Appendix I: Selection of Calibration Targets for the Model

Note: a tabular summary is presented in Table 2 in the main manuscript.

Incidence

Historically, estimates of major depression incidence derived from large prospective studies, such as the Lundby Study [1], the Stirling County Study [2] and the Baltimore Epidemiologic Catchment Area (ECA) follow-up [3]. These studies have reported incidence rates between 2.0 per 1000/year and 4.5 per 1000/year, and have generally observed higher rates in women than in men. More recently, several studies have reported much higher incidence rates. The Finnish ODIN study [4] produced an estimate of 28.5 per 1000/year (approximately 3%), and the Netherlands NEMESIS study [5] reported 2.72 per 100 person-years [6]. These studies used lifetime assessment interviews at baseline to determine who was at risk for a first episode, an approach that has been shown not to be accurate [7,8], so the higher estimates probably mean that these were not truly first incidence studies, but rather included some recurrent cases. Another complicating factor is that several studies have reported very high incidence rates in adolescent samples [9,10]. In these studies, the cumulative incidence over a few years was of similar magnitude to lifetime prevalence estimates from adult community samples. In high school aged adolescents, Lewinsohn et al. reported a one year first incidence of major depression of 7.1% in females and 4.5% in males [10]. Very high incidence in the 12-24 year old age group has also been observed in Canada [11].The high incidence in adolescents must decline with advancing age so that the lifetime

prevalence produced by the model would not be excessively high. The targets for model calibration in the initial year were those from Lewinsohn: 7.1% annually in women and 2.9% in men [10] at the time of entry to the model along with Kruijshaar et al.'s estimate of lifetime prevalence at 30% in women and 20% in men [12].

Point Prevalence

Point prevalence is formally defined as the frequency of disease in a population at a point in time. In psychiatric epidemiology, point or current prevalence usually means a brief period prevalence, typically 30 days. A 1994 review of the historical literature by Wittchen et al. placed the point prevalence of major depression at about 3% [13]. In the NEMESIS study, the one month prevalence was 3.4% for women and 1.9% for men [14]. Murphy et al, placed this parameter within the range of 2.2% to 2.6% [15], citing estimates from the Stirling County Study, ECA Study [16] and an Edmonton study [17]. As such, there is fairly consistent evidence that approximately 2-3% of the population have major depression at any one point in time. In the Canadian Community Health Survey: Mental Health and Wellbeing (CCHS 1.2), with exclusion of apparent bipolar cases, 1.8% of respondents had a major depressive episode in the past 30 days [18].

Lifetime Prevalence

The two most widely cited estimates are those from the National Comorbidity Survey (17.1%) [19] and its replication (16.2%) [20]. The CCHS 1.2 in Canada reported

a 12.2% lifetime prevalence [18], similar to the 12.8% figure reported by the European ESEMeD studies [21]. Given evidence of recall failure with historical assessment [7,12], these are probably all underestimates, an hypothesis that has received support from studies using modeling approaches [12]. A lifetime prevalence of 32% in high school aged women and 16% in high school aged men was reported by Lewinsohn et al. [10]. An estimate of this type may have reduced susceptibility to recall bias since the episodes evaluated occurred in greater temporal proximity to the interview. This idea is consistent with Kruijshaar's assertion that lifetime prevalence is probably higher than retrospective estimates suggest: she estimated that it probably falls in the range of 30% to 20% respectively in women and men [12].

Mortality

The impact of major depression on mortality has mostly been investigated by studies that followed clinical subjects over time. Such estimates may not be generalizable to community populations. As such, the relative risk for mortality of 1.8 arising from a systematic review conducted by Wulsin et al. [22] is probably an over estimate. For this reason, a somewhat arbitrary value of 1.1 was selected as a calibration target for the visual simulation. However, a sensitivity analysis was carried out, see Appendix II and Table 3 in the paper.

Recurrence

In the 12-14 year follow-up of the Baltimore ECA studies, approximately 50% of subjects who had lifetime major depression had a recurrence during the follow-up interval [3]. There was no sex difference in the recurrence rate, but recurrent episodes, on average, were found to be briefer than initial episodes. The National Collaborative Depression Study [23] found a higher rate of recurrence in women. A proviso is that the National Collaborative Study did not use a general population sample. In this study, recovered subjects had an 85% chance of having a recurrence during the following 15 years. Furthermore approximately half of subjects who remained well for five years after recovery had a relapse within the next 10 years. In a more highly recurrent group, the same study found that 41% relapsed within a year, and 74% within 5 years [24]. These figures provide an indication that the rate of recurrence changes over time, with increasing time since recovery being associated with a diminished probability of recurrence.

The Canadian National Population Health Survey prospectively follows a cohort of Canadians who were randomly selected from the population in 1994 and 1995. They are interviewed every two years with an interview that includes the CIDI Short Form for Major Depression [25]. Of 8368 subjects with no episodes of major depression in the first four interview cycles, 175 had an episode in the final cycle – a frequency of approximately 2%. Subjects with one episode in the previous four cycles (n=935), 108 had an episode in the final cycle, an incidence of approximately 12%. Of 303 subjects with more than one episode in the first four cycles, 105 had one in the final cycle,

approximately one third. These results are consistent with the idea that the probability of recurrence increases with successive episodes.

Episode Duration

Data from the NEMESIS study provide the best available data on episode duration, and detailed descriptive analyses have been presented by Spijker [26,27]. This prospective study included interviews at three time points. NEMESIS included a Life Chart Interview to determine episode duration. Analyses of the NEMESIS data indicated that many episodes are brief, the median duration being reported as 3 months, whereas a smaller number of episodes were much longer, so that the mean duration was 8.4 months (with an upper limit of 24 months imposed due to the study design). The proportion of episodes lasting two years or longer was estimated as being approximately 20% [26]. This pattern was described using a lognormal distribution in modeling studies by Vos et al. [28], who included data from several international studies including that of Lewinsohn et al. [29] and Eaton et al. [3]. The probability of remission in the studies reviewed was higher than that of NEMESIS in these studies, and was approximately 90%. The Canadian National Population Health Survey (NPHS) included questions on episode duration, and Markov models based on the NPHS data predicted a one-year recovery rate in the range of 95% [30,31]. Consistent with the pattern seen in the Vos et al. review, the proportion reporting symptom durations of 2-3 weeks (with 2 weeks being the minimum duration in DSM-IV) was high, in the range of 15-20% of episodes in the NPHS [32]. However, the NPHS used a brief version of the CIDI [25], which may have detected

some sub-clinical episodes. The NEMESIS project may be the most credible source of episode duration data, but 80% recovery after two years is more pessimistic than all other studies. Based in the literature, a pattern characterized by approximately 15% recovery after 3 weeks of symptoms, but where 15% remained depressed after two years seemed to be a plausible set of values for calibration targets for the model.

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