			-0.204				-0.141	0.222 **	1.428 **
mental								0.336 **	0.740 **
disability							0.199 **		0.840 **
prevalence t=0									
heart		0.076	0.483 **	0.395 **	0.190 **	0.143 **	0.272 **	0.518 **	-0.220 **
blood pressure	0.358 **		0.418 **	0.046	0.578 **	0.082	0.099	0.356 **	-0.277 **
stroke	0.030	0.238 **		-0.229	0.012	0.086	0.466 **	0.425 **	-0.418 **
lung disease	0.511 **	0.006	0.396 **		0.014	0.301 **	0.841 **	0.627 **	-0.509 **
diabetes	0.540 **	0.014	0.584 **	0.014		-0.069	0.705 **	0.711 **	0.005
cancer	0.191 **	0.050	0.244	0.259 **	-0.023		0.308	-0.128	-1.037 **
mental	0.335 **	0.208 **	0.422 **	0.594 **	0.171 *	0.012		0.512 **	-0.581 **
disability	0.330 **	0.109	0.152	0.423 **	0.127	0.057	0.478 **		-0.065
demographics									
age <75	0.042 **	0.021 **	0.071 **	0.019 **	0.013 **	0.044 **	-0.007 *	0.035 **	0.030 **
age >75	0.038 **	-0.022 **	0.055 **	-0.004	-0.044 **	-0.023 **	0.038 **	0.143 **	0.112 **
black	-0.268 **	0.336 **	0.153 *	-0.363 **	0.210 **	-0.092	-0.225 **	0.447 **	0.244 **
hispanic	-0.441 **	0.095	-0.199	-0.582 **	0.420 **	-0.370 **	0.194 **	0.424 **	-0.073
male	0.336 **	-0.109 **	0.063	-0.146 **	0.364 **	0.366 **	-0.458 **	-0.195 **	0.420 **
ever smoked	0.176 **	-0.009	0.255 **	1.040 **	0.102 *	0.257 **	0.187 **	0.210 **	0.344 **
obese (BMI>30)	0.196 **	0.350 **	0.106	0.059	1.065 **	0.027	-0.032	0.552 **	-0.273 **
high school	-0.169 **	-0.091 *	-0.137 *	-0.356 **	-0.274 **	-0.024	-0.334 **	-0.430 **	-0.029
college	-0.191 **	-0.146 **	-0.252 **	-0.581 **	-0.312 **	0.088	-0.461 **	-0.586 **	-0.168 **
log(time since l.w.)	0.996 **	1.224 **	1.242 **	1.015 **	1.296 **	1.063 **	1.102 **	0.614 **	6.547 **
constant	-6.573 **	-6.121 **	-8.592 **	-7.164 **	-8.016 **	-7.859 **	-6.121 **	-4.433 **	-26.079 **
point 1	0	0	0	0	0	0	0	0	0
point 2	-1.353 **	-1.353 **	-1.353 **	-1.353 **	-1.353 **	-1.353 **	-1.353 **	-2.164 **	-2.176 **
Loading Factor	1	0.625 **	1.637 **	1.085 **	0.678 **	0.244 **	1.308 **	1	1
Probability estimates									
point	p(1,1,1)	p(1,1,2)	p(1,2,1)	p(1,2,2)	p(2,1,1)	p(2,1,2)	p(2,2,1)	p(2,2,2)	
Probability	0.193 **	0.082 **	0	0.024 **	0.085 **	0	0.530 **	0.087 **	
loglike/N	-3.632								

Table 2.4 Goodness-of-Fit

Prevalence Rate (Independent Draws)

	heart		pressure		stroke		lung	
year	data	sim	data	sim	data	sim	data	sim
1992	0.117	0.120	0.347	0.344	0.027	0.027	0.061	0.062
1994	0.138	0.147	0.376	0.393	0.030	0.037	0.074	0.074
1996	0.157	0.172	0.401	0.437	0.039	0.046	0.078	0.087
1998	0.176	0.196	0.435	0.478	0.047	0.055	0.088	0.097
2000	0.199	0.218	0.480	0.516	0.056	0.063	0.093	0.106
2002	0.236	0.241	0.527	0.551	0.064	0.072	0.109	0.113
# cond.	825	853	1843	1949	224	254	380	399
	diabetes		cancer		disability		mental	
year	data	sim	data	sim	data	sim	data	sim
1992	0.104	0.108	0.058	0.058	0.053	0.056	0.072	0.072
1994	0.121	0.130	0.065	0.076	0.094	0.116	0.090	0.095
1996	0.137	0.150	0.078	0.093	0.160	0.164	0.104	0.115
1998	0.151	0.169	0.093	0.111	0.197	0.205	0.118	0.133
2000	0.169	0.185	0.107	0.125	0.224	0.237	0.131	0.148
2002	0.199	0.201	0.125	0.141	0.248	0.264	0.154	0.160
# cond.	695	711	436	500	867	934	540	566
	no conditions		1 cond		2 cond		3 cond.+	
	data	sim	data	sim	data	sim	data	sim
year								
1992	0.475	0.476	0.317	0.311	0.136	0.138	0.072	0.075
1994	0.422	0.390	0.328	0.329	0.149	0.166	0.101	0.115
1996	0.371	0.323	0.326	0.333	0.168	0.191	0.134	0.153
1998	0.324	0.270	0.321	0.326	0.191	0.211	0.163	0.192
2000	0.279	0.230	0.312	0.315	0.215	0.229	0.194	0.226
2002	0.231	0.199	0.295	0.299	0.235	0.240	0.238	0.263

Incidence Rate

	mortality	
year	data	sim
1992	0.000	0.000
1994	0.014	0.009
1996	0.014	0.012
1998	0.016	0.014
2000	0.019	0.017
2002	0.019	0.020

Goodness-of-Fit test			
Prevalence rates		4.05	0.774
(dF = 7)			
Np	3539		
Nu	3500		

Notes: Simulation for HRS 1992 subsample (N=4131)

2.5 Adjusting the Model to European Transitions

In continental Europe, we only have access to cross-sectional data on responses of the type: has the doctor ever told you. Hence, the age distribution is informative about transition rates to the extent that we make assumptions about features of the model which we are willing to assume is similar across the Atlantic. We make those conditions more precise below.

We split the 2004 cross section in two groups based on age. Denote by subscript 0 the first younger group and 1 the second older group. Data takes the form of a set of conditions y and characteristics x for the two samples in year *t=2004*. We have $\{y_{i0}, x_{i0}\}_{i=1,\ldots,n_0}$ and $\{y_{i1}, x_{i1}\}_{i=1,\ldots,n_1}$ in 2004. For convenience also denote by $z = (y, x)$. The data generating process is assumed given by

$$F(z_t \mid z_{t-1}; \theta_0) \tag{2.5}$$

where θ_0 represents the true value of the parameter vector characterizing this DGP. This is essentially our transition model. The dimension of this parameter vector is K.

Indirect Inference

One key assumption allows to make inference based on simulated outcomes is that data from both groups are generated from the same DGP (Eq 1).

Under this assumption, it is possible, for a given value of θ to simulate outcomes of group 0 when they will reach the age of group 1. If the distribution of simulated outcomes or any other moment or auxiliary parameter comes close to that of outcomes of group 1, then it must be that $\theta = \theta_0$. The general class of such estimators is called Simulated Minimum Distance (SMD) (Hall and Rust, 1999) and includes as special cases the method of simulated moments (Pakes and Pollard, 1989) and Indirect Inference (Gourieroux, Monfort and Renault, 1993).

For a given simulation j, denote simulated outcomes by $\{\tilde{z}_{ij}(\theta, z_{i0})\}_{i=1,\ldots,n_0}$. Assume an auxiliary model that yields parameters $\tilde{\gamma}(z_0, \theta)$ *(Px1)* when estimated on this simulated data.

Under assumption 1 and general regularity conditions,

$$E(\tilde{\gamma}_j(z_0, \theta_0)) = \gamma(z_1) \tag{2.6}$$

where $\gamma(z_1)$ are the auxiliary parameters estimated from group 1. Based on *J* simulations, a consistent estimator of the left hand side of (2) for a trial value of θ is given by

$$\gamma(z_0,\theta) = J^{-1}\sum\nolimits_{j=1,..,J}\tilde{\gamma}_j(z_0,\theta) \tag{2.7}$$

Hence, θ_0 can be consistently estimated by

$$\theta_I = \arg\min_\theta g(z,\theta)'\Omega_P g(z,\theta) \tag{2.8}$$

where $g(z,\theta) = \gamma(z_0,\theta) - \gamma(z_1)$ and Ω_P is some positive definite matrix of dimension *P*.

If *P* = *K*, then the model is just identified and θ_I is such that

$$g(z,\theta_I) = 0 \tag{2.9}$$

Auxiliary Model

An important condition for local identification is that $\nabla_\theta g(z,\theta_0)$ be of full rank. Hence the choice of an auxiliary model is important. Because some features of the model are difficult to identify from the cross-sectional information in SHARE, we decide to only re-estimate a subset of the parameters. In particular, we allow the intercept of the hazard to be adjusted and fix other parameters to their U.S. value.

We choose the following auxiliary model for the prevalence of each condition *m*,

$$p_{a,m} = \gamma_{0,m} + \varepsilon_{a,m} \tag{2.10}$$

The parameters of such model can be estimated consistently by OLS. For all health conditions such model can be estimated from the SHARE data using appropriate weights. However, for mortality this is not possible because SHARE is a cross-section. We use each country's life-table mortality profiles to estimate the auxiliary parameters. We weight those by population to get aggregate numbers. These are then compared to the simulated mortality profile in SHARE.

These parameters bear close relationship with the constant and age profile of each condition's hazard. Since the number of structural parameters is equal to the number of auxiliary parameters, the model is just identified. Hence, there is no need to choose a weighting matrix. If estimation reveals that the minimum is not zero, this means the model is misspecified (Alvarez et al., 2001).

Estimation

Because the criterion is effectively a step function (outcomes are discrete), numerical optimization using standard gradient method becomes difficult without having to increase prohibitively the number of replications. Instead we use the Nelder-Mead Simplex algorithm which is not based on gradient methods and hence can optimize non-smooth

functions. We use 50 replications using Halton draws in our simulation. We simulate outcomes of 55-75 year olds 10 years forward such that they are 65-85 in 2014. The 65-85 population in 2004 is used to construct the auxiliary parameters from the simulated and realized data.

Results for SHARE

The next table presents the U.S. estimate of the intercept, the SHARE estimate along with "true" and simulated moments at the SHARE intercept and U.S. intercept.

Table 2.5 True and Simulated Moments

	Hazard Intercept		Moments		
condition	U.S.	Europe	"True"	Simulated at optimum	Simulated at U.S. par
heart	-6.573	-7.098	0.179	0.190	0.266
hypertension	-6.121	-7.040	0.426	0.437	0.539
stroke	-8.592	-9.022	0.051	0.065	0.096
lung	-7.164	-7.522	0.076	0.076	0.102
diabetes	-8.016	-8.416	0.153	0.157	0.195
cancer	-7.859	-9.077	0.071	0.087	0.158
depression	-6.121	-7.069	0.132	0.166	0.216
disability	-4.333	-4.655	0.176	0.187	0.233
Mortality	-26.079	-24.775	0.039	0.037	0.022
criterion				-0.0019	-0.042937

Using U.S. parameters in Europe leads to pretty high prevalence for all conditions. Once, we allow for an intercept shift, we are able to match pretty closely the aggregate prevalence rates among the 65 to 85 population.

2.6 Life-Time Prevalence vs. Current Prevalence of ADL Limitations

The transition model we have estimated takes ADL as an absorbing state. However, the 2004 baseline data in Europe only has current prevalence of ADL. We impute life time prevalence using the HRS 2004 data. In that dataset, we know life time prevalence from 1992 to 2004 as well as current prevalence. Hence, we estimate a probit where the dependent variable is ever had ADL from 1992 to 2004 among those with no current ADL in 2004. We use as regressors the whole set of health conditions and demographics used in the model. We then impute life-time prevalence in the U.S. and Europe based on that probit. Table 2.6 gives the parameter estimates of the probit regression

Table 2.6 Probit Regression Results for Imputation of Life-Time prevalence of ADL Limitations

	par	std	t	p-val
heart	0.244	0.035	6.92	0
hypertension	0.063	0.034	1.88	0.06
stroke	0.293	0.052	5.58	0
lung disease	0.317	0.048	6.59	0
diabetes	0.069	0.040	1.72	0.085
cancer	0.032	0.043	0.75	0.455
mental	0.503	0.040	12.5	0
age	0.014	0.002	7.61	0
black	0.341	0.045	7.51	0
hispanic	0.290	0.059	4.89	0
male	-0.105	0.033	-3.16	0.002
ever smoked	0.054	0.033	1.64	0.1
high school	-0.195	0.041	-4.81	0
college	-0.340	0.042	-8.04	0
obese	0.240	0.036	6.65	0
intercept	-2.338	0.145	-16.15	0

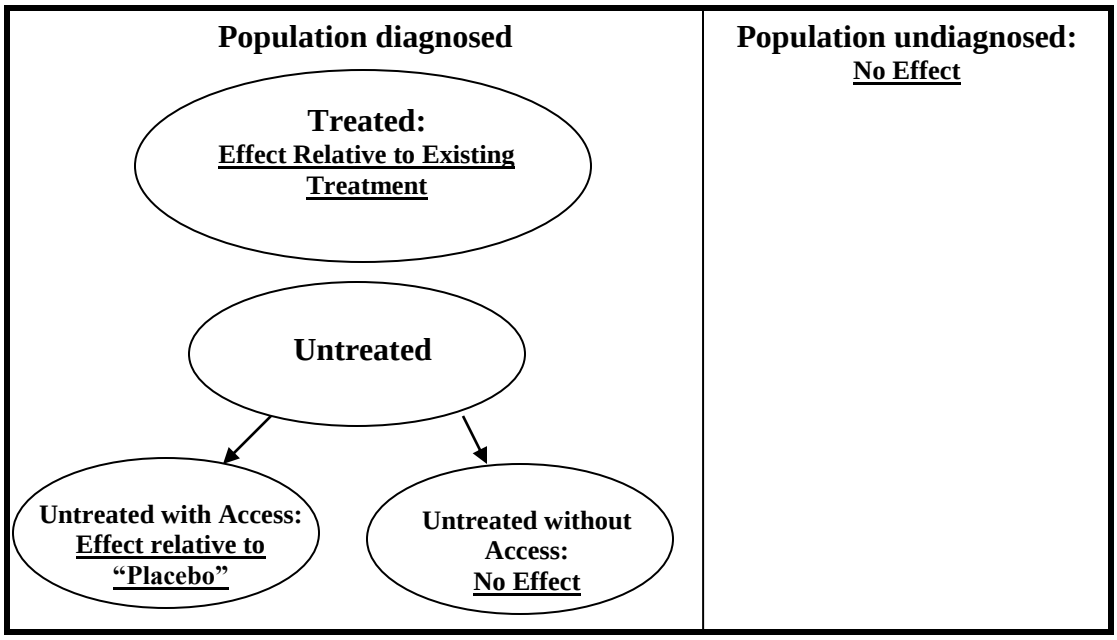
Notes: probit coefficients from HRS 2004 sample of those currently not reporting any ADL where dependent variabie is 1992-2004 prevalence of ADL

3. Calculating the Health Effect of new Drugs

Prior to the introduction of a new drug, it is useful to think of the population as divided into three subgroups: Those undiagnosed for a particular health condition, those diagnosed with a condition and treated with an existing drug, and finally those who are diagnosed but untreated. We can think of the new drug as one that potentially reduces mortality risk or the risk of being diagnosed with another health condition (e.g. a new drug that treats hypertension may reduce the risk of being diagnosed with heart disease).

Figure 3.1 illustrates how each sub-population benefits from a new drug. The treated group may benefit because new drugs are potentially more effective than existing treatments. We will call this the "clinical effect." A fraction of the previously untreated group may however gain access to this treatment. This group will thus experience the full health effect of a new drug (relative to no treatment). We will refer to this as the "access effect". Finally, the remaining untreated individuals do not gain from the introduction of the drug.[3]

Figure 3.1 Effect of a New Drug



In such a population, the average effect of a new drug will be a weighted average of the clinical and access effect. To see this, denote by (α_0, α_1) the fraction of diagnosed individuals who are untreated before and after the introduction of the new drug, respectively, and define $\Delta_\alpha = \alpha_0 - \alpha_1$. Denote P as the probability of being diagnosed

[3] This abstracts from any effect on diagnosis and thus provides a lower bound on the total effect of new drugs.

with a new condition or death, and $RR_{EXISTING} = P_{NEW} / P_{EXISTING}, RR_{PLACEBO} = P_{NEW} / P_{PLACEBO}$ to be the relative risk for those replacing existing therapy with the new drug, and those replacing no therapy with the new drug, respectively. Note that the latter corresponds to the risk given by the new drug, divided by the risk given by placebo treatment. As such, the annual relative risk for the diagnosed population following the introduction of a new drug (relative to the pre-existing situation) is given by

$$\overline{RR} = \frac{[\alpha_1 + \Delta_\alpha RR_{PLACEBO}]P_U + [(1-\alpha_0)RR_{EXISTING}]P_T}{\overline{P}} \tag{3.1}$$

where P_U is the average probability of contracting another condition or death among the untreated, P_T is that average probability among the treated and $\overline{P} = \alpha_0 P_U + (1-\alpha_0)P_T$ is the average probability in the diagnosed population prior to the introduction of the drug.

The first term of the numerator on the right hand side of equation (1) represents the total effect on the untreated, including the access effect, while the second term represents the clinical effect on those that were already treated prior to the new drug introduction. These two effects are weighted by the pre-introduction mean probability of being diagnosed with the new condition or death in the untreated and treated group separately.

For example, suppose a new drug is introduced which potentially reduces mortality for patients diagnosed with cancer. Compared with existing treatment, this drug is 25% more effective. Compared with no treatment, however, it leads to a 50% decrease in mortality risk. Now, suppose 50% of patients diagnosed with Cancer take the existing treatment and that both treated and untreated patient face a survival probability of 75%. Finally assume the introduction of the new drug means that 25% more patients are treated. This leads a 25% reduction in untreated patients. Hence, 25% of the diagnosed population derives no benefit, 25% enjoy a 50% decrease in mortality risk because they move from no treatment to the new therapy, and the remaining 50% of the population enjoy the 25% improvement over existing treatment. The average relative risk is then 0.25+0.25*0.5 + 0.5*0.75 = 0.75 for the diagnosed population.[4] Note that ignoring the access effect amounts to imposing $\Delta_\alpha = 0$. In this case, only the treated will benefit from the new drug. For many diseases, this access effect can be important, particularly when access is relatively low and existing treatments are not easily accessible. The same calculations can be performed for other risks such as the risk of being diagnosed for another health condition.

In Section 3.1, we provide methodologies for estimating each of the components of equation 1. Section 3.1 is devoted to the construction of a list of drugs for each of the

[4] This method accounts for differences in disease severity between untreated and treated individuals. However, note that our approach presumes that the effects of drugs can be appropriately captured by computing the average reduction in risk. An alternative would be to explicitly assign different reductions in risk to different people — e.g., those with different disease severity levels. While the latter approach would be more general, data limitations preclude its implementation: we do not have a panel of data on treatment status, which makes it ultimately impossible for us to separately model disease dynamics for the treated and untreated population.

conditions we consider. For these drugs, the relative risks (*RR)* are then taken from clinical trials in section 3.2. Section 3.3 is devoted to the estimation of the access effect (Δ_α) from claims data. In section 3.4, we calculate the remaining parameters (α_0, P_U, P_T) from the Health and Retirement Study.

3.2 Estimation

For each of the health condition in the transition model, one could in principle consider the whole universe of new drugs and calculate an average effect for each of them. This is likely to be a difficult task. However, breakthrough drugs are the most likely to have clinical effects, and have been in general the most studied and reviewed. This makes the estimated clinical benefits more reliable. For each of our diseases, therefore, we survey the clinical effects for the top 5 selling (or "blockbuster") drugs in that disease group, and assume conservatively that all other drugs outside the top 5 have no therapeutic benefits. Therefore, we estimate the effects of drugs in two parts: calculate the probability that a new drug will be a "top-seller," and apply the expected therapeutic benefit of a top-selling drug.

3.2.1 List of New Blockbuster Drugs

We construct a list of new drugs from INGENIX, a large, nationwide, longitudinal claims-based database (1997-2004).[5] This data set has drug expenditure information from insurance plan enrollees. We use expenditures as a proxy to identify blockbuster drugs. Health conditions in INGENIX are provided at the patient level, which makes it difficult to match drugs to health conditions because patients can take medication for multiple diseases at the same time. For example, it is unclear whether a drug used by a heart disease patient with hypertension is used to treat the heart condition or hypertension. Mapping drugs to Redbook drug class and then to health conditions appears to be a superior strategy. Hence, we first group drugs by class and then assign each class to at least one particular health condition, based on expert opinion and an extensive web search.[6] The result of this class-health condition match is presented in Appendix A.

We rank drugs for each health condition according to revenues in the 2nd year following introduction.[7] We consider new chemical entities (NCEs) as well as reformulation and recombination drugs, but exclude generics. We define the top 5 drugs for each health condition as "Blockbuster drugs". The name of the drug, Redbook drug class, generic name, and the introduction date are presented in Appendix B.

3.2.2 Calculating Effects on Health

[5] Due to the time range of INGENIX dataset, the list was limited to drugs approved by FDA from 1995 to 2002.
[6] A log of the search results is available from the authors upon request.
[7] We deflate expenditures using the general CPI.

For each of the blockbuster drugs, we survey the medical literature for clinical trials. When the trials do not provide an estimate for the health condition we are interested in, we assume the drug has no effect. Hence, these estimates can be seen as conservative. We do the same when the estimate is not statistically significant. When more than one estimate is available, we use the mean of the effects found.

We searched for the impacts of blockbuster drugs on mortality, and on the incidence of all 6 other health conditions under consideration. However, we follow Goldman et al. (2005) in ruling out some causal links, based on expert opinion. For example, we assume that there is a causal link between hypertension and diabetes, but not from hypertension to cancer. We do not investigate the effect of new drugs on recovery or cure rates. Table 1 summarizes results from the survey of the literature for those effects. Appendix C gives detail on the calculation of each estimate. These calculations provide the estimates of $RR_{EXISTING}$ and $RR_{PLACEBO}$ in equation 1.

Table 3.1 Summary of Clinical Effects Found in Medical Literature

	Health Outcome (Relative Risk RR(): New Drug/Control, Control is P=Placebo, E=Existing Treatment)															
	Heart disease		Hypertension		Stroke		Lung Disease		Diabetes		Cancer		Depression		Mortality	
Condition treated	RR(P)	RR(E)	RR(P)	RR(E)	RR(P)	RR(E)	RR(P)	RR(E)	RR(P)	RR(E)	RR(P)	RR(E)	RR(P)	RR(E)	RR(P)	RR(E)
heart diseae					0.475	1							1	1	1	1
hypertension	0.643	1			0.729	1							1	1	1	1
stroke													1	1	1	1
lung disease													1	1	1	0.796
diabetes	0.690	1	1	1	0.533	1							1	1	0.52	1
cancer					1	1							1	1	0.837	0.728
depression															1	1

Notes: See Appendix C for details on the calculations. This matrix assumes a set of causal clinical mechanisms described in Goldman et al. (2004) Empty cell mean that no elevated risk of a new condition is assumed due to the condition treated(no causal effect).

3.2.3 Access Effect

To calculate the access effect, we need to construct an estimate of Δ_α which is the decrease in the fraction of untreated individuals following the introduction of a new drug. We estimate this effect using prescription data from the IMS data.[8] By merging the drug consumption data with data on the introduction date of new drugs (from Appendix B), we get a panel data set of the number of prescriptions consumed monthly for each class before and after the introduction of the top 5 drugs (from 1997.1 to 2004.12).[9] Our strategy is to compute the effect of a launch on prescriptions relative to the trend in prescriptions for a specific class. The statistical model that implements this strategy explains the logarithm of monthly prescriptions in a class *c* as

$$\log(C_{c,t}) = \alpha_c + g_c(t) + \delta_0 L_{c,t}^{0-3} + \delta_3 L_{c,t}^{3-6} + \delta_6 L_{c,t}^{6-12} + \delta_{12} L_{c,t}^{12+} + \varepsilon_{c,t} \qquad (2)$$

α_c are class fixed effects, $g_c(t)$ is some class specific function of calendar time. The variables $L_{c,t}^k$ are indicator functions that take value 1 when a new blockbuster drug has been on the market for k months. Finally ε is some unobserved disturbance with zero mean. We specify linear class-specific time trends: $g_c(t) = \eta_c t$, which was not rejected against a more flexible specification. Hence the total effect of a new drug on prescriptions after 12 months is given by δ_{12}. We also include interaction terms to differentiate if the new drug is a reformulation or a new chemical entity (NCE). This interaction measures the effect of reformulation drug relative to a new NCE, i.e. a negative coefficient indicates that the effect of reformulation is smaller than the effect of a NCE. Table 2 presents estimation results.

[8] http://www.imshealth.com
[9] We use the USC-5 classification which results in 22 classes for the purpose of estimation.

Table 3.2 Access Effect Regression Results

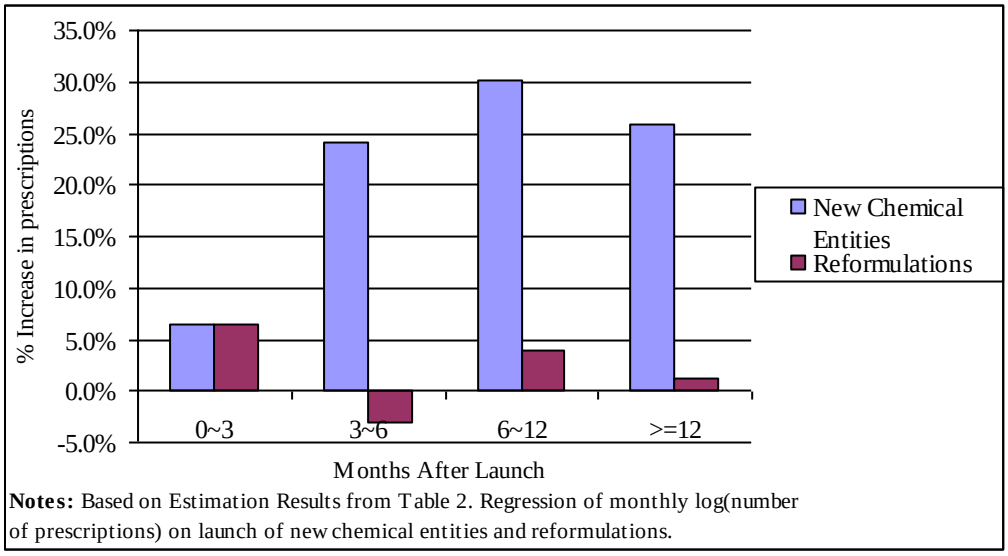
	Coefficient	P-Value	
Launched 0~3 Months	0.064	0.543	Number of observations: 2711
(Launched 0~3 months)*Reformulation	0.001	0.993	
Launched 3~6 Months	0.241	0.076	
(Launched 3~6 months)*Reformulation	-0.272	0.060	R-Square: 0.973
Launched 6~12 Months	0.301	0.033	
(Launched 6~12 months)*Reformul	-0.262	0.064	Time period: Jan 1997~Dec 2004
Launched >=12	0.258	0.035	
(Launched >=12 months)*Reformulation	-0.245	0.049	

Notes: OLS regression of log(number of prescriptions). Standard errors allow for clustering at the USC-5 class level.

New chemical entities tend to have a relatively strong effect on the number of prescriptions after 3 months. After one year, there is a 32% increase in the number of prescriptions. This estimate is statistically significant at the 10% level. On the other hand, the effect for reformulations is small and negligible. Figure 2 presents the estimates of the effect separately for NCEs and reformulations. A statistical test confirms that it is very unlikely that prescriptions increase following the introduction of a reformulation.[10] The effect for NCEs is used to compute the Δ_α assuming that this effect comes from more individuals being treated rather than more prescriptions awarded by existing patients.

[10] In principle, it would be possible to isolate a separate effect for each health conditions since there are generally more than one drug class that treats a condition. The problem is that for some conditions (stroke, diabetes and depression) few classes are used hence leading to identification problems. Estimates from such specifications did not yield differences that were statistically different from each other.

Figure 3.2 Access Effect



Notes: Based on Estimation Results from Table 2. Regression of monthly log(number of prescriptions) on launch of new chemical entities and reformulations.

3.2.4 Access and Incidence Rates by Conditions

Three more estimates are needed to compute average relative risks from equation 1. First, we need to know, for each condition, the fraction of diagnosed individuals not taking existing drugs (α_0). Second, we need estimates of the incidence rates for those treated (P_T) and untreated (P_U). We use the Health and Retirement Study (HRS) for that purpose. The HRS is a nationally representative longitudinal study of the age 50+ population. It asks about lifetime prevalence of the seven conditions we use as well as the consumption of drugs for those diagnosed with these conditions. It also tracks mortality. Mortality rates from the HRS follow closely figures from life-tables (Adams et al., 2003).[11] Most of the differences are attributable to the fact that HRS samples the non-institutionalized population.

To construct estimates of the transition rates (*P*), we use hazard models estimated on the 1992-2002 waves of the HRS. The hazard models include baseline demographics, prevalence indicators at the previous wave, risk behaviors, and age. Table 3 gives the lifetime prevalence in 2004 of various conditions, the fraction untreated among the diagnosed population and predicted transition rates based on hazard models.

[11] The HRS conducts exit interviews with relatives for deceased respondents. If a respondent's status in one wave is unknown, an interview is attempted in following waves until it can be established.

Table 3.3 HRS Disease Prevalence, Drug Usage, and Predicted Incidence Rate

		fraction untreated before	reduction in fraction	Predicted Incidence Rate Prior to Introduction For									
				Heart disease		Hypertension		Stroke		Depression		Mortality	
condition treated	prevalence	introduction	untreated	untreated	treated	untreated	treated	untreated	treated	untreated	treated	untreated	treated
heart disease	0.253	0.338	0.173					0.026	0.030	0.028	0.031	0.037	0.047
hypertension	0.546	0.110	0.110	0.048	0.050			0.022	0.023	0.024	0.024	0.026	0.027
stroke	0.080	0.632	0.096							0.039	0.040	0.063	0.069
lung disease	0.102	0.467	0.140							0.040	0.047	0.047	0.053
diabetes	0.176	0.183	0.183	0.068	0.071	0.074	0.081	0.032	0.032	0.029	0.030	0.041	0.040
cancer	0.141	0.772	0.060					0.022	0.022	0.026	0.021	0.040	0.037
mental	0.165	0.426	0.150									0.032	0.029

Notes: Calculations from HRS 2004 data. Sample weights used.

Of the 54.6% of individuals aged 50+ in 2004 with hypertension, only 11% do not take medication for that condition according to the HRS. A somewhat larger fraction with diabetes and heart disease does not take medication (18.3% and 33.8%). Cancer and stroke are the two conditions with the fewest respondents treated with drugs (77.2% and 63.3% are untreated). The next column present the estimate of Δ_α : the reduction in the fraction untreated following introduction of a new drug. Applying the effect calculated of 31.8% found in the previous section leads to a substantial reduction in the fraction untreated for most diseases. Finally predicted average incidence rates prior to introduction are similar across groups of treated and untreated patients, if not higher in the treated group. Hence, we explicitly take into account of the fact that benefits for the untreated may be lower than for the treated because their condition is less severe.

3.3 Estimates of Average Effects

3.3.1 Average Effect of Blockbuster Drugs

We use estimates along with previously estimated parameters to construct the average relative risks from equation 1. Table 4 gives the results for each of the causal link we identified in Table 1.

Table 3.4 Average Health Effect of a New Blockbuster Drug

	Average Risk Reduction Following Introduction of New Blockbuster Drug							
condition treated	heart	hypertension	stroke	lung disease	diabetes	cancer	depression	mortality
heart			0.919				1.000	1.000
hypertension	0.964		0.974				1.000	1.000
stroke							1.000	1.000
lung disease							1.000	0.887
diabetes	0.945	1.000	0.917				1.000	0.910
cancer			1.000				1.000	0.930
depression								1.000

These estimates are conservative, since they do not include effects on the undiagnosed population. We have also assumed drugs other than those in the Top 5 list had no effect on health. Moreover, whenever we could not find a clinical effect from a peer-reviewed study we have assumed that a new drug has no effect.

3.3.2 Fraction of Blockbuster Drugs (1998-2002)

We use data from the Food and Drug Administration (FDA) to compute how many new chemical entities (NCEs) were introduced over the 1998-2002 period. We compute the fraction of blockbuster NCE as a fraction of all NCE over the period using the year in

which they were approved by the FDA. We map each approved drug to health condition(s) by using the indications listed by the FDA in its annual report. We exclude reformulations and recombination drugs for two reasons. First, indications are only given for NCEs so that we cannot do the mapping for reformulation and recombination drugs. Second, reformulation and recombination drugs are not likely to have clinical effects over existing treatments because they simply recombine or reformulate existing treatments. This leaves the possibility that they have an access effect. But we could not find any access effect for those drugs in section 3.3. Hence, we can ignore such drugs in our calculations. Table 5 presents the results for the fraction of blockbuster NCEs from 1998-2002. The fraction of new blockbuster drugs is quite different across diseases ranging from 10% for hypertension to 67% for stroke (only one new NCE for depression is approved by the FDA over the period and it is a blockbuster drug).

Table 3.5 Probability of a New Blockbuster Drug for Each Health Condition, 1998-2002

New drugs	Heart		Hypertension		Stroke		Lung Disease		Diabetes		Cancer		Depression	
	total	top	total	top	total	top	total	top	total	top	total	top	total	top
1998	3	0	3	0	0	0	1	0	0	0	3	1	1	1
1999	1	0	1	0	0	0	2	0	2	2	5	2	0	0
2000	2	1	1	0	2	1	1	1	3	0	4	0	0	0
2001	2	0	2	1	1	1	2	0	0	0	2	1	0	0
2002	2	1	3	1	0	0	0	0	0	0	2	0	0	0
Total	10	2	10	2	3	2	6	1	5	2	16	4	1	1
Average	2	0.4	2	0.4	0.6	0.4	1.2	0.2	1	0.4	3.2	0.8	0.2	0.2
Fraction top		0.20		0.20		0.67		0.17		0.40		0.25		1.00

Notes: Information on new chemical entities taken from the FDA websites. The FDA lists indications for each drug which were then mapped to our set of conditions. The top-selling drugs are identified in Appendix A according to revenues, two years after introduction according to the INGENIX database.

4. Innovation Module

The innovation module translates changes in market size into new innovation. Previous research has found that, on the margin, a one percent increase in pharmaceutical revenues leads to a four percent increase in the annual number of new drugs (Acemoglu and Linn, 2004). We use this value of four in our baseline scenarios, but consider a range of estimates from zero to five.

Assuming that revenues are proportional to the number of sick consumers, we can readily translate the elasticity into a parameter that relates market size to new drugs. Since we know the baseline levels of sick consumers in each disease group, and the number of new drugs in each disease group, this implies a relationship between patients and new molecules.

Table 1 illustrates our method. We begin with the estimated annual number of new drug introductions in each disease group, and the number of patients (in 2005) with each disease. These are shown in the first two rows of the table, for each disease. If the elasticity of new drug introductions is 4.0, then a one percent increase in market size generates a four percent increase in the number of new drugs. These calculations are displayed in the third and fourth rows of the table. We then compute the number of new patients required to generate a single drug — this is simply the ratio of the increase in market size (of 1%), to the increase in the number of new drugs (of 4%). This is the last row of the table. Varying the elasticity from 4% to other values is straightforward, and causes our estimate of market size per drug to vary correspondingly.

Table 4.1: Estimated effects of market size on innovation.

	Diseases						
Baseline Figures 2005	heart	hypert	stroke	lung disea	diabetes	cancer	mental
baseline number of new drugs	2	2	0.6	1.2	1	3.2	0.2
baseline market (millions)	122.4	68.9	10.1	12.7	23.2	14.9	24.5
Predicted Change in Market							
change in market	6.48	2.79	1.10	0.88	1.22	1.05	2.14
% change	5.3%	4.1%	10.9%	6.9%	5.3%	7.1%	8.7%
Change in New Drugs Using elasticity of 4							
% change in number of new drugs	21.2%	16.2%	43.7%	27.7%	21.0%	28.3%	34.9%
absolute change in number of drugs	0.423	0.324	0.262	0.332	0.210	0.906	0.070
Implied required change in market size to generate one new drug	15.3	8.6	4.2	2.6	5.8	1.2	30.6

This method provides us with the number of new drugs for each disease. The probability of a top-seller in each disease group is then applied to these results to generate the number of new top-sellers each year. The realization is drawn from a binomial trial for each new drug. The realization of $d_{m,t}$, the number of new top-seller drugs, is then applied to health transition probabilities. For example, the mortality probability of individual *i*, $P^T_{m,it}$,after applying the clinical effect $\overline{RR}_m$ is

$$P^T_{m,it} = [1 + h_{m,it-1}\left(\overline{RR}_m\right)^{d_{m,t}}]P^U_{m,it}\,. \tag{4.2}$$

We assume there is 10 year lag between the decision to start research on a new drug and the time it arrives on the market. Hence, new drugs at time t depend on changes in market size at t-10.

5. Costs and Benefits

5.1 Value of Remaining Life-Years

Denote by $n_{a,t}$ the number of people of age *a* alive in alive in year *t*. In any given year, the value of discounted life-years ahead can be calculated from the simulation. Using a discount rate ρ and a value of a statistical life year v, this is given by

$$N_{a,t} = v\sum_{s=t}^{T}\rho^{-(s-t)}n_{a+(s-t),s} \tag{5.1}$$

We use a discount rate of 3% to discount benefits as well as expenditures.

5.2 Medical and Drug Expenditures

Because the HRS does not have accurate information on total medical expenditures and total drug expenditures, we use the Medical Expenditure Panel Study (MEPS) to construct cost regressions. We regress these expenditure on the same demographics we have in the model as well as age and health condition indicators. Few differences in the definition of variables are observed. We use the sample of age 50+ individuals in MEPS. The regressions are performed separately for male and female as well as for each type of expenditure (drug and medical). The regression takes the form:

$$y_{i,t} = \beta_a a_{it} + x_{it}\beta_x + h_{it}\beta_h + \varepsilon_{it} \tag{5.2}$$

Medicare Current Beneficiary Survey (MCBS) provides a better medical cost expenditure estimation for elderly(age 65+). We mapped the MEPS regression results to MCBS average values for the elderly, by adjusting the constant and age variable coefficients. Table 5.1 gives the final results after MEPS regression and mapping MEPS to MCBS:.

Table 5.1 Cost Regression Results for Female and Males aged 50+

Drug Expenditure	female		male	
(annual $)	coeff	s.e.	coeff	s.e.
heart	670.78	50.72	3212.32	232.74
hypertension	593.41	42.24	392.94	193.84
stroke	545.88	81.75	2665.75	375.12
lung	572.19	107.04	2565.87	491.17
diabetes	1075.22	56.95	2150.18	261.34
cancer	477.58	84.79	4268.14	389.09
mental	967.90	49.27	1024.93	226.07
disability	935.43	89.92	8150.39	412.63
age<68	3.17	5.02	37.78	23.05
age>68	-4.00	5.29	145.78	24.29
age 68	-36.11	79.19	1801.86	363.37
black	-151.62	57.44	-481.06	263.57
hispanic	-229.83	62.99	-286.53	289.05
smoke ever	49.72	39.99	312.61	183.52
obese	150.00	44.10	-52.18	202.39
l.t. highschool	-26.23	44.53	64.35	204.33
college	-90.11	61.90	479.82	284.05
constant	835.44	95.50	2735.13	438.25
R-square	0.21		0.32	
Medical expenditure	female		male	
annual ($)	coeff	s.e.	coeff	s.e.
heart	626.43	41.76	3976.53	336.93
hypertension	581.76	35.41	880.40	285.68
stroke	477.00	69.07	2453.71	557.21
lung	702.77	77.02	1885.78	621.37
diabetes	986.95	47.87	1324.49	386.23
cancer	158.61	73.65	5746.56	594.14
mental	762.65	56.21	2059.72	453.50
disability	936.47	97.48	11134.07	786.39
age<68	25.87	4.08	41.28	32.93
age>68	12.20	4.97	114.46	40.13
age 68	-1.11	67.43	573.70	544.02
black	33.05	51.20	-477.30	413.03
hispanic	-99.43	54.81	-106.81	442.16
smoke ever	56.98	35.08	448.36	283.02
obese	208.62	39.61	406.22	319.53
l.t. highschool	40.98	40.16	1031.26	323.96
college	62.65	46.98	1473.59	379.02
constant	599.46	82.36	1903.32	664.44
Sample size	9141		6205	
R-square	0.13		0.12	

Notes: OLS regression results using robust standard errors on MEPS data

For Europe, we adjust costs using the ratio of expenditure per capita across countries. These figures are given by the OECD. Table 5.2 provides detail on the calculations

Table 5.2 Total Expenditure on Pharmaceutical and Non-Pharmaceutical Services by Country

	Total expenditure per capita $USD 2004 PPP		Ratio Country vs. US	
	Non-pharma	pharma	Non-pharma	pharma
Denmark	2610	271	0.49	0.36
France	2562	597	0.48	0.80
Germany	2566	439	0.48	0.58
Greece	1786	376	0.33	0.50
Italy	1880	512	0.35	0.68
Netherlands	2691	350	0.50	0.47
Spain	1617	477	0.30	0.64
Sweden	2478	347	0.46	0.46
U.S.	5351	751	1.00	1.00
Source:	OECD Health Data 2005			

6. Stochastic Simulation and Weighting

The horizon for each simulation is 2005 to 2150 by which time all 2060 new entrants are all dead. We start the simulation with the HRS and SHARE 2004 samples. We adjust weights so that they match 2004 population counts provided by the United Nations' Population Program. We do this by age in order to smooth out bumps in the age distribution. Each year, the population of age 55 respondents in 2004 is added back adjusting their weights for projected demographic trends. Table 6.1 presents forecasted growth rates. By using the age 55 2004 cohort repeatedly and only adjusting for growth, we do not take into account of composition effects due to different growth rates across different segment of the population (say obese population)

Table 6.1 Population Age 55-59 Growth Rate Projections from United Nations

year	SHARE	US
2010	0.009	0.028
2015	0.014	0.021
2020	0.021	0.002
2025	0.003	-0.015
2030	-0.017	-0.005
2035	-0.017	0.005
2040	-0.009	0.016
2045	-0.006	0.013
2050	-0.009	0.007

Notes: Annual growth rates from UN Population Forecasts age 55-59 group

Since the sample size for each age group is small, weighting introduces a significant amount of variability. Do reduce it, we use two replicate datasets of the new cohorts and adjust appropriately the weights.

We use an average of 30 replications of the simulation in order to reduce simulation noise. Each replication takes roughly 5 minutes on a HP DL145 Linux box running on 2 dual core Intel 2.2 GHZ processors with 8 GB of RAM (programmed with OxMetrics). Since we run many scenarios for different parameter values we make use of parallel computing on 2 DL145 machines (total of 8 processors) using a message passing interface (MPI). Each processor is assigned a scenario, performs the calculations, and writes the result to file.

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Appendix A Mapping from Drug Class to Health Conditions

Heart Disease	Hypertension	Stroke	Lung Disease	Diabetes	Cancer	Depression
Antibiot, Penicillins	Cardiac, ACE Inhibitors	Thrombolytic Agents, NEC	Antibiot, Penicillins	Antidiabetic Ag, Sulfonylureas	Antibiot, Antifungals	Psychother, Antidepressants
Antihyperlipidemic Drugs, NEC	Cardiac, Beta Blockers	Antiplatelet Agents, NEC	Vaccines, NEC	Antidiabetic Agents, Insulins	Antiemetics, NEC	Antimanic Agents, NEC
Cardiac Drugs, NEC	Vasodilating Agents, NEC	Coag/Anticoag, Anticoagulants	Antibiot, Cephalosporin & Rel.	Antidiabetic Agents, Misc	Antineoplastic Agents, NEC	
Cardiac, ACE Inhibitors	Cardiac, Alpha-Beta Blockers		Antibiot, Tetracyclines		Folic Acid & Derivatives, NEC	
Cardiac, Antiarrhythmic Agents	Hypotensive Agents, NEC		Antibiotics, Misc		Gonadotrop Rel Horm Antagonist	
Cardiac, Beta Blockers	Cardiac, Calcium Channel		Antituberculosis Agents, NEC		Immunosuppressants, NEC	
Cardiac, Cardiac Clycosides	Symnpatholytic Agents, NEC		Sulfonamides & Comb, NEC		Interferons, NEC	
Cardiac, Cardiac Glycosides	Sympatholytic Agents, NEC		Sulfones, NEC		Blood Derivatives, NEC	
Hemorrheologic Agents, NEC	Diuretics, Loop Diuretics		Tuberculosis, NEC		Antibiot, Aminoglycosides	
Vasodilating Agents, NEC	Diuretics, Potassium-Sparing		Antibiot, B-Lactam Antibiotics			
Blood Derivatives, NEC	Diuretics, Thiazides & Related		Antibiot, Erythromycn&Macrolid			
Cardiac, Calcium Channel	Cardiac Drugs, NEC		Anticholinergic, NEC			
Diuretics, Loop Diuretics			Autonomic, Nicotine Preps			
Diuretics, Potassium-Sparing						
Diuretics, Thiazides & Related						
Thrombolytic Agents, NEC						

Antiplatelet Agents, NEC						
Coag/Anticoag, Anticoagulants						
Source: Web search and expert opinion. Printouts of the sources are available upon requests.						

Appendix B Top 5 Drugs by Health Condition

(1) Heart Disease

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	LIPITOR	Antihyperlipidemic Drugs, NEC	Atorvastatin Calcium	New Ingredient	1996.12
2	ZETIA	Antihyperlipidemic Drugs, NEC	Ezetimibe	New Ingredient	2002.10
3	PLAVIX	Antiplatelet Agents, NEC	Clopidogrel Bisulfate	New Ingredient	1997.11
4	CARTIA XT	Calcium Channel Blocker	Diltiazem Hydrochloride	New Formulation	1998.7
5	WELCHOL	Anti-hyperlipidemic, NEC	Colesevelam Hydrochloride	New Ingredient	2000.5

(2) Hypertension

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	CARTIA XT	Cardiac, Calcium Channel	Diltiazem Hydrochloride	New Formulation	1998.7
2	TRACLEER	Vasodilating Agents, NEC	Bosentan	New Ingredient	2001.11
3	BENICAR	Cardiac Drugs, NEC	Olmesartan Medoxomil	New Ingredient	2002.4
4	AVAPRO	Cardiac Drugs, NEC	Irbesartan	New Ingredient	1997.9
5	DIOVAN	Cardiac Drugs, NEC	Valsartan	New Ingredient	1996.12

(3) Stroke

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	PLAVIX	Antiplatelet Agents, NEC	Clopidogrel Hydrochloride	New Ingredient	1997.11
2	AGGRENOX	Antiplatelet Agents, NEC	Dipyridamole + Aspirin	New Combination	1999.11
3	AGRYLIN	Antiplatelet Agents, NEC	Anagrelide Hydrochloride	New Ingredient	1997.3
4	ARIXTRA	Coag/Anticoag, Anticoagulants	Fondaparinux Sodium	New Ingredient	2001.12
5	INNOHEP	Coag/Anticoag, Anticoagulants	Tinzaparin Sodium	New Ingredient	2000.7

(4) Lung Disease

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	ADVAIR DISKUS	Adrenals & Comb, NEC	Fluticasone Propionate+ Salmeterol Salmeterol Xinafoate	New Combination	2000.8
2	FLOVENT	Adrenals & Comb, NEC	Fluticasone Propionate	New Formulation	1996.3
3	BIAXIN XL	Antibiot, Erythromycn&Macrolid	Clarithromycin	New Formulation	2000.3
4	AUGMENTIN XR	Antibiot, Penicillins	Amoxicillin + Clavulanate	New Formulation	2002.9
5	ZYVOX	Antibiotics, Misc	Linezolid	New Ingredient	2000.4

(5) *Diabetes*

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	ACTOS	Antidiabetic Agents, Misc	Pioglitazone Hydrochloride	New Ingredient	1999.7
2	AVANDIA	Antidiabetic Agents, Misc	Rosiglitazone Maleate	New Ingredient	1999.5
3	REZULIN	Antidiabetic Agents, Misc	Withdrawn	New Ingredient	1997.1
4	GLUCOPHAGE XR	Antidiabetic Agents, Misc	Metformin Hydrochloride	New Formulation	2000.10
5	GLUCOVANCE	Antidiabetic Ag, Sulfonylureas	Glyburide + Metformin Hydrochloride	New Combination	2000.7

(6) Cancer

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	GLEEVEC	Antineoplastic Agents, NEC	Imatinib Mesylate	New Ingredient	2001.5
2	CASODEX	Antineoplastic Agents, NEC	Bicalutamide	New Ingredient	1995.10
3	TEMODAR	Antineoplastic Agents, NEC	Temozolomide	New Ingredient	1999.8
4	XELODA	Antineoplastic Agents, NEC	Capecitabine	New Ingredient	1998.4
5	AROMASIN	Antineoplastic Agents, NEC	Exemestane	New Ingredient	1999.10

(7) Depression

	Drug Name	Class	Active Ingredient	Innovation Type	Introduction Date
1	LEXAPRO	Psychother, Antidepressants	Escitalopram Oxalate	New Indication	2002.8
2	PAXIL CR	Psychother, Antidepressants	Paroxetine Hydrochloride	New Formulation	1999.2
3	CELEXA	Psychother, Antidepressants	Citalopram Hydrovromide	New Ingredient	1998.7
4	EFFEXOR XR	Psychother, Antidepressants	Venlafaxine Hydrochloride	New Formulation	1997.1
5	WELLBUTRIN SR	Psychother, Antidepressants	Buproprion Hydrochloride	New Formulation	1996.10

Appendix C Details and Reference for Calculation of Clinical Effects in Table 3.1

Causal Link					
From	To	Drug	Control Group	Reference	Calculation
heart	stroke	LIPITOR	Placebo	Schwartz, G. G., Olsson Ag, Ezekowitz Md, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes the MIRACL study a randomized controlled trial. Journal of the American Medical Association. 2001;285(13):1711-1718.	translate RRR into annual RRR by assuming RRR to be conatant over years
hypertenstion	heart	LIPITOR	Placebo	Sever, P. S., Dahlof, B., Poulter, N. R., et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. Lancet. 2003;361(9364):1149-1158.	translate RRR into annual RRR by assuming RRR to be conatant over years
hypertension	stroke	LIPITOR	Placebo	Sever, P. S., Dahlof, B., Poulter, N. R., et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial--Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial.[comment]. Lancet. 2003;361(9364):1149-1158.	translate RRR into annual RRR by assuming RRR to be conatant over years
diabetes	heart	LIPITOR	Placebo	Colhoun, H. M., Betteridge, D. J., Durrington, P. N., et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): Multicentre randomised placebo-controlled trial. Lancet. 2004;364(9435):685-696.	translate RRR into annual RRR by assuming RRR to be conatant over years
diabetes	stroke	LIPITOR	Placebo	Colhoun, H. M., Betteridge, D. J., Durrington, P. N., et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): Multicentre randomised placebo-controlled trial. Lancet. 2004;364(9435):685-696.	translate RRR into annual RRR by assuming RRR to be conatant over years
lung disease	mortality	ZYVOX	Vancomycin	ZYVOX label at FDA: http://www.fda.gov/cder/foi/label/2005/021130s008,009,021131s009,010,021132s008,009lbl.pdf	RRR=cure rate in treatment group/ cure rate in control group
diabetes	mortality	ACTOS or AVANDIA	Placebo	Michael Sheehan, Current Therapeutic Options in Diabetes Mellitus, Clinical Medicine and Research, 2003, Vol. 1, No. 3 Kay-Tee Khaw, Nicholas Wareham, Robert Luben, Sheila Bingham, Suzy Oakes, Ailsa Welch,Nicholas Day. Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European Prospective Investigation of Cancer and Nutrition (EPIC-Norfolk).British Medical Journal. Volume 322(7277), 6 January 2001, pp 15-18.	Both lower Hemoglobin A1C levels by 1.5 percentage points,a 1 % increase in HbA1c leads a relative risk increase of 1.28 relative to placebo, so RRR= 1/(1.28)(1.5))= 0.52.
cancer	mortality	TEMODAR+radiotherapy	radiotherapy	Stupp et al. Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastmoa, New England Journal of Medicine, March 10, 2005	RRR=average of RRR in each clinical trial, which is translated tinto annual RRR by assuming RRR to be conatant over years
		TAXOTERE+XELODA	TAXOTERE	FDA drug label of XELODA: http://www.fda.gov/cder/foi/label/2005/020896s016lbl.pdf	
cancer	mortality	GLEEVEC	Interferon-α+Cytarabine	Roy L, Guilhot J, Krahnke T et al. Survival Advantage from Imatinib Compared with the Combination Interferon-α plus Cytarabine in Chronic-phase Chronic Myelogenous Leukemia: Historical Comparison Between Two Phase 3 Trials. Blood. 2006;108:1478-1484.	translate RRR into annual RRR by assuming RRR to be conatant over years

Notes: all the values not available from clinical literature are imputed as 1, i.e., assuming no clinical effect.