

# Screening for a Chronic Disease: A Multiple Stage Duration Model with Partial Observability\*

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## Abstract

We estimate a dynamic multi-stage duration model to investigate how early detection of diabetes can delay the onset of lower extremity complications and death. We allow for partial observability of the disease stage, unmeasured heterogeneity, and endogenous timing of diabetes screening. Timely diagnosis appears important. We evaluate the effectiveness of two potential policies to reduce the monetary costs of frequent screening in terms of lost longevity. Compared to the status quo, the more restrictive policy yields an implicit value for an additional year of life of about \$50,000, while the less restrictive policy implies a value of about \$120,000.

*Keywords:* Screening, partial observability, chronic disease.

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# 1 Introduction

According to the U.S. Center for Disease Control (CDC) 75% of health care expenditures and 70% of all deaths in the U.S. are attributable to chronic diseases, including heart conditions, cancer, stroke, and diabetes (CDC 2009). Earlier detection of these chronic diseases can yield substantial savings and better health outcomes. To achieve these goals, the Affordable Care Act (ACA) of 2010 subsidizes not only primary preventive measures, such as improvements in diet, but also secondary preventive measures. For example, beginning in 2014 all insurance plans will be required to cover many screening tests without any co-payment. However, the empirical evidence that increased screening will save resources or even improve health outcomes is mixed (Cutler 2008). Knowing earlier that an individual has a chronic disease does not imply that screening can delay disease progression or increase longevity.

The "gold standard" for evaluating the benefits versus costs of alternative screening policies is the randomized controlled trial (RCT). RCTs provide a simple approach to solve the problem of unobserved heterogeneity, but their usefulness for policy evaluations can be limited in many important situations. When the outcomes monitored are relatively rare, they can be quite expensive. They are difficult to conduct for long follow-up periods. In the context of dynamic decision-making, the treatment protocols specified in RCTs may not yield results generalizable to community settings. This is especially the case when there are many different outcomes occurring over long time horizons and numerous intermediate outcomes that might require additional interventions. These are all key issues when one studies diabetes, and the sample size of an RCT would have to be very large and the follow-up period very lengthy for it to have sufficient statistical power and time to measure many relevant relationships.

A potentially important alternative is to use observational data like we do

in this study. Large, longitudinal, administrative data sets are becoming increasingly available to researchers, but their effective use requires one to address directly how unobserved heterogeneity impacts both observed treatment choices and outcomes over time. Econometric solutions for dealing with such issues in analyzing observational data have been developed, including for dynamic problems like those examined here, but there is still much progress to be made. In this study we incorporate many of these advances and add in a key component that is relevant for studying diabetes and many other diseases.

Diabetes mellitus is a complex chronic disease. It can affect eyesight, kidneys, cardiovascular systems, and nervous systems affecting the lower extremities. The incidence of diabetes is increasing in the U.S. and elsewhere, reflecting increased obesity of the population in part. The disease progresses through several stages, each with increasingly debilitating consequences. Once an individual reaches a more advanced diabetes stage it is impossible to undo the physiological damage; it can eventually lead to death. Prevalence is high among the elderly (Sloan et al. 2008). The early stages of the disease are typically non-symptomatic, but without interventions, irreversible physiological damage will continue to accrue. Like many other chronic illnesses, diabetes can be much more costly to treat if detected later. Regular screening for diabetes potentially can help the patient and her physician recognize when it is appropriate to undertake behavioral modifications and start medications and other therapies to slow the disease's progression.

Screening is costly, and the optimal screening regimen depends on a comparison of the marginal benefit and the marginal cost of screening. The marginal benefit from more frequent screening depends on the probability that screening will reveal useful information and the value of this information in slowing the disease's progression. This is the primary focus of this paper. This study

uses a dynamic multi-stage discrete duration model to investigate the effectiveness of early detection of diabetes mellitus through screening in delaying the progression of complications and death.

An evaluation of screening for diabetes encounters at least four econometric issues. First, ascertainment of diagnosis in particular and care more generally is endogenous. Second is the importance of partial observability of the disease state; the person could have the disease for a long time without being diagnosed. Third, since people and diseases differ in aspects unobservable to the researcher, there is likely unobserved heterogeneity. Fourth, the probability of adverse outcomes increases with duration and progression of the disease.

Our estimation strategy deals with each of these four econometric problems. We address endogeneity and unmeasured heterogeneity issues by using discrete factor models (Heckman and Singer, 1984; Mroz 1999). This approach has been used previously by Picone et al. (2003), Glewwe and Jacoby (2004), Bhattacharya (2005), Mroz and Savage (2006), and Liu et al. (2010) among others. We simultaneously account for multiple disease stages, partial observability of disease progression, endogeneity of the timing of diagnoses, and health outcomes. We control for partial observability by modeling empirically all potential exact times of disease (or stage) onset and integrating over all these potential onset times. The bounds for these integrations come from the last time period a person was known to not have the disease and the first time the individual was known to have the disease.

These time periods during which we are uncertain about precisely when the individual progressed to the next disease stage constitute a key feature of this analysis. Not only is this an econometric issue to be addressed; it is a real, substantive issue for analyzing disease progression and treatments. Many individuals will not recognize that they have progressed to diabetes or to more

advanced stages if they do not see a health care professional who can diagnose their condition. If the period of time during which the disease is present but unobserved and untreated is long, then the individual may progress much more rapidly to more severe disease stages, possibly resulting in amputation or death.

We find that earlier diagnosis of diabetes, and presumably the treatments that follow diagnosis, delays the onset of lower extremity complications including amputation. For example, a one year delay in the diagnosis of diabetes increases the probability that five years later she will have a lower extremity complication (or worse) by 11% (6.6% points out of a baseline of 59%). Transitions to high severity lower extremity complications, or worse, within five years would increase by 27%. However, because the number of individuals who transition to severe stages is relatively low, the total number of additional high severity LEC cases is correspondingly low. Our parameter estimates also allow us to conduct counterfactual analysis and policy simulations. For example a policy that restricts the number of visits that Medicare covers to two per year at most for healthy individuals will save \$476 per beneficiary, but it would cost about 0.004 per person in years of life during a 15-year span. These would imply an implicit value of a year of life of about \$119,000.

The rest of the paper is organized as follows: Section 2 provides a background on diabetes and the decision process to screen. Section 3 describes the econometric strategy and Section 4 the data. Section 5 presents our empirical specification, including the method for accounting for endogeneity of treatments, which is followed by results in Section 6. Section 7 discusses the marginal effects and policy simulations. Finally, Section 8 presents conclusions and implications.

## 2 Background

Diabetes mellitus is a complex disease, potentially adversely affecting several organ systems, including the eyes, the cardiovascular system, the kidneys, and legs and feet. It reduces life expectancy. Complications of the legs and feet, lower extremity complications (LECs), are common. They may be classified into stages, with each successive stage being increasingly more severe. In this study, we defined five mutually exclusive stages (Table 1): no diabetes or "healthy" and four diabetes stages. The disease stages are: (1) diabetes only, no LEC ( $D_1$ ); (2) low LEC ( $D_2$ ); (3) medium LEC ( $D_3$ ); and (4) high LEC ( $D_4$ ). Persons in  $D_1$  may have no symptoms or at most mild symptoms, such as thirst which could reflect other factors. In  $D_2$ , the person has mild complications of the legs or feet, e.g., loss of feeling in the feet, which might be treated by prescribing special shoes to prevent foot injuries. In  $D_3$ , the person experiences possibly severe infections, bruises on a leg or swelling and/or pain in a foot.  $D_4$  includes gangrene or infections of the bone or bone marrow, which if untreated can lead to amputation or even death.

Each period the individual has the option of visiting a physician who diagnoses whether or not she has diabetes and the stage of the disease from  $D_1$  to  $D_4$ . Early diagnosis of  $D_1$  as well as later stages leads to earlier treatment. This potentially can slow down the disease progression and adverse health shocks. If these screening visits were costless, the individual would visit a physician every period and the disease would be perfectly monitored. In practice very few individuals visit a physician each period for screening, since it is costly in terms of time and out-of-pocket medical or other expenditures (e.g., for transportation). Several factors affect the individual's decision to have a screening visit including time since last visit and whether she has some disease symptoms. Writing, solving, and estimating a complete dynamic optimization model is outside the

scope of our study. Instead we model the individual's decision to have a screening visit at each point in time and examine how this interacts with disease progression. This is a function of observed and unobserved disease characteristics, and observed individual and location specific characteristics as well as unobserved heterogeneity.

Screening visits serve two purposes. First, they assess whether or not the individual's diabetes' status has progressed since the previous screening visit. Second, if the disease has progressed, the patient and her physician use this information to adjust the sequence of treatments. These sequences of treatment choices affect the patient's probabilities of progressing to more advanced disease stages. The actual set of treatments chosen by the patient, however, is not observed in our data set. As a consequence, we assume that the impacts of these treatment decisions can be captured by the measures of each disease stage's durations in the hazard functions of moving to more severe, higher disease stages. Provided that the distributions of the future disease stages and exogenous variables are captured by the current period's variables (a first order Markov assumption),<sup>1</sup> our formulations approximate the optimal sequence of screening visits and treatment decision rules chosen by the patient and her health care provider.

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<sup>1</sup>That is, in a stochastic dynamic optimization model the expected value of the future value function conditional on any set of choices made today can be perfectly forecast by current period variables. See, for example, Blundell, Magnac, and Meghir(1997) and Liu, Mroz and Adair(2009).

## 3 A Discrete-Time Model of a Chronic Disease, Screening Visits, and Health Shocks

### 3.1 Setup

The Medicare claims data we use only record information about physician visits and diagnoses for individuals after they enrol in Medicare at age 65. In addition, before we observe the first post-age 65 screening visit we do not have any information about the individual’s health, including presence or absence of chronic diseases such as diabetes. For this reason we must account for left truncation of the data.

We break time into discrete time intervals. We allow for three arbitrary time periods before one becomes 65 ( $t = 1, 2, 3$ ), and we use these time intervals to model individuals’ initially observed diabetes states. As the model relies on the time spent with diabetes as a determinant of disease progression, we arbitrarily set each of these three periods to have lengths of five years. Once one turns 65, time periods are for a quarter ( $t = 4, 5, \dots$ ). During any of the first three time periods, an individual may have diabetes ( $D_1$ ) and also may transit to low severity extremity complications ( $D_2$ ), but it is not until the person’s first post-age 65 screening visit that we as researchers can observe her diabetes status.<sup>2</sup>

Starting in period four and until the time of a first screening visit ( $t_{FV} \geq 4$ ), we model potential disease progression through its initial two stages. After the first screening visit ( $t > t_{FV}$ ), we model the quarterly progression of diabetes

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<sup>2</sup>We exclude from the analysis any individual who had already advanced to disease stage 3 ( $D_3$ ) by the time of the first observed screening visit after becoming 65. In preliminary analyses, we used having reached stage 3 diabetes or worse by the time of the first post-age 65 visit as an endogenous selection mechanism. This had little effect on the parameter estimates for visits and disease progression after age 65, but it greatly increased the computational burden. Thus, we simplified the model by eliminating these severely ill individuals and focusing on individuals whose length of time in the various diabetes stages are more precisely measured. Persons with stage 3 diabetes have severe deformities (Charcot foot and/or cellulitis) and are likely to have relatively continuous medical care.



through all of its stages and the timing of screening visits in all subsequent time periods. Observations are right censored at time  $T$  when the person dies or leaves the sample for some another reason. We assume censoring not due to death is ignorable.

In total there are 12 different equations in our likelihood function: two pre-age 65 hazards (for  $D_1$  and  $D_2$ ), two post-age 65-before first visit hazards (for  $D_1$  and  $D_2$ ), four post-age 65-after first doctor visit hazards (for  $D_1, D_2, D_3, D_4$ ), two visit equations (first visit after age 65 and subsequent visits) and two health outcomes equations (amputation and death). Below we describe the likelihood function and our parametric assumptions.

## 3.2 Functional Form Specifications

### 3.2.1 Disease Progression

At a particular time period an individual can be either healthy or in one of the four diabetes stages ( $D_1, \dots, D_4$ ). Once a person enters a more severe disease stage, it is impossible to return to a less severe one. Let the hazard function for the progression to  $D_1$  at time  $t > t_{FV} \geq 4$  is

$$h_t^{D_1} \left( D_{1t} = 1 | X_t^{D_1}, e_k, D_{1t-1} = 0 \right) = \Lambda \left( X_t^{D_1} \beta_{D_1} + \rho_{D_1}(e_k) \right) \quad (1)$$

where  $\Lambda(z)$  is the logit function  $e^z / (1 + e^z)$ ,  $X_t^{D_1}$  is a vector of time invariant and time varying explanatory variables,  $e_k$  is the unmeasured heterogeneity assumed to be discrete with  $K$  heterogeneity points and  $\rho_{D_1}(\cdot)$  is a polynomial of degree  $J \leq K - 1$ .

Let  $t_{D_j}$  be the time at which the individual progresses to  $D_j$  ( $j = 1, \dots, 4$ ).

The hazard functions for  $D_j$  ( $j = 2, \dots, 4$ ) at time  $t \geq t_{D_{j-1}}$  are given by

$$h_t^{D_j} \left( D_{jt} = 1 | t^{D_1}, \dots, t^{D_{j-1}}, X_t^{D_j}, e_k, D_{jt-1} = 0 \right) = \Lambda \left( X_t^{D_j} \beta_{D_j} + \sum_{l=2}^j \delta_{j-1,l} (t^{D_{l-1}}) + \rho_{D_j} (e_k) \right) \quad (2)$$

where  $t^{D_{l-1}} = t - t_{D_{l-1}}$  is the length of time since the  $D_{l-1}$  onset and  $\delta_{l,j}(\cdot)$  is a quadratic function for  $l = 2, \dots, j$  and  $j = 2, \dots, 4$ . Our specification allows for the hazard functions to depend on duration in each of the previous stages, and it allows for different sets of regressors depending on the stage. The two pre-age 65 and two post-age 65 before first visit hazard functions for  $h_t^{D_1}$  and  $h_t^{D_2}$  have a functional form similar to eq. (1) and eq.(2), but we do not restrict their parameters to be identical to those in eq. (1) and eq. (2).

### 3.2.2 Visits and Health Shocks

The probability of a screening visit in period  $t$  ( $t = t_{FV} + 1, \dots, T$ ) depends on the current stage  $D_j$  ( $j = 1, \dots, 4$ ) as follows:

$$\begin{aligned} & \Pr (V_t = 1 | t^{D_1}, \dots, t^{D_j}, Z_t, e_k) \\ &= \Lambda \left( Z_t \beta_V + \sum_{l=1}^j \alpha_{0l} (t^{D_l}) + \rho_V (e_k) \right) \end{aligned} \quad (3)$$

where  $\alpha_{0l}(t^{D_l})$  is a quadratic function with an intercept. We restrict  $\beta_V$  and  $\rho_V(e_k)$  to be the same irrespective of disease stage, but allow for different intercepts and different duration coefficients for each stage. For a healthy individual, this probability is  $\Lambda(Z_t \beta_V + \rho_V(e_k))$  and for an individual that only progressed to  $D_1$ , this probability is given by  $\Lambda(Z_t \beta_V + \alpha_{01}(t^{D_1}) + \rho_V(e_k))$ . Among the regressors are variables affecting the probability of a visit but otherwise not af-

fecting health or diabetes progression (exclusion restrictions). We use distances to the nearest health providers as our exclusion restriction. The specification of the probability of the first visit is identical to eq. (3), but we do not restrict  $\beta_V$  and  $\rho_V(e_k)$  to be the same as in eq. (3).

Finally, let  $d_1$  and  $d_2$  be two observable health outcome shocks, amputation and death. As the disease progresses, the hazard of such an outcome occurring is likely to increase. For an individual at stage  $D_j$ , the hazard of  $d_{ct}$  during each time period is

$$\Pr(d_{ct} = 1 | t^{D_1}, \dots, t^{D_j}, W_t, e_k) = \Lambda \left( W_t \beta_{cd} + \sum_{l=1}^j \alpha_{cdl}(t^{D_l}) + \rho_{cd}(e_k) \right) \quad (4)$$

for  $c = 1, 2$ . As with visits we restrict the coefficients ( $\beta_{cd}$ ) to be the same irrespective of the disease stage, but allow for different intercepts and different duration coefficients for each disease stage the person entered by date  $t$ .

### 3.2.3 Unmeasured Heterogeneity

Unmeasured heterogeneity, e.g., overall unmeasured health, affects the hazard of progression to a higher disease stage, probabilities of a screening visit, amputation and death. For each of the events we assume a discrete heterogeneity distribution which we model as a polynomial

$$\rho_q(e_k) = \rho_q \left( \frac{k-1}{K-1} \right) = \rho_{q1} \left( \frac{k-1}{K-1} \right) + \dots + \rho_{qJ} \left( \frac{k-1}{K-1} \right)^J \quad (5)$$

where  $k = 1, \dots, K$ ,  $K$  is the number of heterogeneity points,  $J \leq K - 1$  is the degree of the polynomial, and  $q = 1, \dots, Q$  where  $Q = 12$  is the number of equations in the model. We estimate  $\Pr(e_k)$  subject to the restrictions that

each probability is non-negative and  $\sum_{k=1}^K \Pr(e_k) = 1$ .

Note that the underlying heterogeneity terms  $e_k = (k - 1) / (K - 1)$  for  $k = 1, \dots, K$  form a set of equally spaced points on the unit interval. If we were to allow the heterogeneity terms in each of the 12 equations to be a  $K - 1$  order polynomial, then in each equation it would be possible to map from this set of equally spaced  $K$  points on the unit interval to any arbitrary set of  $K$  or fewer points on the real line. With a large enough value of  $K$ , the resulting multi-variate distribution then could represent any arbitrary 12-dimensional discrete distribution function with a finite number of support points.<sup>3</sup>

### 3.3 The Likelihood Function

Based on the hazards and probabilities (eqs. 1-4), the likelihood function for an individual with any possible transition combination conditional on unmeasured heterogeneity  $e_k$  and the matrix of all possible explanatory variables  $\mathbf{M} = (\vec{\mathbf{X}}^{D_1}, \dots, \vec{\mathbf{X}}^{D_4}, \vec{\mathbf{Z}}, \vec{\mathbf{W}})$ <sup>4</sup> is

$$\begin{aligned}
& L(t_{D_1}, \dots, t_{D_4}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M}) = \\
& L_H(T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M})^{1(t_{D_1} \geq T)} \times L_{D_1}(t_{D_1}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M})^{1(t_{D_2} \geq T > t_{D_1})} \\
& \times L_{D_2}(t_{D_1}, t_{D_2}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M})^{1(t_{D_3} \geq T > t_{D_2})} \\
& \times L_{D_3}(t_{D_1}, t_{D_2}, t_{D_3}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M})^{1(t_{D_4} \geq T > t_{D_3})} \\
& \times L_{D_4}(t_{D_1}, \dots, t_{D_4}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M})^{1(T > t_{D_4})} \tag{6}
\end{aligned}$$

<sup>3</sup>The formulation used by Mroz (1999) is a special case of this. To obtain his linear discrete factor distribution, one would use  $K - 1$  degree polynomials restricted to be proportional to each other across all pairs of the 12 components.

<sup>4</sup> $\vec{\mathbf{X}}^{D_j}$  is the sequence of all possible values of  $X^{D_j}$  ( $X_1^{D_j}, \dots, X_T^{D_j}$ ) for  $j = 1, \dots, 4$ . We also define  $\vec{\mathbf{Z}}$  and  $\vec{\mathbf{W}}$  the same way.

$L_H \left( T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right)$  is the likelihood function for an individual who did not progress to  $D_1$  by period  $T$  with a sequence of visits  $\vec{V} = (V_4, \dots, V_T)$  and health shocks  $\vec{d}_c = (d_{c4}, \dots, d_{cT})$ .  $L_{D_1}(\cdot)$  is the likelihood function for an individual who entered stage  $D_1$  at  $t_{D_1}$ , but did not progress to  $D_2$  by terminal period  $T$ . Similarly, we define  $L_{D_2}(\cdot)$ ,  $L_{D_3}(\cdot)$ , and  $L_{D_4}(\cdot)$ . These individual likelihood functions depend on the hazard functions for disease progression, the probability of visits, and the probabilities of health shocks. For example  $L_{D_4}(\cdot)$  is given by

$$\begin{aligned} & L_{D_4} \left( t_{D_1}, \dots, t_{D_4}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right) \\ &= \left[ \prod_{j=1}^4 \Pr(D_j = t_{D_j}) \right] \times \Pr(\mathbf{V}_4^{t_{FV}}) \times \Pr(\mathbf{V}_{t_{FV}+1}^T) \\ & \quad \times \Pr(\mathbf{d}_{1,t_{FV}}^T) \times \Pr(\mathbf{d}_{2,t_{FV}}^T) \end{aligned}$$

where  $\Pr(D_1 = t_{D_1})$  is the probability of an individual contracting  $D_1$  at period  $t_{D_1}$  and  $\Pr(D_j = t_{D_j})$  for  $j = 2, \dots, 4$  is the probability of an individual contracting  $D_j$  at period  $t_{D_j}$ .  $\Pr(\mathbf{V}_4^{t_{FV}})$  is the probability of having the first visit at  $t = t_{FV}$ .  $\Pr(\mathbf{V}_{t_{FV}+1}^T)$  is the probability of the sequence of visits from  $t = t_{FV} + 1$  to  $t = T$ .  $\Pr(\mathbf{d}_{c,t_{FV}}^T)$  for  $c = 1, 2$  is the probability of the sequence of outcomes  $d_{ct}$  from  $t = t_{FV}$  to  $t = T$ . Appendix A contains the details on the construction of  $L_H(\cdot)$ ,  $L_{D_1}(\cdot)$ ,  $L_{D_2}(\cdot)$ ,  $L_{D_3}(\cdot)$ , and  $L_{D_4}(\cdot)$ .

### 3.3.1 Partial Observability and Early Detection of a Disease

To avoid the unrealistic assumption that the individual's stage is continuously monitored at each  $t$  (i.e., the individual visits a physician every period), we incorporate partial observability by the individual and her physician of the disease stage into the likelihood function. We do this by integrating over the possible time spans during which an individual is known from our data to have progressed

to a higher disease stage.<sup>5</sup> In particular, we assume that the first date at which a claim reports a diabetes stage is the latest period ( $t_{\max j}$ ) a person could enter that stage. The date of the visit immediately prior to that is assumed to be the latest date that we observe the person without the diabetes stage. The period immediately following this date is the earliest date ( $t_{\min j}$ ) a person could enter that stage. The actual (unobserved) date at which the person enters the stage is in the range

$$t_{\min j} \leq t_j \leq t_{\max j}$$

for  $j = D_1, \dots, D_4$ . Conditional on  $e_k$ , the individual likelihood function for the observed series ( $t_{\min D_1}, t_{\max D_1}, \dots, t_{\min D_4}, t_{\max D_4}, T$ ) is obtained by integrating over all possible starting and ending values of  $t_{D_1}, t_{D_2}, t_{D_3}$ , and  $t_{D_4}$ :

$$L\left(t_{\min, D_1}, \dots, t_{\max, D_4}, T, \vec{V}, \vec{d} | e_k, \mathbf{M}\right) = \sum_{t_{D_1} = t_{\min D_1}}^{\min\{t_{\max D_1}, T\}} \left[ \sum_{\substack{t_{D_2} = \max\{t_{D_1}, t_{\min D_2}\} \\ t_{D_2} \geq t_{D_1}}}^{\min\{t_{\max, D_2}, T\}} \left[ \sum_{\substack{t_{D_3} = \max\{t_{D_2}, t_{\min D_3}\} \\ t_{D_3} \geq t_{D_2}}}^{\min\{t_{\max D_3}, T\}} \left[ \sum_{\substack{t_{D_4} = \max\{t_{D_3}, t_{\min D_4}\} \\ t_{D_4} \geq t_{D_3}}}^{\min\{t_{\max D_4}, T\}} L\left(t_{D_1}, \dots, t_{D_4}, T, \vec{V}, \vec{d} | e_k, \mathbf{M}\right) \right] \right] \right] \right]. \quad (7)$$

Uncertainty about precisely when the individual progressed to the next stage is a key feature of this analysis, not just an econometric issue to be addressed. If the time during which the disease is present but unobserved and untreated is long, then the individual may progress to more severe disease stages much more rapidly.

An advantage of our model is that we can model the length of time a person spends with any stage of the disease without it having been diagnosed. We defined  $t_{D_j}$  as the time at which the individual progresses to diabetes stage  $D_j$ ,

<sup>5</sup>This is similar to the strategy used by Mroz and Weir(1990) to address the partial observability of lactational amenorrhea in their life-cycle model of fertility control.

so  $t^{D_j} = t - t_{D_j}$  is the length of time of stage  $D_j$  that the individual has been in that state since its onset. We calculate the time spent with undiagnosed stage  $D_j$  as  $t^{D_j^u} = \min\{t^{D_j}, t_{\max D_j} - t_{D_j}\}$ . Delay in time to diagnosis of diabetes and its complications has a potential permanent effect on the person's health and longevity because of consequent delay in treatment. These  $t^{D_j^u}$ 's are our main explanatory variables. They allow us to ascertain whether or not more frequent visits, and the resulting earlier diagnosis, could reduce disease progression. Without modeling explicitly the process of disease stage acquisition and  $t^{D_j^u}$ 's in an environment with partial observability, one could not separate the true causal effects of early diagnosis from lead time biases. These types of bias arise because more frequent screenings mechanically diagnose disease stages at shorter true duration times on average, and this leads to a spurious relationship between the frequency of screening and longer waiting times to the future adverse events. Of course the length of time with an undiagnosed disease stage depends on the unobserved time of entering the stage, but that is captured in eq (7).

### 3.3.2 Estimation

Finally, the unconditional log-likelihood function is:

$$L(\theta) = \sum_{i=1}^N \ln\left(\sum_{k=1}^K \Pr(e_k) L\left(t_{\min D_{1i}}, \dots, t_{\max D_{4i}}, T_i, \vec{V}_i, \vec{d}_i | \theta, e_k, \mathbf{M}_i\right)\right), \quad (8)$$

where  $\theta$  is the vector of parameters and  $\Pr(e_k)$  is the probability of the discrete heterogeneity point  $e_k$ .<sup>6</sup> We maximize this likelihood function using GQOPT with respect to all of the parameters in  $\theta$  in the twelve outcome equations.

We estimate the likelihood with different number of heterogeneity points ( $K$ ),

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<sup>6</sup>We wrote a FORTRAN program to estimate this likelihood function, which is available from the corresponding author upon request.

including  $K = 1$  (no heterogeneity and no correlation among the equations). We report the results for eight points of support ( $K = 8$ ) and third degree polynomials in the underlying heterogeneity factor ( $J = 3$ ). Adding the eighth point of support barely improved the likelihood function value over using seven points of support.

## 4 Data

We use data from interviews conducted for the National Long-Term Care Survey (NLTC), a longitudinal study of elderly persons. The screening process began with a random sample of persons aged 65 and older in 1982. Respondents were tracked in five-years intervals (1989, 1994, 1999, and 2004) with additional persons added to the sample in later waves. Over the five NLTC cohorts, more than 40,000 individuals were interviewed. We only use NLTC data from 1994, 1999 and 2004 interviews, because Medicare claims data are only available since 1991. The NLTC interviews provide information on the sample person's demographic characteristics, date of birth, gender, race, marital status, and years of schooling.

An advantage of NLTC is that Medicare claims data, both for Part A (services provided by institutions such as hospitals) and Part B (services provided by physicians and other health professionals) have been merged with NLTC. These claims data provide information on diagnoses and procedures performed by date of service. Data on diagnosis were first added to Part B claims data in 1991. Furthermore, NLTC respondents were merged with National Death Index (NDI) data, providing the respondent's death dates through 2004.

Using NLTC interviews for 1994, 1999, and 2004, Medicare claims data for 1991-2004, and NDI data through 2004, we create a panel with the individual Medicare beneficiary by quarter as the observational unit. We select individuals



born between 1926 and 1939. This restriction ensures that all individuals were at least age 65 when they enter the sample. We also drop individuals with less than 2 years of data and individuals who had progressed to medium severity LEC ( $D_3$ ) or higher by the time of the first visit. Our final sample size consists of 9,417 individuals observed over a total of 261,916 quarters (Panel A, Table 2), the time periods used in this study. A quarter may be sufficient for some individuals to notice disease symptoms and visit a doctor. Moreover, visits more frequent than once in a quarter are likely to be predominantly follow up visits.

## 5 Empirical Specification

There are 12 different equations in the likelihood function: two pre-age 65 hazards (for  $D_1$  and  $D_2$ ), two post-age 65-before first visit hazards (for  $D_1$  and  $D_2$ ), four post-age 65-after first doctor visit hazards (for  $D_1, D_2, D_3, D_4$ ), two visit equations (first visit after age 65 and subsequent visits) and two health outcomes equations (amputation and death), respectively.

### 5.1 Dependent Variables

**Stages:** A person is in one or more of five mutually exclusive stages during a quarter. When a person transitions to a higher stage in a quarter, the person is assumed to have been in the higher stage throughout the quarter.

We assume that once a person transitions to a higher stage she cannot return to a lower stage. Furthermore, a person in a particular stage has experienced all prior stages in the past, albeit at times unknown to us, unless explicitly documented in prior claims.

**Visits:** The role of a visit is to diagnose whether the individual has the disease ( $D_1$ ) and any of its progression stages ( $D_2, D_3$ , and  $D_4$ ). We assume that the following specialities screen for diabetes (with Medicare provider type

codes in parentheses): general practice (01), cardiology (06), family practice (08), internal medicine (11), endocrinology (46), and clinical laboratory (69). Once a person progresses to diabetes only ( $D_1$ ), we add podiatry (48) to the list of specialities. A podiatrist is a non-physician who specializes in diseases of the lower extremities. Diagnoses on claims to other types of health professionals are less likely to contain information on diabetes, even if this disease is present.

**Outcomes:** In each period, the individual may experience two types of adverse health outcomes: (1) a person’s toe, foot, or leg is amputated<sup>7</sup> and (2) death. Other diabetes-related health shocks, e.g., heart attacks and strokes, were not explicitly modeled because they do not affect higher LEC transitions.

## 5.2 Explanatory Variables

Explanatory variables fall into four categories: (1) early diagnosis (our main explanatory variable); (2) duration dependence; (3) demographic variables; and (4) exclusion restrictions.

**Early Diagnosis:** The effects of early diagnosis are measured using the time with undiagnosed  $D_1$ ,  $D_2$ ,  $D_3$ , and  $D_4$  and their squares. We defined these variables in Section 3. These variables are different from the duration of the time already spent in the four disease stages after the stage is ascertained by screening. If early diagnosis is beneficial, then one would expect undiagnosed duration to increase the probability of progression to the next stages and possibly increase mortality and amputation probabilities. Given partial observability of diabetes stages, the effect of these times with undiagnosed disease depend on the integration implicit in eq. (7).<sup>8</sup> We assume that a visit that diagnoses the disease leads to treatment. Thus, earlier diagnosis leads to earlier treatment.

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<sup>7</sup>Since two or more amputations are rare events in our data set, we only model time to the occurrence of the first amputation.

<sup>8</sup>Mroz and Weir (1990) discuss identification of the distribution governing a partially observed process for a simpler model than that analyzed here.

We do not have comprehensive data on treatment.

**Duration Dependence:** Duration dependence is measured by a quadratic function of the time in quarters from the period the individual enters a particular stage in eqs. (2) and (3). In addition, we allow for a discrete shift in the hazard and probability arguments at entry to any stage. All duration dependence terms can vary independently for each disease stage.

**Demographic and Health Characteristics:** We include binary variables in all equations for gender, educational attainment, marital status, arthritis, and race.<sup>9</sup> We expect more highly educated and married persons to have better health outcomes. To control for age and cohort effects, we also include a year trend and its square, and the year in which the individual turned age 65. Age and generational changes in diet, for example, might affect diabetes outcomes.

**Exclusion Restrictions:** We use distances to the nearest health providers as exclusion restrictions affecting the probabilities of visits but not directly influencing disease progression or health shocks. Distance is computed, for each sample person, from the center of the person’s zip code of residence to the center of the zip code of each health care provider type. For each individual, we select the shortest distances to such providers. The NLTCs only provides area of residence information at the level of the primary sampling unit (PSU), which is a Standard Metropolitan Area for persons living in such areas and a rural area of a state for others. For each PSU, we calculate the distance from the centroid of the zip code of residence of each Medicare beneficiary to the centroid of the zip code of nearest provider based on the speciality code. We expect an increase in the minimum distance to be negatively related to the probabilities of visits but not to affect disease progression or health shocks after controlling for visits.

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<sup>9</sup>These variables were obtained from the NLTCs screener file using the latest available year.

## 6 Results

Of the 9,417 persons in our sample (col. 1, Panel A, Table 2), 66.1% were never diagnosed with diabetes during the observational period, 10.7% had a diabetes diagnosis without an LEC ( $D_1$ ), while 13.9%, 5.3%, and 4.1% were observed to have progressed to  $D_2$ ,  $D_3$ , and  $D_4$ , respectively. Of the 261,916 quarter/person observations in our sample (col. 2), 77.5% are observed healthy,<sup>10</sup> 10.6% are observed in state  $D_1$ , 7.2% in  $D_2$ , 2.8% in  $D_3$ , and 1.9% in  $D_4$ . Overall, 7.8% of individuals die during the observational period; we observe 27.8 quarters per person on average. Mortality is 6.4% for healthy individuals and increases to 14.7% and 18.4% for those in  $D_3$  and  $D_4$  states, respectively. Amputations spike upwards at stage  $D_4$ , with 13.1% of those entering this stage having at least one lower extremity amputation; but amputation is very rare before this stage. The number of quarters with a visit rises by stage. Healthy individuals visit a physician in 47.8% of the quarters, but once diagnosed with low severity LEC ( $D_2$ ), this probability increases to over 80%.

Table 2 (Panel B) describes results for our main explanatory variable, time without diagnosed diabetes and its lower extremity complications. The mean quarter at which diabetes is diagnosed is 16.2 (slightly over four years). The mean potential range for undiagnosed diabetes is 3.2 quarters (almost 10 months) with 41.5% of our sample having a range of zero and a maximum of 55 quarters. For  $D_2$ ,  $D_3$ , and  $D_4$  the mean ranges of potential undiagnosed disease are much smaller and the percentage of zero quarters with undiagnosed LEC is much larger (col. 2-4). This is because once a person is diagnosed with diabetes, she tends to have more frequent visits. Finally, Table 2 (Panel C) describes our time invariant explanatory variables. Most persons are white (88%) and about half are male, married, and have at least finished high school. The mean minimum

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<sup>10</sup>More precisely, 77.5% of the person/quarters take place before the first diagnosis of diabetes.

distance in miles to the nearest provider is 1.1 for visits overall and 5.5 miles for podiatrists.

Table 3 presents key parameter estimates and standard errors with eight points of support for the heterogeneity distribution. We only report transition to diabetes and LECs after the first visit, adverse health outcomes (death and amputation), and screening visits. Other transitions, the pre-age 65 outcomes and the first post age-65 visit, were estimated to control for endogenous initial conditions but are not shown (available from the corresponding author on request).

Consider the effects of the length of time with undiagnosed diabetes ( $D_1$ ) on the transitions to more severe disease stages ( $D_2$  and  $D_4$ ) and death. The parameter estimates on each of these linear terms for time with undiagnosed diabetes ( $D_1$ ) in row 1 of Table 3 are positive, while the parameter estimates on the quadratic terms are negative (row 2). These imply positive but decreasing marginal effects of time without a diagnosis on the hazards of these adverse outcomes occurring.<sup>11</sup> At this disease stage, the principal therapies are drugs, improved diet and more and more regular exercise. These results imply that persons who screen less often for diabetes, and consequently have longer stretches when they have diabetes but are unaware of it, pay a long-term health penalty.

For some categories of persons with LECs, the parameter estimate on the linear term is negative, but the parameter estimate on the squared term is positive. This implies that the initial negative effect of increased time with a particular undiagnosed diabetes stage is followed by increasingly positive marginal effects. Rows 3 and 4 show that time with undiagnosed low severity LEC ( $D_2$ ) has such a U-shape effect on the hazards for medium severity LEC ( $D_3$ ); there is a similar pattern for high severity LEC ( $D_4$ ). Both troughs, however,

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<sup>11</sup>The turning points are at 13 to 55 quarters, which would be an extreme length of time with unmeasured diabetes.

are at quite short durations, i.e., three and five quarters, respectively. At the low severity LEC stage, therapies include use of special shoes. We expect that wearing such shoes would defer adverse outcomes of diabetes complications of the lower extremities. While this is generally so, there appears to be a short period during which minor undiagnosed complications have no apparent adverse effects of not wearing specialized shoes.

The duration dependence parameters usually imply a U-shaped effect of duration on transitions. For example, total time with diabetes, including both undiagnosed time and time after onset (col. 2-3, rows 10-11), has a U-shaped effect on the transition probabilities to the low LEC stage ( $D_2$ ) and medium LEC stage ( $D_3$ ); the inflection points are around 28 quarters (seven years) and 23 quarters (six years). Similarly, time in the low LEC stage (col. 3, rows 13-14) has a U-shape effect on the transition to the medium LEC stage (inflection point around 21 quarters) and time in the medium LEC stage has a U-shape effect on the transition probability to the high LEC stage (col. 4, rows 16-17) with an inflection point of around 26 quarters. These somewhat lengthy estimated spells of negative duration dependence could reflect a failure to allow for disease-stage specific individual heterogeneity.

The hazards of death and amputation increase considerably when one enters either stage  $D_3$  or  $D_4$  (cols 5-6, rows 15 and 18).  $D_4$  especially carries an extensive risk for both amputation and death. Surprisingly, we find that an increase in the time one has undiagnosed  $D_3$  or  $D_4$  appears to reduce, relatively, the risks of death (rows 5-8, col. 5). The estimates also suggest that an increase in the total time spent with  $D_4$  yields relatively lower (though still quite high) risks of death and amputation (rows 19-20, cols 5-6). It is important to note that  $D_3$  (cellulitis and charcot foot) or  $D_4$  (osteomyelitis and gangrene) produce high levels of discomfort which leads to visits and diagnoses. It is highly unlikely

a person will spend a long time with these conditions without knowing it and without seeking medical assistance. Indeed our data show that about 80% of all observations at risk of developing either  $D_3$  or  $D_4$  spend no quarters with the stage undiagnosed. Our data also indicate that at most only 37 individuals could have a range of undiagnosed stage  $D_3$  diabetes for more than 3 quarters, and only 15 observations, at most, could have a range of undiagnosed  $D_4$  for more than two quarters. The limited number of observations with long exposures of undiagnosed diabetes with severe symptoms also suggest that we should be careful in the interpretation of the duration effects associated with the higher disease stages.

Results for the demographic characteristics and arthritis on disease progression and outcomes (rows 21-25) are generally consistent with previous studies (Sloan et al., 2010). For example, whites are less likely to develop diabetes, but once they have diabetes the effects of race on further complications, death, amputation are not uniform and mostly not significant. Male, low education, not married, and having arthritis lead to worse health outcomes. For screening visits, the exclusion restrictions are statistically significant, and the parameter estimates have the anticipated signs (col. 7, rows 26-27).

Table 4 displays the heterogeneity points of support for the different transitions and the implied probabilities for each of the eight points of support. All of the coefficients associated with these mass points and weights are statistically significant. The probabilities associated with the mass points range from 0.012 to 0.326, which indicates that there is no point with extremely small or large weight. Additionally, there are no extreme mass points in any of the specifications. The implied correlations between the heterogeneities points of the different equations (Table 5) are mostly positive and small when negative. This seems plausible in that, for example, the unmeasured heterogeneity associ-

ated with faster transitions to  $D_1$  is positively correlated with the unmeasured heterogeneities associated with all disease progressions, amputation, death, and visits.

## 7 Marginal Effects and Policy Simulations

We conduct two sets of simulations using the parameter estimates in Tables 3 and 4 to describe the benefits and costs of different screening trajectories for diagnosing the onset of diabetes. In the first we set we use a very mechanical rule. We compare longer-term outcomes from the immediate detection of the onset of diabetes to those same outcomes when diabetes progresses and is undetected for exactly four quarters. In the second set we consider somewhat more policy relevant experiments where we restrict the frequency of screening for diabetes to at most only once (or twice) per year; current policy does not restrict the number of times one can be screened for diabetes. We then compare longer-term outcomes from the restricted and unrestricted environments. We simulate 10,000 individuals from age 65 to age 80 for each of these experiments. Demographic characteristics and a diagnosis of arthritis are based on the sample population distribution, and the unmeasured heterogeneity points of support are simulated based on results in Table 4.

In the first set of simulations we impose that the person was healthy at the start of age 65 ( $t = 4$ ) but becomes diabetic in the next quarter ( $t = 5$ ). The experiment is to screen everyone at  $t = 5$  for diabetes and compare those outcomes to ones obtained when there was no screening for diabetes until date  $t = 9$ . The former had a zero length period of unobserved diabetes while the latter group experiences exactly one year of undiagnosed diabetes. After the initial screening visit ( $t = 5$  or  $t = 9$ ) which detects diabetes stage  $D_1$  (or higher for  $t = 9$ ) with probability one, all subsequent screening visits follow the



data generating process described by the full set of parameter estimates.

Table 6 contains estimates of this effect of a one year delay in detecting diabetes on the progression to more severe stages, amputation, and death over a five year time horizon. Even with immediate detection of first onset of diabetes, 23.8% of the simulated population progresses to low severity LEC ( $D_2$ , or worse) within one year. A one year delay in screening would result in an additional 3.9% of the observations progressing to at least this stage. Five years after becoming diabetic, 59% of the immediately diagnosed would have progressed to low severity LEC, and this would increase by 6.6 percentage points if the diagnosis were delayed for one year. Mortality within five years of being diabetic would increase by 44 deaths per 10,000 because of the one year delay in diagnosis. In general, these marginal effects are not large, but they are not trivial either.

For the second set of simulations we examine what would happen to life cycle trajectories from age 65 to age 80 if those without a prior diabetes diagnosis were limited to at most only one diabetes screening visit per year. After being observed with diabetes, all subsequent visits (and disease and outcome progressions) follow the processes defined by the model estimates. We assume that the first visit per year, if there is one, is the screening visit for that year. We compare these restricted simulated outcomes to the status quo that allows one to make as many screening visits as they would like each year. We also examine a less extreme policy of allowing each person to have up to two diabetes screening visits per year before being observed with diabetes.

In the top row of Table 7 we report cumulative results for the simulations of the status quo over all quarters from age 65 to age 80. In the first column we see that with no restrictions on diabetes screening that there would be 38.9 visits on average over this 15-year period. If we were to restrict individuals to have no more than one screening visit before they had been diagnosed with diabetes,

the total number of screening visits would fall by 15.6, or about 40% (including the unrestricted ones taking place after the first diabetes diagnosis). If instead we limited the number of screening visits for detecting  $D_1$  to at most two per year, there would be 9.54 fewer doctor visits over the 15-year horizon compared to the status quo. These figures represent the gross cost savings in terms of the number of screening visits prevented by the policies.

The bottom panel of Table 7 describes the consequences of these policies in terms of life-span and time spent in health relatively healthy states from age 65 to age 80 relative to the status quo. On average lifespans would shrink by 0.0677 quarters (about six days) if there were a limit of one screening visit per year and by 0.0161 quarters for a restriction of no more than two screening visits before being diagnosed with diabetes. The more restrictive policy change (one per year maximum) would reduce the number of quarters without any lower extremity conditions by 0.154 quarters (two weeks), and the less restrictive policy change (two per year) would reduce the time spent without LEC complications by 0.039 quarters.

While these impacts seem small, they are not inconsequential. If we assume no discounting and a \$50 cost per screening visit, the more restrictive policy would save about \$780 per person entering age 65 without diabetes. In terms of the effects on one's lifespan, these savings come at a cost of 0.0677 quarters of life or about 0.017 fewer years of life. This policy implies an implicit value of a year of life of about \$45,900 ( $\$780/0.017$ ). The less restrictive policy change would have a much smaller reduction in the number of doctor visits and considerably smaller impacts on longevity. The undiscounted cost savings from fewer visits would only be about \$476 ( $\$50 \times 9.53$ ), and this would only cost about 0.004 fewer years of life. These would imply an implicit value of a year of life of about \$119,000 ( $\$476/.004$ ).

We use a similar approach to calculate the costs in terms of "quality-adjusted" years, i.e., years without a LEC. The one visit per year restriction implies a willingness to pay of about \$20,300 ( $\$780/ (.1540/4)$ ) for an additional year of quality lifetime. The less restrictive policy implies a value of a year of quality life of more than \$48,000 ( $\$476/ (.039/4)$ ). Many current estimates place the value of a year of life at about \$100,000, (Viscusi and Aldy 2003) so the more restrictive policy change to only one visit per year might undervalue its implicit costs relative to the cash savings from funding fewer screening visits; the less severe restriction on screening visits would slightly undervalue the savings relative to the benefits from the extended lifespans.

## 8 Discussion, Conclusion, and Extensions

This paper develops a model of screening for a chronic disease that allows for analysis of the effects of early diagnosis of the disease on disease progression and other health outcomes. The model incorporates partial observability of the disease as a key component. This allows us to assess the benefits and costs of different screening scenarios. We apply the model to diabetes mellitus.

According to the U.S. Preventive Services Task Force (USPSTF) currently there is insufficient evidence on the benefits of routine screening for type 2 diabetes in asymptomatic adults unless they have high blood pressure (USPSTF 2008). The American Diabetes Association recommends testing at three-year intervals, but there are no conclusive randomized controlled trials (RCTs) that have documented health benefits of more frequent screening of diabetes (USPSTF 2008). Our results indicate there are small individual health benefits for early diagnosis of diabetes. These are consistent with limited findings from the RCTs (USPSTF 2008).

Although many individual features of our model are not new, they have

not been combined in a single application. Relevant previous studies include: multiple-state duration models with endogenous treatment (Eberwein et al. 1997, Eberwein et al. 2002, Heckman and Navarro 2008, Abbring and Heckman 2008, Richardson and van den Berg 2008); competing risk (Honore and Lleras-Muney 2006); unobserved heterogeneity (Heckman and Singer 1984); partial observability (Mroz and Weir 1990); and discrete factors (Heckman and Singer 1984, Mroz 1999). Due to improvements in computation, combining these features is feasible now when it would have been infeasible a decade ago.

The study benefits from recent availability of administrative data. Such data allow researchers to study dynamic processes for many individuals over a long time period. Administrative data, of course, have important limitations, but they are relatively inexpensive and are likely to become more detailed and even less expensive to collect and use. They will constitute key components of future research because of the inherent limitations of RCTs for assessing longer term outcomes. Developing methods for analyzing data from surveys linked with administrative records, as in this study, and dealing with their important deficiencies should receive a high priority.

Perhaps the most important feature of our study is in accounting for partial observability. By modeling the earliest and latest possible dates of onset of the stage, we infer the length of being in a stage without knowledge of the exact time of entering the stage. We study how this measure affects subsequent transitions in diabetic stages and outcomes. As in past research, accounting for unobserved heterogeneity has proven important here. However, we do not allow for the emergence of chronic health shocks, and these are likely to be important for modelling many health transitions.

Further research should incorporate these extensions. First, rather than defining a general measure of visits, there should be more explicit measurement

of specific treatments. Data on the Medicare prescription drug program is just becoming available, and it is not yet possible to incorporate long-term effects of drug treatment for this reason. Second, in our model determinants of visits, such as the exclusion restrictions, do not depend on the disease stage, a restriction which could be relaxed. Third, our unmeasured heterogeneity is time invariant within each equation. A potential extension would be to introduce short and long term unobserved health shocks evolving as the individual ages.

In conclusion, this study provides a promising approach for evaluating how the duration of unobserved events affects outcomes of interest using administrative data.

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**Table 1: Disease Progression**

Stage	Progression	Condition	ICD9-CM code
1	Healthy		
2	Diabetes mellitus only ( $D_1$ )	Diabetes mellitus only	250.xx
3	Low severity lower extremity complication ( $D_2$ )	Neuropathy	250.6 357.2 355.xx
		Paresthesia	782.xx
		Pain in feet	729.5
		Diabetic Amyotrophy	358.1
4	Medium severity lower extremity complication ( $D_3$ )	Cellulitis	681.1 682.6 682.7
		Charcot foot	707.1
5	High severity lower extremity complication ( $D_4$ )	Osteomyelitis	730.06 730.07 730.16 730.17 730.26 730.27
		Gangrene	250.7 785.4

**Table 2: Summary Statistics**

**Panel A: Dependent Variable**

	Progression		Outcomes		Screening
	Individuals	Quarters	Death (%)	Amputation (%)	Visits per quarter (%)
Overall			7.8	1.1	54.2
Stages (%)					
Healthy	66.1	77.5	6.4	0.6	47.8
Diabetes only ( $D_1$ )	10.7	10.6	6.2	0.3	67.9
Low severity LEC ( $D_2$ )	13.9	7.2	9.9	0.5	81.3
Medium severity LEC ( $D_3$ )	5.3	2.8	14.7	1.4	85.6
High Severity LEC ( $D_4$ )	4.1	1.9	18.4	13.1	88.9
Sample size	9,417	261,916			

For Individuals, stage is at last quarter observed in data; for quarters, stage is at last quarter observed in data except for visits.

**Panel B: Main Explanatory Variable (undiagnosed disease)**

Disease Progression	No. of individuals	Mean quarter of diagnosed	Range of Undiagnosed Disease		
			Mean	% of zeros	Maximum
Diabetes only ( $D_1$ )	3,187	16.24 (12.52)	3.21 (5.41)	41.5	55
Low severity LEC ( $D_2$ )	2,183	22.53 (12.32)	0.89 (2.83)	72.7	42
Medium severity LEC ( $D_3$ )	878	24.74 (12.74)	0.64 (2.32)	78.9	32
High Severity LEC ( $D_4$ )	381	25.10 (12.66)	0.41 (1.72)	85.3	20

**Panel C: Time Invariant Explanatory Variables**

Variable	Mean
Arthritis (%)	1.67
White (%)	87.97
Male (%)	45.16
Married (%)	57.38
High-school + (%)	48.83
Year Turned 65 (1991=0.1)	0.67 (0.36)
Mean Distance GP (10 miles)	0.11 (0.16)
Mean Distance Podiatrist (10 miles)	0.55 (0.84)

**Table 3: Results with Eight Points Heterogeneity**

Explanatory Variables	Disease				Outcomes		Visits
	$D_1$	Lower Extremity Complication			Death	Amputation	
		$D_2$	$D_3$	$D_4$			
(1)	(2)	(3)	(4)	(5)	(6)	(7)	
<b>Early Diagnosis</b>							
1) Time with undiagnosed diabetes		0.0571 <sup>***</sup>	0.0067	0.0440 <sup>**</sup>	0.0690 <sup>***</sup>	-0.0151	0.0087
		(0.0134)	(0.0127)	(0.0182)	(0.0215)	(0.0295)	(0.0177)
2) Time with undiagnosed diabetes sq		-0.0014 <sup>***</sup>	-0.0002	-0.0004	-0.0016 <sup>***</sup>	0.0007	-0.0009 <sup>***</sup>
		(0.0004)	(0.0003)	(0.0004)	(0.0006)	(0.0006)	(0.0001)
3) Time with undiagnosed low severity LEC			-0.0306	-0.1848 <sup>*</sup>	0.0270	-0.0783	-0.0008
			(0.0353)	(0.1014)	(0.0494)	(0.2131)	(0.0179)
4) Time with undiagnosed low severity LEC sq			0.0053 <sup>***</sup>	0.0172 <sup>*</sup>	0.0005	-0.0572	0.0034 <sup>***</sup>
			(0.0018)	(0.0092)	(0.0035)	(0.0477)	(0.0004)
5) Time with undiagnosed medium severity LEC				-0.1495	-0.1331	0.3300	0.0052
				(0.1102)	(0.0930)	(0.2362)	(0.0177)
6) Time with undiagnosed medium severity LEC sq				0.0007	0.0032	-0.0758	-0.0081 <sup>***</sup>
				(0.0082)	(0.0029)	(0.0596)	(0.0005)
7) Time with undiagnosed high severity LEC					-0.0617 <sup>**</sup>	0.0384	0.0116
					(0.0285)	(0.0273)	(0.0178)
8) Time with undiagnosed high severity LEC sq					0.0004 <sup>**</sup>	-0.0010	0.0000
					(0.0002)	(0.0006)	(0.0001)
<b>Duration Dependence</b>							
9) Has diabetes					-0.4125 <sup>*</sup>	-0.6026	0.3760
					(0.2109)	(0.4776)	(0.7075)
10) Time with diabetes		-0.2535 <sup>***</sup>	-0.0194 <sup>**</sup>	0.0215	-0.0041	0.0057	-0.0349 <sup>***</sup>
		(0.0092)	(0.0083)	(0.0136)	(0.0120)	(0.0248)	(0.0037)
11) Time with diabetes square		0.0045 <sup>***</sup>	0.0004 <sup>***</sup>	-0.0003	0.0002	0.0000	0.0012 <sup>***</sup>
		(0.0003)	(0.0001)	(0.0002)	(0.0002)	(0.0002)	(0.0001)
12) Has low severity LEC					1.2104 <sup>***</sup>	0.6192	0.0807
					(0.2176)	(0.5994)	(0.7143)
13) Time with low severity LEC			-0.3033 <sup>***</sup>	-0.0202	-0.0454 <sup>**</sup>	-0.1016 <sup>*</sup>	-0.0246 <sup>***</sup>
			(0.0142)	(0.0228)	(0.0219)	(0.0537)	(0.0081)

**Table 3 (Continuation): Results with Eight Points Heterogeneity**

Explanatory Variables	Disease				Outcomes		Visits
	$D_1$	Lower Extremity Complication			Death	Amputation	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<b>Duration Dependence (Cont.)</b>							
14) Time with low severity LEC sq			0.0073 <sup>***</sup>	0.0008	0.0005	0.0028 <sup>**</sup>	0.0003
			(0.0004)	(0.0007)	(0.0006)	(0.0013)	(0.0003)
15) Has medium severity LEC					0.2421	0.2934	0.1893
					(0.2479)	(0.7295)	(0.7087)
16) Time with medium severity LEC				-0.3640 <sup>***</sup>	0.0391	0.1606 <sup>**</sup>	-0.0005
				(0.0270)	(0.0412)	(0.0663)	(0.0121)
17) Time with medium severity LEC sq				0.0071 <sup>***</sup>	-0.0018	-0.0049 <sup>**</sup>	-0.0004
				(0.0008)	(0.0014)	(0.0022)	(0.0004)
18) Has high severity LEC					0.7214 <sup>**</sup>	4.4580 <sup>***</sup>	0.4368
					(0.2893)	(0.5515)	(0.7104)
19) Time with high severity LEC					-0.0892 <sup>*</sup>	-0.4532 <sup>***</sup>	-0.0682 <sup>***</sup>
					(0.0452)	(0.0674)	(0.0168)
20) Time with high severity LEC sq					0.0040 <sup>***</sup>	0.0115 <sup>***</sup>	0.0016 <sup>***</sup>
					(0.0015)	(0.0022)	(0.0005)
<b>Other Variables</b>							
21) White	-0.3636 <sup>***</sup>	0.1621 <sup>**</sup>	0.0055	-0.3096 <sup>**</sup>	0.0198	0.3509	0.0274
	(0.0667)	(0.0721)	(0.0991)	(0.1523)	(0.1019)	(0.2560)	(0.0521)
22) Male	0.2863 <sup>***</sup>	-0.3414 <sup>***</sup>	0.2232 <sup>***</sup>	0.2865 <sup>**</sup>	0.2194 <sup>***</sup>	0.6862 <sup>***</sup>	-0.2534 <sup>***</sup>
	(0.0471)	(0.0534)	(0.0750)	(0.1247)	(0.0729)	(0.1807)	(0.0287)
23) High-school+	-0.2599 <sup>***</sup>	-0.1336 <sup>*</sup>	-0.1802 <sup>*</sup>	-0.0096	-1.4441 <sup>***</sup>	-0.4602 <sup>**</sup>	-0.2042 <sup>***</sup>
	(0.0603)	(0.0679)	(0.0914)	(0.1488)	(0.1421)	(0.2241)	(0.0396)
24) Married	-0.2041 <sup>***</sup>	-0.0428	-0.1246	-0.1086	-0.1461	-0.7102 <sup>***</sup>	0.0524
	(0.0517)	(0.0581)	(0.0824)	(0.1357)	(0.0914)	(0.1999)	(0.0333)
25) Arthritis	0.6789 <sup>***</sup>	1.1341 <sup>***</sup>	0.5066 <sup>**</sup>	0.0608	0.5434 <sup>**</sup>	0.5645	1.2819 <sup>***</sup>
	(0.1561)	(0.1772)	(0.1958)	(0.3185)	(0.2349)	(0.6194)	(0.0716)
<b>Exclusion Restrictions</b>							
26) Weighted mean distance to general physician							-0.2274 <sup>***</sup>
							(0.0772)
27) Weighted mean distance to podiatrist							-0.0252 <sup>*</sup>
							(0.0130)
Log Likelihood					-346,036.05		

Standard errors in parentheses. <sup>\*\*\*</sup>, <sup>\*\*</sup> and <sup>\*</sup> indicate statistical significance at the 1%, 5%, and 10% level respectively.

Note: All equations include a year trend and its square, and the year in which the individual turned age 65.

These 7 equations were estimated jointly with 5 others that describe the diabetes progressions' "initial conditions."

Those estimates can be obtained by contacting the corresponding author.

**Table 4: Distribution of the Effects of Unobserved Heterogeneity by Point of Support**

Heterogeneity Point ( $e_k$ )	Probability	Disease				Outcomes		Visits
		$D_1$	$D_2$	$D_3$	$D_4$	Death	Amputation	
1	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	0.12	0.22	0.09	0.01	0.16	0.24	0.87	0.97
3	0.33	0.46	0.48	0.09	0.20	0.50	1.14	2.16
4	0.27	0.69	0.97	0.20	0.17	0.74	1.03	3.36
5	0.08	0.89	1.39	0.29	0.11	0.93	0.76	4.36
6	0.10	1.06	1.53	0.31	0.09	1.04	0.54	4.94
7	0.01	1.18	1.22	0.23	0.14	1.02	0.59	4.91
8	0.02	1.22	0.27	-0.02	0.33	0.86	1.13	4.03
Expected Value		0.57	0.71	0.14	0.16	0.60	0.90	2.70
Standard Deviation		0.30	0.48	0.10	0.06	0.28	0.31	1.38

**Table 5: Correlation Matrix with Eight Points of Support**

	$D_1$	$D_2$	$D_3$	$D_4$	Death	Amputation	Visits
<b>Diabetes (<math>D_1</math>)</b>	1.00						
<b>Low severity LEC (<math>D_2</math>)</b>	0.26	1.00					
<b>Medium severity LEC (<math>D_3</math>)</b>	0.25	0.29	1.00				
<b>High severity LEC (<math>D_4</math>)</b>	0.03	-0.05	-0.07	1.00			
<b>Death</b>	0.29	0.28	0.28	0.03	1.00		
<b>Amputation</b>	0.04	0.00	-0.01	0.28	0.06	1.00	
<b>Visit</b>	0.23	0.22	0.22	0.01	0.24	0.03	1.00

**Table 6: Marginal Effect of a One Year Delay in Diagnosing Diabetes**

Increase in probability of progressing to a higher stage by year					
Stage	One	Two	Three	Four	Five
Low severity LEC ( $D_2$ )	0.0391 [0.2382]	0.0550 [0.3943]	0.0610 [0.4835]	0.0657 [0.5436]	0.0660 [0.5922]
Medium severity LEC ( $D_3$ )	0.0051 [0.0279]	0.0174 [0.1019]	0.0245 [0.1614]	0.0286 [0.2053]	0.0328 [0.2390]
High Severity LEC ( $D_4$ )	0.0004 [0.0022]	0.0042 [0.0126]	0.0089 [0.0274]	0.0117 [0.0420]	0.0155 [0.0559]
Amputation	0.0001 [0.0016]	0.0005 [0.0042]	0.0018 [0.0072]	0.0029 [0.0122]	0.0044 [0.0175]
Death	0.0001 [0.0016]	0.0005 [0.0040]	0.0018 [0.0065]	0.0029 [0.0111]	0.0044 [0.0160]

Note: Baseline in brackets

Note: In each of the 10,000 simulations, we specify that the person got diabetes in the second quarter at age 65 ( $t=5$ ). To calculate the marginal effect of early diagnosis, we compare the outcome of those who were diagnosed on the quarter of diabetes onset to those who were not diagnosed until a year later ( $t=9$ ).

**Table 7: Policy Simulations Restricting the Number of Covered Visits for Health Individuals**

	Visits	Number of quarters				
		Alive	Without amputation	Less than high LEC	Less than medium LEC	Less than low LEC
Baseline	38.9393	55.9818	55.5771	54.0502	50.0424	42.3388
<b>Reduction in visits and adverse health outcomes: 15 years follow-up</b>						
Savings in quarters of screening visits						
Only 1 visits/year	15.6219					
Only 2 visit/year	9.5368					
Adverse health effects in quarters						
Only 2 visits/year		0.0677	0.0836	0.1172	0.0893	0.1540
Only 1 visit/year		0.0161	0.0284	0.0419	0.0282	0.0390

Baseline: The predicted average of the same individuals using the parameters estimates.

Only 2 visits/year: The predicted average of the same individuals allowing them to have at most two visit until diagnose with diabetes.

Only 1 visit/year: The predicted average of the same individuals allowing them to have at most one visit until diagnose with diabetes.



## Appendix A

### Likelihood Function

We categorize observations into five categories that are defined by whether or not we observe an individual progressing to each disease stage. Here we present the likelihood function for each category conditional on the unobserved heterogeneity. We assume away the possibility of reaching diabetes stage 3 ( $D_3$ ) before the time of the first post-age 65 screening.

**Category 1:** Did not progress to  $D_1$  by the terminal period  $T$ :

$$\begin{aligned}
L_H \left( T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right) &= Sur(D_1 = T | \cdot) \times \Pr(\mathbf{V}_4^{t_{FV}} | \cdot) \times \Pr(\mathbf{V}_{t_{FV}+1}^T | \cdot) \\
&\quad \times \Pr(\mathbf{d}_{1,t_{FV}}^T | \cdot) \times \Pr(\mathbf{d}_{2,t_{FV}}^T | \cdot) \\
Sur(D_1 = T | e_k, \mathbf{M}) &= \prod_{t=1}^3 \left( 1 - h_t^{D_1^{P65}}(\cdot) \right) \prod_{t=4}^{t_{FV}} \left( 1 - h_t^{D_1^{FV}}(\cdot) \right) \prod_{t=t_{FV}+1}^T \left( 1 - h_t^{D_1}(\cdot) \right) \\
\Pr(\mathbf{V}_4^{t_{FV}} | e_k, \mathbf{M}) &= \Pr(V_4^{FV} = 1 | \cdot) \prod_{t=4}^{t_{FV}-1} \left( 1 - \Pr(V_t^{FV} = 1 | \cdot) \right) \\
\Pr(\mathbf{V}_{t_{FV}+1}^T | e_k, \mathbf{M}) &= \prod_{t=t_{FV}+1}^T \left[ \Pr(V_t = 1 | \cdot) \right]^{1(V_t=1)} \left[ 1 - \Pr(V_t = 1 | \cdot) \right]^{1-1(V_t=1)} \\
\Pr(\mathbf{d}_{c,t_{FV}}^T | e_k, \mathbf{M}) &= \prod_{t=t_{FV}}^T \left[ \Pr(d_{ct} = 1 | \cdot) \right]^{1(d_{ct}=1)} \left[ 1 - \Pr(d_{ct} = 1 | \cdot) \right]^{1-1(d_{ct}=1)}
\end{aligned}$$

where  $Sur(D_1 = T)$  is the probability of an individual surviving to  $T$  without  $D_1$ ,  $\Pr(\mathbf{V}_4^{t_{FV}})$  is the probability of having the first visit after turning age 65 at  $t = t_{FV}$  and  $\Pr(\mathbf{V}_{t_{FV}+1}^T)$  is the probability of the sequence of visits from  $t = t_{FV} + 1$  to  $t = T$ .  $\Pr(\mathbf{d}_{c,t_{FV}}^T)$  for  $c = 1, 2$  is the probability of the sequence of outcomes  $d_{ct}$  from  $t = t_{FV}$  to  $t = T$ .

**Category 2:** Progress to  $D_1$  at  $t_{D_1}$  and did not progressed to  $D_2$  by  $T$  :

$$\begin{aligned}
L_{D_1} \left( t_{D_1}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right) &= \Pr(D_1 = t_{D_1} | \cdot) \times Sur(D_2 = T | \cdot) \times \Pr(\mathbf{V}_4^{t_{FV}} | \cdot) \\
&\quad \times \Pr(\mathbf{V}_{t_{FV}+1}^T | \cdot) \times \Pr(\mathbf{d}_{1,t_{FV}}^T | \cdot) \times \Pr(\mathbf{d}_{2,t_{FV}}^T | \cdot) \\
Sur(D_2 = T | t_{D_1}; e_k, \mathbf{M}) &= \prod_{t=t_{D_1}}^T \left( 1 - h_t^{D_2}(\cdot) \right)
\end{aligned}$$

where  $Sur(D_2 = T | \cdot)$  is the probability of an individual surviving to  $T$  without  $D_2$  after contracting  $D_1$  at  $t_{D_1}$ .

$\Pr(D_1 = t_{D_1} | \cdot)$  is the probability of an individual contracting  $D_1$  at period  $t_{D_1}$  which depends on whether  $t_{D_1}$  is before or after  $t_{FV}$ . There are 3 possible scenarios for  $\Pr(D_1 = t_{D_1} | \cdot)$ :

a) if  $t_{D_1} \leq 3$  ( $D_1$  before age 65)

$$h_{t_{D_1}}^{D_1^{P65}}(\cdot) \prod_{t=1}^{t_{D_1}-1} \left( 1 - h_t^{D_1^{P65}}(\cdot) \right),$$

b) if  $3 < t_{D_1} \leq t_{FV}$  ( $D_1$  after age 65, but before the first post-65 screening)

$$h_{t_{D_1}}^{D_1^{FV}}(\cdot) \prod_{t=1}^3 \left(1 - h_t^{D_1^{P65}}(\cdot)\right) \prod_{t=4}^{t_{D_1}-1} \left(1 - h_t^{D_1^{FV}}(\cdot)\right),$$

c) if  $t_{FV} < t_{D_1}$  ( $D_1$  after the first post-65 screening)

$$h_{t_{D_1}}^{D_1}(\cdot) \prod_{t=1}^3 \left(1 - h_t^{D_1^{P65}}(\cdot)\right) \prod_{t=4}^{t_{FV}} \left(1 - h_t^{D_1^{FV}}(\cdot)\right) \prod_{t=t_{FV}+1}^{t_{D_1}-1} \left(1 - h_t^{D_1}(\cdot)\right).$$

**Category 3:** Progressed to  $D_1$  at  $t_{D_1}$ , progressed to  $D_2$  at  $t_{D_2}$ , and did not progress to  $D_3$  by  $T$ :

$$\begin{aligned} L_{D_3} \left( t_{D_1}, t_{D_2}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right) &= \Pr(D_1 = t_{D_1} | \cdot) \times \Pr(D_2 = t_{D_2} | \cdot) \\ &\quad \times \text{Sur}(D_3 = T | \cdot) \times \Pr(\mathbf{V}_4^{t_{FV}} | \cdot) \\ &\quad \times \Pr(\mathbf{V}_{t_{FV}+1}^T | \cdot) \times \Pr(\mathbf{d}_{1,t_{FV}}^T | \cdot) \times \Pr(\mathbf{d}_{2,t_{FV}}^T | \cdot) \\ \text{Sur}(D_3 = T | t_{D_1}, t_{D_2}; e_k, \mathbf{M}) &= \prod_{t=t_{D_2}}^T \left(1 - h_t^{D_3}(\cdot)\right) \end{aligned}$$

where  $\text{Sur}(D_3 = T | \cdot)$  is the probability of an individual surviving to  $T$  without  $D_3$  after contracting  $D_2$  at  $t_{D_2}$ .

$\Pr(D_2 = t_{D_2} | \cdot)$  is the probability of an individual contracting  $D_2$  at period  $t_{D_2}$ . There are 6 possible scenarios for  $\Pr(D_2 = t_{D_2} | \cdot)$ :

a) if  $t_{D_1} \leq t_{D_2} \leq 3$

$$h_{t_{D_2}}^{D_2^{P65}}(\cdot) \prod_{t=t_{D_1}}^{t_{D_2}-1} \left(1 - h_t^{D_2^{P65}}(\cdot)\right)$$

b) if  $t_{D_1} \leq 3 < t_{D_2} \leq t_{FV}$

$$h_{t_{D_2}}^{D_2^{FV}}(\cdot) \prod_{t=t_{D_1}}^3 \left(1 - h_t^{D_2^{P65}}(\cdot)\right) \prod_{t=4}^{t_{D_2}-1} \left(1 - h_t^{D_2^{FV}}(\cdot)\right)$$

c) if  $t_{D_1} \leq 3 < t_{FV} < t_{D_2}$

$$h_{t_{D_2}}^{D_2}(\cdot) \prod_{t=t_{D_1}}^3 \left(1 - h_t^{D_2^{P65}}(\cdot)\right) \prod_{t=4}^{t_{FV}} \left(1 - h_t^{D_2^{FV}}(\cdot)\right) \prod_{t=t_{FV}+1}^{t_{D_2}-1} \left(1 - h_t^{D_2}(\cdot)\right)$$

d) if  $3 < t_{D_1} \leq t_{D_2} \leq t_{FV}$

$$h_{t_{D_2}}^{D_2^{FV}}(\cdot) \prod_{t=t_{D_1}}^{t_{D_2}-1} \left(1 - h_t^{D_2^{FV}}(\cdot)\right)$$

e) if  $3 < t_{D_1} \leq t_{FV} < t_{D_2}$

$$h_{t_{D_2}}^{D_2}(\cdot) \prod_{t=t_{D_1}}^{t_{FV}} \left(1 - h_t^{D_2^{FV}}(\cdot)\right) \prod_{t=t_{FV}+1}^{t_{D_2}-1} \left(1 - h_t^{D_2}(\cdot)\right)$$

f) if  $3 < t_{FV} < t_{D_1} \leq t_{D_2}$

$$h_{t_{D_2}}^{D_2}(\cdot) \prod_{t=t_{D_1}}^{t_{D_2}-1} \left(1 - h_t^{D_2}(\cdot)\right)$$

**Category 4:** Progressed to  $D_1$  at  $t_{D_1}$ , progressed to  $D_2$  at  $t_{D_2}$ , progressed to  $D_3$  at  $t_{D_3}$ , and did not progress to  $D_4$  by  $T$ :

$$\begin{aligned} L_{D_M} \left( t_{D_1}, t_{D_2}, t_{D_3}, T, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right) &= \left[ \prod_{j=1}^3 \Pr(D_j = t_{D_j} | \cdot) \right] \times Sur(D_4 = T | \cdot) \\ &\quad \times \Pr(\mathbf{V}_4^{t_{FV}} | \cdot) \times \Pr(\mathbf{V}_{t_{FV}+1}^T | \cdot) \\ &\quad \times \Pr(\mathbf{d}_{1,t_{FV}}^T | \cdot) \times \Pr(\mathbf{d}_{2,t_{FV}}^T | \cdot) \\ Sur(D_4 = T | t_{D_1}, t_{D_2}, t_{D_3}; e_k, \mathbf{M}) &= \prod_{t=t_{D_3}}^T \left(1 - h_t^{D_4}(\cdot)\right) \\ \Pr(D_3 = t_{D_3} | t_{D_1}, t_{D_2}; e_k, \mathbf{M}) &= h_t^{D_3}(\cdot) \prod_{t=t_{D_2}}^{t_{D_3}-1} \left(1 - h_t^{D_3}(\cdot)\right) \end{aligned}$$

where  $Sur(D_4 = T | \cdot)$  is the probability of an individual surviving to  $T$  without  $D_4$  after contracting  $D_3$  at  $t_{D_3}$  and  $\Pr(D_3 = t_{D_3} | \cdot)$  is the probability of an individual contracting  $D_3$  at period  $t_{D_3}$ .

**Category 5:** Progressed to  $D_1$  at  $t_{D_1}$ , progressed to  $D_2$  at  $t_{D_2}$ , progressed to  $D_3$  at  $t_{D_3}$ , and progressed to  $D_4$  at  $t_{D_4}$ :

$$\begin{aligned} L_{D_4} \left( t_{D_1}, \dots, t_{D_4}, \vec{V}, \vec{d}_1, \vec{d}_2 | e_k, \mathbf{M} \right) &= \left[ \prod_{j=1}^4 \Pr(D_j = t_{D_j} | \cdot) \right] \times \Pr(\mathbf{V}_4^{t_{FV}} | \cdot) \\ &\quad \times \Pr(\mathbf{V}_{t_{FV}+1}^T | \cdot) \times \Pr(\mathbf{d}_{1,t_{FV}}^T | \cdot) \times \Pr(\mathbf{d}_{2,t_{FV}}^T | \cdot) \\ \Pr(D_4 = t_{D_4} | t_{D_1}, t_{D_2}, t_{D_3}; e_k, \mathbf{M}) &= h_t^{D_4}(\cdot) \prod_{t=t_{D_3}}^{t_{D_4}-1} \left(1 - h_t^{D_4}(\cdot)\right) \end{aligned}$$

where  $\Pr(D_4 = t_{D_4} | \cdot)$  is the probability of an individual contracting  $D_4$  at period  $t_{D_4}$ .