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Time Trends in the Prevalence of Neurocognitive Disorders and Cognitive Impairment in the United States: The Effects of Disease Severity and Improved Ascertainment

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Abstract

BACKGROUND: Trends in the prevalence of cognitive impairment (CI) based on cognitive assessment instruments are often inconsistent with those of neurocognitive disorders (ND) based on Medicare claims records.

OBJECTIVE: We hypothesized that improved ascertainment and resulting decrease in disease severity at the time of diagnosis are responsible for this phenomenon.

METHODS: Using Medicare data linked to the Health and Retirement Study (1992–2012), we performed a joint analysis of trends in CI and ND to test our hypothesis.

RESULTS: We identified two major contributors to the divergent directions in CI and ND trends: reductions in disease severity explained more than 60% of the differences between CI and ND prevalence over the study period; the remaining 40% was explained by a decrease in the fraction of undiagnosed individuals.

DISCUSSION: Improvements in the diagnoses of ND diseases were a major contributor to reported trends in AD and CI. Recent forecasts of CI and ND trends in the U.S. may be overly pessimistic.

Keywords

time trends; cognitive impairment; neurocognitive disorders; severity; underdiagnosis; Medicare; ascertainment; health and retirement study; disease prevalence; telephone interview for cognitive status

Introduction

Cognitive impairment (CI) is a natural outcome of the progression of Alzheimer's disease (AD) and other neurocognitive disorders (ND); therefore, time-trends in the prevalence of

ND and CI are expected to be concordant. However, recent research demonstrates a lack of consistency in estimating the directions of these trends: CI measures decline with time, while clinical data show increasing trends for the prevalence of AD and related dementias.

Recent studies have concluded that the prevalence of CI in the U.S. is on the decline based on measurements of CI using cognitive tests [1] or through the prevalence of “dementia” that is calculated from CI measures using an established threshold [2] (also reviewed in [3, 4]). Notably the study using the National Long-Term Care Survey (NLTC) showed a decrease in crude CI prevalence for age 65+ from 9.2% in 1984 to 6.7% in 2004 [1]. In this study, CI was multiply defined as 3+, 4+, or 5+ Short Portable Mental Status Questionnaire [5] errors, and/or a caregiver report of Alzheimer’s disease/dementia, or similar problems requiring concurrent substantial supervision. Another study, based on the Health and Retirement Study (HRS) also reported a decline in the prevalence of CI for age 65+ from 11.6% in 2000 to 8.8% in 2012. In this case, CI was defined using the score on a battery of tests based on the Telephone Interview for Cognitive Status (TICS); the prevalence of CI was calculated using an established threshold cut-point [2].

In contrast to trends in CI prevalence, studies based on clinical data report an increase in the prevalence of AD and other NDs leading to dementia. The Alzheimer’s Association recently concluded that, even though the incidence of AD has been decreasing, its prevalence has been increasing over the past 25 years in the U.S. [6]; another study projected that the number of people with AD will triple by 2050 [7]. A recent Canadian [8] retrospective cohort study found a simultaneous trend of decreasing incidence and increasing prevalence of dementia over a relatively short 8-year time period from 2005/06 to 2012/13, with the age-standardized prevalence increasing from 21.35% to 27.87%. Other studies also demonstrated increases in dementia prevalence in UK [9], another Canadian study [10], and pooled European data [11] (also reviewed in [12]).

Overall, the literature suggests that the prevalence of AD and other NDs are on the rise, while the prevalence of CI has been declining over recent decades. The divergent directions of the trends in these two closely-related outcomes appear counterintuitive. We hypothesized that this apparent contradiction can be explained by changes in disease severity and in the fractions of undiagnosed individuals and that these changes can be quantified in terms of the time trends of two-way frequencies of individuals i) with CI and without ND and ii) without CI and with ND, respectively. To test this hypothesis, we used HRS survey data linked to Medicare administrative claim records (1998–2010) to evaluate the trends in the prevalence of AD and other NDs (based on Medicare diagnosis) against the trends in the prevalence of CI (based on the TICS) for the same individuals. Research based on the Aging, Demographics, and Memory Study [13] (ADAMS)—a detailed study of a subset of the HRS population identified as being at high risk for the presence of ND that included in-person physician evaluations—has shown the TICS, as administered in the HRS, to be a good measure of CI and clinical dementia [14]. TICS-based measures correctly classified 78% of all ADAMS participants with dementia (76% of self-respondents and 84% of those represented by a proxy) [15]. Other studies [16–18] focused on the relationships between dementia diagnoses made using the ADAMS protocol [13] and Medicare claims; they found that Medicare claims and ADAMS agreed on 85% of subjects with a kappa statistic of 0.70

with the sensitivity and specificity of Medicare claims being 0.85/0.89 for dementia and 0.64/0.95 for AD [18, 19].

Joint analyses of CI and ND prevalence trends require maximally precise evaluation of trends of CI and ND separately including analyses of their uncertainties. Therefore, additional scrutiny was given to the selection of ICD-9 codes and the properties of the resulting trends in ND. We further hypothesized that trends in cognitive impairment derived from tests of cognitive status would be highly dependent on the threshold cut-points used to define cognitive impairment. Finally, since several critical factors, such as changes in the age structure of the population, and individual-level characteristics (most notably educational attainment) influence the direction and magnitude of the time-trends in CI and ND prevalence, we controlled for the effects of these factors.

The contributions of the current paper are as follows. First, in contrast to most previous studies which analyzed CI or ND separately (primarily due to the paucity of data sources allowing simultaneous evaluation of these trends) our study addressed both CI and multiple specific ND diagnoses by combining Medicare data with cognitive assessments. Second, rather than choosing one of the established threshold cut-points to dichotomize a wide range of cognitive scores into *impaired* and *non-impaired*, our study carefully considered all possible CI thresholds—important because the estimated trend in CI was highly sensitive to the choice of threshold cut-points. Third, our study analyzed a broad spectrum of ND diseases, estimating and comparing their prevalences and time trends. We show that, although each ND can lead to some level of CI, each disease has unique properties that warrant individual attention in addition to the overall effect on aggregate levels of CI. The results in the current paper confirm that both CI and ND measures are informative, clarify the roles of disease severity and underdiagnosis, and underscore the need to account for these effects in evaluating the success of health care delivery, planning for further improvements and interventions, and predicting future disease burdens, including financial costs.

Methods

The Health and Retirement Study (HRS) is an ongoing national longitudinal survey that has been fielded every other year since 1992. It collects data on a battery of demographic and socioeconomic characteristics including education, nursing home residence, and activities of daily living. The HRS also includes the modified Telephone Interview for Cognitive Status (TICS)—a widely-used instrument designed to measure cognitive ability [20]. The HRS version of the TICS produces a cumulative score between 0 and 35 points based on the following cognitive function tests: 10-word immediate and delayed recall to test memory (20 pts. total); serial 7s subtraction test of working memory (5 pts.); counting backwards for attention (2 pts.); responsive naming to assess language (2 pts.); and recall of the date (3 pts.), day of week (1 pt.), and president and vice-president (2 pts.) to test orientation. The linked Medicare data contain information on individual-level administrative records on health-care claims paid for by Medicare Part A (facility-based services) or Medicare Part B (professional services) during the 1992–2012 period. Medicare data contain information on

the exact dates of diagnosis as defined by the International Classification of Disease 9th Edition, Clinical Modification (ICD-9).

Dementia is an umbrella term for several different neurocognitive or memory-related disorders leading to loss of physical and social functioning as well as cognitive impairment (CI); dementia is often used interchangeably with CI [6]. Therefore, we consider a broad spectrum of neurocognitive-related diseases (Table 1) that could lead to the development of CI, individually or as a part of the composite measure “All neurocognitive disorders”. An individual was considered to have a disease at a given time if there was at least one primary or secondary diagnosis record with a preselected disease-specific ICD-9 code (Table 1) in any of four primary Medicare data files (physician carrier, inpatient, outpatient, and skilled nursing facility) during the 12 months prior to the selected time. Because an individual can have multiple diagnoses, he/she could be selected for several disease-specific analyses. If an individual had any listed disease, then he/she was selected for analysis of the composite measure “All neurocognitive disorders”.

Individuals aged 65+ at the time of their interviews in waves 4–10 (1998–2010) of the HRS were selected as potentially eligible for this study. We excluded individuals who were enrolled in Medicare Advantage, a private managed-care alternative to traditional Medicare, during the 12 months prior to their interview (17.9% of total sample) and/or who had missing cognitive scores for unknown reasons (0.1% of total sample).

Two approaches were used to account for remaining individuals with missing TICS scores (in our data all such cases were individuals who were unable/unwilling to take the TICS but received a proxy assessment instead). In both approaches, we used information drawn from a proxy interview to fill in or approximate the missing TICS scores. First, in the “filled” approach, missing TICS values were imputed using linear regression with Medicare disease diagnosis, nursing home residence, education, self-reported memory problems, difficulties using a phone and managing money, and several demographic variables as predictors. This resulted in individuals having continuous TICS values with lower numbers representing increased levels of CI. In the “filled” approach, CI was defined using an arbitrary predetermined threshold, e.g., if the chosen threshold was 9, then the individuals with CI were those who had TICS ≥ 9 . Second, in the “base” approach, we used proxy assessment fields to assign cognitive status to individuals with missing TICS. Four variables in the proxy interviews were measured across all waves and hence were used: i) ever get lost in a familiar environment; ii) ever wander off and not return by himself/herself; iii) can be left alone for an hour or so; and iv) ever see or hear things that are not really there. In the “base” approach, CI was defined for three alternative thresholds: i) TICS ≥ 13 for individuals with measured TICS or one or more negative responses in the proxy interview; ii) TICS ≥ 8 or 2+ negative responses in the proxy interview; and iii) TICS ≥ 4 or 3+ negative responses in the proxy interview. The three numerical thresholds (13, 8, and 4) were selected for use in the “base” definition because they separated the same fractions of proxy-respondents, respectively, in the “filled” approach as the 1+, 2+, and 3+ negative-response criteria in the “base” approach. Moreover, the cut-point value 8 is a recognized and validated threshold for predicting dementia using TICS [21].

The empirical time and age-specific CI and ND prevalences were calculated as the ratio of the respective numbers of cases to the total number of subjects at-risk (Table 2). Age-adjusted prevalence was calculated by summing the age-specific estimates over all age groups weighted by population weights from the U.S. standard population aged 65+ for the year 2000. The time-trends of the age-adjusted prevalences were evaluated using the average annual percent change (or the annual rate of change of the prevalence) which was estimated using a log-linear model: $\log(p(t)) = a + b(t-2000) + \varepsilon_t$ or $p(t) = p_{2000} \exp(b(t-2000))$, where t was calendar year, and ε_t was the error term of the log-linear regression. The estimate of the average annual percent change was given by $100b$, expressed in percentage form [22]. We used weighted least squares for estimation, where the weights were the reciprocals of the variance estimated for each time-specific age-adjusted prevalence.

The joint prevalence of CI and ND can be represented through two-way relative frequencies as $p_{CI} = f_{11} + f_{10}$ and $p_{ND} = f_{11} + f_{01}$: where f_{ij} 's represent individuals with CI and ND (f_{11}), with CI and without ND (f_{10}), and without CI and with ND (f_{01}). The term f_{01} is the fraction of non-severe cases and the term f_{10} is the fraction of undiagnosed individuals. The difference between p_{ND} and p_{CI} is defined as $p_{ND} - p_{CI} = f_{01} - f_{10}$. Accordingly, the differences between the time trends of p_{ND} and p_{CI} are governed by the time trends of disease severity (represented by f_{01}) and the fraction of undiagnosed cases (represented by f_{10}). The prevalences p_{ND} and p_{CI} and the fractions f_{01} and f_{10} were calculated empirically for each HRS wave and then modeled using ordinal linear regression: $a_t + b_t(t-2004)$, where a_t is the intercept in the middle of the study period and b_t is the slope that estimates the time-trend of the respective measure. Taking coefficients at t in $p_{ND} - p_{CI} = f_{01} - f_{10}$ (or calculating the derivative) we connect slopes for these measures: $b_{t,ND} - b_{t,CI} = b_{t,01} - b_{t,10}$. Under the assumption that p_{ND} is increasing and p_{CI} is decreasing over time, it follows that $b_{t,01} > 0$ and $b_{t,10} < 0$, which implies that $b_{t,01} - b_{t,10} > -b_{t,10} > 0$ and $b_{t,01} - b_{t,10} > b_{t,10} > 0$. Hence, we can define that two positive ratios $b_{t,01} / (b_{t,ND} - b_{t,CI})$ and $-b_{t,01} / (b_{t,ND} - b_{t,CI})$ to represent the proportions of the total difference between the ND and CI trends explained by the separate, divergent trends in disease severity and underdiagnosis. The prevalence of CI depends on the value chosen for the numerical threshold cut-point (13, 8, or 4) used in the base definition, the first two of which were chosen because the estimated intercepts for p_{ND} and p_{CI} were close. Specifically, we chose TICS = 13 for all ND and TICS = 8 for other major conditions. For each choice, the prevalence of CI in the population was approximately equal to the prevalence of cases with the corresponding disease classification. Moreover, because education and sex distributions can also change over time, we adjusted for sex and education in addition to adjusting for age; comparisons of the age-adjusted and age-sex-education-adjusted estimates are provided in Figure 4.

Results

The summary statistics for the analytic sample are presented in Table 2. The temporal trend of each variable between waves 4 and 10 of the HRS was represented by an Odds Ratio (OR) estimated using a logistic regression model with the wave number as the sole predictor. An OR > 1 implies an increasing trend in a given variable over the study period. Detailed information including Z-statistics and one-way p-values for the Cochran-Armitage tests for linear trend is presented in Supplementary Table 1.

Annual percentage changes (APC) in the mean age-adjusted prevalence of CI over the 12-year study period are shown in Figure 1. Although our results confirmed the results of previous studies [1, 2], the identified downwards trend in CI was strongly dependent on the value of the threshold cut-point, especially at lower levels (higher CI). The proportions of individuals with TICS 2, 3, and 4 increased over the study period. The calculations were repeated (Supplementary Figure 1) for both sexes, white and black races, and for individuals with three different levels of education (less than high-school graduate; GED/high-school graduate; and some college or more). The results were consistent for all of the sub-groups, except for the lowest education group.

Over the same time-period, the prevalence of the combined measure of all neurocognitive disorders (Table 1) went up (Figure 2). The primary contributors to the observed trends in *all neurocognitive disorders* were: AD, dementia due to senility, persistent mental disorder (PMD), and memory loss. The prevalence of AD increased from 1.87% in 1998 to 2.96% in 2010 with an annual percentage change (APC) of 4.08% (5.08% for males; 3.78% for females). After 2008, the prevalence pattern of AD leveled off. Over the same time period the prevalence of persistent mental disorders increased from 8.98% to 13.66%. Memory loss, codes for which were first introduced in October 2003, quickly diffused over 2003–2005 and reached 5.05% in 2010. The prevalence of dementia due to senility did not exhibit changes with time. The time patterns of the top 11 diseases are shown in Supplementary Figure 2.

The results of the CI/ND joint analysis show that, as expected, three diseases identified in Figure 2 (i.e., AD, senile dementia, and dementia PMD) plus vascular dementia had the lowest average TICS scores (Figure 3). The results also show that the threshold cut-point of 8 was highly conservative as even the lowest disease-specific mean TICS score was above this level. For the 11 diseases with the largest prevalence (Table 2), we evaluated the time patterns of the fractions of individuals with severe CI. The results are shown in Supplementary Figure 3. For most NDs, the fractions of severe CI went down with time. This was consistent with our hypothesis that the expansion of the diagnosed pool would include less severe cases. Figure 4 displays the prevalences of CI and ND (p_{CI} and p_{ND}) and the relative frequencies of the two-way analysis f_{11} , f_{10} , and f_{01} . The calculations were performed for both definitions of CI (base and filled) with the TICS threshold estimated to have similar levels of CI and ND prevalence. The figure indicates (see second header line in each panel) that the trends in disease severity explained more than 60% of the differences between the trends of CI and ND (for filled dataset); the remaining 40% was explained by the trends in underdiagnosis. Comparisons of the results obtained using the base and filled data as well as the adjusted and unadjusted estimates showed that the estimates were stable.

Discussion

Recent studies reported a decline in CI [1–4] and increases in the prevalence of AD and other NDs [7–10]. Our study provides further support for these trends and identifies two major contributors behind the previously observed trends: reductions in disease severity explain more than 60% of the difference between CI and ND prevalence over the study

period and decreases in the fractions of undiagnosed individuals are responsible for the remaining 40%.

For over three decades AD has been the focus of epidemiologic studies and health forecasting in the U.S. and other industrialized countries. It has drawn interest due to: i) the additional future burden expected due to the growing size of the elderly population; ii) changes in the primary provision of AD care from institutional to community settings; and iii) new innovative methods of pharmacotherapy leading to revisions of AD management [23]. Since the mid-1980s multiple publications have referred to AD as an epidemic [24] and have forecasted dramatic increases in AD prevalence accompanied by severe CI. One study estimated that 43% of AD cases will need high levels of care—equivalent to that of a nursing home [25]—resulting in enormous costs of care with little chance that these costs can be reduced in the future. In contrast, recent studies show that populations born later have lower risks of dementia, probably because of higher education levels and better prevention of vascular diseases [26]. Dementia risk may be decreasing among older adults [26–28] due to secular decreases in cerebrovascular diseases [29] and better control of vascular-disease risk factors including smoking, hypertension, and high cholesterol; adverse trends in obesity and diabetes could have contributed to increases in dementia prevalence absent these other effects [28].

We demonstrated that differences in the CI and ND trends are related to decreased disease severity and decreased fractions of undiagnosed cases. The trends in ND severities are represented by the changes in two-way relative frequencies that measure the fractions of individuals with a specific ND diagnosis but without CI (calculated using a threshold cut-off point). Similarly, the fraction of undiagnosed individuals is given by the two-way relative frequency of individuals with CI but without a ND diagnosis. Both effects can be explained, in part, by improvements in diagnostic procedures and associated improvements in early diagnosis and diagnostic accuracy. In this case, observed trends of both disease severity and ascertainment would represent two distinct consequences of the same process: improvement in ND diagnostics. However, the observed trends in severity could potentially reflect improved care of AD/ADRD resulting in a reduction in the level of associated CI, while expanded diagnoses occur among all levels of severity. In this case the observed trends would reflect both positive and negative trends in health care. Although definitive conclusions regarding the underlying health-care-related causes of the observed trends in disease severity and ascertainment are not possible within the scope of this study, it is likely that recent changes in approaches to AD/ADRD diagnosis could explain our results.

The neuro-pathophysiological processes of AD/ADRD begin many years before the diagnosis is established, implying that the observed prevalence increases could be explained if earlier diagnoses were being established in later years. The 2011 National Institute on Aging-Alzheimer's Association (NIA-AA) workgroup summarized experience in dementia after previous diagnostic criteria originally developed in 1984 and proposed new criteria and guidelines for diagnosing AD [30–34] that define three stages of AD—preclinical AD, mild cognitive impairment (MCI) due to AD, and dementia due to AD—and incorporate biomarker tests [35]. These new criteria could result in earlier diagnoses of AD/ADRD, e.g., they suggest that in some cases, MCI is actually an early stage of AD or another dementia.

The diagnostic criteria for MCI revised in 2003 [36, 37] and in 2013 [38] made easier the identification of different types of MCI due to dementia and causes not related to dementia such as depression, anxiety, drug use, and other non-neurodegenerative disorders [38]. Published estimates of the incidence and prevalence of MCI are highly dependent on the specific criteria used for diagnostic classification [39], underscoring the importance of using comparable instrumentation for trend analysis. While we could meet this requirement using the TICS instrument with a fixed threshold for the CI trend analysis, the corresponding analyses of the Medicare diagnostic codes were impacted by changes in diagnostic practice for ND diseases that were beyond our control. Biomarker tests (e.g., for amyloid-beta accumulation, neuronal dysfunction, or neurodegeneration) also included in the new criteria and guidelines for AD are essential for identifying individuals at early stages as well [40]. Moreover, new diagnostic approaches such as the tests for blood-brain barrier leakage [41] and other innovations [42] may increase the proportion of diagnoses of early AD among patients both before and after onset of MCI.

An alternative explanation of our findings is the possible impact of CI-reducing therapy. If this is the case, then the proportion of less severe cases of AD/ADRD would accumulate over time. However, numerous strategies for pharmacologic [43, 44] treatment of AD have been shown to be of limited effectiveness in reducing cognitive impairment in AD/ADRD patients. Although some innovative non-pharmacological therapies [45–47] may improve or stabilize cognitive function, performance of daily activities, behavior, mood, and quality of life in patients with AD, the current consensus is that non-pharmacologic therapies (as well as pharmacologic therapies) do not slow or stop the damage and destruction of neurons that cause Alzheimer's symptoms and make the disease fatal [48]. At least for now treatment of AD is not a factor for reducing severity of ND although it can improve survival thus influencing ND severity through increasing the fraction of patients with severe CI. A detailed evaluation of the prevalence time trends in terms of the relative contributions of incidence and mortality trends is possible based on further updates of a recently-developed partitioning approach [49, 50].

Our study can help in developing more realistic forecasts of the prevalence of CI, AD, and other NDs in the U.S. The major challenge for the future is to develop new strategies for AD diagnosis, treatment, and care, targeting patients at a high risk of institutional placement. A specific focus on these high-risk patients and evaluation of their CI severity could lead to more effective management of the disease, and possibly to lower overall costs.

ND-specific analyses showed that NDs are a heterogeneous group of health disorders. In addition to different pathogenesis and prognoses, NDs can differ substantially with respect to the associated rates of *severe* CI: AD, vascular, and PMD dementias are associated with relatively high proportions of *severe* CI (70–80%) while other forms (e.g., dementia due to alcohol use) are more uniformly distributed between the *severe* and *non-severe* levels of impairment. We believe the most likely explanation for these trends is improvements in ascertainment due to the availability of more effective diagnostic procedures. The increases in the time-trends for AD and other NDs are suggestive of an under-diagnosis of these conditions in the past, especially at earlier stages of disease which are characterized by lower severity of CI, i.e., previously undiagnosed/misdiagnosed cases are now more likely to

be identified (increasing ND prevalence in the general population) at an earlier stage of the disorder (decreasing CI prevalence among ND patients). The very same diagnostic enhancements contributed to changes in coding patterns as new codes designed to reflect improved knowledge of ND pathology were introduced, which in turn, affected ND trends when these were based on records obtained from administrative health claim sources. For example, *memory loss* did not appear until 2004, after which the use of the code diffused rapidly (Figure 2). Another example is “senile dementia” which is no longer recommended for use as diagnosis [6]; even so, the use of this diagnosis code is widespread and has seen only a minor decline. Finally, improved diagnostic procedures also affected ND prevalence rates through the phenomenon of mixed dementia. Modern diagnosis quality is increasingly able to identify symptoms of multiple NDs in a single individual [6]. This pushes up the prevalence of the individual NDs involved as well as aggregate estimates that fail to account for the joint effects of multiple NDs.

Our study identified important limitations in the use of strict threshold methods for deriving cognitive evaluations of dementia [2]. The results presented in Figure 3 show that estimates of dementia prevalence based on data derived from the survey instrument/threshold approach could have poor sensitivity and specificity when applied to the Medicare population: less than 50% of cases are correctly predicted for models of ND (i.e., $f_{11} = 0.5p_{ND}$) and CI (i.e., $f_{11} = 0.5p_{CI}$). The results presented in Figure 1 demonstrate strong sensitivity of the estimated trend of CI to the value of the threshold, especially at very low levels of TICS consistent with more severe CI. Because the distribution of TICS (Supplementary Figure 4) does not have any modes in the range of candidate thresholds (e.g., 4–13) but rapidly increases instead, the estimates of CI prevalence based on any given threshold may be unstable. Moreover, the area with TICS 5–11 shrunk with time, but the respective cases moved not only to higher TICS (a highly positive tendency) but also to lower TICS (as follows from Figure 1), i.e., the fraction of patients with more severe CI increased. Such nonlinear dynamics indicate that conclusions based on any single threshold cut-point value concerning the annual percent change may not be generalizable to the population in question.

In sum, the underlying reasons behind divergent trends in CI and ND are largely positive and associated with success in the health care system over the study period 1998–2010. The severity of diagnosed cases and the fraction of undiagnosed individuals both decreased during these years. This is likely due, in part, to improvements in the ascertainment of NDs. This suggests that recent forecasts of CI and ND trends in the U.S. may be overly pessimistic.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Annual percent change (APC) of age-adjusted indicators $I(T < T_{thr})$ of low TICS scores using values for the TICS threshold cut-point (T_{thr}) in the range 2–27.

Figure 2. Time trends of age-adjusted prevalence for selected diseases from the memory disease group. Each point represents ND prevalence at the mean date of the interview of a specific wave of HRS data.

Figure 3.

Mean values and error bars for standard errors of TICS scores for individuals with any of 20 diseases. Closed and open dots correspond to original measurements (i.e., without proxy respondents) and filled (with imputed data) data, respectively. The first two columns in the right side of this figure show the number of measurements of TICS for individuals with a given disease for the filled (column 1) and base (column 1) datasets. The differences between them are the number of proxy respondents. The next three columns show the fractions of proxy respondents with 1+, 2+, and 3+ negative responses.

Figure 4.

Age-adjusted prevalence of CI (open dots) and ND (closed dots) (p_{CI} and p_{ND}) and the relative frequencies of the two-way analysis f_{11} (thin solid), f_{10} (dashed), and f_{01} (thick solid). The second header line in each panel shows the type of CI imputation (Base or Filled), the threshold used, and the percent explained difference between CI and ND trends calculated, respectively, without and with additional adjustments for sex and education. NA for senile dementia means that the difference between CI and ND prevalence was not significant.

Table 1.

Memory-loss/cognitive impairment-related diseases selected for our study (with respective ICD-9-CM codes).

Disease	Description	ICD-9-CM
Alzheimer's Disease	Alzheimer's disease	331.0
Hepatolenticular Degeneration	Hepatolenticular degeneration	275.1
Dementia (Senile)	Dementia due to senility, including confusional state or delirium superimposed on senile dementia (290.3)	290.0–290.3
Vascular Dementia	Dementia due to arteriosclerosis (vascular dementia)	290.40–290.43
Dementia (Alcohol)	Dementia due to alcohol, including alcoholic encephalopathy (291.2)	291.0–291.9
Dementia (Drugs)	Dementia due to drugs	292.82
Transient Psychotic Conditions	Transient organic psychotic conditions	293.0–293.9
Dementia PMD	Persistent mental disorders due to conditions classified elsewhere: includes organic psychotic brain syndromes (chronic), not elsewhere classified	294
Non-psychotic Mental Disorders	Specific nonpsychotic mental disorders following organic brain damage, including senility with mental changes of nonpsychotic severity, mild memory disturbance due to organic brain damage (310.1) and other specified mild memory disturbance (310.8)	310.0–310.9
Cerebral Degeneration, Excluding AD	Other (and other than AD) cerebral degenerations, including frontotemporal dementia (331.1), senile degeneration of brain (331.2), communicating hydrocephalus (331.3), idiopathic normal pressure hydrocephalus (331.5), cerebral degeneration in diseases classified elsewhere (331.7), other cerebral degeneration (331.8), Reye's syndrome (331.81), dementia with Lewy bodies (331.82), mild cognitive impairment, so stated (331.83), and cerebral degeneration, unspecified (331.9).	331.1–331.9
Other Demyelinating Diseases	Other demyelinating diseases of central nervous system	341.0–341.9
Encephalopathy (Not Elsewhere Classified)	Encephalopathy, not elsewhere classified including Encephalopathy, unspecified (348.30), metabolic encephalopathy (348.31), other encephalopathy (348.39)	348.3
Toxic Metabolic Encephalopathy	Toxic metabolic encephalopathy	349.82
Hypertensive Encephalopathy	Hypertensive encephalopathy (437.2), transient global amnesia (437.7)	437.2, 437.7
Cognitive Deficits (Late Effects)	Cognitive deficits following (late effects of) cerebral hemorrhage or infarction (438.0), unspecified late effects of cerebrovascular disease (438.9), other late effects of cerebrovascular disease (438.89)	438.0, 438.9, 438.89
Hepatic Encephalopathy	Hepatic encephalopathy	572.2
Memory Loss/Amnesia	Memory loss: amnesia (retrograde); memory loss NOS (780.93), altered mental status (780.97)	780.93, 780.97
Neurologic Neglect Syndrome	Neurologic neglect syndrome	781.8
Senility NOS	Senility NOS	797
Cognitive Disorder due to Injury	Cognitive impairment due to intracranial or head injury (850–854, 959.01), cognitive impairment due to late effect of intracranial injury (907.0)	850–854, 959.01, 907.0
Jakob-Creutzfeldt Disease	Jakob-Creutzfeldt disease	046.1

Table 2.

Characteristics of HRS study population by wave

Variable	1998	2000	2002	2004	2006	2008	2010	OR	p-value
Number of Selected Individuals	8857	8416	8789	8956	8923	8000	7148		
Available TICS	7774	7318	7662	8027	8253	7411	6511		
TICS from proxy	1083	1098	1127	929	670	589	637	0.900	<.0001
TICS: 0–6	119	71	79	98	135	95	65	0.992	0.6846
TICS: 7–11	335	302	291	307	311	257	273	0.982	0.1150
Age: 65–74	4534	4312	4596	4769	4780	4127	3354	0.987	0.0024
Age: 75–84	3187	2951	3012	2954	2870	2639	2640	0.992	0.0695
Age: 85–94	1055	1072	1085	1128	1170	1128	1050	1.037	<.0001
Age: 95+	81	81	96	105	103	106	104	1.078	0.0001
Nursing Home Residents	579	574	677	641	685	643	684	1.059	<.0001
HMO coverage (7–11 months)	243	193	123	111	197	167	134	0.958	0.0042
Alzheimer's Disease	172	198	247	286	303	286	245	1.101	<.0001
All Neurocognitive Disorders	818	808	941	1026	1062	1126	1087	1.101	<.0001
Hepatolenticular Degeneration	0	1	0	0	0	1	3	1.840	0.0541
Dementia (Senile)	262	224	245	253	243	227	213	1.003	0.7867
Vascular Dementia	62	65	82	93	81	82	60	1.040	0.0782
Dementia (Alcohol)	12	3	8	11	14	14	10	1.112	0.0812
Dementia (Drugs)	0	0	0	0	0	0	0		
Transient Psychotic Conditions	82	68	98	81	100	114	87	1.074	0.0005
Dementia PMD	255	266	345	393	423	426	430	1.135	<.0001
Non-psychotic Mental Disorders	72	51	61	56	56	35	37	0.927	0.0049
Cerebral Degeneration, Excluding AD	170	158	185	218	234	236	205	1.089	<.0001
Demyelinating Diseases, Other	11	6	3	5	3	5	3	0.846	0.0587
Encephalopathy (Not Elsewhere Classified)	38	44	42	54	59	52	77	1.144	<.0001
Toxic Metabolic Encephalopathy	10	8	7	8	15	11	16	1.148	0.0211
Hypertensive Encephalopathy	14	13	13	9	16	13	10	0.999	0.9859
Cognitive Deficits (Late Effects)	106	121	141	143	128	141	142	1.067	0.0001
Hepatic Encephalopathy	3	5	4	4	3	4	7	1.110	0.2670
Memory Loss/Amnesia	0	0	1	71	137	340	397	2.273	<.0001
Neurologic Neglect Syndrome	1	2	5	2	0	4	2	1.060	0.6485
Senility NOS	23	21	18	26	14	18	20	0.990	0.8224
Cognitive Disorder due to Injury	117	120	139	165	186	189	202	1.141	<.0001
Jakob-Creutzfeldt Disease	0	0	0	0	0	0	0		