

## Web-based application to project the burden of Alzheimer's disease

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### Abstract

**Background:** Health care planning and research would benefit from tools that enable researchers to project the future burden of Alzheimer's disease (AD) and evaluate the effect of potential interventions.

**Methods:** We created a web-based application of the AD prevalence model developed by Brookmeyer et al (*Am J Public Health* 1998;88:1337–42; *Alzheimers Dement* 2007;3:186–91). The user defines the disease parameters and any interventions that may either reduce risk or slow disease progression. We expanded the parameters to include the cost and weights for disability-adjusted life years.

**Application:** The secure, web-based application generates detailed AD projections for each calendar year to 2050, and allows users to create personal accounts for them to save, retrieve, and modify the input parameters. The flexibility of the application is illustrated with a forecast for the state of Maryland, USA.

**Conclusions:** The application generates AD burden projections, costs, and disability-adjusted life years, along with changes associated with potential interventions.

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### Keywords:

Forecasting; Disease burden; Multi-stage disease model; Web-tool; Costs; Preventative therapy; Disability-adjusted life years (DALYs)

## 1. Introduction

Projecting the future burden of Alzheimer's disease (AD) is critical for health care planning. Additionally, researchers and policy makers are interested in evaluating the effect of potential interventions that may reduce disease risk or slow disease progression. Brookmeyer et al [1,2] developed and implemented a multistage, incidence to prevalence disease model to estimate and project the prevalence of AD. The model allows for the introduction of potential interventions that either reduce the risk of or slow progression of AD to assess the effect of interventions on the burden of disease. We have expanded the Brookmeyer et al [1,2] model to incorporate alternative health burden measures (years of life lost [YLL] and disability-adjusted life years [DALYs]) and the economic costs of disease. These measures can be

incorporated into decisions regarding resource allocation [3] and in cost-effectiveness studies for new therapies [4,5]. We created a web-based application to implement the model, allowing anyone to generate his/her own projections based on his/her particular parameters. The user may specify inputs related to AD incidence, disease progression, and the effect of AD on mortality, costs, and DALYs. The web-based application generates annual projections of AD prevalence, costs, YLL, DALYs by age, gender, and stage for each year, up to 2050. The application allows the user to easily generate multiple “what if” scenarios by varying the underlying assumptions, i.e., input parameters. In this report, we describe the web-based application and illustrate its flexibility for making both global and local forecasts.

## 2. Web-based application

We created a web-based application using the Brookmeyer et al [1,2] model. It is located on a secure-server within the Department of Biostatistics, Bloomberg School of Public Health, Johns Hopkins University (available at: <http://www.biostat.jhsph.edu/project/globalAD>).

Conflict of interest: H Michael Arrighi was an employee of and owns stock in Elan and is currently an employee of JANSSEN Alzheimer Immunotherapy Research & Development, LLC.

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The Brookmeyer et al [1,2] model forecasts the prevalence of disease by estimating annual age, gender, and stage-specific prevalence rates and then applies these to population projections. The annual prevalence rates are estimated using a stochastic multistage discrete-time Markov model. The model is general and may be used to project the burden of AD globally, for the U.S., for a specific country or region of interest.

### 2.1. Inputs

Global, by United Nations regions [6], and U.S [7] population projections for the years 2000–2050 by age and gender are provided in the web-based application. Alternatively, the user may upload other population projections for any specific country or region of interest.

Table 1 lists the required inputs for the web-based application. The inputs include current and future background mortality rates for the population, age, and gender-specific incidence rates for AD, the annual transition probability from early to late stage disease, and the effect of AD on mortality. For each of these inputs, the user may use either the default value or enter their own value. For instance, the user may specify the risk of progression from early to late stage to evaluate different definitions of disease stages. For the population background mortality rates, the user may upload rates or change the default rates by a multiplier (i.e., increase rates by 20%, multiplier 1.2). However, our sensitivity investigations have revealed that the results are relatively insensitive to the specification of that multiplier.

The user may evaluate the effect of potential interventions that either delay the onset of disease (i.e., reduce the incidence rate), or slow disease progression (i.e., reduce the rate of transition from early to late stage disease). If the intervention delays disease onset, the user specifies the relative amount to which the intervention decreases the incidence of disease (i.e., to delay the onset of disease by roughly 1 year on average, the default incidence rates would decrease by 12%). If the intervention delays disease progression, the user must specify the average number of years that the intervention would delay the progression of disease to an advanced stage. The calendar year the interventions take effect must be specified.

The application also calculates DALYs and costs associated with AD. DALYs are the sum of YLL and years lost due to disability and are calculated according to methods proposed by Murray [14]. We provide default values for the disability weights for early and late stage disease [13], which may be modified by the user.

Users may estimate cost associated with the prevalence forecast. The user may input costs for direct or indirect medical costs to treat or the hours spent by caregivers to care for a patient with AD. Forecasts of costs may be in current or future dollars by including an annual inflation factor.

Table 1  
Inputs and outputs of the web-based application

Inputs	Outputs
Population forecasts*	AD prevalence <sup>‡‡</sup>
Background mortality rates <sup>†</sup>	AD incidence <sup>‡‡</sup>
AD incidence rates <sup>‡</sup>	Costs <sup>‡‡</sup>
Annual transition probability from stage 1 to 2 disease <sup>§</sup>	Disability Adjusted Life Years (DALYs) <sup>‡‡</sup>
Impact of AD on mortality <sup>¶</sup>	Prevalence rate <sup>§§</sup>
Years during which an intervention is introduced**	Median survival <sup>§§</sup>
Effect of intervention on disease incidence**	
Effect of intervention on disease progression**	
Disability weights <sup>††</sup>	
Costs of AD**	

\*Global population projections by UN region of the world [6] and US population projections [7] are provided.

<sup>†</sup>Default values provided by age (60–100), gender, and year (1959–2050) based on historic and projected US mortality rates [8].

<sup>‡</sup>Default values provided based on meta analysis of worlds incidence rates by age (60–100) [9].

<sup>§</sup>Default value is 0.167, based on approximate mean duration of 6 years living with AD before care equivalent to nursing home [10].

<sup>¶</sup>Default values assumes no increase in mortality for stage 1 disease and effect of mortality on stage 2 disease is to add 11% per year (additive model) [12].

\*\*User supplies (optional).

<sup>††</sup>Default values are 0.45 for stage 1 and 0.94 for stage 2 [13].

<sup>‡‡</sup>By age (60–100), gender, stage for years 2000–2050.

<sup>§§</sup>By age (60–100) and gender for years 2000–2050.

### 2.2. Outputs

Outputs of our web-based application include age, gender, stage, and calendar year counts of prevalent and incident cases of AD, DALYs, and costs (Table 1). Age, gender, and calendar year-specific prevalence rates are produced. The web-based application produces an html page and several figures displaying the results of the forecast (e.g., prevalence by gender, stage, and calendar year). In addition, a text file is created with the results which may be imported into statistical software for further analysis or creation of customized figures.

## 3. Illustration of the web-based application for local forecasts: Maryland, USA

The flexibility of the web-based application is illustrated by projecting the prevalence and cost of AD for the state of Maryland (MD), USA. MD population projections by gender and age (in single years of age from 60 to 84, and pooled for those aged 85 years and older) for the calendar years 2004–2030 were downloaded from the U.S. Census Bureau [15]. We forecast the formal costs of caring for persons with AD in 2009 dollars, assuming that the costs are \$23,160 for early stage and \$82,957 for late stage disease (adapted from Fox [16]) and calculated into 2009 dollars using the Bureau of Labor Statistics inflation calculator ([www.bls.gov/data/](http://www.bls.gov/data/))

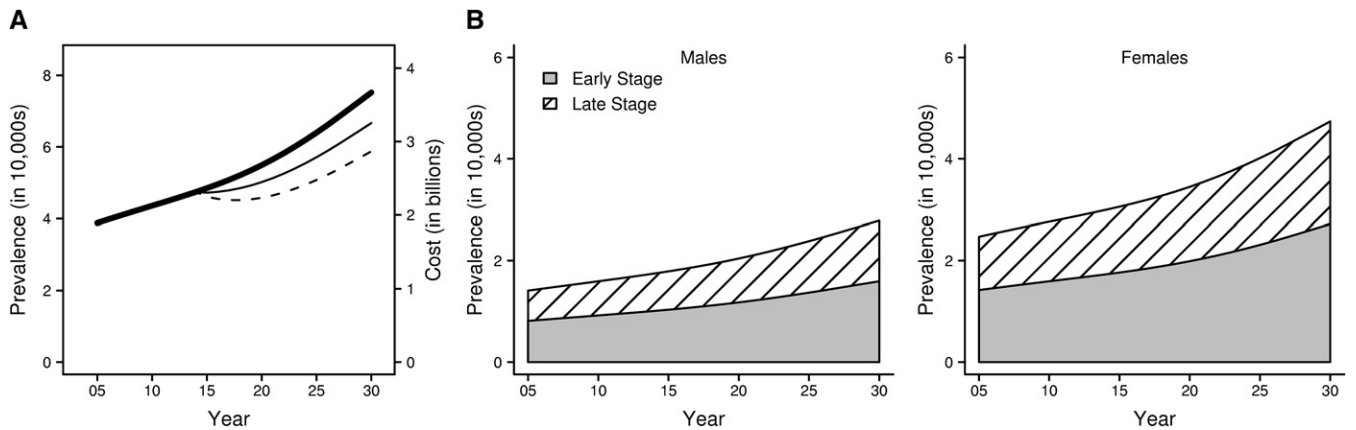


Fig. 1. Examples of graphical displays created from the output of the web-based application. Panel A displays the estimated prevalence (in 10,000s) and costs of caring for persons with AD (in billions of 2009 dollars) for 2005–2030 for the state of Maryland, USA. The figure displays prevalence and cost assuming no intervention (thick solid black line) and preventative interventions introduced in 2015 that delays onset of disease on average 1 year (thin solid black line) or 2 years (thin dashed black line). Panel B displays the estimated prevalence of AD (in 10,000s) by gender and stage for 2005–2030 for the state of Maryland, USA.

[inflation\\_calculator.htm](#)). Formal costs include costs of medical care and social services, and we assume that persons with early stage disease are similar to community residents with AD and persons with late stage disease require institutional care. We performed the following forecasts: (1) no intervention, (2) preventative intervention introduced in 2015 that delays disease onset by 1 year (multiply incidence rates by 0.88), and (3) preventative intervention introduced in 2015 that delays disease onset by 2 years (multiply incidence rates by 0.75). The input files for the example with additional explanations are available on-line (<http://www.biostat.jhsph.edu/project/globalAD/programs.htm#md>).

We estimate that the current (2009) prevalence of AD in MD is approximately 42,600 and the cost of formal care for persons with AD in MD is approximately 2.1 billion dollars (Fig. 1, Panel A: thick solid black line). Slightly more than 60% of the cases are women and nearly 40% of the cases are late stage cases regardless of calendar year (Fig. 1, Panel B). We forecast that the prevalence of and the formal costs of caring for persons with AD in MD will increase by nearly 75% by 2030 to 75,200 cases and 3.7 billion dollars, respectively (Fig. 1, Panel A: solid black line). The effect of the preventative interventions is to decrease the prevalence of AD in 2030 by 8500 (approximately 11%) or 16,400 (approximately 22%) if the intervention delays disease onset by an average of 1 or 2 years, respectively (Fig. 1, Panel A: thin solid and dashed lines, respectively).

#### 4. Discussion

We have adapted a multistage incidence to prevalence disease model into a web-based application that allows users to project the burden of AD globally or locally. We provide default inputs or the user may specify his/her own. Inputs, such as population projections or incidence rates, may need to be modified before using the application. The user may run the application multiple times, varying one or two input param-

eters, to generate a variety of exploratory “what if” scenarios or sensitivity analyses.

The burden of disease has been quantified using prevalence, incidence, costs, YLL, and DALYs. Costs may focus on a particular aspect, as in the example, where AD cost was limited to the cost of formal care under the assumption that early stage is equivalent to community care and late stage is equivalent to institutionalized care. Additionally, the effect of an intervention on either incidence or progression may be assessed.

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