

Reduce the burden of dementia now.

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A Call to Arms:

Although Congress has allocated substantial funding to accelerate dementia research, nearly all attempts to find effective preventions and treatments for dementia have failed. Current dementia therapies offer little hope. They provide only modest clinical benefits and have limited impact on the unrelenting progression of disease. With few means to slow the epidemic, the projected increase in Alzheimer's and dementia cases over the next 30 years will prove overwhelming for a health care system that is ill-equipped to manage treatment, care, and costs. However, an opportunity to ***immediately forestall the onset of new dementia cases*** and to reduce morbidity in those with existing dementia has been largely overlooked. Stated succinctly, we believe that **we have an unprecedented opportunity to reduce the burden of dementia now.**

As demonstrated by Brookmeyer et al., in 1998,¹ the one-year onset delay of dementia would substantially decrease dementia prevalence. Presently, the only path to achieve this goal is lifestyle intervention. An important, tangible, and overlooked approach to reduce the burden of dementia is by preventing delirium. Delirium is common in older adults,² and while dementia increases the risk for delirium it is becoming clear that delirium also substantially increases the risk for subsequent dementia. This dangerous symbiotic relationship contributes to increased suffering, morbidity, mortality, and health care costs. Delirium may accelerate cognitive decline and can unmask dementia pathology in cognitively normal or mildly impaired individuals, reducing time to dementia diagnoses. Yet, randomized trials demonstrate that multicomponent nonpharmacological interventions, can in some instances reduce the risk of delirium by nearly 40%. To realize this potential we need to improve recognition of delirium, to implement strategies to prevent delirium, and to instigate major research programs to better understand the biology of delirium.

The international drive to illuminate Delirium: development of a campaign & implementation of programs

We propose an ambitious multi-stakeholder campaign of research, care, and advocacy to address the problem of delirium. Just as the Leon Thal Symposia (LTS) 2007-2010 helped lead to today's advances in Alzheimer's research and care public policies, *we seek to apply* this approach once again: to launch an international public health campaign, "IDID" (International Drive to Illuminate Delirium), to advance and synergize the field of delirium along five pillars: Awareness, Policy, Diagnosis, Burden, and Biology; with the goal of improving care and developing better strategies to prevent and treat delirium [Figure]. Longer term efforts will be required to better understand the etiology of delirium, and mechanistic links between delirium and dementia..



Awareness & Policy:

Delirium prevention offers opportunities for meaningful dementia prevention *right now*. A growing body of evidence suggests that delirium represents a sentinel event that is indicative of increased brain vulnerability,³ and can result in enhanced risk of persistent cognitive decline, including dementia.² Therefore, increasing awareness among patients, primary care physicians, and hospitals might help to target and reduce the problem. Patients and family members need to be aware of the risks and consequences of delirium. Despite the obvious clinical importance of delirium, implementation of prevention programs, particularly for high-risk older adults with mild cognitive impairment or dementia, is currently not considered a high priority for most hospital systems.

Furthermore, care providers need to know how to identify and appropriately treat delirium and hospitals need to take an active role in monitoring at-risk patients for delirium. That means regular screening and diagnosis of delirium, as well as implementation of appropriate and effective treatments for delirium. Importantly, a campaign to forestall dementia by preventing delirium could spur implementation of ambitious policies that may ultimately lead to effective delirium prevention programs at 25% of hospitals worldwide by 2020, 50% by 2024, and 75% by 2028, which would target a

potentially preventable driver of cognitive decline and dementia in older adults. These policies would represent a new standard of care that includes comprehensive screening for delirium risk, widespread roll-out of preventive strategies, systematic assessment for incident delirium, and appropriate management of delirium with reduction in its attendant complications.

Diagnosis:

A critical aspect of assessing the population burden of delirium is case identification. We know the importance of this seemingly simple notion because of the example set by dementia researchers. Generally accepted criteria helped standardize case assessment, refined our counts of cases, enabled us to differentiate types of dementia, and allowed us to study the epidemiology of dementia. Our dementia criteria have been revisited and refined, further pushing the field toward discovering the etiology of disease. Currently, there is a lack of an accepted reference standard definition of delirium. This is exacerbated by a lack of consensus across the multiple approaches that exist in different disciplines and across the variety of case identification methods that can be applied in different clinical settings and patient populations. As demonstrated by dementia studies, an accurate and standardized approach to case identification is an essential prerequisite for public health surveillance, quality monitoring, risk factor identification, and biomarker discovery. Achieving the goals of standardized screening and diagnoses would advance knowledge of etiology and pathophysiology of delirium, and could enable development of more effective prevention and perhaps treatment options.

Burden & Biology of disease:

Delirium research lags far behind dementia research. We still do not have a solid understanding of the scope of the problem nor the costs associated with it. And yet, previously published estimates suggest the burden of delirium is very high both in cost and in human suffering. Despite the huge potential of studying the interface between delirium and dementia, the biological pathways by which these disorders are intertwined is little understood. Delirium is strongly associated with the development of new-onset dementia and acceleration of existing cognitive decline. It may be that interventions for delirium could result in secondary prevention of dementias, but research into the extent to which delirium and dementias are driven by either distinct or shared pathophysiological processes remains in its infancy.³ However human patho-epidemiological and animal model studies indicate that new pathological features may arise during episodes of delirium and it is crucial to research the mechanisms by which inflammatory, neurotransmitter and metabolic perturbations link delirium to long-term cognitive decline across different clinical settings.^{4,5} Only in the last decade has the call for large-scale longitudinal studies on delirium been answered. A limited number of studies that are currently underway will track cognitive status before, during, and after an acute stressor, coupled with imaging and other biomarker assessments, and will address how much of the population burden of chronic cognitive impairment might in fact be attributable to acute decline precipitated by delirium.

Low Hanging Fruit:

A starting point in this campaign would be to focus on an easily addressable aspect of the problem. A prevention program targeting delirium could be implemented swiftly with adequate buy-in from policy makers and the health care community. While such programs exist and have proven efficacy and cost-effectiveness, largescale implementation is lagging despite the fact that these programs hold the potential to dramatically improve clinical outcomes, quality and safety of care, and importantly, forestall long-term cognitive decline. A pre-operative screening and prevention program might make an immediate impact on dementia because: 1) rates of postoperative delirium in surgical patients aged 65+ are high, ranging from 15- to over 50% and from 70- to over 80% of intensive care unit (ICU) patients; and 2) older patients who undergo *elective* outpatient surgery often experience post-operative delirium, potentially increasing the risk of accelerated cognitive decline and dementia. With implementation of a global standard of care, including appropriate pre-operative screening, counseling, and post-operative care, a significant number of high-risk individuals might be spared the adverse effects of delirium and increased risk of dementia. With such an approach, high-risk patients can make informed decisions, weighing the risks and benefits of surgery; high-risk patients who proceed with a surgery could be closely monitored for delirium and treated appropriately with nonpharmacologic interventions.

Effective programs have been developed and tested across many clinical settings beyond surgery. However, it is important to acknowledge that not all delirium will be preventable and not all episodes of delirium that are prevented by interventions will have an impact on dementia trajectories. A greater appreciation of the biological underpinnings of

delirium and the key determinants of new brain injury will be essential to identify points of intervention in these populations.

Alzheimer's & Dementia Championing IDID

The Journal will help support this effort with a Special Topics Section; workgroups to address each pillar; and presentation of a preliminary action plan. Reports included in the special topic section will provide a roadmap to address research gaps, spur a public health awareness campaign, and generate health policy objectives. Increased research funding targeted for delirium prevention is essential to advance this cause. Through this unified public health effort, we seek to reduce the burden and prevalence of dementia through immediate implementation of effective programs to prevent delirium.

Selected References:

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