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The deprivation cascade hypothesis of dementia

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ABSTRACT

There are significant disparities in dementia risk and care burden in the global population. This review provides evidence of the effects of deprivation, understood as the absence of environmental resources required for brain health. Deprivation increases dementia risk and care burden due to biological, environmental, and social dimensions of risk. It is hypothesized that the major mediator between deprivation and dementia is reduced educational and professional attainment. It argues for structural interventions centered around improved attainment, particularly for girls and women across the globe, improved funding for primary and social care, and a rights-based approach to brain health to improve access to these resources and thereby reduce dementia disparities.

1. Introduction: the need for an adequate theory of dementia risk disparities

Any aging person is at risk of developing dementia. But risk for dementia and other chronic health conditions is not distributed equally throughout the population due to the existence of "social gradients in health" which lead to worse outcomes for people on the disadvantaged side of social inequities [1]. Socioeconomic status or poverty is the major factor defining these social gradients. However, they are also conditioned by other factors within different contexts, including relative and absolute amounts of deprivation, social position, and social participation [1].

This article will focus specifically on dementia through the lens of social inequity. It takes as a starting point the existence of over 50 million people living with dementia worldwide, with this number expected to triple by 2050 [2]. Furthermore, women continue to outnumber men in dementia risk by approximately two to one, and global forecasts of future risk show that this disparity will be maintained [2]. Dementia is understood here as a clinical syndrome rather than a particular biological disease (like Alzheimer's disease). This article therefore focuses on "all the different kinds of dementia" [3] understood as "a diffuse clinical syndrome representing the gradual accumulation of multiple pathologies, arising from multiple interlocking risk factors over the life course" [4]. Recent literature suggests that around 45 % of dementia cases are associated with 14 modifiable risk factors that center around less educational attainment, worse physical, mental and social health, and air pollution [5]. Risk is relevant across the lifetime. Meta-analyses show that these factors affect dementia risk according to exposure at different periods of life [5]. They include risk factors from early life (less education), midlife (hearing loss, brain injury, hypertension, alcohol consumption, obesity), and late life (smoking, depression, social isolation, physical inactivity, diabetes, air pollution) [5]. Finally, dementia rates are actually falling in rich countries, suggesting that improved overall public health is having a positive impact on dementia reduction [6].

This article does not align with the widespread idea that lifestyle is the fulcrum of modifiable risk. It has been argued that lifestyle behaviors are only the "tip of the iceberg" of dementia risk from a public health point of view [7]. Several longitudinal studies suggest that lifestyle behaviors alone do not adequately explain how low socioeconomic status leads to increased risk of dementia [8,9]. The "lifestyle" framing of dementia is symptomatic of simplistic thinking about the causes of dementia, and is reminiscent of the amyloid cascade hypothesis of Alzheimer's disease, according to which the brain protein amyloid defines and causes dementia [10]. Both lifestyle and amyloid are seductive ways of understanding dementia since they offer simple explanations of dementia (they conceptualize risk along one dimension), and are actionable (they offer precise targets), although they both have low therapeutic impact [9,10]. Furthermore, neither amyloid nor lifestyle address questions of health justice and equity [7,11] as well as obvious gaps between efforts of "cure" and "care" in research, policy making, and advocacy [12]. However, moving away from either amyloid or

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lifestyle in dementia means a move towards complexity and often involves a "long-list" of contributions to risk [13] that is less palatable to researchers, policymakers and citizens.

This article therefore aims to offer a hypothesis to satisfy the simultaneous need to account for the complexity of dementia risk within the population, but minimize the imprecision of a plan of action to reduce risk and improve care in ways that are both fair and efficacious. It will do so by drawing on a multidimensional definition of the concept of "deprivation" [14] to promote understanding of dementia risk through the lens of inequalities in ways that make sense to researchers, policymakers, and citizens alike. Understanding dementia through the lens of socioeconomic disparities [15] allows us to see that modifiable risk factors, including lifestyle behaviors, "cluster" with socioeconomic factors [5] and therefore helps us to understand "the causes of the causes" [16] of increased risk in different populations. To look beyond lifestyle means studying and ultimately changing the different living conditions and social structures in which people grow, live, and work.

In ways that are independent of lifestyle behaviors, socioeconomic status is very robustly associated with dementia risk [17]. This review will draw on empirical literature to argue that deprivation leads to a cascade that not only increases the risk of dementia, but leads to an increased care burden and a vicious cycle of intergenerational deprivation, leading to even further dementia risk. It closes with concrete steps that could be taken to reduce brain health disparities in the population.

2. Three dimensions of deprivation in the context of dementia

In the context of public health, when we talk about deprivation, we usually refer to deprived neighborhoods, areas and regions of the world and how people living within these areas have lower income and reduced life opportunities in ways that lead to worse health outcomes across all different kinds of diseases worldwide [18]. Life expectancy and the risk of developing non-communicable diseases varies greatly between countries, and importantly, within countries [1,18]. Many "deprivation indices" using calculations of area-based deprivation have been elaborated and shown their use in application to the study of health [19,20]. Furthermore, beyond purely financial considerations, deprivation has a strong social component and refers to ways in which a person may be disconnected from their society and healthy social interactions for reasons that include economic considerations but are not reducible to them [21].

Studies of environmental or "ecological" indices of deprivation have shown that poorer people living in wealthy areas have better outcomes than people with similar economic conditions living in deprived areas (for example [22]). The reverse is also true for richer people living in poorer areas [23]. In this sense, it is recognized that deprivation is a property of the environments in which people grow, live, and work. However, it is well recognized that ecological measures of deprivation do not account for individual differences in health outcomes based on individual deprivation, for example within the same neighborhood [24]. There is also a growing literature on individual deprivation indices from different countries that are more appropriate to the needs of patient-facing, clinical care, albeit with the caveat of limited applicability in different sociocultural contexts [20].

For the purposes of this review to understand dementia risk and care burden, deprivation will be understood as "any lack of environmental resources leading to an unmet need" from a brain health point of view [14]. Deprivation for dementia is best understood along three dimensions: economic, social, and sensorimotor [14]. Economic deprivation is when "households struggle to meet their basic needs" [25], whereas social deprivation includes other domains such as "years of education, income, wealth, health insurance status, lifetime job stability" [26]. Sensorimotor deprivation results from an impoverished interaction between the organism and its environment in ways that do not stimulate the body and brain so as to maximize brain health [27,28].

Understanding deprivation along three dimensions acknowledges the common theme of "lack of resources" of the word "deprivation" (from Latin *dēprīvō*, to deny some necessity) but does not reduce risk to any one of these dimensions. In other words, from the point of view of brain health, deprivation allows for a focus on health justice and resource distribution throughout the population without reducing considerations of these resources to economic ones. That said, socioeconomic disparities are the most important resources to consider from a public health point of view of brain health [15,18] because of the causal asymmetry between different kinds of deprivation: economic and social deprivation are likely to lead to sensorimotor deprivation through reduced time, space, and other resources for activities like physical activity [29], whereas sensorimotor deprivation does not in itself lead to socioeconomic deprivation [7]. Therefore, we should be as ambitious as possible about improving economic and social resource distribution.

3. The deprivation cascade hypothesis of dementia risk and burden

Pause to imagine the following case: two identical twins are separated at birth and live, grow and work in very different environments. Twin One has adequate access to quality education, societal resources, leisure time, safe and stimulating environments. Twin Two lives and grows in a polluted, unsafe and stressful environment. Though they have an almost identical genetic profile, Twin Two will have a higher risk of developing dementia later in life.

Economic, social, and sensorimotor deprivation conspire to form a cascade of interlocking risk and increased care burden (Fig. 1). Here, these "interlocking risk factors" [4] are understood along three major dimensions of risk: biological, social, and environmental.

At the center of this bio-social-environmental model is lower attainment for deprived individuals, which affects health along these three dimensions due to interactions between them [30]. Less education is the most important risk factor for dementia as revealed by several longitudinal studies and meta-analyses [5]. However, it was found in a Swedish natural study cohort that "without mediation through adult socioeconomic position, education cannot be uncritically considered a modifiable risk factor for dementia" [31]. Moreover, attainment is not just about educational attainment, but also professional attainment, which serves as a reminder of the lifelong effects of social connectedness and deprivation on professional outcomes and socioeconomic position [32]. Indeed, a study from England found that "the association between socioeconomic status and dementia incidence in a contemporary cohort of older adults may be driven by wealth rather than education" [33].

The "achievement gap" is a multi-factorial phenomenon and may involve the early linguistic environment of deprived children who experience a "word gap" that goes on to affect their linguistic and cognitive abilities later in life [34], though the size and meaning of this "word gap" phenomenon is not certain [35]. Attainment also depends on other factors, including social class [36], minority status [37], and the "summer learning gap" between more and less disadvantaged families [38]. A final aspect of this achievement gap concerns sex and gender disparities in dementia risk. Regions of the world in which dementia risk is set to increase the most [2], including the Middle East and sub-Saharan Africa, are also regions in which women's rights, including access to education and work, are not adequately protected.

Let us now consider the more specifically biological consequences of deprivation for dementia risk. The biological dimension of the relationship between deprivation and dementia can best be summarized as a reduction of an individual's "intrinsic capacity" [39]. Intrinsic capacity is defined by the World Health Organization as "the composite of all the physical and mental capacities that an individual can draw on at any point in time" [39]. Though there is no absolute consensus as to the composite dimensions of intrinsic capacity [40], here we will focus on a recent proposal to integrate the concept of intrinsic capacity into our understanding of dementia [41]. Intrinsic capacity is useful for

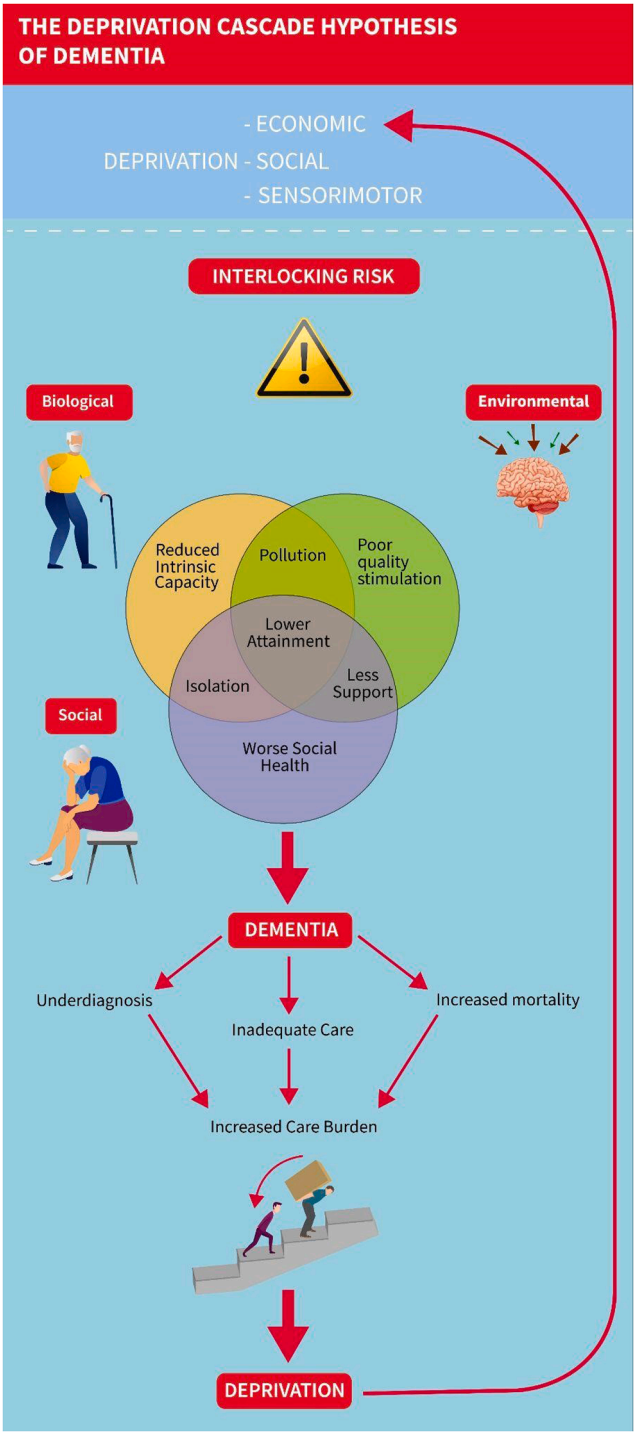

Fig. 1. The deprivation cascade hypothesis of dementia. Different forms of deprivation of environmental resources lead to worsened brain health and increased care burden. Policy making centered around improving educational and professional attainment to reduce long-term economic, social, and sensorimotor deprivation should be a priority for dementia prevention.

understanding non-specific contributions to dementia along biological dimensions ("psychological, cognitive, locomotor, sensory and vitality" [41]). The idea is that the more intrinsic capacity an individual has, the more they can resist the changes in their brain that lead to dementia. This positive "glass half full" [41] view of functioning focuses on what capacity the individual has left, whereas "frailty" is the "glass half empty" [41] view of functioning which focuses on the way in which non-specific cumulative health deficits lead to worsened functioning and cognitive decline [42,43]. A related concept to frailty is comorbidity, and both are associated with deprivation [44,45]. Other biological factors affecting intrinsic capacity include poverty's effect on the neuroendocrine stress axis because of the "consequences of poverty-related adversity early in children's lives" affecting brain development and cognitive performance throughout the lifetime [46].

Further aspects of the biology of deprivation and dementia include greater exposure to air pollution of poorer neighborhoods [47], a robust risk factor for dementia [5,48]. Discussing pollution allows us to move into the more specifically environmental contributors to risk. These can be summarized as centered around poor-quality stimulation of the brain and body by the environment in ways that do not favor brain health [28]. Chronic noise exposure may also be an important risk factor for dementia [49], to which poor socioeconomically deprived individuals are more exposed [50]. Beyond pollution and stress, deprived individuals have less access to leisure, i.e. less free time in which they can perform a variety of physically, mentally, and socially stimulating activities that protect against dementia across the lifetime [51].

Due to social deprivation, deprived individuals have less social support, leading to further emotional and personal stress along with worse health outcomes more generally [52]. Economic deprivation is a well-established mechanism of a "loneliness pathway" [53]. There has been a growing literature on the application of the concept of social health [54] to dementia [55,56], to which we now turn so as to consider the social dimension of interlocking risk. A lack of social contact has been consistently associated with increased risk of cognitive decline [57–59]. But beyond the quantitative nature of social interactions, there are constituent qualitative dimensions of social health that apply to individuals and their social environment including social autonomy, support, and participation [56]. Furthermore, social health also takes into account an individual's own appraisal of their social interactions, which is very relevant to dementia [56]. Feelings of loneliness in particular are associated with neurobiological imaging markers of vulnerability to cognitive decline, bringing us back to the biological dimension of interlocking risk [60].

Finally, it is important to recognize how deprivation leads to worse dementia outcomes beyond risk of onset. In particular, low socioeconomic status is associated with missed or delayed diagnosis [61], particularly in poorer countries [2]; reduced access to adequate care [62], increased mortality [63] and morbidity [64]. All of these lead to major disparities in dementia care for disadvantaged people [64]. This creates a vicious cycle of an increased care burden that leads to further intergenerational deprivation [65], and therefore a greater dementia risk and burden for future generations.

4. Conclusion - Intervening in the deprivation cascade

The "deprivation cascade hypothesis of dementia" suggests that economic, social, and sensorimotor deprivation lead to reduced attainment, heightened risk and increased care burden associated with dementia. The purpose of this review is not only to encourage the further study of socioeconomic disparities in dementia, but to motivate intervention in the deprivation cascade [7]. Beyond the first step of including deprivation as an explicit risk factor for dementia in prevention guidelines [14], there are three major considerations: upstream structural interventions for the purpose of prevention; matching care and cure funding; and the right to a healthy environment.

Structural interventions require changing the broader contexts in which health operates. In other words, such interventions for dementia require changing the "social, physical, economic, or legislative environments" in which risk for dementia is most present [66]. There are many examples of successful structural interventions in public health that researchers and policy makers can draw on, since many successful interventions are often "disease-agnostic" and improve health outcomes across different diseases [67]. The recent Lancet Commission on dementia [5] recommends the following categories of structural

interventions: fiscal, marketing, legislative/accessibility, and housing policies, all of which have been shown to be effective for other conditions. Improving socioeconomic mobility, changing living environments, and maximizing access to healthy behaviors should be the focus of such interventions [67].

However, this deprivation hypothesis puts reduced attainment at the heart of the relationship between deprivation and dementia risk. It is therefore hypothesized that, long-term, policy making to improve educational and professional attainment would lead to the greatest reduction in dementia risk. Victor Hugo famously stated, "*He who opens a school door, closes a prison*," i.e. early education is an effective means of prevention of criminal behavior. In an analogous way applied to health care rather than the penal system, it is hypothesized here that a society that can improve educational and professional outcomes for its disadvantaged members will have better outcomes for later-life dementia. In other words, "*open a school door early, ease the demand on memory clinics later.*" Existing successful attainment interventions show the plurality of approaches that could be useful to this end [68].

Meanwhile, there is major economic interest in both private and public funding of biomedical dementia research to find a cure [69]. However, if we study funding through the lens of deprivation and its impact on risk and care burden, then the urgency of improving the funding of primary and social care becomes very apparent [70]. Researchers as well as advocacy groups should be vocal advocates of the idea that the funding between "cure" and "care" for dementia be more closely matched, without which, "cure" research becomes a silver bullet approach [12], and carers are left without adequate access to healthcare resources.

Finally, arguably the best way to understand a fair approach to issues of risk and care is rights-based. Dementia prevention, treatment, and care can best be understood through the lens of the right to a healthy environment, adopted by the United Nations in 2022 as a human right [71]. This right requires application across the spectrum of dementia risk, from younger members of society [72] to people living with different stages of dementia [73]. Through the lens of deprivation and other forms of inequity like "racism, classism, sexism, and homophobia" [74], dementia shows us how oppressive forces conspire to push certain populations into "ability transitions" like cognitive decline in ways that increase their dependence on access to external resources like caregivers [75]. It is vital that we act against those oppressive forces as a collective so as to expand access to brain and bodily health across all of society, and that the research the community undertakes attempts to address the importance of these factors.

However, there are limitations to our position. The a priori hypothesis based on this review does not respect the principle of "nothing about us without us" as regards disadvantaged populations, who should be more involved in a more democratic view of dementia research in our societies. It is unlikely that researchers alone will provide adequate models of dementia to face up to the public health challenge before us [7,11,12], and elaborating more useful theories and action plans will require collaboration with different populations [76], through a form of activist research [7]. A logical next step would be more widespread use of qualitative research with at-risk populations [77,78], policymakers [79], and healthcare providers [80] to establish the needs and challenges facing the kind of interventions required to make our societies healthier and fairer.

CRediT authorship contribution statement

Timothy Daly: Writing – review & editing, Writing – original draft, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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