Actionable Causes of Alzheimer's disease

*** Ronald N. Kostoff**

Research Affiliate, School of Public Policy, Georgia Institute of Technology, USA

ABSTRACT

A monograph identifying the full spectrum of actionable Alzheimer's Disease (AD) contributing factors has been published recently.[1] Elimination of these actionable contributing factors offers the promise of 1) potentially preventing and reversing AD in selected cases, and 2) dramatically lowering AD healthcare costs by circumventing the need for a) expensive high technology AD diagnostics and treatments and b) expensive extended maintenance and care of individuals with AD. The advanced text mining/information retrieval methodology used to identify the AD contributing factors may be of interest to professionals in the areas of text mining, information retrieval, literature-based discovery, text analytics, and big data, while the medical/biomedical findings may be of interest to AD researchers and clinicians, as well as health policy professionals and decision-makers.

Keywords: Alzheimer's Disease, Dementia, Text Mining, Information Technology, Adverse Events, Risk Factors, Contributing Factors.

INTRODUCTION

Alzheimer's disease (AD) is a brain disease, and the most common form of dementia. Currently, it affects those 65 years old and above overwhelmingly; incidence increases with age. AD has an environmental component, and there have been many high-technology additions to the environment in the past few decades that may adversely impact AD incidence and prevalence statistics in the future. The mainstream medical approach to treating AD has been centered around drug therapy mainly. How effective has it been? Bredesen states: "In the case of Alzheimer's disease, there is not a single therapeutic that exerts anything beyond a marginal, un-sustained symptomatic effect, with little or no effect on disease progression.

Furthermore, in the past decade alone, hundreds of clinical trials have been conducted for AD, at an aggregate cost of billions of dollars, without success. This has led some to question whether the approach taken to drug development for AD is an optimal one".[2]

I have developed a general holistic medical principle for preventing or reversing disease: "At the present time, removal of cause is a necessary, but not necessarily sufficient, condition for restorative treatment of disease to be effective." To *prevent* AD, or any disease, the foundational causes that underlie the disease symptoms need to be identified and removed as comprehensively, thoroughly, and rapidly as possible. To *reverse* AD (if irreversible damage has not been done and strong genetic predisposition is not a dominant factor), the preventive steps above need to be implemented, and treatments to reverse progression (if necessary) need to be applied. The first step in both AD prevention and reversal protocols is to identify the full spectrum of potential AD foundational causes/contributing factors. The recent monograph[1] takes this first step for AD.

***Address for correspondence:**
Dr. Ronald N. Kostoff,
13500 Tallyrand Way, Gainesville, VA, 20155, USA.
Phone.no: 571-248-2661
Email: rkostoff@gmail.com

Access this article online

Official Publication of

Phcog.Net
Bringing Medicinal Plants Researchers Together

Website: www.jscires.org

DOI: 10.5530/jscires.6.1.7

METHODOLOGY

General Concept

The methodology employed in[1] identified actionable foundational causes (tangible items over which we have some control, such as smoking, food additives, pesticides, etc) linked directly to AD, or indirectly through surrogate endpoints for AD (surrogate endpoints are early/intermediate markers thought to predict longer-term clinical benefit, and are used by the FDA to accelerate drug approval).[3]

Why was the surrogate endpoint concept used as part of[1] ? Direct links between potential contributing factors and AD are established through satisfying conditions such as Koch's Postulates, Bradford Hill criteria, or other causation criteria. However, for diseases that emerge late in life, such as AD, linking potential causes/contributing factors to the disease directly could require many decades to validate potential causes that occur early in life. Therefore, to avoid the enhanced risk of populations being exposed to potentially harmful substances for many decades while waiting for definitive links between the potential causes and AD to be demonstrated, identifying links between the potentially harmful substances and shorter-term/intermediate markers of AD (surrogate endpoints) could lead to precautionary risk mitigation.

Specific Approach

Two overlapping approaches were used to identify potential AD contributing factors. First, a complex query focused on potential causes linked directly to AD (e.g., "increased risk for AD"), or linked to its surrogate endpoints (e.g., "produced hyperphosphorylated tau", "accelerated neurofibrillary tangles", "caused cognitive decline", "induced amyloid beta", etc), was applied to the ~100,000 Medline articles that had Alzheimer* as a Title or MeSH term (the full query is shown in Chapter 7 of [1]). The ~5,000 most recently published articles were reviewed to identify potential AD contributing factors.

Second, cause-related MeSH and text terms (e.g., "exposed", "induced", etc) were generated that would link to MeSH and text representations of potential AD actionable foundational causes in the ~100,000 Medline articles (e.g., "nerve agent *exposure*", "smoking-*induced*"). The potential AD foundational causes ("nerve agent", "smoking") would then be separated from the cause-related linking terms ("*exposure*", "*-induced*"). Both factors that linked directly to AD (e.g., "risk factor for AD") and to surrogate endpoints (e.g., "risk factor for tau hyperphosphorylation") were included. Surrogate endpoints for AD additional to those used in the complex query of the previous paragraph were identified over the course of the study (e.g., "impaired BBB integrity", "induced neurotoxicity", "produced cholinergic hypofunction and tissue lesions"), and could be useful for future studies of this type.

RESULTS

Approximately 600 actionable foundational causes of AD were identified. This full spectrum of causes covered the general areas of Lifestyle, Iatrogenic, Bio-toxic, Occupational/Environmental, and Psychosocial/Socio-economic. Genetic causes were not examined in detail, since they are not viewed as actionable at the present time.

CONCLUSIONS

Perhaps the main driver of these actionable foundational AD causes is the use of modern technology that is inadequately regulated and inadequately safety-tested, especially for long-term safety. These deficiencies lead to national health policies that are inherently contradictory. The major economies pursue policies of rapid economic growth, which tends to involve adjusting regulatory practices to accelerate the introduction and implementation of new and relatively untested technologies. At the same time, these major economies sponsor large research efforts to combat diseases such as AD, while they are accelerating the expansion of many of the technologies that are contributing factors to AD. The situation can be viewed metaphorically as two people in a boat taking on water, where one person is bailing out the water furiously, and the other person is drilling holes in the bottom. The AD situation can be repeated for many, if not most, chronic diseases. Serious progress in preventing and reversing chronic diseases will require a re-orientation of national health and economic policies.

ACKNOWLEDGEMENT

I acknowledge the contributions of Drs. Yi Zhang, Jing Ma, Alan L. Porter, and Henry A. Buchtel to the monograph on which this Research Note is based.

CONFLICT OF INTEREST

None

ABBREVIATIONS USED

None

REFERENCES

1. Kostoff RN, Zhang Y, Ma J, Porter AL, Buchtel HA. Prevention and reversal of Alzheimer's Disease. Georgia Institute of Technology. 2017. PDF. <https://smartech.gatech.edu/handle/1853/56646>
2. Bredesen DE. Reversal of cognitive decline: A novel therapeutic program. Aging. 2014;6(9):707-17. https://doi.org/10.18632/aging.100690 ; PMid:25324467 PMCid:PMC4221920.
3. Accelerated Approval. US FDA. 2014. http://www.fda.gov/ForPatients/Approvals/Fast/ucm405447.htm.

How to cite this article: Kostoff RN. Actionable Causes of Alzheimer's disease. J Scientometric Res. 2017;6(1):51-53.