Situated Prevention: Framing the "New Dementia"

Annette Leibing

In the early 1980s, biographies and autobiographies from U.S. authors about living with dementia often depicted the dramatic search for a diagnosis,[1] at a period of time when Alzheimer's disease was only starting to become better known to the general population — even among some doctors.[2] During the 1990s — declared the "decade of the brain" by former president George Bush — this changed, and a greater awareness regarding the first signs of dementia resulted in much earlier diagnoses. In some contexts this resulted in what Adelman[3] called the "Alzheimerization of aging": a concentration of resources going to research about Alzheimer's disease to the detriment of other aging-related issues. This was increasingly paired with a hyper-vigilance among aging individuals, leading to a general anxiety regarding signs of forgetfulness.[4] However, interventions generally only began when symptoms interfered with daily life, and the whole idea of prevention remained absent from public discourses on dementia, except for rather ambiguous ideas about "brain training" in the later years (e.g., learning languages and doing crossword puzzles).

What I want to call here the "new dementia" consists mainly of two recent and profound epistemological changes.[5] 1. Current research agendas show a major effort to develop means for reliable, early, ideally presymptomatic detection (through biomarkers such as found in the cerebrospinal fluid and through brain scans) or of detecting very early symptoms, therefore placing a lot more importance on mild cognitive impairment (MCI) than in the past.[6] Some also argue that first noticeable changes should be called Mild Behavioral Impairment (MBI),[7] since slight behavioral alterations seem to precede cognitive impairment — both extremely imprecise signs of change observed usually in the elderly, though sometimes in younger individuals as well. The category "mild cognitive impairment" that has existed at least since the 1960s[8] refers to the observation that initial complaints of memory loss may or may not develop into a dementia. Now, however, MCI is becoming increasingly part of the general dementia syndrome, although this perception is contested and context-dependent on (see below).

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2. The focus of this article will be on the second change, although it often cannot be separated from the first point. Until recently dementia was understood by the general public in many countries as a mixture of destiny and family history,[9] and the afore-mentioned recommendation of "brain training" almost the only preventive practice aging people and health professionals were aware of.[10] Now, however — and similar to arguments made regarding other syndromes (e.g., Parkinson's disease, schizophrenia) — researchers argue that interventions for Alzheimer's patients happen far too late, a point that is also commonly made in explaining the need for early detection. A common argument today and widely propagated by media internationally, is that "[o]nce someone has dementia there is already an advanced stage of brain degeneration. It takes an estimated 10 to 20 years for dementia to become obvious (…). But if we can identify people in this pre-symptomatic phase, (…) we may be able to treat them with drugs and recommend lifestyle changes that delay or even stop the disease's progression."[11]

In the following pages these recent changes will be briefly discussed, followed by the central argument of this article, namely that what I call "the new dementia," and especially the aspect of prevention, needs to be "situated." My claim is that paying more attention to a critical contextualization of prevention will lead to a more nuanced analysis of recent changes in dementia research and to a greater awareness of what is at stake for aging individuals.

The New Dementia

Starting more or less in 2007,[12] changes in the conceptualization of dementia have resulted in (a) an intense and contested search for predictive biomarkers in a pre-clinical phase — often targeting individuals in their 40s or even earlier; (b) the study of very first signs — the greater emphasis on Mild Cognitive Impairment already mentioned — and finally, (c) the insight that the prevention of dementia is possible. One reason for these conceptual changes springs from the need to explore new avenues of treatment after the continued failure of drug trials and the limited effect of currently existing specific medications for dementia.[13] A 2012 study by the Pharmaceutical Research and Manufacturers of America (PhRMA) showed that in the 13 previous years, 101 Alzheimer's drugs failed in testing and so would not reach the market.[14] As I have argued elsewhere,[15] early detection and preventive measures — a "critical turning point in the history of the field"[16] — were not only related to the growing insight that current specific dementia medications were inefficient (with sometimes severe side effects), but that, in effect, dementia, especially in very old age, is tied up with the overall breakdown of the aging organism, rather than a neatly isolated, specific disease. As Richards and Brayne had already argued in 2005,[17] "It is timely to interrogate the term Alzheimer's Disease. In older age groups, AD seems to be a diffuse clinical syndrome representing the gradual accumulation of multiple pathologies, arising from multiple interlocking risk factors over the life course. The term Alzheimer's syndrome seems more appropriate." And Molin and Rockwood[18] in their critical discussion of an early detection of dementia point out that "biomarkers' ability to distinguish normal subjects from AD patients lessens with age. The typical pattern of AD-related (…) brain changes seen in the young old (…) appears to be less salient in very old patients (…), despite similar levels of cognitive impairment." In other words, for older people it is the complexity and the accumulation of many co-existing conditions that seem to be strongly related to cognitive decline, something that is nearly impossible to cure or slow down with a single drug. It is among the affected younger old that the typical Alzheimer's pathology is more easily distinguishable from an aging process, something that would confirm Alois Alzheimer's description in 1907 of the early onset form of dementia as "peculiar" and different from the syndrome detected in older people — a point that has been debated ever since.[19]

Further, earlier studies showing a high correlation between first signs and a concomitant dementia among patients recruited from clinical settings were relativized by more recent research in community settings, in which early signs of forgetfulness developed less often into a dementia. These insights serve to question the usefulness of the category "Mild Cognitive Impairment" understood as an early phase of Alzheimer's syndrome. Finally, clinical trials testing substances which are supposed to clear the brain's most prominent biomarker, ß amyloids, has not lead to any improvement of dementia, showing that looking only at ß amyloids will probably not lead to a cure, something that is now well known and accepted, including by the pharmaceutical industry.[20] Recent headlines concerning the Pharma company Pfizer announcing its desisting from research on dementia, is but one sign of the difficulty of targeting a complex condition like Alzheimer's disease (as well as other kinds of dementia), and especially the hope for a blockbuster drug.

Related to the idea of early detection and intervention is the growing awareness that prevention of dementia might be possible: One third of cases could be prevented, mostly through lifestyle interventions, suggests a recent *Lancet* commission,[21] though oth-

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ers are skeptical about making such direct links.[22] In other words, often-heard public health recommendations, easily merged with ideas regarding active and successful aging — for instance, avoiding sedentarism, smoking, and unhealthy food — are now also applicable to dementia:

> [L]arge cohort studies have implicated multiple health factors that may increase the risk for developing cognitive decline and dementia thought to be caused by AD. (. . .) In particular, vascular risk factors such as hypertension, hypercholesterolemia, and diabetes have been associated with an increased risk of dementia.[23]

Cardiovascular risk factors have previously been linked to *vascular dementia* (due to mini strokes), although even in this case, until recently, prevention was not explicitly a major public health issue. Now, however, the once separate categories "vascular dementia" and "Alzheimer's disease" are increasingly perceived as merging with regard to aetiology and common risk factors.[24] The link between Alzheimer's disease and cardiovascular risk factors has been known at least since the beginning of the 1990s, but was widely ignored, largely because Tacrine, the first dementia-specific medication arrived on the market in 1993[25] and a blockbuster drug approach tended to be privileged over a more complex explanatory pathway.

The recent reconfiguration of the conception of dementia as preventable is gaining currency circulating internationally, and with it the recommendation to manage risk factors such as diabetes, depression, hypertension, smoking, poor diet, hearing loss in middle age, air pollution, as well as ongoing education and cognitive stimulation. However, prevention is not an unproblematic or straightforward concept, hence my claim that prevention needs to be contextualized — that more attention needs to be paid to "situated prevention."

Short Overview of Prevention as a Sociological Object

It is a commonplace and widely propagated notion these days that prevention should be seen as an investment in one's health, which at the same time lowers costs of health care systems increasingly solicited by the aging baby boomers. Social scientists have frequently criticized this kind of reasoning as neo-liberal and paternalistic, which has the effect of shifting blame for healthcare costs onto those who do not adhere to public health recommendations.

Much has been written about prevention by social scientists, so that here only a short overview of arguments will be provided.[26] Scholars have shown, for example, that preventive measures — those that are at the heart of public health campaigns — can be understood as a biomedicalization of the life course[27] with regard to a "new public health."[28] Keywords in critical prevention discussions are, among others, healthism, the normalization of the body, responsibilization, and risk management.[29] Related to this is the important critique that neoliberal ideologies are transforming public responsibilities and structural factors into private concerns[30] or, as Mayes[31] recently observed regarding obesity, "a focus on the individual is ethically questionable, ineffective and ignores relevant research that suggests systemic factors, not individual choices, are behind the epidemic." Aronowitz[32] further warns of the danger of conflation, when — as it well might well happen with "the new dementia" — being at risk is experienced as illness itself, leading to the possibility of years lived in anxiety, as well as stigma and unnecessary interventions.

I want to link the following reflections about the "new dementia" to existing discussions on prevention, lifestyle and public health[33] and, equally, to studies within the domain of a critical gerontology, especially

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Table 1

Clinical trials for the prevention of dementia currently found on ClinicalTrials.gov; light gray shade: trial in both U.S. and Europe; italics: allopathic drugs; underlined: plant-based drug

U.S.-American trials	Intervention	European trials	Intervention
Disease Prevention in Clinical Practice Base on Patient Specific Physiology	Lifestyle modification	**Norway:** Anthocyanins as Dementia Prevention?	Plant-based medication
… Prevention of MCI and Eventual Alzheimer's Disease Using F18 Futemetamol	*2 drugs (anti-depressants) and placebo*	**France, Italy, Netherlands, Spain, Sweden, Switzerland, United Kingdom:** European Prevention of Alzheimer's Dementia (EPAD) Longitudinal Cohort Study (LCS)	*Personalized drugs or multiple drugs in development*
GeneMatch: A Program of the Alzheimer's Prevention Registry to Match Individuals to Studies Based on APOE Genotype	Get a pool of individuals for future preventive clinical trials (*first study using the pool sponsored by Novartis*)	**Germany:** Physical Activity and Cerebral Metabolism in the Elderly: a Randomised Controlled Trial	Aerobic training
Gray Matters: Multi-domain Lifestyle Behavioral AD Prevention RCT	Health education program — lifestyle	**Ireland, UK**: idem	idem
Alzheimer's Prevention Registry: A Program to Accelerate Enrollment into Studies	none	**Switzerland:** Move for Your Mind – Pilot Trial	Exercise, Vitamin D
Early Detection and Prevention of MCI	Behavioral: Heart Health Intervention	**Italy:** Physical Exercise for Prevention of Dementia	Exercise
Exercise in Asymptomatic Pre-Alzheimer's Disease Pilot Study	Aerobic	**Denmark:** Patient Participation in Prevention of Loss of Functions	Behavioral — lifestyle
Follow-up Study of the AD Anti-Inflammatory Prevention Trial	*2 nonsteroidal anti-inflammatory drugs* (no prevention found); further observation of enrolled individuals	**Germany**: Effect of Cognitive Intervention in AD on Functional Cortical Networks in fMRI	Behavioral — cognitive training (tertiary prevention)
Prevention of AD by Vitamin E and Selenium (PREADVISE)	Alphatocopherol and Selenium	**Germany**: Neuro-Prevention INVADE-2 (follow-up)	Standardized cranial MRIs (detection of mini strokes and bleedings)
Prevention of Cognitive Decline in AD by Ingested Interferon Alpha	*Aricept and IFN-alpha2A*		
Gingko Biloba Prevention Trial in Older Individuals	Gingko Biloba		
AD Anti-Inflammatory Prevention Trial (ADAPT)	*Aleve and Celebrex*		
AD Prevention Trial	*Estrogen and Progesterone*		

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to what Stephen Katz[34] has called "lifestyle in social context." Recommendations in public health campaigns concerning both successful aging[35] and the prevention of dementia target individuals making responsible choices, which, as Katz writes, should take into account how "the recent individualistic story of lifestyle, the one that leads to improving or lengthening lifespan, [...] positions lifestyle in the myriad of life chances, status hierarchies and social contexts."[36]

Situated Prevention

Situatedness emphasizes the context-dependency of a phenomenon — here, prevention. As defined by Chandler and Munday,[37] situatedness relates to

> [t]he dependence of meaning (and/or identity) on the specifics of particular sociohistorical, geographical, and cultural contexts, social and power relations, and philosophical and ideological frameworks, within which the multiple perspectives of social actors are dynamically constructed, negotiated, and contested.

One aspect of Donna Haraway's well-known reflections on situated knowledge[38] is especially relevant to this article, namely her claim that situatedness does not mean relativism, but responsibility regarding multiple existing kinds of knowledge. In other words, it makes a difference which of the many existing or possible (moral) narratives are being privileged when talking about the prevention of dementia.

Situatedness can be studied on different levels. In this article, an analysis comparing major prevention initiatives in North America (especially in the U.S.) and in Northern Europe will be emphasized. There are differences that can be observed between nations or, more precisely, between different epistemic cultures[39] — that is, "glocal" scientific models and traditions and their translations into concrete recommendations and ways of living. The following differences, detected when comparing North-American and European preventive initiatives might initiate a discussion about how the conceptualization of prevention and its concomitant recommendations can have an impact on the way individuals age.

Methods Overview

Relying on the author's earlier studies on epistemological changes in dementia research, the general context of this article has been conceptualized.[40] Recent national and transnational major research initiatives (clinical trials) in Europe and North America targeting prevention of dementia (studies that were often conceived in combination with an early detection) were then listed, and the general objectives of these initiatives studied. The main source was the site ClincalTrials.gov (n=22 relevant trials in North America and Europe) and related sites that provided additional information regarding the listed trials. The websites of different Alzheimer Societies/Associations — arguably the most influential sources for those worrying about dementia — were studied in order to see which prevention trials were discussed on those sites, as well as explicit recommendations posted for their readers (the U.S. Alzheimer's Association, Alzheimer Society Canada, and Alzheimer Europe and its sub-sections). Although Alzheimer's Society and Associations were more often a direct source of information in the U.S. when compared with Europe,[41] other informational material in Europe (newspaper articles, community groups, etc.) rely on them in order to inform their readers and members.

A summative content analysis[42] provides a first reflection on the discovered differences and their possible impact on older individuals and societies at large, although further (ideally longitudinal) studies are needed in order to determine how explicit and implicit recommendations from those prevention studies are being concretely incorporated into people's everyday lives and transformed into health and social policies in different countries.

Prevention Studies in Europe and in North America

Studying recent European and U.S. clinical trial initiatives found on the site *ClinicalTrials.gov*, it appears at first sight that the objectives and study designs of preventive interventions are similar: Recommendations of lifestyle changes and pharmaceutical interventions can be found on both continents. However, in Europe, only the EPEAD study is testing allopathic drug interventions. "As yet, there is no preventative or curative treatment for Alzheimer's disease," one reads on the Alzheimer Europe website, while a major initiative funded by them — The European Collaboration on Dementia — targets lifestyle changes as the future treatment options.

On both continents early detection and early intervention is recommended. After a survey conducted in 2011 by the Harvard School of Public Health and Alzheimer Europe in the U.S. and four European countries, a "great public desire to seek early diagnosis of Alzheimer's" emerged.[43] This result indicates that the recent turn towards a "new dementia" has reached, at least partly, the general public on both continents. Financed by Bayer Pharmaceuticals, this survey was conceived in order to see whether individuals in those five countries were interested in early testing (67%

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Table 2

U.S. American and European major intervention trials with the objective of preventing dementia

North America		Europe	
Trial name	Intervention/objective	Trial name	Intervention/objective
A4 trial (Anti-Amyloid Treatment in Asymptomatic Alzheimer's) *One drug*	… whether an anti-amyloid antibody can slow memory loss caused by Alzheimer's disease.	**FINGER (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability)** Lifestyle/ cardiovascular	A 2-year multidomain intervention including *nutritional guidance, physical activity, cognitive training, increased social activity, and intensive monitoring and management of metabolic and vascular risk factors.*
LEARN (Longitudinal Evaluation of Amyloid Risk and Neurodegeneration) ß amyloid development	… evaluate the rate of cognitive change in approximately 500 clinically normal older individuals who "screen-fail" for the A4 trial on the basis of their screening PET imaging not demonstrating evidence of elevated amyloid accumulation … but meet all other A4 study eligibility criteria.	**EPAD (European Prevention of AD)** *Several drugs*	The project will select around 1 500 people from this EPAD cohort to take part in early stage "adaptive" clinical trials of *drugs designed to prevent Alzheimer's dementia.*
API (Alzheimer's Prevention Initiative) Several sub-studies; e.g.: **Autosomal Dominant Alzheimer's Disease (ADAD) Trial** *One drug* **API Generation Study** *Two drugs*	To identify *pre-symptomatic treatments or interventions* that will postpone, slow or prevent the disease's progression. … members of an extended family in Colombia. Many share a rare genetic mutation that typically triggers Alzheimer's symptoms around age 45. The trial focuses on whether an *"anti-amyloid" antibody treatment called crenezumab* can stave off Alzheimer's disease. This study focuses on whether *two investigational drugs* – an active immunotherapy (CAD106) and a BACE (beta-secretase 1) inhibitor (CNP520) – can prevent or delay the onset of Alzheimer's symptoms.	**PREVENT Dementia study** Lifestyle/ cardiovascular	U.K. study: research focuses on people in middle age to identify biological and psychological factors which may increase the risk of dementia in later life. Once identified, we would like to select those people at high risk and intervene in this process. These interventions might be *lifestyle changes or measures to affect the risk of an individual developing* dementia.
DIAN (Dominantly Inherited Alzheimer Network) (international sites) *Changes before first symptoms*	…to study changes in people who carry an Alzheimer's disease mutation to determine *how the disease process develops before there are any symptoms.*	**CAIDE (Cardiovascular Risk Factors, Aging and Incidence of Dementia)** *Cardiovascular/ lifestyle*	Finnish study: the purpose is to investigate the *connection between social, lifestyle, and cardiovascular risk factors* and cognition, dementia, and structural changes in the brain.

Table 2 continued on page 710

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Table 2 *(continued)*

U.S. American and European major intervention trials with the objective of preventing dementia

North America		**Europe**	
Trial name	Intervention/objective	Trial name	Intervention/objective
TOMORROW Trial *One drug*	3,500 asymptomatic individuals, some of whom have the Alzheimer's risk gene (APOE-e4) or the TOMM40 risk gene. The trial will explore whether the *anti-diabetes drug pioglitazone can prevent mild cognitive impairment* due to Alzheimer's disease.	**EDPI (European Dementia Prevention Initiative)** Sub-project **EU–HATICE (Healthy Ageing Through Internet Counselling in the Elderly)** *Cardiovascular risk factors*	Initiative linked to FINGER, MAPT, and PreDIVA for a stronger int'l collaboration. 1. An internet intervention platform to optimize treatment of *cardiovascular disease in the elderly;* 2. Test this new intervention to investigate whether new cardiovascular disease and cognitive decline can be prevented.
IDRP (Institute for Dementia Research and Prevention) *Early detection*	…a platform for the collection of data which identify the most important risk factors …, *elucidate novel targets for the design of new therapeutic interventions, and develop new test* for more effective detection and monitoring the earliest stages of dementia.	**MAPT (Multidomain Alzheimer Preventive Trial)** *Cardiovascular risk factors/lifestyle*	A French 3-year multicenter RCT evaluating the efficacy of isolated supplementation with ω-3 fatty acid, isolated multidomain intervention, or their combination in the prevention of cognitive decline in frail individuals who are at least 70 years old. *Also group training sessions (physical exercise, cognitive training, and nutritional advice) and yearly personalized preventive consultations* that aim to identify dementia and frailty risk factors *(vascular risk factors, nutritional problems, sensory deficits, mood disorders, and walking difficulties).*
EMERGE (also in Europe) *Drug*	To evaluate the efficacy and safety of Aducanumab (BIIB037) in subjects with early Alzheimer's disease (Phase 3). Also European countries, sponsored by U.S. company (Biogen).	**PreDIVA (Prevention of dementia by intensive vascular care)** *Cardiovascular risk factors/lifestyle*	A Dutch 6-year long multicenter RCT comparing *standard and intensive care of cardiovascular risk factors in preventing dementia* **a**nd disability in older people: a multi-component intensive vascular care addresses *hypertension, hypercholesterolemia, smoking habits, excessive weight, physical inactivity, and diabetes mellitus*, which are strictly controlled with medication and lifestyle interventions.

were interested). This high degree of interest needs to be seen in conjunction with high expectations regarding currently available medications as effective in slowing down the progression of AD, especially in Poland (63%) and the U.S. (47%), while the other European countries score lower in this regard.

Both the U.S. and E.U. Alzheimer Societies describe currently available medications as having only a temporary effect for some patients, and make clear that some risk factors (age, gender, genetics) cannot be changed, but suggest there are modifiable risk factors that have an influence on the epidemiology (and epigenetics) of dementia. On the U.S. website, hope exists

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that in the future, drugs will be developed that address the complexity of the dementia syndrome: "many of the new drugs in development aim to modify the disease process itself, by impacting one or more of the many wide-ranging brain changes that Alzheimer's causes. (…) Many researchers believe successful treatment will eventually involve a 'cocktail' of medications aimed at several targets, similar to current state-of-the-art treatments for many cancers and AIDS."[44] Although lifestyle factors are mentioned, prevention trials are clearly described as Pharma-based interventions, and larger trials are then listed, which cannot be found on the ClinicalTrials.gov website, but that have been strongly mediatized in the last years.

When looking at those larger, transnational and relatively well mediatized clinical trials, differences between Europe and the U.S. become more clear-cut.

Discussion

All in all, a tendency exists in which prevention in the North American context — though this may be less accentuated in Canada[45] — is described as primarily emphasizing drug interventions, while in Europe lifestyle changes are more in the foreground. As an example:

> The participants [from the U.S.] receive solanezumab, an antibody-based drug that aims to reduce brain amyloid-beta, which recently failed to improve mild Alzheimer's dementia. Despite the failure, researchers speculate the drug may be effective in preventing dementia in people who have amyloid-beta aggregates in the brain.[46]

The PREVENT study, based in the U.K., is an example of how the same problem (early detection and prevention) is described as being achieved primarily through lifestyle-related changes:

> Recent research suggests changes in the brain may precede symptoms of Alzheimer's disease by many years. (…) Our research (…) focuses on people in middle age to identify biological and psychological factors which may increase the risk of dementia in later life. Once we have identified which factors are changing we would like to select those people at high risk and intervene in this process. These interventions might be lifestyle changes or measures to affect the risk of an individual developing dementia.[47]

The North American dementia models rely more often on brain-based biomarkers compared to European studies, while the latter seem to privilege the heart-head connection ("what is good for your heart is good for your brain") as the central model framing preventive interventions, although, as Anstey and Peters[48] argue, the heart-head connection is often communicated in an oversimplified way and, therefore, is sometimes as reductionist as some proposed drug interventions.[49] Also the use of medications in the first case is based on a logic of biomarkers generally found in tissues and body fluids made visible (regarding different kinds of biomarkers), while in the European context medications are being used primarily in order to improve concomitant health conditions (diabetes, hypertension, etc.) conceived as risk factors — two different kinds or levels of biomarkers and medication use.[50]

This difference is especially relevant today, a time in which health and illness are increasingly being conceived using a future-oriented process Metzler calls "biomarkerization."[51] One of the consequences of this process is the blurring of previously existing boundaries between health and illness, and more inclusive thinking regarding presymptomatic individuals who easily become presymptomatic patients. And although brain-based biomarkers are often indeterminate — as is the case with those linked to Alzheimer's disease — their central feature, that of being a sign and therefore suggesting concreteness and certainty, can transform a single person, or even whole groups, into individuals who are apparently at greater risk of contracting or already having the disease. As Baker[52] convincingly showed, the great interest in research on biomarkers is directly linked to the desire for more cost-effective and quicker drug development — see, for example, the current large patient register initiatives for prevention trials.

However, the differences detected between European and North American prevention studies are not as clear-cut as they might seem at first sight. First, many of the trials based in Europe also include samples from North America, and vice-versa (e.g., the EMERGE study is also taking place in several European countries). Furthermore, major joint initiatives, dominated by the pharmaceutical industry, have been sharing forces in order to reduce the costs of clinical trials, speed up the time of recruitment, and standardize procedures across sites, making it difficult to separate results of these studies from commercial interests.[53] As an example, the U.K.-based Dementia Discovery Fund (see http://www.theddfund.com/) works with researchers from around the world and is clearly drug-focused: "Our goal is to invest over $200m over fifteen years to support the creation of novel disease-modifying drugs for dementia," it reads on their website, of an initiative that is sponsored by "[t]he Department of Health, the charity Alzheimer's Research UK and (…)

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six pharmaceutical firms [that] have raised $100m (£65m) to invest in early-stage, novel treatments for (…) dementia (…) [T]he company is joined by the US drugmakers Johnson & Johnson, Biogen, Eli Lilly and Pfizer, and Japan's Takeda."[54]

The international, U.S.-based Global Alzheimer Platform[55] has a similar objective: "the GAP Foundation is joining together leading academic researchers, pharmaceutical companies, nonprofit organizations and foundations, and governments around the world to reduce the time, cost and risk of Alzheimer's clinical trials, in order to speed innovative medicines to those with or at risk of Alzheimer's disease." This initiative is associated with the European EDPI study (see table 2).

Future studies, including social science research, will need to pay attention to whether over time Americans begin to get a different message than Europeans about approaches to preventing Alzheimer's, how the "new dementia," including the reading of biomarkers, will influence local health policies, and whether any of this will have specific impacts on aging individuals' attitudes toward themselves and others. Although it is not clear how exactly risk for dementia should be managed, what is apparent is that individualized attitudes are not enough.

It might be though that the international initiatives (here: those targeting European *and* U.S. publics) influence or even render irrelevant the differences detected between the American and European prevention studies. Molin and Rockwood[56] believe that the turn toward integrating pre-clinical phases into the dementia syndrome itself will continue to be more important in North American, with the result that these differences will persist. European researchers also are more sceptical of the concept of Mild Cognitive Impairment than their American counterparts,[57] which means that some forgetfulness is treated as a normal part of aging and so, is less likely to be pathologized.

A significant factor explaining these differences is the media, an important vehicle of knowledge transmission. In the U.S., historically the media has become more closely related to interest groups and is less controlled by the state than in Europe.[58] Additionally, and related to the previous point, pharmaceutical products may be advertised in the U.S., but generally not in Europe, which suggests that it is easier for U.S. companies to transmit desired messages — and the underlying scientific models — to clients, prescribing doctors, and policy makers as compared to Europe.[59] Furthermore, as Hunt, Kreiner and Brody[60] showed for the U.S., national guidelines that instruct and guide the majority of prescribing clinicians are often heavily influenced by the pharmaceutical industry, in many cases resulting in "polypharmacy": the prescription of more drugs to moderate the effects of already-prescribed medications.

Although the differences between European and American media and Pharma practices are not new — and, in fact, well-known ideas — the point here is that facts regarding the "new dementia" are generally being propagated as if they were universal facts and situational differences are rarely taken into account.

For instance, since most dementia risk factors are correlated with socioeconomic status, management of them is dependent on access, for those at risk, to certain resources, so the prevention of dementia becomes in part a political discussion about living conditions in different societies. Or, as Strighini et al.[61] recently recommended in a *Lancet* article, "socioeconomic adversity should be included as a modifiable risk factor in local and global health strategies, policies, and health-risk surveillance."

Another point to consider is that in some regions of the world (generally, parts of richer nations) dementia prevalence and incidence rates are declining, for instance in the U.S.,[62] Holland,[63] Sweden,[64] and England.[65] These findings are creating some optimism — and the sense we might move "from muddled diagnosis to treatable mechanisms."[66] But they also show that preventive interventions are tightly linked to sociopolitical factors: The longitudinal multi-domain Dutch PreDiva study ("Prevention of dementia by intensive vascular care"), aimed at reducing cardiovascular risk factors through nurse-led interventions targeting individualized lifestyle changes and drug treatments for hypertension and diabetes, arrived at no significant result. Researchers think that this is due to the fact that in Holland people are already quite well taken care of, through good quality health care, with regard

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to the most important risk factors, and they suspect a major impact of the studied interventions would have been noticeable in contexts with a less efficient health care system. The study nevertheless showed some effect for people who had untreated hypertension at baseline.[67]

Researchers publishing in the two British journals *The Lancet* and *BMJ* that were involved in the "statin war" — also relevant to dementia research because of a possible preventive effect of statins on cardiovascular health — debated the usefulness of aggressive prescription of statins in the U.S. against its lower rate of prescription in Europe (where it tends to be combined with a greater emphasis on the "Mediterranean diet"). This is another example of a debate that shows that differences must not be merely acknowledged, but that, ideally, the origins of such differences, and their impacts on people's lives, need to be understood.[68]

Conclusion

Major scientific insights generally circulate internationally and key findings are taken to be universally valid. When comparing conceptions of the "new dementia" and actual preventive dementia trials in North America with those in Europe, the core arguments are the same: current interventions happen too late, and preventable risk factors play a role in the aetiology of the "new dementia" (although this might only hold true for a mixed dementia and not necessarily the "pure" form of Alzheimer's disease[69]). However, the translation of those core arguments into established facts happens in different ways, and this situatedness needs to be acknowledged in order to see that public health recommendations not only often ignore those factors that are linked to socio-political and economic issues, but also that they differ between sites. In sum, the central questions are whether different prescriptions will also have different impacts on the epidemiology of dementia and on what Nikolas Rose[70] called "somatic individuals" — the ever-increasing links being established between someone's biology and his or her conduct.

Future studies, including social science research, will need to pay attention to whether over time Americans begin to get a different message than Europeans about approaches to preventing Alzheimer's, how the "new dementia," including the reading of biomarkers, will influence local health policies, and whether any of this will have specific impacts on aging individuals' attitudes toward themselves and others. Although it is not clear how exactly risk for dementia should be managed, what is apparent is that individualized attitudes are not enough: many commonly recommended changes evoke state responsibilities (providing good education, better food for all, cleaner air etc.), while others are individual choices, modified by lifestyle changes or by drugs[71] (for an extensive discussion see note 71), although this simple division between the state and the individual's responsibility obscures many complicating factors. It remains problematic that much of what constitutes "lifestyle" is usually considered an individual choice, ignoring the role society plays in providing conditions for choice (e.g., parks in neighborhoods, good schooling).

It is important to disentangle the many co-existing narratives and see which are being privileged by whom, how early detection and prevention are being framed, whose interests the newer models serve, and what early detection means within a therapeutic landscape of uncertainty (e.g., until now biomarkers were not considered specific to dementia, and overlap with normal aging and other pathologies). The analytical category of "situated prevention" proposed here might contribute to a greater awareness regarding the framing of different factors involved in the "new dementia," since risk factors come to life within moral narratives.

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References

1. D. F. McGowin, *Living in the Labyrinth: A Personal Journey through the Maze of Alzheimer's Disease* (New York: Delacorte Press, 1993).
2. B. Reisberg, *A Guide to Alzheimer's Disease* (New York: The Free Press, 1981); J. Gubrium, *Oldtimers and Alzheimer's: The Descriptive Organization of Senility* (Greenwich: Jai Press, 1986). Note: In the following I will use "dementia" and "Alzheimer's disease" (AD) interchangeably (employing the common, more colloquial use of the terms), although, in reality, a distinction needs to be made: it should be stated that AD is a syndrome, the most common form of a dementia and, since the 1980s, has meant the early and late onset form. The term was coined in 1910 by Kraepelin who, at that time, was referring to the early-onset, pre-senile form of the disease (see J. Ballenger, *Self, Senility and Alzheimer's Disease in Modern America: A History* [Johns Hopkins University Press, 2006]).

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https://doi.org/10.1177/1073110518804232 Published online by Cambridge University Press

3. R. C. Adelman, "The *Alzheimerization* of Aging," *Gerontologist* 35, no. 4 (1995): 526-532; R. C. Adelman, "The Alzheimerization of Aging: A Brief Update," *Experimental Gerontology* 33, nos. 1-2 (1998): 155-157.
4. R. L. Beard, *Living with Alzheimer's: Managing Memory Loss, Identity, and Illness* (New York: New York University Press, 2016).
5. Another major shift in the understanding of the dementia syndrome preceded the two changes here described as part of the "new dementia": a widening of the category once exclusively steeped in a cognitive paradigm, which now integrated once-peripherical behavioral symptoms into the main syndrome. See A. Leibing, "From the Periphery to the Center: Treating Noncognitive, Especially Behavioral and Psychological, Symptoms of Dementia," in J. Ballenger, P. Whitehouse, C. Lyketsos, P. Rabins, and J. Karlawish, eds., *Treating Dementia: Do We Have a Pill for That?* (Baltimore: The Johns Hopkins University Press, 2009): 74-97.
6. R. Peters, "The Prevention of Dementia," *International Journal of Geriatric Psychiatry* 24, no. 5 (2009): 452–458.
7. F. E. Taragano, R. F. Allegri, H. Krupitzki, D. Sarasola, C. M. Serrano, and C. Lyketsos, "Mild Behavioral Impairment and Risk of Dementia," *Neurology* 70 (2008): A282.
8. See, e.g., V. A. Kral, "Senescent Forgetfulness: Benign and Malignant," *Canadian Medical Association Journal* 86 (1962): 257-260; see J. Golomb, A. Kluger, and S. H. Ferris, "Mild Cognitive Impairment: Historical Development and Summary of Research," *Dialogues in Clinical Neuroscience* 6, no. 4 (2004): 351-367.
9. See J. Ballenger, *Self, Senility and Alzheimer's Disease in Modern America: A History* (Johns Hopkins University Press, 2006); A. Leibing, "Narrowing Worlds: On Biography and Alzheimer's Disease in Brazil," in A. Leibing, ed., *The Medical Anthropologies in Brazil* (Berlin: VWB-Verlag, 1997): 221-242.
10. F. Vidal, "Brainhood, Anthropological Figure of Modernity," *History of the Human Sciences* 22, no. 1 (2009): 5-36; S. J. Williams, S. Katz, and P. Martin, "Neuroscience and Medicalisation: Sociological Reflections on Memory, Medicine and the Brain," in M. Pickersgill and I. van Keulen, eds., *Sociological Reflections on the Neurosciences* (Emerald Group Publishing Limited, 2011): at 231-254.
11. ASC (Alzheimer Society Canada), "Making the Case for Dementia Prevention," 2017, *available at* <http://www.alzheimer.ca/en/Home/Research/Alzheimer-Society-Research-Program/past-ASRP-recipients/Researcher-profiles/Barry-Greenberg> (last visited November 2017).
12. Alzheimer's Association, "2009 Alzheimer's Disease Facts and Figures," *Alzheimer's & Dementia* 5, no. 3 (2009): 234-270.
13. P. Whitehouse, "The Diagnosis and Treatment of Alzheimer's: Are We Being Irresponsible?" in M. Boenink, H. van Lente, and E. Moors, eds., *Emerging Technologies for Diagnosing Alzheimer's Disease, Innovating with Care* (Palgrave Macmillan, 2016): at 21-39; M. Lock, "Detecting Amyloid Biomarkers: Embodied Risk and Alzheimer Prevention," *Biosocieties* 8, no. 2 (2013): 107-123; see Leibing, *supra* note 5; A. Leibing, "The Earlier the Better: Alzheimer's Prevention, Early Detection, and the Quest for Pharmacological Interventions," *Culture, Medicine & Psychiatry* 38, no. 2 (2014): 217-236.
14. D. Roland, "Big Pharma Backs New $100m Dementia Venture Fund," *The Telegraph*, March 17, 2015, *available at* <http://www.telegraph.co.uk/finance/newsbysector/pharmaceuticalsandchemicals/11477304/Big-Pharma-backs-new-100m-dementia-venture-fund.html> (last visited August 7, 2018).
15. See Leibing, *supra* note 13; A. Leibing, "Tense Prescriptions? Alzheimer Medications and the Anthropology of Uncertainty," *Transcultural Psychiatry* 46, no. 1 (2009): 180-206; Leibing, *supra* note 13; A. Leibing, "Dementia in the Making: Early Detection and the Body/Brain in Alzheimer's Disease," in A. Swinnen M. and Schweda, eds., *Popularizing Dementia, Public Expressions and Representations of Forgetfulness* (Bielefeld: Transkript, 2015): at 275-294; A. Leibing, "On Short Cuts: The Complexity of Studying the Early Diagnosis and Prevention of Alzheimer's Disease," in M. Boening, H. van Lente, and E. Moors, eds., *Emerging Technologies for Diagnosing Alzheimer's Disease: Innovating with Care* (Palgrave, 2016): 41-62.
16. Z. S. Khachaturian and A. S. Khachaturian, "The Paradox of Research on Dementia-Alzheimer's Disease," *Journal of Prevention of Alzheimer's Disease* 3, no. 4 (2016): 189-191.
17. M. Richards and C. Brayne, "What Do We Mean by Alzheimer's Disease?" *BMJ* 341 (2010): at 865.
18. P. Molin and K. Rockwood, "The New Criteria for Alzheimer's Disease: Implications for Geriatricians," *Canadian Geriatrics Journal* 19, no. 2 (2016): 66-73, at 70.
19. A. Alzheimer, "Über eine eigenartige Erkrankung der Hirnrinde," *Allg Zschr Psychiatr Psych Gerichtl Med* 64 (1907): 146-148.
20. G. Strobel, "After Solanezumab: Where Should Alzheimer's Research Go?" *Alzforum*, January 31, 2017, *available at* <https://www.alzforum.org/news/conference-coverage/after-solanezumab-where-should-alzheimers-research-go> (last visited August 7, 2018). This does not mean that ß amyloid-based medications have been abandoned. In a recent article with the title "Anti-amyloid drug pipeline shows no sign of drying up" (see M. B. Rogers, "Anti-amyloid Drug Pipeline Shows No Sign of Drying Up," *Alzforum*, *available at* <http://www.alzforum.org/news/conference-coverage/anti-amyloid-drug-pipeline-shows-no-sign-drying> (last visited August 7, 2018), one researcher explained that many other mechanisms interact with amyloid processes: "Instead of a linear amyloid cascade, it's more of a swirling eddy." It is too early to see whether this more holistic view will later on be part of conceptualizing new classes of drugs and how the multiple factors will be translated into marketing and public health campaigns.
21. G. Livingston et al., "Dementia Prevention, Intervention, and Care," *The Lancet* 390, no. 10113 (2017): 2673-7234.
22. R. L. Kane, "Interventions to Prevent Age-Related Cognitive Decline, Mild Cognitive Impairment, and Clinical Alzheimer's-Type Dementia," *AHRQ Publication* no. 17-EHC008-EF (2017); K. Anstey and R. Peters, "Oversimplification of Dementia Risk Reduction Messaging Is a Threat to Knowledge Translation in Dementia Prevention Research," *Journal of Prevention of Alzheimer's Disease* 5, no. 1 (2018): 2-4.
23. R. A. Sperling et al., "Toward Defining the Preclinical Stages of Alzheimer's Disease," *Alzheimer's & Dementia* 7, no. 3 (2011): 280-292, at 282.
24. See, e.g., J. Attems and K. A. Jellinger, "The Overlap between Vascular Disease and Alzheimer's Disease: Lessons from Pathology," *BMC Medicine* 12 (2014): 206; see also author Leibing (2014), *supra* note 13; Leibing (2015, 2016), *supra* note 13; but see Anstey and Peters, *supra* note 22.
25. See Leibing, *supra* note 13.
26. For a more detailed analysis, see A. Petersen and D. Lupton, *The New Public Health: Health and Self in the Age of Risk* (London: Sage, 1997); K. Bell, D. McNaughton, and A. Salmon, eds., *Alcohol, Tobacco and Obesity: Morality, Mortality and the New Public Health* (London: Routledge, 2011); S. Alvarez, *Prévention et vieillissement: l'expérience individuelle du vieillissement face à la norme contemporaine du "bien vieillir*," Ph.D. thesis in Sociologie, Université de Grenoble, France, 2014; J. K. Shim, *Heart-Sick: The Politics of Risk, Inequality, and Heart Disease* (New York: New York University Press, 2014); among others.
27. A. E. Clarke et al., "Biomedicalization: Technoscientific Transformations of Health, Illness and U.S. Biomedicine," *American Sociological Review* 68, no. 2, (2003): 161-194.
28. See Petersen and Lupton, *supra* note 26; Bell, McNaughton and Salmon, *supra* note 26, at 201; K. Bell and J. Green, "On the Perils of Invoking Neoliberalism in Public Health Critique," *Critical Public Health* 26, no. 3 (2016): 239-243; see also A. Leibing and A. Kampf, "Neither Body nor Brain: Com-

The Journal of Law, Medicine & Ethics, 46 (2018): 704-716. © 2018 The Author(s)

https://doi.org/10.1177/1073110518804232 Published online by Cambridge University Press

paring Attitudes to Prostate Cancer and Alzheimer's Disease," *Body & Society* 19, no. 4 (2013): 61-91, at 65ff.

29. See, e.g., M. Foucault, "Technologies of the Self," in L. H. Martin, H. Gutman, and P. H. Hutton, eds., *Technologies of the Self: A Seminar with Michel Foucault* (Amherst, MA: The University of Massachusetts Press, 1988): 16-49; B. Cruikshank, "Revolutions Within: Self-Government and Self-Esteem," in A. Barry, T. Osborne, and N. Rose, eds., *Foucault and Political Reason: Liberalism, Neo-Liberalism, and Rationalities of Government* (Chicago, IL: University of Chicago Press, 1996); A. Petersen, "Risk, Governance and the New Public Health," in A. Petersen and R. Bunton, eds., *Foucault, Health and Medicine* (London/New York: Routledge, 1998): 189-206; E. Hache (2007) "La responsabilité, une technique de gouvernementalité néolibérale?" *Raisons politiques* 4, no. 28 (2007): 49-65.
30. See Bell and Green, *supra* note 28; V. Ridde, "Reducing Social Inequalities in Health: Public Health, Community Health or Health Promotion?" *Health Promotion and Education* 14, no. 2 (2007): 63-67, 111-114.
31. C. Mayes, *The Biopolitics of Lifestyle: Foucault, Ethics and Healthy Choices* (London/New York, Routledge, 2016): at 4.
32. R. A. Aronowitz, "The Converged Experience of Risk and Disease," *Milbank Quarterly* 87 (2009): 417–442; also M. J. Kreiner and L. M. Hunt, "The Pursuit of Preventive Care for Chronic Illness: Turning Healthy People into Chronic Patients," *Sociology of Health and Illness* 36, no. 6 (2013): 870-884.
33. See, e.g., Mayes, *supra* note 31.
34. S. Katz, "Active and Successful Aging: Lifestyle as a Gerontological Idea," *Recherches sociologiques et anthropologiques* 44, no. 1 (2013): 33-49.
35. See, e.g., S. Lamb, ed., *Successful Aging? Global Perspectives on a Contemporary Obsession* (London: Rutgers University Press, 2017).
36. See Katz, *supra* note 34, at 44.
37. D. Chandler and R. Munday, *Oxford Dictionary of Media and Communication*, Oxford University Press, 2011, *available at* <http://www.oxfordreference.com/view/10.1093/acref/9780199568758.001.0001/acref-9780199568758-e-2501> (last visited August 7, 2018).
38. D. Haraway, "Situated Knowledges: The Science Question in Feminism and the Privilege of Partial Perspective," *Feminist Studies* 14, no. 3 (1988): 575-599.
39. K. Knorr-Cetina, *Epistemic Cultures, How the Sciences Make Knowledge* (Cambridge, MA: Harvard University Press, 1999).
40. See, for example, A. Leibing, "The Earlier the Better: Alzheimer's Prevention, Early Detection, and the Quest for Pharmacological Interventions," *Culture, Medicine & Psychiatry* 38, no. 2 (2014): 217-236. A. Leibing, "From the Periphery to the Center: Treating Noncognitive, Especially Behavioral and Psychological, Symptoms of Dementia," in J. Ballenger, P. Whitehouse, C. Lyketsos, P. Rabins, and J. Karlawish, eds., *Treating Dementia: Do We Have a Pill for That?* (Baltimore: The Johns Hopkins University Press, 2009): 74-97.
41. See Alzheimer Europe, "Five-Country Alzheimer's Disease Survey," 2018, *available at* <http://www.alzheimer-europe.org/Research/Value-of-Knowing> (last visited January 2018).
42. H. F. Hsie and S. E. Shannon, "Three Approaches to Qualitative Content Analysis," *Qualitative Health Research* 15, no. 9 (2005): 1277-1288.
43. See Alzheimer Europe, *supra* note 41.
44. Alzheimer's Association, *2016 Alzheimer's Disease Facts and Figures*, *available at* <http://www.alz.org/documents_custom/2016-facts-and-figures.pdf> (last visited December 2016).
45. It is possible that parts of the Canadian research community are more critical regarding the 'new dementia' when compared with U.S. American tendencies: "The 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD4) recommended that the criteria for MCI due to AD be used cautiously and only in specialized clinical practice. Specifically, the CCCDTD4 considered it premature to refer to brain amyloidosis as an asymptomatic state of AD and rejected the label "preclinical AD" as proposed by the NIA-AA. Moreover, ethical and financial impact of its use would be considerable. IWG's definition of "asymptomatic at risk" has been endorsed only for research purposes" (Molin and Rockwood, 2016):67.
46. M. Kegel, "Top Researchers Believe Prevention Is the Future of Alzheimer's Research," *Alzheimer's News Today*, April, 13, 2017, *available at* <https://alzheimersnewstoday.com/2017/04/13/researchers-prevention-future-alzheimers-research/?utm_source=Alzheimer%27s+List&utm_campaign=d341a07f5b-RSS_EMAIL_CAMPAIGN&utm_medium=email&utm_term=0_94425accb7-d341a07f5b-72085009> (last visited August 7, 2018).
47. PREVENT Dementia Study, "Welcome to the PREVENT Dementia Study," (n.d.), *available at* <http://preventdementia.co.uk/> (last visited August 7, 2018).
48. See Anstey and Peters, *supra* note 22.
49. The Alzheimer's Association explains the heart-head connectionon their website, suggesting additionally an explanation of why some people show no symptoms of dementia, even when after autopsy they were found to have the typical biomarkers, neurofibrillary plaques and amyloid tangles in their brain (and vice versa — dementia, but no biomarkers), an apparent contradiction that has been used by a number of critical social scientists in order to deconstruct dominant dementia models: "Several conditions known to increase the risk of cardiovascular disease — such as high blood pressure, diabetes and high cholesterol — also increase the risk of developing Alzheimer's. Some autopsy studies show that as many as 80 percent of individuals with Alzheimer's disease also have cardiovascular disease. (…) Some autopsy studies suggest that plaques and tangles may be present in the brain without causing symptoms of cognitive decline unless the brain also shows evidence of vascular disease" (see <http://www.alz.org/research/science/alzheimers_prevention_and_risk.asp> [last visited August 7, 2018]).
50. See M. Baker, "In Biomarkers We Trust?" *Nature Biotechnology* 23, no. 3 (2005): 297-304; I. Metzler, "Biomarkers and Their Consequences for the Biomedical Profession: A Social Science Perspective," *Future Medicine* 7, no. 4 (2010): 407-420.
51. After Metzler (*id.*).
52. See Baker, *supra* note 50.
53. See, e.g., K. Applbaum, "Is Marketing the Enemy of Pharmaceutical Innovation?" *Hastings Center Report* 39, no. 4 (2009): 13-17; S. Sismondo, "Pharmaceutical Company Funding and Its Consequences: A Qualitative Systematic Review," *Contemporary Clinical Trials* 29 (2008): 109-113.
54. J. Kollewe, "GlaxoSmithKline, $100m UK Fund Launches to Find Cures for Dementia," *The Guardian*, October 21, 2015, *available at* <https://www.theguardian.com/business/2015/oct/21/gsk-launches-global-fund-to-prevent-and-treat-dementia> (last visited August 7, 2018).
55. GAP (Global Alzheimer's Platform, (n.d., *available at* <http://globalalzplatform.org/> (last visited August 7, 2018); see also J. Cummings et al., "Re-engineering Alzheimer Clinical Trials: Global Alzheimer's Platform Network," *Journal of Prevention of Alzheimer's Disease* 3, no. 2 (2016): 114-120.
56. See Molin and Rockwood, *supra* note 18, at 66.
57. Peter Whitehouse, personal information.
58. D. C. Hallin, "Comparing Mass Media in Europe and the United States," *Insights on Law & Society* 5, no. 3 (2005): 1-4.
59. J. A. Greenberg and D. Herzberg, "Hidden in Plain Sight Marketing Prescription Drugs to Consumers in the Twentieth Century," *American Journal of Public Health* 100, no. 5 (2010): 793-803.
60. L. M. Hunt, M. Kreiner, and H. Brody, "The Changing Face of Chronic Illness Management in Primary Care: A Qualitative

The Journal of Law, Medicine & Ethics, 46 (2018): 704-716. © 2018 The Author(s)

https://doi.org/10.1177/1073110518804232 Published online by Cambridge University Press

Study of Underlying Influences and Unintended Outcomes," *Annals of Family Medicine* 10, no. 5 (2012): 452-460.
61. S. Stringhini et al., "Socioeconomic Status and the 25 × 25 Risk Factors as Determinants of Premature Mortality: A Multicohort Study and Meta-analysis of 1·7 Million Men and Women," *The Lancet* 389, no. 100075 (2017): 1229-1237.
62. K. C. Manton, X. L. Gu, and S.V. Ukraintseva, "Declining Prevalence of Dementia in the U.S. Elderly Population," *Advances in Gerontology* 16 (2005): 30-37.
63. E. M. C. Schrijvers, B. F. J. Verhaaren, P. J. Kroudstaal, A. Hofman, M. A. Ikram, and M. M. B. Breteler, "Is Dementia Incidence Declining? Trends in Dementia Incidence Since 1990 in the Rotterdam Study," *Neurology* 87, no. 19 (2012): 1456-1463.
64. C. Qiu, E. von Strauss, L. Backman, B. Winblad, and L. Fratiglioni, "Twenty-Year Changes in Dementia Occurrence Suggest Decreasing Incidence in Central Stockholm, Sweden," *Neurology* 80, no. 20 (2013): 1888-1894.
65. F. E. Matthews, A. Arthur, L. E. Barnes, J. Bond, C. Jagger, L. Robinson, and C. Brayne, "A Two-Decade Comparison of Prevalence of Dementia in Individuals Aged 65 Years and Older from Three Geographical Areas of England: Results of the Cognitive Function and Ageing Study I and II," *The Lancet* 382, no. 9902 (2013): 1405-1412.
66. V. Hachinski and L. Sposato, "Dementia: From Muddled Diagnoses to Treatable Mechanisms," *Brain* 136 (2013): 2652-2656.
67. T. Fagan, "PreDiva Trial Falls Short," *Alzforum*, August 12, 2016, *available at* <http://www.alzforum.org/news/conference-coverage/prediva-trial-falls-short> (last visited August 7, 2018).
68. R. DuBroff and M. de Lorgeril, "Cholesterol Confusion and Statin Controversy," *World Journal of Cardiology* 7, no. 7 (2015): 404–409.
69. R. Y. Jo and W. J. Jagust, "Vascular Burden and Alzheimer Disease Pathologic Progression," *Neurology* 79 (2012): 1349-1355.
70. N. Rose, "The Politics of Life Itself," *Theory Culture & Society* 18, no. 6 (2001): 1-30.
71. L. Nelson and N. Tabet, "Slowing the Progression of Alzheimer's Disease: What Works?" *Aging Research Reviews* 23 (2015): 193-209.

The Journal of Law, Medicine & Ethics, 46 (2018): 704-716. © 2018 The Author(s)

https://doi.org/10.1177/1073110518804232 Published online by Cambridge University Press