Individuals with dementia and populations with dementia

Introduction

The impacts of dementia cut across levels of analysis. For people living with dementia, it causes increasing disability and dependence on others over time. Much of dementia care provision relies on informal care, with attendant stresses on family and friend care partners, and the amount of informal care provision is disproportionately high among women care partners vs. men and in low- and middle-income countries (LMICs) vs. high-income countries due to the sparsity of formal care systems in those countries[1]. Care costs to health care systems and countries are high. No cure exists, and current disease modifying Alzheimer's disease drugs have substantial drawbacks such as small effect sizes on cognition and function[2], high risk of amyloid-related imaging abnormalities[3], and high financial costs[4]. Furthermore, the risks and benefits of these drugs are poorly understood among groups typically underrepresented in research and at greater risk of Alzheimer's disease dementia (e.g., individuals who identify as Black/African American and Hispanic/Latinx) given exclusion criteria for many common comorbidities of aging and poor representation in randomized controlled trials[4,5]. These consequences of dementia and its treatment make a focus on primary prevention critical.

Primary prevention focuses on prevention of a disease before it ever occurs via risk reduction and can be implemented at an individual or population level. A population level lens is typical of public health approaches, while medical approaches focus on individuals[6]. Most preventive dementia interventions evaluated do not take a population level approach, instead aiming at individual level risk reduction, and this is exactly the issue that Daly addresses in his review in Cerebral Circulation - Cognition and Behavior[7]. Daly uses the image of an iceberg to illustrate his conceptualization of interventions on health behavior as a surface level strategy; intervention at levels where people live, work, and play as a shallow level strategy; and intervention on structural political, social, and economic factors as a deep strategy. He argues that shallow and deep level interventions (vs. surface), have not been adequately implemented in dementia prevention approaches. In this commentary, I provide additional context for understanding considerations in dementia prevention from a population-based public health perspective and across levels of influence.

The population-based public health approach vs. the individual approach to dementia prevention

Daly's review calls to mind Rose's classic epidemiology manuscript, *Sick individuals and sick populations*[8], and the title of this commentary is a nod to that piece. In his paper, Rose emphasizes that the approaches to disease prevention at the individual and population levels are different. The individual prevention approach identifies high risk people and reduces risk among only them, seeking to cut the high risk tail off the distribution (Fig. 1, individual approach). This is the approach taken by the multi-domain interventions for dementia prevention which Daly critiques. They include components focusing on modifying various health behaviors such as promoting physical activity, healthy diet, smoking cessation, treatment of hypertension, and management of other vascular risk factors among high-risk individuals. The population approach, on the other hand, seeks to reduce risk across the population, effectively shifting the whole distribution to the left (Fig.1, population approach). The same risk factors mentioned previously could be intervened upon at the population level instead of the individual level. Clear examples of individual vs. population level interventions on the same risk factors for dementia have been described[9], with the evidence for population level interventions recently reviewed[10]. One example of a population level physical activity intervention for primary dementia prevention is for communities to install bike lanes and walking paths to make physical activity safer and easier. The key intuition here is that although the population approach may impart a small risk reduction for an individual, this approach will have a larger impact across the population than the individual approach would. Importantly, the population and individual prevention approaches are not mutually exclusive, and Rose states that they seldom operate in conflict with one another. This is notable because many of the multi-domain dementia prevention strategies Daly discusses are part of prevention and treatment guidelines and approaches for other conditions (e.g., diabetes, cardiovascular disease), and individuals and their doctors will wish to engage in individually tailored strategies in addition to any population-level prevention strategies being undertaken. For example, intensive blood pressure control is a feasible risk reduction strategy for cognitive impairment and dementia[11]. A joint approach would pair this individual level prevention with population level cardiovascular risk factor reduction strategies (e.g. no smoking policies), which are likely partially responsible for recent declines in dementia incidence in the US and Europe[12]. Thus, researchers and practitioners taking an individual approach and those taking a population approach to dementia prevention can work together, and interventions which address multiple levels of influence can be designed. As Daly points out, interventions across the surface, shallow, and deep levels of the dementia iceberg are needed, with new and intensive focus on the deep levels.

Dementia determinants across levels

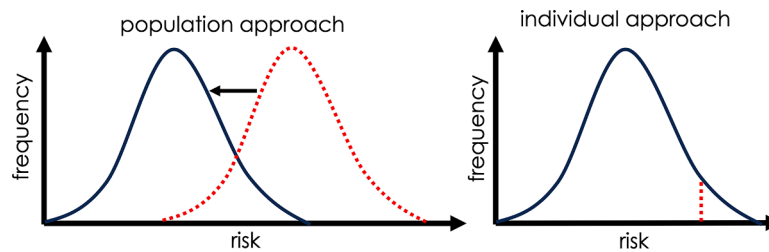The dementia iceberg is meant to provoke much needed

Fig. 1. Population approach vs. individual approach to prevention. High risk is represented by the red dotted line.

conversation and debate in the field about where to place our limited intervention resources, but it was not designed to lay out the key variables, provide detailed levels of influence, and explain relationships between them. To provide this type of insight and understanding, it is necessary to couple the dementia iceberg with other frameworks and models of health determinants. Although there are multiple relevant frameworks and models, I will focus on two which have been recently been described in Alzheimer's disease and related dementias: Ecological Systems Theory[13,14] and Population Neuroscience-Syndemics of Alzheimer's Disease and Related Dementias[15].

Ecological Systems Theory focuses on structural and social determinants of health (S/SDOH). It describes human development and how individuals and nested, increasing levels of S/SDOH interact to influence relevant human outcomes (e.g., dementia)[13]. The inner levels of S/SDOH map roughly onto the shallow level of Daly's dementia iceberg. The outermost level, or macrosystem, which consists of cultural and subcultural norms, beliefs, policies, practices, and the like, maps onto the deep level of the dementia iceberg. A suggested set of measures for use in dementia studies has been developed based on this framework [16]. The dementia application of Ecological Systems Theory specifically focuses on a framework for the macrosystem as it applies to dementia[14]. The authors define the macrosystem as follows: "…bias-based value systems that consistently underlie a culture as a whole and are expressed and transmitted intergenerationally through exo-, micro-, and meso-systems through public policies that steer institutional and individual biases across time (p. 3174)"[14]. They describe multiple macrosystem factors and the evidence for their influence on dementia risk including capitalism, structural racism, xenophobia, religious biases, structural genderism, sexism, homophobia, and ageism[14]. Interventions on the macrosystem in this framework would involve intervening on these bias-based value systems and their affiliated policies.

The Population Neuroscience-Syndemics of Alzheimer's Disease and Related Dementias Framework incorporates brain, behavior, and population sciences to promote brain health and prevent brain disease at the population level[15]. It considers the brain across contextual levels and the lifecourse in a way that is consistent with Ecological Systems Theory, and it uses study design and analytic methods to promote internal and external validity of studies. Syndemics occur when two or more health conditions negatively interact amongst themselves and with S/SDOH [17]. The term comes from "synergistic epidemics". This Framework posits that in populations experiencing syndemic risk factors, including sociocultural, political, economic, and environmental factors, S/SDOH and diseases cluster and interact, amplifying negative health consequences[15]. In this Framework and its associated model, this interaction promotes stress and biological aging, co-occurrence of physical and mental health disorders, and increases risk of dementia. Key syndemic risk and protective factors with importance for dementia include culture, religion, gender norms, discrimination, education, disability, government policies, war and conflict, migrant and refugee related-factors, reproductive health agency, climate change, pollution, and poverty. Many of these factors map onto the deep level of the dementia iceberg. Interventions in this framework could be multilevel, focus on interrupting co-occurrence and interactions of S/SDOH with biological and health conditions, and promote resilience factors.

In agreement with Daly's review, Ecological Systems Theory and the Population Neuroscience-Syndemics of Alzheimer's Disease and Related Dementias Framework suggest that addressing biological pathways to dementia without addressing S/SDOH will not lead to substantive and lasting risk reduction. Although Ecological Systems Theory emphasizes bidirectional influences of the varying ecological levels, authors of the dementia framework point out that the beliefs and bias systems inherent in the macrosystem direct the lower-level systems and pattern what is possible within them[14]. This parallels a key argument that Daly makes—the deeper levels of the dementia iceberg, corresponding with outer levels of Ecological Systems Theory, can affect the shallower levels, but the reverse direction of influence is either not possible or very difficult. As Daly points out, this further implies that emphasizing individual-level intervention without addressing S/SDOH factors that pattern who can access and benefit from such interventions is likely to widen inequality. Another key theme described in the Population Neuroscience-Syndemics of Alzheimer's Disease and Related Dementias Framework is that of interaction within and across levels of dementia determinants. The combination of these ideas of 1) directional influence (intervening on structural factors can also impact individual level, but not vice versa) and 2) interaction effects suggests it would be potentially synergistically impactful across levels to prevent dementia by directing interventions at the macrosystem or deep levels along with other levels of intervention.

Conclusions

Daly's review and the metaphor of the iceberg of dementia risk contributes importantly to the literature by providing an at a glance tool to initiate discussion and action planning in dementia prevention. Additional context regarding population vs. individual level prevention and multilevel frameworks in dementia can inform how to implement population level primary prevention of dementia.

CRediT authorship contribution statement

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Declaration of Competing Interest

References

[1] Global Status Report On the Public Health Response to Dementia, World Health Organization, Geneva, 2021.

[2] S.F. Ackley, J. Wang, R. Chen, M.C. Power, I.E. Allen, M.M. Glymour, Estimated effects of amyloid reduction on cognitive change: a Bayesian update across a range of priors, Alzheimer's & dementia: the journal of the Alzheimer's Association (2023).

[3] M. Filippi, G. Cecchetti, E.G. Spinelli, P. Vezzulli, A. Falini, F. Agosta, Amyloid-related imaging abnormalities and β-amyloid–targeting antibodies: a systematic review, JAMA Neurol. (2022).

[4] J.J. Manly, M.M. Glymour, What the aducanumab approval reveals about Alzheimer disease research, JAMA Neurol. 78 (11) (2021) 1305–1306.

[5] T.S. Anderson, J.Z. Ayanian, J. Souza, B.E. Landon, Representativeness of participants eligible to be enrolled in clinical trials of aducanumab for alzheimer disease compared with medicare beneficiaries with alzheimer disease and mild cognitive impairment, JAMA 326 (16) (2021) 1627–1629.

[6] H.V. Fineberg, Public health and medicine: where the twain shall meet, Am. J. Prev. Med. 41 (4) (2011) S149–SS51.

[7] T. Daly, The iceberg of dementia risk: empirical and conceptual arguments in favor of structural interventions for brain health, Cerebral Circulation-Cognition and Behavior (2023) 100193.

[8] G. Rose, Sick individuals and sick populations, Int. J. Epidemiol. 30 (14) (1985) 32–38.

[9] S. Walsh, I. Govia, L. Wallace, E. Richard, R. Peters, K.J. Anstey, et al., A whole-population approach is required for dementia risk reduction, Lancet Healthy Longev 3 (1) (2022) e6–e8.

[10] S. Walsh, L. Wallace, I. Kuhn, O. Mytton, L. Lafortune, W. Wills, et al., Population-level interventions for the primary prevention of dementia: a complex evidence review, EClinicalMedicine 70 (2024) 102538.

[11] F.M. Elahi, S. Alladi, S.E. Black, J. Claassen, C. DeCarli, T.M. Hughes, et al., Clinical trials in vascular cognitive impairment following SPRINT-MIND: an international perspective, Cell Rep Med 4 (6) (2023) 101089.

[12] F.J. Wolters, L.B. Chibnik, R. Waziry, R. Anderson, C. Berr, A. Beiser, et al., Twenty-seven-year time trends in dementia incidence in Europe and the United States: the Alzheimer Cohorts Consortium, Neurology 95 (5) (2020) e519–ee31.

[13] U. Bronfenbrenner, The Ecology of Human development: Experiments by Nature and Design, Harvard university press, 1979.

[14] P.B. Adkins-Jackson, K.M. George, L.M. Besser, J. Hyun, M. Lamar, T.G. Hill-Jarrett, et al., The structural and social determinants of Alzheimer's disease related dementias, Alzheimer's & dementia: the journal of the Alzheimer's Association 19 (7) (2023) 3171–3185.

[15] C.E. Shaaban, J.F. Trani, G.M. Babulal, Sex & Gender Special Interest Group of the ISTAART Diversity Disparities Professional Interest Area. Integrating population neuroscience and syndemics frameworks to better understand global sex and gender-based risk in Alzheimer's disease and related dementias, Alzheimer's & Dementia 19 (2023) e074149.

[16] S.D. Stites, S. Midgett, D. Mechanic-Hamilton, M. Zuelsdorff, C.M. Glover, D. X. Marquez, et al., Establishing a Framework for Gathering Structural and Social Determinants of Health in Alzheimer's Disease Research Centers, Gerontologist 62 (5) (2021) 694–703.

[17] M. Singer, N. Bulled, B. Ostrach, E. Mendenhall, Syndemics and the biosocial conception of health, Lancet North Am. Ed. 389 (10072) (2017) 941–950.

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