11/03/15 PRESENTATION: PROPOSALS FOR INCREASING WELLNESS AND PREVENTION

<TARGET><BILL></BILL><SUBJECT>11-03-15 PRESENTATION PROPOSALS FOR INCREASING WELLNESS AND PREVENTION</SUBJECT><COMM>HHSS29</COMM></TARGET>

STATE CAPITOL
P.O. Box 110001
Juneau, AK 99811-0001
907-465-3500
fax: 907-465-3532

550 West Seventh Avenue, Suite 1700
Anchorage, AK 99501
907-269-7450
fax 907-269-7461
www.Gov.Alaska.Gov
Governor@Alaska.Gov

Governor Bill Walker
STATE OF ALASKA

March 4, 2016

The Honorable Paul Seaton
Alaska House of Representatives
State Capitol, Room 102
Juneau, AK 99801

Dear Representative Seaton:

Thank you for your letter on behalf of the House Health and Social Services Committee regarding safety and wellness promotion in the various State departments. I am pleased to hear that you are interested in these efforts, and each department is eager to assist in continuing this dialogue.

All departments encourage full participation in AlaskaCare Wellness programs that are outlined on the Department of Administration's web site. In addition, I have enclosed a compilation of innovations and concepts that each department has provided in regard to wellness and safety promotion, as well as a list of contacts for each department should the Committee wish to follow up further.

Thank you for starting this dialogue, and we hope that it will continue. Any insight or suggestions you may have are welcome. I am confident that we can all work together to continue to improve prevention efforts to keep State workers healthy and on the job.

Sincerely,

Bill Walker
Governor

Enclosure

cc: The Honorable Bert Stedman, Health and Social Services Chair, Alaska State Senate

Safety and Wellness Efforts of State Departments

Department of Revenue

The department has an organized employee fitness program. Many employees have fit-bits and challenge each other to work-week contests for getting the most steps. They support the use of the stairs instead of the elevator in efforts to promote fitness. Further, healthy foods are encouraged at office potlucks. As needed, ergonomic assessments are completed and tailored to fit the needs of individual employees. This is essential to reducing back, neck, and repetitive stress injuries. The department trains staff on prevention of workplace violence, instructing on how to react in the case of an active shooter. They also send out emails reminding staff to be careful when roads are icy.

Department of Law

The department holds an annual "fun run" for department employees and their families with the proceeds of the event donated to charity. Reminders are emailed to ensure employees are aware that their insurance covers counseling programs and substance abuse treatment. The criminal division includes a motivational speaker at the yearly District Attorney Victim Witness Paralegal Conference that focuses on the importance of caring for oneself and strategies on how to cope with horrific situations on a daily basis. Various offices have incorporated a buddy system for leaving the building at night. The department has installed AED machines at each office location and provides training to keep certified AED and CPR responders on site. Emergency coordinators are identified and offices are equipped with an emergency kit on each floor.

Department of Corrections

The department routinely emails safety information to all staff. They have implemented a Safety Data Sheet repository available at all times to all staff using online services. Video safety training simulators were purchased to reduce training costs for fire prevention. Safety "tool box" briefings are often conducted at facilities with maintenance personnel. Proper use of tools and ladders are reviewed and discussed. Larger internal work tasks are reviewed and discussed ahead of time to provide the proper job hazard analysis and awareness. Pre-planning often exposes risk and hazards that can be mitigated, reducing injuries and lost time days from work. Employees are reminded through email and yearly training of wellness programs that are currently available through their bargaining units, available gym discounts, and that confidential counseling services are available through the Employee Assistance Program. The department is continually looking for cost-effective methods and opportunities to educate staff and promote safety practices and awareness.

Department of Public Safety

DPS puts a large emphasis on physical fitness. The Troopers hold an annual Alaska State Troopers Adventure Relay, stretching from Fairbanks to Seward. Teams of DPS members also participate in the Wish Upon the North Star fundraiser (adventure relay) as well as the Torch Run for the Special Olympics. DPS bike riders are encouraged to participate in Anchorage's official Bike to Work Day. The Department encourages employees to walk or exercise on breaks and works with the nonprofit Fraternal Order of Alaska State Troopers to purchase exercise equipment for rural locations to help promote fitness and well-being in regions where commercial gyms are not available.

Additionally, safety briefings are conducted at the beginning of each training session. The department hangs wall posters to remind Officers to check their equipment and ensure that they are prepared for duty, mentally and physically. Automated external defibrillator and first aid kits are

installed in buildings. Fire safety press releases for employees and the public are sent out to increase fire safety knowledge.

Department of Environmental Conservation
The department has a policy to support employees who choose to engage in physical fitness activities, allowing adjustments to work schedules to accommodate employees' individual fitness efforts. Some staff choose to participate in daily group walks to exercise and promote comradery.

New employees are made aware of their building's emergency exits, muster areas, defibrillators, and first aid kits. A fire safety monitor is assigned to each floor to safely guide staff to the muster area and account for staff in the event of an emergency. There are hand sanitizers in all offices, and hallways are maintained to be clear and free of tripping hazards. Ergonomic keyboards, chairs, and consultations are available upon request on an as-needed basis, as are standup desks. Where appropriate, safety signage is posted around the workplace, and periodic building-wide fire drills are held in all locations.

To enhance communication skills and de-escalate tense situations and address potential workplace violence concerns, the department encourages staff to take the free Department of Administration Division of Personnel's Learn Alaska courses (for remote staff, if resources allow for travel), including Valuing Diversity and Customer Service Excellence. CPR/First Aid training is offered if it is a job requirement, and training specific each job is provided for all fields.

Department of Health and Social Services
On a routine basis the department's divisions work with the Department of Administration to coordinate fire drills and seek consultations on ergonomically-sound work stations. Two online training sessions have been created to assist in recognizing potentially violent situations in the workplace and preventing/responding to them professionally. The department drafted new DHSS workplace violence prevention policies and procedures. As part of an effort to offer employee safety and wellness training, Stress Management and Stress Management at Work webinars and group and individual coaching sessions were conducted by AETNA coaches (Employee Assistance Program, Supervisory Unit) in 2015 for at least 120 staff trainees and participants.

The Division of Juvenile Justice offers Secondary Trauma training to help staff address traumatic impacts of working with delinquent juveniles and their families. The Office of Children's Services has safety committees established in all five of the agency's administrative regions that meet routinely to evaluate safety issues, address concerns, and identify areas of improvement. The Division of Senior and Disabilities Services has created a wellness team to encourage and promote healthy activities within the workplace, to equip employees with stress coping mechanisms, and to provide the tools to foster a team environment. The team has hosted a wide range of wellness related activities including a Division-wide "Healthy Harvest" potluck, decorating each break room corkboard with wellness information including: financial fitness presentations, stress reduction demos, superfoods tasting sessions, daily walks on breaks and lunch, and much more. The Division of Public Assistance encourages employees to walk each day. They also encourage them to get outside during their lunch hour or to participate in other activities like stretching at their desks.

Further, the Division of Alaska Pioneer Homes has invested in mechanical lifts for safe movement/lifting of residents which has contributed to the safety and wellbeing of direct care staff and residents. The Division of Public Health sponsors a number of activities to encourage a culture

of safety and wellness. The "Healthy Division Worksite Wellness Program" includes an intranet site that directs employees to health promotion and wellness resources, policies to encourage the presence of healthy food and beverage choices at meetings, "wellness work scheduling" that facilitates employees' ability to engage in wellness activities, and a "healthy employee recognition" for staff who set a positive example for others to become or stay healthy. From October 2014 to August 2015, 248 of the division's 488 employees (51 percent) participated in Division-sponsored "health challenge" events. The next such event is an Iditarod-themed, friendly team competition between the Division's 22 public health centers to encourage tracking of steps and miles.

Department of Natural Resources
The department trains staff in preparation for work assignments that may present risk. These trainings include offering helicopter crash training; as well as, learn to return, bear safety, snow machine and ATV safety, swift water rescue, and many more, depending on the work at hand. Safety briefings are conducted before field trips, and staff are provided with appropriate equipment to keep them safe. The Office of Project Management and Permitting starts each meeting with a safety minute. Further, staff members encourage each other to stay active and to get outdoors, promoting a healthy lifestyle.

Department of Transportation
The department requires monthly safety meetings of all employees and has instituted specific safety training for all disciplines. Safety meetings are used to present information, discuss problems, create new ideas, and to discuss recent accidents and injuries. The department has established an employee concerns program in the construction division so that individuals can bring forward issues of concern, and a safety minute is required at the start of all department and regional meetings. In an effort to evaluate the department's safety culture, a series of survey questions has been developed and distributed to department personnel. Once the responses are compiled, the department will be able to assess the areas that need improvement.

Department of Labor and Workforce Development
The Department has been proactive in reducing the number of workplace injuries for all State workers through outreach efforts. The Occupational Safety and Health Consultation and Training Section in the Department of Labor and Workforce Development is offering free consulting services to reduce the occurrences of workplace injuries to all departments. The department hosts a safety minute at bi-weekly staff meetings and a quarterly safety message is distributed.

Department of Fish and Game
The department has a culture for promoting and enjoying healthy outdoor activities such as hunting, fishing, and wildlife viewing, and the department hosts several outdoor events, open to employees and the public. Several employees participate and even volunteer their time towards this effort. A few of those events include the "Becoming an Outdoors Woman" program which teaches rifle, shotgun, and handgun cleaning and maintenance and wilderness first aid and CPR/AED. Alaskans Afield teaches classes on outdoor survival and small game hunting. There are several camps offered for youth including Alaska Conservation Camp and Outdoor Youth Days. Hunter Education Camps and Skills Clinics are offered as well. Through a partnership between members of the public and professional scientists, interested individuals, families, community organizations, and school are able to become involved in learning more about our local wildlife.

Department of Education and Early Development
The department posts appropriate bulletins and materials in the staff room that address issues regarding safety, as well as computer stretches to encourage healthy habits. Additionally, staff are allowed appropriate breaks and allowed to physically move more frequently from the workspace to support good physical fitness. When the department is setting up or replacing workstations, it invests in spaces that allow employees to stand, and allows for purchases of ergonomic keyboards and office furniture.

Department of Commerce, Community, and Economic Development
The department has informally organized fit-bit challenges to encourage one another to make healthy changes in activity levels. The Alaska Energy Authority (AEA), has ActiveHealth provide quarterly educational sessions and one-on-one coaching with interested individuals. They also promote an online webinar series which is conducted over the lunch hours. Last January, a 12-week "Healthy Choices" challenge was held to encourage an increase in healthy habits. AEA has a team for the Heart Run in April. Groups of employees regularly run and walk on their lunch hour. Further, health and fitness tips are posted in the breakrooms, stairwells, and the elevator.

Department of Military and Veterans Affairs
All of the uniformed and many of the civilian members of the Alaska Department of Military and Veterans Affairs engage in regular physical training. Uniformed members must meet strict height/weight and fitness standards.

Within the Division of Homeland Security and Emergency Management, safety is a constant and active concern for all personnel. During disaster events, daily safety briefings are given to all participating staff and partners identifying threats and hazards while in the affected community or while travelling to or from communities. Acclimation briefings assist out-of-state partners arriving in Alaska to support disasters; these briefings include expectations for climate, culture, health, and safety for people new to Alaska. During weather or health hazard events, briefings on travel, safety, and health and safety precautions and procedures are a more than daily occurrence. The Division also provides active shooter training, and cyber security and hygiene training.

Legislative Liaisons

Updated: February 9, 2016

Department/Agency	Liaison	Session, Interim	Cell	Fax	Alternate	Office	Cell
Administration	Minta Montalbo	465-1176	529-2851	465-2135	Cheri Lowenstein	465-5655	957-9157
Alaska Court System	Nancy Meade	463-4736, 264-8264	230-7176	463-3475	Doug Wooliver	463-4750	748-7313
Commerce, Community, & Economic Development	Micaela Fowler	465-2503	209-3070	465-5442	Hannah Lager	465-5533	
Corrections	Sherrie Daigle	465-4645	575-3705	269-7390	April Wilkerson	465-3460	723-4646
Education & Early Development	Marcy Herman	465-2803	723-7567	465-4156	Heidi Teshner	465-2875	321-4107
Environmental Conservation	Alida Bus	465-5871	500-4747	465-5070	Claire Fishwick	465-5065	
Fish & Game	Kevin Brooks	465-6138	321-4656	465-2332	Abby Smith	465-6141	209-3037
Governor: Office of Management & Budget	Joy Wilkinson	465-4677	209-8439	465-3640	Craig Kahklen	465-3559	957-4203
Health & Social Services	Anthony Newman	465-1611	321-3989	465-3068	Sarah Woods	465-1631	
Labor & Workforce Development	Anna Latham	465-4531	957-8737	465-2784	Joe Thomas	465-2702	957-5334
Law-Civil	Cori Mills	465-2132	957-3224	465-2075	Susan Pollard	465-2168	957-2168
Law-Criminal	Kaci Schroeder	465-4037	957-2167	465-4043	John Skidmore	269-6308	
Military & Veterans Affairs	Ron Clarke	465-4600, 428-6007	723-6840	428-6019	Michael O'Hare	428-7066	529-2406
Natural Resources	Courtney Sanborn	465-4730, 269-8429	280-9055	465-3886	Ed Fogels	269-8423	830-9107
Public Safety	Allison Hanzawa	465-5505	465-7782	465-4362	Kelly Howell	465-4336, 269-5591	952-5118
Revenue	Jerry Burnett	465-3669	321-4499	465-2389	Stephanie Alexander	465-6829	419-0701
Transportation & Public Facilities	Mike Lesmann	465-4772	957-2321		Mary Siroky	465-8974	321-0550
University of Alaska	Chris Christensen	463-3086	242-5299	463-3938	Michelle Rizk	450-8187	322-9625

Governor's Office Contacts	
Darwin Peterson	Legislative Director
Lacy Wilcox	Deputy Legislative Director
Natasha McClanahan	Assistant Legislative Director
Liz Williams	Legislative Office Assistant

Phone: 465-4021 Fax: 465-3147

Meeting Name: **House Health and Social Services Committee**

Scheduled Start: **11/3 10:00 AM**

Registered Witnesses:

#	Name	LIO Site	Affiliation	Testimony	Location	Agenda Item (if specified)
1	Mike Barnhill	Offnet	Dept. of Administration	Q	Juneau	Presentations
2	Jay Butler	Offnet	Dept. of Health & Social Services	Q	Anchorage	Presentations
3	Mark Erickson	Offnet	Dept. of Health & Social Services	Yes	Anchorage	Presentations
4	Nelly Ayala	Offnet	Dept. of Health & Social Services	Yes	Anchorage	Presentations

Reconvened at 11am to call of the chair.

#	Name	LIO Site	Affiliation	Testimony	Location	Agenda Item (if specified)

Meeting Name: **House Health and Social Services Committee**

Scheduled Start: **11/3 4:00 PM**

Registered Witnesses:

#	Name	LIO Site	Affiliation	Testimony	Location	Agenda Item (if specified)
1	Mark Erickson	Offnet	Alaska Psychiatric Institute	Q	Anchorage	Presentations
2	Jay Butler	Offnet	Dept. of HHSS	Q	Anchorage	Presentations

Invited Testimony: that was in person House HSS 11/3/15

Rep. Talerico & Jeff Goodall

Rep Tarr and Pat Sidmore

Rep. Seaton

- Nelly Ayala, Diabetes Prevention and Control Manager for the Division of Public Health: on diabetes prevention and wellness efforts

- **Dr. Mark Erickson,** Psychiatrist, Alaska Psychiatric Institute, will be available for questions and comment on biological issues related to behavioral health and on Adverse Childhood Experiences.
- **Pat Sidmore,** Planner, Alaska Mental Health Board, will be available for questions and comment on Adverse Childhood Experiences.
- **Dr. Jay Butler,** Chief Medical Officer and Director of Public Health, will be available for general questions and comments.

Today's order:

1. Rep Talerico: Safety Minutes to reduce accidents in the work place
    a. There are no documents for this presentation.

2. Nelly Ayala, Diabetes Prevention and Control Manager for the Division of Public Health: on diabetes prevention and wellness efforts
    a. Presentation attached

3. Rep Tarr: Understanding and preventing ACEs Adverse Childhood Experiences
    a. Documents attached

4. Rep Seaton: How a better understanding of the immunological causes of depression and other mental health concerns could provide a primary care a prevention window into reducing Alaska's behavioral health needs
    a. Documents attached

Invited testimony-Available for questions / comments:

- **Dr. Mark Erickson,** Psychiatrist, Alaska Psychiatric Institute, will be available for questions and comment on biological issues related to behavioral health and on Adverse Childhood Experiences.

- **Pat Sidmore,** Planner, Alaska Mental Health Board, will be available for questions and comment on Adverse Childhood Experiences.

- **Dr. Jay Butler,** Chief Medical Officer and Director of Public Health, will be available for general questions and comments.

FYI-DOA – staff Mike Barnhill will try to attend the meeting in person or on the phone to hear proposals only (not for questions/comments). Comm Fisher was invited but unable to attend at short notice.

Nutrition and Behavioral Health

How a better understanding of the immunological causes of depression and other mental health concerns could provide a primary care a prevention window into reducing Alaska's behavioral health needs

- A growing body of literature shows that inflammation and inflammatory markers such as pro-inflammatory cytokines, have a strong association with depression. In cases of major depression the inflammatory response system is often activated. Higher levels of inflammation also appear to increase the risk for the development of new depression cases. [Cytokines and Depression- How your immune system causes depression. Immunology of Major Depression. A Meta-analysis of Cytokines in Major Depression. Association of high-sensitivity C-reactive protein with *de novo* major depression]
- There are many known environmental factors that may elevate the risk of depression and that are associated with inflammation including stress, poor diet, and vitamin D deficiency. For example, studies have found that dietary interventions significantly lowered certain inflammation markers that have been associated with depression [So depression is an inflammatory disease….]
- Other studies have found association between vitamin D supplementation and reduced inflammatory markers associated with depression, as well as an association between vitamin D deficiency and suicide. [So depression is an inflammatory disease, but where does the inflammation come from? Suicidal Patients are deficient in vitamin D, associated with a pro-inflammatory status in the blood]
- Furthermore, vitamin supplementation is associated with an increased sense of wellbeing [So depression is an inflammatory disease, but where does the inflammation come from? Randomized comparison of the effects of the vitamin D3 adequate intake versus 100 mcg (4000 IU) per day on biochemical responses and the wellbeing of patients. Reanalysis of study finds vitamin D improves feelings of well-being in subjects with frequent respiratory tract infections]
- Last year, an expert panel found sufficient scientific evidence to support increase the Daily Recommended Intake of omega-3 of military members especially before combat. In fact, given the evidence for the reduction of depressive symptoms and suicide prevention, the panel found "It would be unethical to not attempt elevating the omega-3 status among military personnel." [The Response of an Expert Panel to Nutritional Armor for the Warfighter]

- Behavioral health is a very important topic in Alaska. Right now we face a shortage of needed services, both because of a lack of parity in our current pay structure and because of a limited number of providers.
- Physicians and primary care providers report spending a good amount of time providing behavioral health care they were not trained to provide because they do not have somewhere to refer their patients.
- However, physicians can and do ask their patients about environmental factors such as diet. If the state or state-wide provider groups support physicians by providing information on the immunological causes of issues like depression (e.g. inflammation) and the modifiable environmental factors (e.g. diet, sleep, nutrition), primary care providers could help moderate some mental health concerns and even prevent *de novo* cases. This would reduce the stress on our behavioral health system as we work to expand access to it.

From the authors of So Depression is an inflammatory disease, but where does the inflammation come from?:

"The identification of a number of potential factors that are known sources of inflammation, and their correlation to quality evidence linking those factors to increased risk of depression, provides mechanistic support for inflammation as one of the mediating pathways to both risk and neuroprogression in depression. The pivotal element is that most of these are plastic, and amenable to intervention, both therapeutic and preventative. While inflammation has suggested a number of very promising anti-inflammatory therapies, including statins, aspirin, pioglitazone and celecoxib, the latter preventative need is perhaps the more pressing [14,250,251]. Psychiatry largely lacks an integrated model for conceptualizing modifiable risk factors for depression. It has, therefore, lacked conceptually and pragmatically coherent primary prevention strategies, prioritizing the treatment of established disorders. Yet the rationale, targets and imperative to focus on prevention of depression at a population level is clear." Berk, et al. BMC Medicine. Page 10.

Cytokines and Depression
How your immune system *causes* depression

by Ronald S. Smith

Chapter 7:

Immunological Evidence Supporting The Immune-Cytokine Model of Depression

The Immune-Cytokine Model of Depression (ICMD) is an entirely new concept for understanding the riddle of depression. This is the only model of depression to bridge the conceptual and diagnostic gap between physical and mental disorders.[1,2] ICMD views depression to be any number of chronic physical-biological disorders that have mental-emotional symptoms. From the perspective of ICMD, depression isn't really a disease, but rather a multifaceted sign of chronic immune system activation. During chronic immune system activation, greater than normal amounts of various cytokines are secreted. The cytokines produce the multifaceted signs and symptoms of depression. This chapter summarizes the extensive immunological evidence supporting ICMD. Chapter 7 reviews the evidence from biological psychiatry supporting ICMD.

Cytokines Cause The Symptoms Of Depression

Cytokines are at the heart of the immunological basis of depression since they provoke a wide spectrum of neuropsychiatric symptoms when given to human volunteers. The profound effects of cytokines on mood, thought and behavior were first discovered in the early 1980's. For the first time in history, physicians had found molecules made by the human body which, when given to humans, produced all the symptoms necessary for the diagnosis of depression.

These discoveries are of monumental importance. They should have dazzled every psychiatrist and psychologist in the world, but quite surprisingly, mental health professionals had meager interest in these discoveries. Most psychologists and psychiatrists were (and still seem to be) engrossed in their own theories of psychopathology and had little time or interest in psychiatric discoveries coming from other disciplines, especially when they came from something as seemingly unrelated as immunology.

Interferon-alpha Interferon-alpha (INFα) is a cytokine released by activated monocytes and macrophages. It has a number of beneficial effects on various immune cells[3], but it also has many very debilitating neuropsychiatric consequences.[4] Priestman[5] in 1980 was one of the first to report some of INFα's neuropsychiatric effects. A few year later Rohatiner et al.[6] published a more detailed study. They gave INFα intravenously for seven days to eleven volunteers and observed the effects. All volunteers became feverish, fatigued and lacked appetite. They were socially withdrawn, slow to answer questions, lost interest in their surroundings and slept most of the day. In one week, these volunteers developed nearly all the symptoms necessary for the diagnosis of major depressive episode. Their brain waves also became abnormal and were suggestive of a brain degenerative disease.

A year later, Adams et al.[7] did a longer term (four week, ten patient) study on the effects of INFα. For the first few days fever, headache, aching muscles and other flu like symptoms occurred, but they did not persist. They were replaced by symptoms of severe depression. From the end of the first week to the end the fourth week, eight of

So depression is an inflammatory disease, but where does the inflammation come from?

Michael Berk[1234*], **Lana J Williams**[12], **Felice N Jacka**[12], **Adrienne O'Neil**[15], **Julie A Pasco**[16], **Steven Moylan**[1], **Nicholas B Allen**[7], **Amanda L Stuart**[1], **Amie C Hayley**[1], **Michelle L Byrne**[7] and **Michael Maes**[18]

- *Corresponding author: Michael Berk mikebe@barwonhealth.org.au

BMC Medicine 2013, **11**:200 doi:10.1186/1741-7015-11-200
Published: 12 September 2013

Abstract

Background

We now know that depression is associated with a chronic, low-grade inflammatory response and activation of cell-mediated immunity, as well as activation of the compensatory anti-inflammatory reflex system. It is similarly accompanied by increased oxidative and nitrosative stress (O&NS), which contribute to neuroprogression in the disorder. The obvious question this poses is 'what is the source of this chronic low-grade inflammation?'

Discussion

This review explores the role of inflammation and oxidative and nitrosative stress as possible mediators of known environmental risk factors in depression, and discusses potential implications of these findings. A range of factors appear to increase the risk for the development of depression, and seem to be associated with systemic inflammation; these include psychosocial stressors, poor diet, physical inactivity, obesity, smoking, altered gut permeability, atopy, dental cares, sleep and vitamin D deficiency.

Summary

The identification of known sources of inflammation provides support for inflammation as a mediating pathway to both risk and neuroprogression in depression. Critically, most of these factors are plastic, and potentially amenable to therapeutic and preventative interventions. Most, but not all, of the above mentioned sources of inflammation may play a role in other psychiatric disorders, such as bipolar disorder, schizophrenia, autism and post-traumatic stress disorder.

Keywords:

Depression; Inflammation; Cytokines; Diet; Obesity; Exercise; Smoking; Vitamin D; Dental cares; Sleep; Atopic; Gut; Oxidative stress

Abstract

Neuroimmunomodulation. 2014;21(2-3):123-30. doi: 10.1159/000356540. Epub 2014 Feb 14.

Immunology of major depression.

Müller N[1].

Author information

Abstract

High levels of several proinflammatory components of the immune system, such as interleukin-6, C-reactive protein, tumor necrosis factor (TNF)-α, or neopterin in patients suffering from major depression (MD) point to the involvement of an inflammatory process in the pathophysiology of MD. The direct and indirect effects of cytokines on neurotransmitter storage and release - mediated by microglia cells and astrocytes - are discussed. The tryptophan/kynurenine metabolism is one of the indirect mechanisms because the enzyme indoleamine 2,3-dioxygenase - a key enzyme of this metabolism in the central nervous system - is driven by pro- and anti-inflammatory cytokines and degrades serotonin. Moreover, neuroactive kynurenines such as kynurenic acid and quinolinic acid act on the glutamatergic neurotransmission as N-methyl-D-aspartate antagonists and agonists, respectively. Alterations of the serotonergic, noradrenergic and glutamatergic neurotransmission have been shown with low-level neuroinflammation and may be involved in symptom generation. Epidemiological and clinical studies show a role for inflammation as a risk factor for MD. A large-scale epidemiological study in MD clearly demonstrates that severe infections and autoimmune disorders are lifetime risk factors for MD. The vulnerability-stress-inflammation model matches with this view as stress may increase proinflammatory cytokines and even contribute to a lasting proinflammatory state. Further support comes from the therapeutic benefit of anti-inflammatory medications such as the cyclo-oxygenase-2 inhibitors, TNF-α antagonists and others, and the anti-inflammatory and immunomodulatory intrinsic effects of antidepressants.

PMID: 24557045 [PubMed - indexed for MEDLINE]

PubMed

Abstract

Full text links

ELSEVIER FULL-TEXT ARTICLE

Biol Psychiatry. 2010 Mar 1;67(5):446-57. doi: 10.1016/j.biopsych.2009.09.033. Epub 2009 Dec 16.

A meta-analysis of cytokines in major depression.

Dowlati Y[1], Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, Lanctôt KL.

Author information

Abstract

BACKGROUND: Major depression occurs in 4.4% to 20% of the general population. Studies suggest that major depression is accompanied by immune dysregulation and activation of the inflammatory response system (IRS). Our objective was to quantitatively summarize the data on concentrations of specific cytokines in patients diagnosed with a major depressive episode and controls.

METHODS: We performed a meta-analysis of studies measuring cytokine concentration in patients with major depression, with a database search of the English literature (to August 2009) and a manual search of references.

RESULTS: Twenty-four studies involving unstimulated measurements of cytokines in patients meeting DSM criteria for major depression were included in the meta-analysis; 13 for tumor necrosis factor (TNF)-alpha, 9 for interleukin (IL)-1beta, 16 for IL-6, 5 for IL-4, 5 for IL-2, 4 for IL-8, 6 for IL-10, and 4 for interferon (IFN)-gamma. There were significantly higher concentrations of TNF-alpha ($p < .00001$), weighted mean difference (WMD) (95% confidence interval) 3.97 pg/mL (2.24 to 5.71), in depressed subjects compared with control subjects (438 depressed/350 nondepressed). Also, IL-6 concentrations were significantly higher ($p < .00001$) in depressed subjects compared with control subjects (492 depressed/400 nondepressed) with an overall WMD of 1.78 pg/mL (1.23 to 2.33). There were no significant differences among depressed and nondepressed subjects for the other cytokines studied.

CONCLUSIONS: This meta-analysis reports significantly higher concentrations of the proinflammatory cytokines TNF-alpha and IL-6 in depressed subjects compared with control subjects. While both positive and negative results have been reported in individual studies, this meta-analytic result strengthens evidence that depression is accompanied by activation of the IRS.

PMID: 20015486 [PubMed - indexed for MEDLINE]

BJPsych | The British Journal of Psychiatry (2010) 197, 372–377. doi: 10.1192/bjp.bp.109.076430

Association of high-sensitivity C-reactive protein with *de novo* major depression

Julie A. Pasco, Geoffrey C. Nicholson, Lana J. Williams, Felice N. Jacka, Margaret J. Henry, Mark A. Kotowicz, Hans G. Schneider, Brian E. Leonard and Michael Berk

Background
Although there is cross-sectional evidence that changes in the immune system contribute to the pathophysiology of depression, longitudinal data capable of elucidating cause and effect relationships are lacking.

Aims
We aimed to determine whether subclinical systemic inflammation, as measured by serum high-sensitivity C-reactive protein (hsCRP) concentration, is associated with an increased risk of *de novo* major depressive disorder.

Method
Major depressive disorder was diagnosed using a clinical interview (SCID–I/NP). This is a retrospective cohort study; from a population-based sample of 1494 randomly selected women recruited at baseline during the period 1994–7, 822 were followed for a decade and provided measures of both exposure and outcome. Of these women, 644 (aged 20–84 years) had no prior history of depression at baseline and were eligible for analysis.

Results
During 5827 person-years of follow-up, 48 cases of *de novo* major depressive disorder were identified. The hazard ratio (HR) for depression increased by 44% for each standard deviation increase in log-transformed hsCRP (ln-hsCRP) (HR = 1.44, 95% CI 1.04–1.99), after adjusting for weight, smoking and use of non-steroidal anti-inflammatory drugs. Further adjustment for other lifestyle factors, medications and comorbidity failed to explain the observed increased risk for depression.

Conclusions
Serum hsCRP is an independent risk marker for *de novo* major depressive disorder in women. This supports an aetiological role for inflammatory activity in the pathophysiology of depression.

Declaration of interest
M.B. has received grant/research support from the Stanley Medical Research Foundation, MBF, National Health and Medical Research Council, Beyond Blue, Geelong Medical Research Foundation, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Organon, Novartis, Mayne Pharma, Servier and AstraZeneca. He has been a paid consultant for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, Lundbeck and Pfizer, and a paid speaker for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Janssen-Cilag, Lundbeck, Organon, Pfizer, Sanofi Synthelabo, Solvay and Wyeth.

PubMed

Abstract

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Suicidal patients are deficient in vitamin D, associated with a pro-inflammatory status in the blood.

Grudet C[1], Malm J[2], Westrin A[3], Brundin L[4].

Author information

Abstract

BACKGROUND: Low levels of vitamin D may play a role in psychiatric disorders, as cross-sectional studies show an association between vitamin D deficiency and depression, schizophrenia and psychotic symptoms. The underlying mechanisms are not well understood, although vitamin D is known to influence the immune system to promote a T helper (Th)-2 phenotype. At the same time, increased inflammation might be of importance in the pathophysiology of depression and suicide. We therefore hypothesized that suicidal patients would be deficient in vitamin D, which could be responsible for the inflammatory changes observed in these patients.

METHODS: We compared vitamin D levels in suicide attempters (n=59), non-suicidal depressed patients (n=17) and healthy controls (n=14). Subjects were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, and went through a structured interview by a specialist in psychiatry. 25(OH)D2 and 25(OH)D3 were measured in plasma using liquid-chromatography-mass-spectrometry (LC-MS). We further explored vitamin D's association with plasma IL-1β, IL-6 and TNF-α.

RESULTS: Suicide attempters had significantly lower mean levels of vitamin D than depressed non-suicidal patients and healthy controls. 58 percent of the suicide attempters were vitamin D deficient according to clinical standard. Moreover, there was a significant negative association between vitamin D and pro-inflammatory cytokines in the psychiatric patients. Low vitamin D levels were associated with higher levels of the inflammatory cytokines IL-6 and IL-1β in the blood.

CONCLUSION: The suicide attempters in our study were deficient in vitamin D. Our data also suggest that vitamin D deficiency could be a contributing factor to the elevated pro-inflammatory cytokines previously reported in suicidal patients. We propose that routine clinical testing of vitamin D levels could be beneficial in patients with suicidal symptoms, with subsequent supplementation in patients found to be deficient.

KEYWORDS: Cytokines; Depression; IL-1β; IL-6; Inflammation; Suicidality; TNF-α; Th-1; Th-2

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Randomized comparison of the effects of the vitamin D_3 adequate intake versus 100 mcg (4000 IU) per day on biochemical responses and the wellbeing of patients

Reinhold Vieth*[1], Samantha Kimball[1], Amanda Hu[1] and Paul G Walfish[2,3]

Address: [1]Department of Laboratory Medicine and Pathology, University of Toronto, Canada, [2]Department of Medicine, Pediatrics, and Otolaryngology, University of Toronto, Canada and [3]Medicine and Endocrine Oncology Program, Mount Sinai Hospital, Toronto, Canada

Email: Reinhold Vieth* - rvieth@mtsinai.on.ca; Samantha Kimball - skimball@uoguelph.ca; Amanda Hu - amanda.hu@utoronto.ca; Paul G Walfish - walfish@mshri.on.ca

* Corresponding author

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Abstract

Background: For adults, vitamin D intake of 100 mcg (4000 IU)/day is physiologic and safe. The adequate intake (AI) for older adults is 15 mcg (600 IU)/day, but there has been no report focusing on use of this dose.

Methods: We compared effects of these doses on biochemical responses and sense of wellbeing in a blinded, randomized trial. In Study 1, 64 outpatients (recruited if summer 2001 25(OH)D <61 nmol/L) were given 15 or 100 mcg/day vitamin D in December 2001. Biochemical responses were followed at subsequent visits that were part of clinical care; 37 patients completed a wellbeing questionnaire in December 2001 and February 2002. Subjects for Study 2 were recruited if their 25(OH)D was <51 nmol/L in summer 2001. 66 outpatients were given vitamin D; 51 completed a wellbeing questionnaire in both December 2002 and February 2003.

Results: In Study 1, basal summer 25-hydroxyvitamin D [25(OH)D] averaged 48 ± 9 (SD) nmol/L. Supplementation for more than 6 months produced mean 25(OH)D levels of 79 ± 30 nmol/L for the 15 mcg/day group, and 112 ± 41 nmol/L for the 100 mcg/day group. Both doses lowered plasma parathyroid hormone with no effect on plasma calcium. Between December and February, wellbeing score improved more for the 100-mcg/day group than for the lower-dosed group (1-tail Mann-Whitney $p = 0.036$). In Study 2, 25(OH)D averaged 39 ± 9 nmol/L, and winter wellbeing scores improved with both doses of vitamin D (two-tail $p < 0.001$).

Conclusion: The highest AI for vitamin D brought summertime 25(OH)D to >40 nmol/L, lowered PTH, and its use was associated with improved wellbeing. The 100 mcg/day dose produced greater responses. Since it was ethically necessary to provide a meaningful dose of vitamin D to these insufficient patients, we cannot rule out a placebo wellbeing response, particularly for those on the lower dose. This work confirms the safety and efficacy of both 15 and 100 mcg/day vitamin D_3 in patients who needed additional vitamin D.

Study finds vitamin D improves feelings of well being in subjects with frequent respiratory tract infections

A reanalysis of a double-blind, randomized controlled trial of the effects of supplementation [Vitamin D_3 Supplementation in patients with frequent respiratory tract infections. Bergman et al.] found that those patients who significantly increased their vitamin D blood serum levels also reported their wellbeing to be 'better than before'. Vitamin D supplementation also have an effect on anti-depressant use.

Read the full news article at www.vitamindcouncil.org/

Read the original study at www.bmjopen.bmj.com

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The response of an expert panel to Nutritional armor for the warfighter: can omega-3 fatty acids enhance stress resilience, wellness, and military performance?

Coulter ID[1].

An expert panel unanimously agreed that omega-3 fatty acids should have a Daily Recommended Intake for military members. The panel concluded that evidence for cardiovascular, immunological, and surgical benefits was strong, as was the evidence for a reduction in depressive symptoms and suicide.

The final conclusion was that based on the studies, it would be unethical to not attempt to elevate omega-3 levels.

Abstract available at: www.ncbi.nlm.nih.gov/pubmed

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Review

Vitamin D and Depression: A Systematic Review and Meta-Analysis Comparing Studies with and without Biological Flaws

Simon Spedding

Nutritional Physiology Research Centre, University of South Australia, City East Campus, North Tce, Adelaide, SA 5000, Australia; E-Mail: spedding@adam.com.au; Tel.: +61-439-687-866; Fax: +61-882-900-498

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Abstract: Efficacy of Vitamin D supplements in depression is controversial, awaiting further literature analysis. Biological flaws in primary studies is a possible reason meta-analyses of Vitamin D have failed to demonstrate efficacy. This systematic review and meta-analysis of Vitamin D and depression compared studies with and without biological flaws. The systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The literature search was undertaken through four databases for randomized controlled trials (RCTs). Studies were critically appraised for methodological quality and biological flaws, in relation to the hypothesis and study design. Meta-analyses were performed for studies according to the presence of biological flaws. The 15 RCTs identified provide a more comprehensive evidence-base than previous systematic reviews; methodological quality of studies was generally good and methodology was diverse. A meta-analysis of all studies without flaws demonstrated a statistically significant improvement in depression with Vitamin D supplements (+0.78 CI +0.24, +1.27). Studies with biological flaws were mainly inconclusive, with the meta-analysis demonstrating a statistically significant worsening in depression by taking Vitamin D supplements (−1.1 CI −0.7, −1.5). Vitamin D supplementation (≥800 I.U. daily) was somewhat favorable in the management of depression in studies that demonstrate a change in vitamin levels, and the effect size was comparable to that of anti-depressant medication.

Keywords: Vitamin D supplementation; depression; biological plausibility; meta-analysis; systematic review; 25OHD

1. Introduction

Depression affects 350 million people worldwide, is the leading cause of disability and the fourth-leading cause of the global disease burden [1]. However, the effectiveness of conventional treatments for depression is questioned: meta-analyses of drug treatments demonstrate minimal difference from placebo, comparisons of real and sham electroconvulsive therapy show little difference after a month, and the evidence for the use of specific cognitive interventions is weak [2]. Therefore we examined the evidence for other approaches to the management of depression.

The association between depressive disorders and Vitamin D deficiency from a lack of sun exposure is well established and was first noted two thousand years ago [3], therefore we considered the evidence for the effectiveness of Vitamin D supplementation.

Vitamin D is a unique secosteroid hormone formed mainly by photosynthesis, so an indoor lifestyle and sun-avoidance leads to deficiency (25OHD <50 nmol/L) [4]. Vitamin D deficiency is now a global public health problem affecting a billion people worldwide [5]. Even in sunny Australia, deficiency affects one third of the population [6], with much higher rates observed in migrant populations [7,8]. There has been an increase in the prevalence of Vitamin D deficiency [9] and a ten-fold increase in spending on supplements in the US over the last decade [10].

Knowledge of Vitamin D has grown exponentially [11] and 95% of our current knowledge was published in the last 15 years [12]. This demonstrates new mechanisms and diseases associated with deficiency including cancer, cardiovascular disease, diabetes, and premature mortality [4]. Whilst Vitamin D was believed to follow Funk's model of vitamins, having a single mechanism and function limited to calcium and bone metabolism [13], the mechanisms of action of Vitamin D are now recognized to be endocrine, paracrine and autocrine via Vitamin D receptors (VDRs) [14] affecting most physiological systems, including the brain [15]. The enzymes necessary for the hydroxylation of 25hydroxyvitamin D (25OHD) to the active form 1,25dihydroxyvitamin D are present in the hypothalamus, cerebellum, and substantia nigra [16]. Vitamin D modulates the hypothalamic-pituitary-adrenal axis, regulating adrenalin, noradrenaline and dopamine production through VDRs in the adrenal cortex [17]; and protects against the depletion of dopamine and serotonin centrally [18]. Therefore, biological plausibility for the action of Vitamin D in depression has been established.

Epidemiological evidence shows that Vitamin D deficiency is associated with an 8%–14% increase in depression [19–22] and a 50% increase in suicide [23]; however, causality and efficacy of supplementation remain controversial [10,24] awaiting confirmation by systematic review and meta-analysis.

Four systematic reviews of Vitamin D efficacy in depression, but no meta-analysis, have been published [25–28]. These reviews provide conflicting results due to the limited number of studies found and the inclusion of inappropriate studies. Based on six RCTs deemed relevant, the Institute of Medicine (IOM) [25] concluded there was "inconclusive evidence of an effect" although four of these RCTs showed a beneficial effect of Vitamin D supplementation in depression. The inclusion of the other two studies [29,30] described by the IOM as "RCTs of Vitamin D" was inappropriate as; one used calcium and not Vitamin D as the intervention, and the other was not an RCT in the opinion of

the study authors as the intervention decreased 25OHD levels. Similarly, consistent conclusions could not be drawn from the other systematic reviews [26–28], as these found so few of the primary studies.

These reviews mirror the inconsistent results found across Vitamin D research as demonstrated by the twenty four conflicting meta-analyses for falls, fractures, and all-cause mortality [31]. The reason Vitamin D meta-analyses fail to produce useful results is thought to be biological flaws in primary studies. These flaws lead to null results [32] as the intervention does not change the Vitamin D status however these flaws may be overlooked when evaluating the research for Vitamin D and other nutrients [33,34].

The concept of "biological flaws" arises from the work of Heaney and others [33,34], and refers to limitations in the design of primary studies which preclude them from testing the research hypothesis. The hypothesis being addressed in this review is that rectifying Vitamin D deficiency decreases depressive symptoms. However some trials have limitations in their study design that prevent this evaluation. This hypothesis can only be tested if participants are Vitamin D deficient at baseline and then receive a large enough dose of Vitamin D supplements to achieve Vitamin D sufficiency during the trial. Vitamin D deficiency cannot be demonstrated if the level of 25OHD is sufficient or higher or not tested at baseline. An ineffective dose of Vitamin D is one that would not be expected to increase the level of 25OHD from deficient to sufficient.

Trials with these biological flaws may demonstrate the limitations of the study design rather than the effectiveness of Vitamin D supplements for changing health outcomes. The parallel in pharmaceutical research to these nutrient studies with biological flaws would be trialling a drug known to be ineffective or on patients already taking a full dose of the drug. Thus biological flaws are a critical element that differentiates nutrient research from pharmaceutical research.

This review was designed to estimate the effect of Vitamin D supplementation in depression and examine the influence of biological flaws in primary studies on the meta-analyses.

2. Methods

This review followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, systematically identifying and appraising peer-reviewed RCTs reporting on the effect of Vitamin D supplementation for individuals with symptoms of depression with the objectives of investigating:

- the primary evidence for Vitamin D supplementation and depression from RCTs;
- the types of subjects, the dose of Vitamin D supplementation, the control interventions and the measures of outcome used;
- methodological quality of the studies;
- biological flaws in the study design, and
- estimates of the size of the effect.

2.1. Search Approach

A systematic search for relevant RCTs was performed evaluating oral Vitamin D supplementation that included data on depression using four library databases of PsychINFO, MedLine, PubMed and Cochrane online library. Search approaches for the different databases can be obtained from the researchers. All databases were searched from inception to October 2012, with eligible papers limited to English language and human subjects.

2.2. Independence

Two independent researchers investigated the library databases to reduce errors/bias in accessing evidence. The reference lists of four systematic reviews [25–28] were hand-searched to identify other RCTs.

2.3. Eligible Studies

RCTs were included where the intervention was Vitamin D supplementation and excluded where trials were not RCTs or used surrogate interventions. Studies were not excluded on their methodological quality as the entire evidence base was required to address the aims of this research.

2.4. Decision-Making

Relevant publications were identified from title, abstract and study descriptors by one researcher; the decision to include was independently validated by a second and disagreements were referred to third for an independent ruling.

2.5. Critical Appraisal

Methodological quality of articles was critically appraised with PEDro [35]. Trials were rated with a checklist, the PEDro scale. This considers two aspects of trial quality; internal validity of the trial and whether the trial contains sufficient statistical information to make it interpretable. It does not rate external validity or the effect size.

2.6. Data Extraction

Data was extracted for participants, 25OHD levels, study timeframes, interventions, outcome measures, measures of effect, methodological quality scores, and biological flaws.

2.7. Biological Flaws

Biological flaws in primary studies were identified. These studies included:

- inappropriate interventions (interventions that did not include Vitamin D), or
- interventions producing the opposite effect of that intended (interventions that included Vitamin D, but reduced the 25OHD level in the intervention group), or

- ineffective interventions that did not improving Vitamin D status (did not significantly change the 25OHD level), or
- where the baseline 25OHD level was not measured in the majority of participants, or
- where the baseline 25OHD level indicated sufficiency (not deficiency) at baseline.

Studies were grouped according to the presence of biological flaws, and compared by date of publication, methodological quality, outcome measure, and study outcome.

2.8. Meta-Analysis

Meta-analyses were performed using MedCalc where data was available on diagnosis, dose, outcome measure, and biological flaws. Estimates of the size of effect using the standardised mean difference (SMD) were compared according to the presence of biological flaws in primary studies.

For meta-analysis of studies with a continuous measure, MedCalc uses the "Hedges g" statistic as a formulation for the SMD under the fixed effects model. The SMD is the difference between the two means divided by the pooled standard deviation, with a correction for small sample bias. Next the heterogeneity statistic is incorporated to calculate the summary SMD under the random effects model. The total SMD with 95% CI is given both for the Fixed effects model and the Random effects model.

The SMD has no units or dimensions, however using Cohen's rule of thumb for interpretation of the SMD statistic: a value of 0.2 indicates a small effect, a value of 0.5 indicates a medium effect, and a value of 0.8 or larger indicates a large effect.

3. Results

3.1. Systematic Review

From all databases 465 relevant articles were identified with 390 articles remaining after removal of duplicates. After applying inclusion criteria, 375 were removed and 15 articles remained. These included 15 RCTs [30,36–49], nine new RCTs and six identified by previous reviews. Seven of the 15 were published in 2011 and 2012 (Table 1).

There was wide variation in study methodology. The study populations were diverse (Table 1). Smaller studies were performed in patients with specific disorders (depression, seasonal affective disorder, obesity, post-menstrual tension and hospitalized patients) [30,37–39,41–44,47–49], and studies in University students [45,46].

Table 1. Study populations, sample sizes (numbers entering intervention and control groups respectively) and methodological quality score (PEDro Scale).

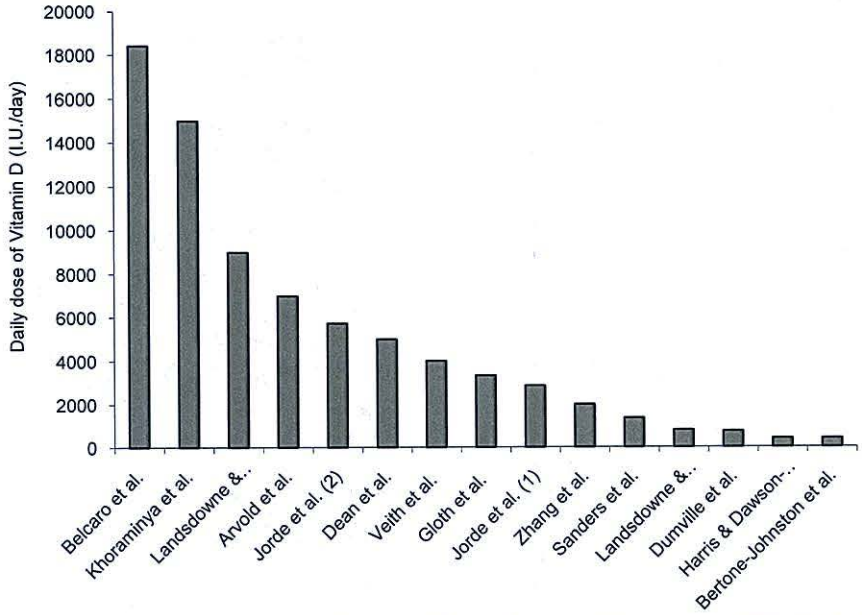
Author	Year	Reference Citation #	Population	Sample Size	Quality Score
Arvold *et al.*	2009	[36]	Individuals with Vit D deficiency (10–25 ng/mL) seen for medical care at a primary healthcare clinic	100 (I 50, C 50)	10
Belcaro *et al.*	2010	[42]	Menopausal women with signs of depression and mood disorder	65 (I 33, C 32)	8
Bertone-Johnson *et al.*	2012	[38]	Postmenopausal Women with depressive symptoms	36,282 (I 18176, C 18106)	11
Dean *et al.*	2011	[45]	Young healthy adults (University students)	128 (I 63, C 65)	11
Dumville *et al.*	2006	[43]	Older women with seasonal affective disorder	2117 (I 912,C 1205)	11
Gloth *et al.*	1999	[44]	Adults with Season Affective Disorder	15 (I 8,C 7)	6.5
Harris & Dawson-Hughes	1993	[30]	Women with seasonal affective disorder	250 (I 125, C 125)	5
Jorde *et al.*	2008	[37]	Overweight and obese adults	441 (IH 150, ILl 142, C 149)	8
Khajehei *et al.*	2009	[46]	University female students with premenstrual syndrome	180 (IOes 60, I 60, C 60)	9
Khoraminya *et al.*	2013	[49]	Adults with major depressive disorder based on DSM-IV criteria, without psychosis	40 (I 20, C 20)	10
Landsdowne & Provost	1998	[39]	Adults with seasonal affective disorder	44 (I 22, C 22)	8
Sanders *et al.*	2011	[47]	Community dwelling older women with seasonal mood disorders	2012 (I 1001, C 1011)	11
Veith *et al.*	2004	[40]	Adults with serum 25(OH)D <61 nmol/L in summer, expected to develop 25(OH)D concentrations <40 nmol/L by winter	64 (I 32, C 32)	10
Yalamanchilli & Gallagher	2012	[48]	Older post-menopausal women with depression	488 (Ioes+Calcitrol 122, Ioes 122, Calcitrol 123, placebo 123)	11
Zhang *et al.*	2011	[41]	Hospitalized patients	32 (I 17, C 15)	9

C = control group and I = intervention group. Where there are two intervention groups; IH is used to indicate where a high dose and IL for where a low dose of Vitamin D supplements were given. Where one intervention group took a hormone, this was designated IOes.

Baseline 25OHD levels were not reported in six papers [36–41] but were performed in eight studies [42–49] (Table 2). For one study [30], Vitamin D data was sought from an earlier paper [50] showing 25OHD levels were not measured at baseline. However 25OHD levels were measured twice during the study. This demonstrated that the 25OHD levels decreased 5% in the intervention group during this part of the study due to the decreased availability of sunlight with the change in season, overwhelming the effect of the low dose of Vitamin D supplements provided.

Daily doses varied from 400 I.U. to 18,400 I.U. across the 15 trials (Figure 1). Three studies [30,38,43] used doses lower that 800 I.U./day. In the Women's Health Initiative [38], the Vitamin D dose would be inadequate to change vitamin levels; the actual dose ingested was ≈200 I.U., as the stipulated dose was 400 I.U. but compliance was 46%. The doses shown in two papers were misprints; reported as 200 mg Vitamin D [42] and 0.25 g of calcitriol [48], equating to millions of international units. However, attempts to clarify this with authors and editors were unsuccessful. The intervention in another study [47] was high dose Vitamin D (500,000 I.U.) probably inducing side effects; a 15% increase in falls and 26% increase in fractures.

Figure 1. Daily dose of Vitamin D per study. This shows the range of equivalent daily doses. (These were calculated after estimating the actual dose rather than using the dose shown in their published papers).



Low doses of 400 I.U. in Harris & Dawson-Hughes [30] and Bertone-Johnson *et al.* [38]; High doses were over 15,000 I.U. per day in Belcaro *et al.* [42] and Khoraminya *et al.* [49]; Jorde *et al.* [37] and Landsdowne & Provost [39] both tested three groups; two differing dosages and one placebo.

Validated outcome measures of depression (Table 2) included Beck Depression Index in three studies [37,45,49] the Profile of Mood States in two studies [30,41] and the mental component score of the SF12 in two studies [43,47]. Questionnaires about pre-menstrual syndrome [46], fibromyalgia [36], and menopause [42] included depression as a domain. One early study used an unvalidated questionnaire [39]. There was no significant differences at baseline measures and methodological quality of studies was generally high (9 out of 11) (Table 1).

Table 2. Key depression outcome measures, within and between group findings.

Author	Year	Outcome Measures	Follow-up Time Period	Within Group Findings	Between Group Findings
Arvold *et al.*	2009	Fibromyalgia Impact Questionnaire	8 weeks	FIQ score Mean pre-post difference total (95%CI) intervention −3.71 (−7.5 to 0.1) ($p < 0.03$), control 1.91 (−2.9 to 6.7) ($p > 0.05$)	$p < 0.05$ favoring intervention
Belcaro *et al.*	2010	Menopause Symptoms Questionnaire	8 weeks	Total average symptom score reduced by 48% for intervention group ($p < 0.05$), control group increased by 10% ($p > 0.05$).	$p < 0.05$ favoring intervention
Bertone-Johnson *et al.*	2012	Burnam Depression Scale	At 2 weeks, then twice yearly for 2 years	Mean overall change (SD) 0.004 (0.143) intervention, −0.002 (0.113) (control)	$p > 0.05$
Dean *et al.*	2011	Beck Depression Index	6 weeks	Baseline: follow up mean (95%CI): Intervention 7.24 (5.58–8.90); 6.40 (4.73–8.07) ($p > 0.05$); control 5.72 (4.09–7.36); 5.38 (3.74–7.02) ($p > 0.05$)	$p > 0.05$
Dumville *et al.*	2006	SF12 mental component	6 months	Mean difference (95%CI) between intervention and control at baseline −0.6 (−1.5 to 0.3) ($p > 0.05$); at follow up 1.8 (−0.8 to 1.2) ($p > 0.05$)	Mean adjusted (age- and baseline score) between group difference (95%CI) −0.49 (−1.34 to 0.81) $p > 0.05$
Gloth *et al.*	1999	SAD-8	1 month	Significant improvement in SAD-8 scores for intervention group, not control (explanatory data not provided)	Significant association between improvement in Vit D levels and SAD-8 scores in overall cohort ($r^2 = 0.26$)
Harris & Dawson-Hughes	1993	Profile of Mood States	3 monthly for 12 months	No difference in pre-post scores for any domain of PoMS for either intervention or control ($p > 0.05$)	No difference between intervention or control change over time in any domain ($p > 0.05$)
Jorde *et al.*	2008	Beck Depression Index (total score)	12 months	Baseline: DD group 4.5 (0.0-24.0); DP group 5.0 (0.0–28.0); PP group 4.0 (0.0–24.0). Follow-up: DD group 3.0 (0.0–23.0) ($p < 0.05$); DP group 4.0 (0.0–26.0) ($p < 0.05$); PP group 3.8 (0.0–18.0)	DD and DP groups change was similar ($p > 0.05$) but significantly greater from PP ($p < 0.05$)

Table 2. *Cont.*

Author	Year	Outcome Measures	Follow-up Time Period	Within Group Findings	Between Group Findings
Khajehei *et al.*	2009	PMS symptom rating form which captured psychological and physical symptoms including depression	Pre-mens for 2 cycles	Mean % total symptoms *Pre:* Dydrogesteron group 52.1%, Calcium plus Vitamin D group 50.7%, Placebo 53.7%. *Post* (respectively): 47.9%, 46.1%, 53.7% Both active treatment groups had significant decreases	The dydrogesterone and calcium plus Vitamin D treatments were significantly more effective than placebo in lessening the severity of PMS symptoms ($p < 0.05$)
Khora-minya *et al.*	2013	24-item Hamilton Depression Rating Scale (HDRS) (1°), 21-item Beck Depression Inventory (BDI) (2°)	Every 2 weeks for 8 weeks	BDI Intervention Wk0 32.45 ± 7.35; Wk2 27.73 ± 7.50; Wk4 20.44 ± 6.56; Wk6 16.73 ± 8.11; Wk8 13.2 ± 8.64 ($p < 0.05$) Control. Wk0 31.65 ± 7.33; Wk2 29.17 ± 6.78; Wk4 25.18 ± 6.93; Wk6 21.00 ± 6.81; Wk8 17.95 ± 6.31 ($p < 0.05$)	$p < 0.05$ for both outcomes, favoring intervention
Lands-downe & Provost	1998	PANAS	5 days	Sig within-group improvements for both active interventions ($p < 0.05$)	Sig improvements for both active interventions cf control for positive and negative affects ($p < 0.05$)
Sanders *et al.*	2011	General Health Questionnaire SF12 (PCS, MCS), WHO Wellbeing Index	3–5 years	Intervention: no intervention SF12 PCS effect size (95%CI) 0.27 (−2.40 to 2.94) 0.23 (−0.88 to 1.34)	Treatment effects SF12 effect size (95%CI) PCS 0.22 (−70.75 to 1.19); MCS 70.14 (−71.00 to 0.72)
Veith *et al.*	2004	Self-developed Wellbeing Scale	2–6 months	Pre-post mean (SD): *600 I.U.* 2.2 (2.0); 2.3 (2.3) ($p > 0.05$) *4000 I.U.* 2.0 (2.3); 1.1 (1.8) ($p < 0.05$)	Significant improvement in wellbeing, favoring higher Vit D dose

Table 2. *Cont.*

Author	Year	Outcome Measures	Follow-up Time Period	Within Group Findings	Between Group Findings
Yalamanchilli & Gallagher	2012	Geriatric Depression Scale	1. HT alone 2. calcitriol alone 3. HT & calcitrol 4. placebo	*% with depression* (pre/post) 13.8%; 8.9%; 9.7%; 7.3%; 8.2%; 6.6% 13.8%; 8.9% All groups $p > 0.05$	No effect on depression in any treatment group compared with placebo ($p > 0.05$)
Zhang *et al.*	2011	Profile of Mood States questionnaire	Average 8 days	Vit D group pre-post 23.1 ± 27.2; 22.4 ± 22.4 $p > 0.05$ Vit C group pre-post 28.6 ± 21.8; 18.8 ± 19.4) $p < 0.05$	$p < 0.05$ favouring Vit D

3.2. Biological Flaws

Biological flaws were found in eight of the 15 studies (Table 3). These flaws limit the ability of these studies to demonstrate a change in vitamin status in the intervention group. The most common flaw, occurring in five studies, was not measuring 25OHD. Two studies [30,38] utilized doses below the minimum effective dose of 600-800 I.U. [51] and one study [45] had such high baseline 25OHD levels that supplements could not improve the Vitamin D status of participants. One intervention was associated with a decrease in 25OHD level [30], and another caused falls and fractures minimising the potential to see any health benefits [47]. Biological flaws were more prevalent (70%) in recent studies (since 2010) than in earlier studies (50%), and in larger studies than in smaller studies (Table 3).

Table 3. Comparison of studies by presence of biological flaws to the study findings and methodological quality.

Study	Biological Flaws NOT Present	Biological Flaw(s) Present	Type of Flaw		Quality Score (Max 11)	Date of Publication	
			25OHD not Assessed	*Dose not Appropriate*			
Belcaro *et al.*		X	X		8		2010
Bertone-Johnson *et al.*		X	X	X (L)	11		2012
Dumville *et al.*		X	X		11	2006	
Harris & Dawson-Hughes		X	X	X (L)	5	1993	
Dean *et al.*		X	X	X (H)	11		2011
Khajehei *et al.*		X		X (I)	9	2009	
Sanders *et al.*		X		X (SE)	11		2011
Yalamanchilli & Gallagher		X		X (I)	11		2012
Total-8 Studies with Biological Flaws	**0**	**8**	**5**	**6**		**3**	**5**
Arvold *et al.*	**X**				***10***	2009	
Gloth *et al.*	**X**				6.5	1999	
Jorde *et al.*	**X**				8	2008	
Khoraminya *et al.*	**X**				10		2013
Landsdowne & Provost	**X**				8	1998	
Veith *et al.*	**X**				10	2004	
Zhang *et al.*	**X**				9		2011
Total—7 studies without flaws	7	**0**	**0**	**0**		**5**	**2**

↑ = significant improvement favouring Vitamin D; Dose incorrect (I), low (L), high (H) or produces side effects (SE).

Of the seven studies without flaws, six [36,37,39,40,44,49] showed improvement in depression with supplementation, whereas six of the nine flawed studies [30,38,42,45–48] had a null result (Table 3). The positive results in two flawed studies maybe due to the unknown contents [46] or the effects of the herbs [42] used in these studies.

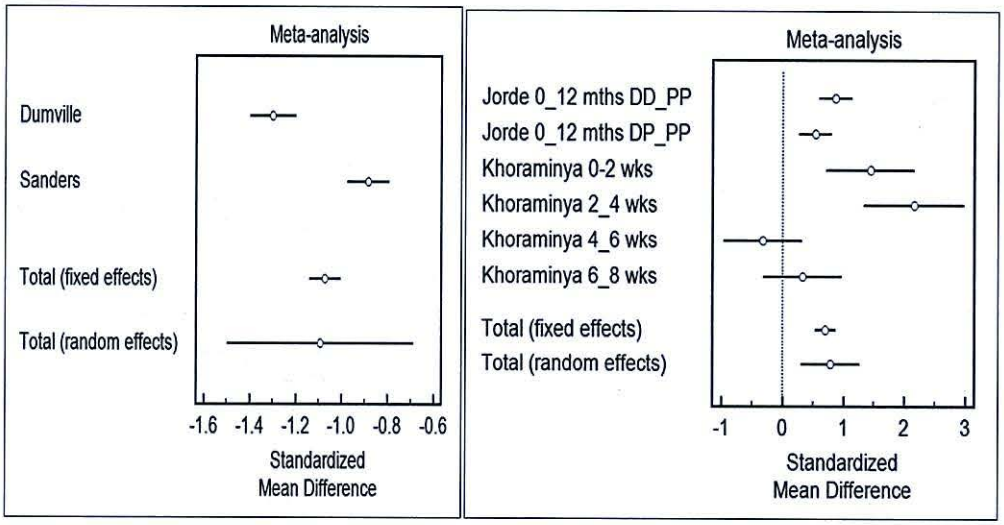
3.3. Meta-Analysis

3.3.1. Meta-Analysis of Studies without Biological Flaws (Right Panel of Figure 2)

Two studies (Jorde *et al.* [37] and Khoraminya *et al.* [49]) were included as they used the same outcome measure; the Beck Depression Inventory.

The standardized mean difference for these studies without flaws is shown in the Right Panel of Figure 2. It shows a statistically significant positive effect of Vitamin D in depression of 0.78 (CI 0.24, 1.27). The random effects model was used due to the diverse populations studied.

Figure 2. The figures show the meta-analysis of studies from the systematic review.



Left Panel—Two studies with biological flaws were combined, Dumville *et al.* [43] and Sanders *et al.* [47]; **Right Panel**—Two studies without biological flaws were combined, Jorde *et al.* [37] and Khoraminya *et al.* [49], showing two intervention groups for Jorde *et al.* [37] (high and low dose Vitamin D) and the data from the Khoraminya *et al.* [49] at 2, 4, 6, and 8 weeks.

The Jorde *et al.* [37] trial (n = 387) had three study groups; two interventions with different doses of Vitamin D and a control. The Khoraminya *et al.* [49] trial (n = 40) compared Vitamin D plus fluoxetine to fluoxetine alone. The studies had similar baseline level of 25OHD (Jorde *et al.* [37] 55 nmol/L) (Khoraminya *et al.* [49] 57 nmol/L), and the doses of Vitamin D over 800 nmol/L in both studies. The participants in both studies were patients; Khoraminya *et al.* [49] depressed patients and Jorde *et al.* [37] obese patients. Depression and obesity overlap, as there is a reciprocal relationship between obesity and depression indicated by the 50% increase in one condition when the other is present [52].

3.3.2. Meta-Analysis of Studies with Biological Flaws (Left Panel of Figure 2)

Options for meta-analysis were examined and performed combining the Dumville *et al.* [43] and Sanders *et al.* [47] studies, due to the diverse outcome variables used in other studies. There was a statistically significant negative effect of Vitamin D administration evident from the forest plot in the

standardized mean differences as shown in the Left Panel of Figure 2. The effect size was −1.1 (CI −0.7, −1.5) (random effects). These studies were of high methodological quality, had similar subjects (community dwelling women aged >70 years) and baseline 25OHD, and used the same outcome measure. The studies differed in the dosing schedule, daily and annually.

4. Discussion

This is the most comprehensive systematic review of randomized controlled trials investigating the effectiveness of Vitamin D in the management of depression. Fifteen RCTs were found, whilst previous reviews captured few of the available RCTs. Although the methodological quality was good, biological flaws were common and more prevalent in recent studies.

For the meta-analysis of studies without biological flaws, the size of the effect was statistically significant being +0.78 (CI 0.24, 1.27). As the measure of effect size was the standardized mean difference (SMD), this was 0.78, using Cohen's Rule-of-Thumb, a SMD of 0.8 is considered to indicate a large effect.

As less than half the study population were deficient the effect of the intervention was diluted such that if all subjects had been deficient the size of the effect would have been higher, perhaps double, 1.5 points on the BDI scale. This is similar to the size of effect seen in a large RCT of antidepressant medication, which was 0.8 point on the BDI scale for the blinded parts of the study and 1.7 points overall [53]. A review of antidepressant efficacy published in the NEJM [54] shows that the effect size of antidepressant medication was increased by selective publication of trials and altering the effect size. However the overall mean weighted effect size value for antidepressants was only 0.15 (CI 0.08, 0.22) for unpublished studies and 0.37 (CI 0.33, 0.41) for published studies. Thus, the effect size of Vitamin D demonstrated in our meta-analysis may be comparable with that of anti-depressant medication. For the meta-analysis of studies with biological flaws, the size of the effect was statistically significant and negative being −1.1 (CI −0.7, −1.5), indicating that Vitamin D supplementation in flawed studies may lead to deterioration in depression.

The main finding is that all studies without flaws and the meta-analysis of studies without biological flaws support the efficacy of Vitamin D supplementation for depression, as compared with the negative results of meta-analysis for studies with biological flaws. The Womens Health Initiative [38] (WHI), with more participants that all the other studies combined, had the highest methodological quality and the most biological flaws leading to non-significant outcomes for both bone strength and mood. Due to its sheer size, the WHI has dominated previous meta-analysis leading to null results.

The main limitation of this review was the diversity of study methodology precluding more extensive meta-analyses, and leaving only two studies in each meta-analysis. The variability in outcome measures and reporting suggest agreement should be sought within the research community to underpin standard conduct and reporting of future studies to support meta-analysis.

5. Conclusion

Traditional evidence, biological plausibility and epidemiological studies indicate Vitamin D has therapeutic effects in depression. There are no previous meta-analyses of Vitamin D and depression as

the evidence was deemed to be insubstantial [25]. This may be due to previous systematic reviews identifying few of the available studies and including RCTs with inappropriate methodology and biological flaws.

Meta-analysis of studies without biological flaws demonstrates that improving Vitamin D levels improves depression, whereas the meta-analysis of flawed studies had a negative result. Heaney [34] identified the most common flaw "baseline status" and the most pernicious flaw "(in)effective dosing". However we found other flaws: not measuring 25OHD levels throughout the study limits the ability to know if the 25OHD level actually changed. In this case, there would be no reason to believe that the intervention caused a biological difference in Vitamin D levels between intervention and control groups. We also found more fundamental biological flaws where the intervention was not Vitamin D but calcium, and caused a decreased in the 25OHD level. These two studies were included in previous systematic reviews but rejected by this review.

The finding that meta-analyses for studies with biological flaws had the statistically significant effect of increasing depression, may lead to a conclusion that some of these trials led to levels for Vitamin D above the therapeutic range. This would be supported by a recent paper indicating that the therapeutic range for 25OHD in depression is 50 and 85 nmol/L [55].

It may be argued that meta-analysis including flawed RCTs reflect the trial methodology more than the efficacy of the intervention, leaving reviewers unable to make valid conclusions about efficacy [34], resulting in uncertainty amongst researchers and clinicians. This has led to calls for more RCTs and less "torturing of the data" by meta-analysis [56]. However, as this review demonstrates, it is excluding biological flaws that will lead to greater understanding of Vitamin D, not simply increasing the quantity of studies.

We note that biological flaws are more frequent in recent studies; this may be due to the belief that vitamins exert a function beyond deficiency. Hence RCTs should test whether using supplementation to correct deficiency is beneficial, rather than testing whether additional supplementation on top of the recommended doses is beneficial in reducing disease [57]. Thus, it is unremarkable that Vitamin D supplementation would not benefit a population that are not deficient or where the dose was ineffective. To test the hypothesis that correcting Vitamin D deficiency leads to an improvement in depression, it is critical to exclude biological flaws from future studies.

The effect size for Vitamin D in depression demonstrated in this meta-analysis is comparable with the effect of anti-depressant medication, an accepted treatment for depression. Should these results be verified by future research, these findings may have important clinical and public health implications.

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Vitamin D Supplementation for Depressive Symptoms: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Jonathan A. Shaffer, PhD, MS Biostats[1], **Donald Edmondson, PhD, MPH**[1], **Lauren Taggart Wasson, MD, MPH**[1], **Louise Falzon, PGDipInf**[1], **Kirsten Homma, BA**[1], **Nchedcochukwu Ezeokoli**[2], **Peter Li, BA**[3], and **Karina W. Davidson, PhD**[1]

[1]Center for Behavioral Cardiovascular Health, Columbia University Medical Center, NY, NY

[2]Department of Chemistry, School of Humanities & Sciences, Stanford University, Stanford, CA

[3]Department of Mathematics, College of Arts and Sciences, New York University, NY, NY

Abstract

Objective—To review the effects of vitamin D supplementation on depression or depressive symptoms in randomized controlled trials. Although low vitamin D levels have been observationally associated with depression and depressive symptoms, the effect of vitamin D supplementation as an antidepressant remains uncertain.

METHODS—MEDLINE, CINAHL, Allied and Complimentary Medicine Database, PsycINFO, Scopus, and The Cochrane Library, and references of included reports (through May 2013) were searched. Two independent reviewers identified randomized trials that compared the effect of vitamin D supplementation on depression or depressive symptoms to a control condition. Two additional reviewers independently reviewed and extracted relevant data; disagreements were reconciled by consensus. The Cochrane Risk of Bias Tool was used to assess study quality. Seven trials (3191 participants) were included.

RESULTS—Vitamin D supplementation had no overall effect on depressive symptoms (standardized mean difference [SMD], −0.14; 95% CI, −0.33 to 0.05; $P = 0.16$), although considerable heterogeneity was observed. Subgroup analysis showed that vitamin D supplementation for participants with clinically significant depressive symptoms or depressive disorder had a moderate, statistically significant effect (2 studies: SMD, −0.60; 95% CI, −1.19 to −0.01; P = 0.046), but a small, nonsignificant effect for those without clinically significant depression (5 studies: SMD, −0.04; CI, −0.20 to 0.12; P = 0.61). Most trials had unclear or high risk of bias. Studies varied in the amount, frequency, duration, and mode of delivery of vitamin D supplementation.

Conclusion—Vitamin D supplementation may be effective for reducing depressive symptoms in patients with clinically significant depression; however, further high quality research is needed.

Address for Correspondence: Jonathan A. Shaffer, PhD, MS*Biostats* Columbia University Medical Center, Center for Behavioral Cardiovascular Health 622 West 168th Street, PH9-318 New York, NY 10032 js3742@columbia.edu; Phone: 212-342-4492; Fax: 212-305-3172.

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Keywords

vitamin D; depression; depressive symptoms; randomized controlled trials; meta-analysis; systematic review

Depression is a highly prevalent and debilitating chronic illness that can be difficult to treat (1, 2), and both depressive disorders and subthreshold depressive symptoms are associated with significant disability, mortality, and health care costs (3, 4). Although the underlying pathophysiology of depression remains unknown and probably involves several mechanisms, a possible role of vitamin D in depression has received considerable attention (5). Indeed, a recent systematic review and meta-analysis (6) of case-control, cross-sectional, and prospective observational cohort studies of depression and vitamin D provided some support for an association of depression with low concentrations of serum 25-hydroxyvitamin D (25[OH]D), the primary circulating form of vitamin D that is used to determine a patient's vitamin D status (7). Although these findings are compelling, the most important questions concerning the association of vitamin D with depression are (1) is the association causal, and (2) does vitamin D supplementation affect depressive symptom level?

We conducted a systematic review and meta-analysis of randomized controlled trials to investigate whether vitamin D supplementation improves -- or potentially worsens-- depressive disorder or depressive symptoms. On the basis of previous narrative reviews (8, 9), we hypothesized that vitamin D supplementation would have a minimal effect on depression in these trials.

Methods

We followed the *Cochrane Handbook for Systematic Reviews* to plan and conduct this meta-analysis (10), and we report our findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (11).

Data Sources and Searches

We systematically identified all randomized controlled trials that examined the effect of vitamin D supplementation on depressive disorder or depressive symptoms. Although it is difficult to detect treatment effects in those with few, if any, baseline depressive symptoms (12), we nonetheless included studies of both nondepressed and depressed individuals because of our interest in determining whether vitamin D supplementation either worsened or improved depression. Potentially relevant articles were identified by searching the biomedical electronic databases Ovid MEDLINE, The Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, Allied and Complimentary Medicine Database, PsycINFO, and Scopus. Dates were searched from inception to the second week of May 2013. Registers of clinical trials were searched for unpublished and ongoing studies. The initial search was conducted on June 1, 2012, and weekly searches were conducted thereafter through May 15, 2013. All relevant subject headings and free-text terms were used to represent vitamin D and depression. Additional records were identified by searching

the reference lists of relevant studies and reviews and by using the Related Articles feature in PubMed and the Cited Reference Search in ISI Web of Science. The search did not have any language or year restrictions, and we considered all studies regardless of their publication status. The exact search terms and search strategies for each database are reported in Table S1 in Supplemental Digital Content 1.

To determine the studies to be included in the meta-analysis, 2 trained reviewers (N.E., P.L.) independently read the title and/or abstract of every record retrieved. All potentially relevant articles were investigated as full text, and differences in opinion between the 2 reviewers were resolved by consensus or in consultation with one of the authors (J.A.S.).

Database Extraction and Quality Assessment

Two additional reviewers (L.F., K.H.) worked independently of each other and in consultation with the first author to extract relevant data from each report. These data included study characteristics (setting, design, randomization, masking, intent-to-treat analyses, sample size, trial entry criteria related to depression and vitamin D, and primary depression measure), participant demographic characteristics (age and sex), and clinical characteristics (baseline concentration of 25[OH]D and depression status). Additional data were extracted to characterize the type, amount, frequency, duration, and mode of delivery of vitamin D supplementation, type of control conditions, and trial requirements regarding the use of nonstudy vitamin D supplementation. Study quality was assessed using the Cochrane Risk of Bias Tool (13), which considers the reporting and adequacy of random sequence generation, randomization concealment, masking of participants, research personnel, and outcome assessors, and methods for dealing with participants who were lost to follow-up or had missing data for other reasons.

Data on mean (SD) depressive symptoms were extracted as the primary end point given that no studies included a diagnosis of depressive disorder as an end point. We used available data to calculate change-from-baseline differences within and between treatments. Change scores were standardized using the SD of change. Two studies (14, 15) reported results as mean (SD) preintervention and postintervention depressive symptom scores but did not provide estimates of the pre-post correlation of depression scores that are required to compute effect sizes. We attempted to contact study authors to request these additional data but ultimately estimated the pre-post correlation of depression scores using published data (16, 17). Two studies included 2 intervention groups with different doses of vitamin D supplementation (14, 18), and 1 study included 2 control groups (15). We pooled means and SDs across the 2 intervention and control groups in these studies to calculate effect sizes.

Statistical Analysis

Data were entered into an electronic database and analyzed using Comprehensive Meta Analysis (version 2.0; BioStat Software, Englewood, NJ) (19). We weighted each study's effect size using the inverse variance method. To summarize intervention effects across trials, we pooled data in random-effects models, which provide more conservative summary effect estimates than fixed-effects models even in the absence of statistically significant between-study heterogeneity (20). Data are expressed as standardized mean differences

(SMDs) and 95% CIs for the primary end point of depressive symptoms. The magnitude of intervention effects was characterized as small (SMD = 0.2), medium (SMD = 0.5), and large (SMD = 0.8) according to Cohen's recommendations (21).

Between-study heterogeneity was assessed using the Cochrane Q statistic, with a significance level set at $P < .10$. The magnitude of heterogeneity was evaluated using the I^2 statistic, and values of 50% or greater were considered indicative of substantial heterogeneity (10). Post hoc subgroup analyses were conducted for baseline depression status (trials of participants with clinically significant depressive symptoms or major depressive disorder vs trials that excluded such participants or whose participants had baseline depressive symptom scores indicative of no or mild depression [22, 23]) and baseline vitamin D status (insufficient vs sufficient [7]). Mixed-effects analyses, in which random-effects models are used to combine studies within subgroups, were used to conduct subgroup analyses, and the Q statistic was calculated to compare intervention effects among studies.

We conducted sensitivity analyses in which we substituted a range of pre-post correlations (r = 0.1, 0.4, 0.8, and 0.9) in depressive symptoms for the 2 studies that did not report these data. An additional sensitivity analysis was conducted that excluded an unpublished thesis that qualified for inclusion in our meta-analysis (15).

Although the validity of procedures for detecting publication bias is limited when the number of studies is as small as in the current meta-analysis (24), we planned to inspect funnel plots and compute Rosenthal's fail-safe N, which provides an estimate of the number of missing studies with nonsignificant effects that would be needed to make a significant P value for the observed aggregate effect nonsignificant (25). Given that we obtain a nonsignificant overall effect, however, we did not conduct these assessments.

RESULTS

Search Results

The search for randomized controlled trials of vitamin D supplementation for depressive disorder or depressive symptoms identified 2394 reports. Details of the study flow are documented in Figure S1, Supplemental Digital Content 1. Of the 1829 nonduplicate articles identified by the initial search, 1797 were deemed ineligible or irrelevant on the basis of their titles and abstracts; the remaining 32 articles, in addition to 2 articles (18, 26) that were identified after the completion of the initial search through weekly database searches, required full reading. Of these 34 potentially eligible articles, 7 randomized controlled trials (14, 15, 16, 26-29) met our criteria for inclusion. Nearly all studies that were excluded at the full-text stage of review did not feature intervention designs; however, we excluded 3 intervention studies that did not feature randomization (30), did not include a depression outcome measure (31), or for which no published data could be identified (32).

Trial Characteristics

Table 1 and **Table 2** detail the characteristics of the 7 randomized controlled trials identified by our search that examined the effect of vitamin D supplementation for depressive

symptoms (total N= 3191; age range, 18-79 years) by participant and study characteristics and depression and vitamin D trial entry criteria, respectively. All trials were published between 2003 and 2013. Two studies required that participants have low levels of 25(OH)D at baseline (18, 29), and participants in a third study (15) of older adults also had baseline concentrations of 25(OH)D consistent with definitions of vitamin D deficiency (<50 nmol/L). Five trials either did not specifically recruit participants with depression (15) or excluded those with depressive disorders, elevated depressive symptoms, and/or current antidepressant use (14, 27 - 29). The baseline depressive symptom scores of the participants in these 5 trials suggest that they had no depressive disorder or minimal, nonclinically significant depressive symptoms (22, 23). The primary end point for all 7 studies was depressive symptom scores, although the specific instruments used to assess depressive symptoms varied.

Characteristics of the vitamin D supplementation used in each of the 7 randomized controlled trials included in this review are reported in **Table 3**. All but one study (18) specified vitamin D_3 (cholecalciferol) as the type of supplement. Mode of delivery, dosage (range, 600-300,000 IU), frequency (daily vs weekly vs one-time administration), and duration (range, 6 weeks to 2 years) of supplementation varied between studies, as did types of control conditions and requirements regarding the use of nonstudy vitamin D supplementation.

Assessment of study quality with the Cochrane Risk of Bias Tool demonstrated at least one unclear or high risk of bias in all but 2 trials (Table S2, Supplemental Digital Content 1) (28, 29). The most common types of bias pertained to randomization concealment (14, 15, 16, 26, 27) and masking of research personnel (14, 15, 18, 26, 27), which were rated as posing a high or unclear risk in 5 of 7 trials.

Effect of Vitamin D Supplementation for Depressive Symptoms

The overall reduction in depressive symptoms associated with vitamin D supplementation was small and nonsignificant (SMD, −0.14; 95% CI, −0.33 to 0.05; $P = 0.16$) **(Figure)**. Analyses of heterogeneity revealed substantial variation among intervention effects ($Q_6 = 20.2$, $P = 0.003$, $I^2 = 70.3$), and SMDs ranged from −0.96 ($P = 0.004$) in favor of vitamin D supplementation to 0.15 ($P = 0.49$) in favor of control.

Subgroup analyses were conducted to identify potential sources of heterogeneity among intervention effects **(Figure)**. The 4 studies of participants whose baseline vitamin D status was sufficient (>50 nmol/L) showed a larger reduction in depressive symptoms (SMD, −0.22; 95% CI, −0.53 to 0.08; $P = 0.15$) than the 3 studies of participants whose baseline vitamin D status was insufficient (SMD, −0.05; 95% CI, −0.31 to 0.20; $P = 0.69$); however, the difference in intervention effects between these 2 subgroups of studies was not significant ($Q_1 = 0.70$, $P = 0.40$) and neither subgroup of studies had a statistically significant intervention effect.

A post hoc subgroup analysis was also conducted to compare studies of participants with clinically significant depressive symptoms and/or major depressive disorder with those that either explicitly excluded participants with clinically significant depression or included

participants with nonclinically significant depressive symptoms at baseline **(Figure)**. These analyses revealed that the effect of vitamin D supplementation on depressive symptoms was moderate and statistically significant in the 2 studies of participants with clinically significant depressive symptoms and/or major depressive disorder (SMD, −0.60; 95% CI, −1.19 to −0.01; $P = 0.046$). In contrast, the effect of vitamin D supplementation on depressive symptoms among trials of nonclinically depressed participants was small and not statistically significant (SMD, −0.04; 95% CI, −0.20 to 0.12; $P = 0.61$). The difference in intervention effects between these 2 subgroups approached statistical significance ($Q_1 = 3.22$, $P = 0.07$). We planned to investigate further sources of heterogeneity by conducting subgroup analyses of dose; however, the use of different amounts, frequencies, and durations of vitamin D in each trial precluded this analysis.

Sensitivity analyses, in which a range of pre-post correlations among depressive symptom scores were substituted for the published estimates used in the primary analyses, did not change the statistical significance of the overall intervention effect or the analyses of between-study heterogeneity among effects. Removal of the unpublished thesis from our analyses also did not change the primary results.

Discussion

This systematic review and meta-analysis report is the first to examine the effect of vitamin D supplementation on depressive symptoms. We found that vitamin D supplementation neither worsened nor improved depressive symptoms across 7 randomized controlled trials, but considerable heterogeneity of study characteristics and intervention effects among studies was observed. Although baseline vitamin D status did not explain the between-study heterogeneity in intervention effects, baseline depression status may have. Whereas vitamin D supplementation was associated with a statistically significant, moderate reduction in depressive symptoms across 2 trials that recruited patients with clinically significant depressive symptoms and/or major depressive disorder, its effect in trials of participants with nonclinically significant depression was small and nonsignificant.

Notwithstanding the biological plausibility of a causal role for vitamin D deficiency in depression (33), the results of this review suggest that the use of vitamin D supplementation to reduce depressive symptoms for individuals without clinicallysignificant depression may not be warranted. Although trials of nonclinically depressed individuals differed considerably in the type of participants they included, their study locations and designs, and characteristics of their intervention and control conditions, 4 of these 5 trials had nonsignificant intervention effects (15, 27-29). These null findings are not entirely surprising given that the association of vitamin D with depressive symptoms has not clearly been established in nondepressed individuals. Although a recently conducted meta-analysis of observational studies of vitamin D deficiency and depression in older adults found a moderate and statistically significant association of lower vitamin D levels with clinically meaningful depression in cross-sectional studies, the studies included in that review had several methodologic biases (6). In particular, cross-sectional studies cannot rule out the possibility of reverse causation in which patients with subthreshold depressive symptoms or depressive disorders have less exposure to sunlight and thus lower vitamin D levels (9).

Interestingly, the same meta-analysis included 3 prospective cohort studies (34-36) that found a statistically significant, 2-fold increased risk of developing clinically significant depression or depressive symptoms among those with low vitamin D levels. To date, however, no study has examined whether vitamin D supplementation offsets the risk of *incident* depressive disorder or depressive episodes, and future randomized controlled trials may thus be needed to do so.

Of note, not all trials of nonclinically depressed participants in this review featured null intervention effects. A trial conducted by Jorde and colleagues (14), which included participants with overweight and obesity, found a small but statistically significant reduction in depressive symptoms with vitamin D supplementation. This trial had an unclear risk of bias in 3 of the 6 domains of the Cochrane Risk of Bias Tool; however, its findings suggest a possible need for additional studies that examine mechanistic aspects of the association of vitamin D with depressive symptoms and vitamin D intervention effects in this distinct population. These findings also hint that overweight and obesity may contribute to some of the observed heterogeneity of effects among the studies included in this meta-analysis, although we could not test this hypothesis given a lack of reported data on overweight and obesity across trials.

Although our subgroup analysis of trials with vs without participants with clinically significant depressive symptoms and/or major depressive disorder suggests a possible explanation for the heterogeneity of intervention effects observed in overall analyses, several characteristics other than participants' baseline depression status differed between the former trials and the latter ones. In particular, characteristics of the vitamin D interventions used in all 7 trials varied, and no 2 studies featured the same dose or duration of vitamin D supplementation. In addition, the trial in which we observed the largest effect of vitamin D supplementation on depressive symptoms not only included participants with major depressive disorder and elevated depressive symptoms (26) but also used vitamin D supplementation as an adjunctive intervention to pharmacotherapy with fluoxetine. The other trial of participants with clinically significant depression used a dose of vitamin D that far exceeds the single, but not necessarily cumulative, doses featured in other studies (18). Vitamin D supplementation was also administered via intramuscular injection in that trial, whereas other trials included in this review administered supplementation via capsule or food. The interaction between vitamin D supplementation and selective serotonin reuptake inhibitors such as fluoxetine, the comparative efficacy of different vitamin D dose amounts, and the implications of using alternate modes of administration of vitamin D supplementation thus remain unknown, and require investigation in future trials.

As a parallel to the present study, it is worth examining studies evaluating the efficacy of omega-3 supplements for depression, which resemble studies of vitamin D for depression in several ways. As with studies of vitamin D for depression, a large proportion of omega-3 trials involve healthy participants or those with subclinical depression (37). Meta-analyses of omega-3 for depression have pooled across these studies and those of participants with clinical depression (37) and concluded that the efficacy of omega-3 for depression is stronger in clinical samples than in nonclinical ones. Similar to the results of one of the studies (26) included in this review, the effect of omega-3 on depression may also be

stronger when used to supplement traditional antidepressants rather than as monotherapy (38). Most importantly, meta-analyses of studies of omega-3 for depression have helped to guide subsequent research, as we hope the current meta-analysis will likewise do.

Several limitations of the current review warrant attention. First, we identified few trials overall, the design characteristics of each of these studies differed considerably, and all but 2 of these trials (28, 29) had at least one unclear or high risk of bias. Although the heterogeneity among studies is indeed striking, it is not unlike the heterogeneity observed among studies of vitamin D for other conditions (39). The overall quality of the evidence from each trial is thus low and poses uncertainty regarding the true effect of vitamin D supplementation on depressive symptoms. Although it is unlikely that poor methodologic quality biased the results of trials of nondepressed participants *toward* the null hypothesis of no intervention effect, it may have inflated the treatment effects observed in the 2 trials of participants with clinically significant depression. Second, some of the decisions that we made while conducting our review may limit the validity of our findings. Although we drafted a protocol and planned extensively before conducting our review and analyses, we did not register the protocol or anticipate in advance all of the analyses that we conducted. In particular, we performed 2 post hoc subgroup analyses given that we could not conduct an a priori analysis of whether differences in vitamin D dose contributed to potential heterogeneity among intervention effects. Nonetheless, these post hoc analyses were informed by reasoned clinical and empirical considerations, and we did not conduct an excessive number of these analyses. A third limitation is that we did not consider whether vitamin D supplementation increased levels of 25(OH)D in each trial, and it is possible that the null effects seen in some trials reflect a failure of the intervention to improve vitamin D status.

The small number of studies included in this review, the considerable heterogeneity among these studies, and the unlikely possibly of detecting intervention effects among nonclinical samples (12) may lead one to wonder whether a systematic review and meta-analysis of vitamin D supplementation for depression at this time is premature. Given the recently published meta-analysis of observational studies of vitamin D deficiency and depression (6), we believe that now is precisely the time to highlight the dearth of evidence for a causal role of vitamin D in relation to depression, and point to the necessary next steps to determine whether any clinical benefit is likely to be gained by vitamin D supplementation.

Notwithstanding these limitations and considerations, this systematic review and meta-analysis report represents a timely contribution to the emerging literature on vitamin D and depression that may inform the development of future clinical trials. Although we found a nonsignificant effect on depressive symptoms associated with vitamin D supplementation, the intervention effects across the 7 randomized controlled trials included in this review varied significantly and considerably. We observed suggestive evidence that vitamin D supplementation may be effective for participants with major depressive disorder or subthreshold, clinically significant depressive symptoms but not for those without; however, other potential sources of the between-study heterogeneity of intervention effects such as obesity exist.

We still have limited data to conclusively address whether vitamin D supplementation is effective as either a unique drug or an adjuvant to pharmacotherapy for the treatment of depression. Future trials are needed that not only target depressed patients but also consider baseline levels of vitamin D (40) and how vitamin D dosing and mode of delivery may contribute to its effects on depressive symptoms. We found no evidence of prior dosing studies for vitamin D supplementation in patients with depression, and it may be time to determine the optimal dose before testing such a dose against placebo in a double-blind trial. Adding vitamin D supplementation to the armamentarium of remedies for depression, although tempting, appears premature based on the evidence that has accumulated on this topic thus far.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

25(OH)D	25-hydroxyvitamin D
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SD	standard deviation
SMD	standardized mean difference
IU	international units
RCT	randomized controlled trial
MDD	major depressive disorder
BDI	Beck Depression Inventory
CES-D	Center for Epidemiologic Studies Depression scale
GDS	Geriatric Depression Scale
HDRS	Hamilton Depression Rating Scale
MADRS	Montgomery-Ashburg Depression Rating Scale
IM	intramuscular

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Study, Year (Reference)	Mean Difference in Depressive Symptoms (95% CI)	Z	P
Dean et al., 2011 (28)	-0.12 (-0.46 to 0.23)	-0.66	0.51
Bertone-Johnson et al., 2012 (27)	0.06 (-0.02 to 0.14)	1.37	0.17
Jorde et al., 2008 (14)	-0.29 (-0.52 to -0.06)	-2.51	0.01
Hogie-Lorenzen et al., 2003 (15)	0.15 (-0.28 to 0.58)	0.69	0.49
Kjaergaard et al., 2012 (29)	0.01 (-0.25 to 0.27)	0.09	0.93
Mozaffari-Khosravi et al., 2013 (18)	-0.35 (-0.76 to 0.06)	-1.68	0.09
Khoraminya et al., 2012 (26)	-0.96 (-1.62 to -0.31)	-2.89	0.00
Random-effects model for all studies	**-0.14 (-0.33 to 0.05)**	**-1.41**	**0.16**
Nondepressed			
Dean et al., 2011 (28)	-0.12 (-0.46 to 0.23)	-0.66	0.51
Bertone-Johnson et al., 2012 (27)	0.06 (-0.02 to 0.14)	1.37	0.17
Jorde et al., 2008 (14)	-0.29 (-0.52 to -0.06)	-2.51	0.01
Hogie-Lorenzen et al., 2003 (15)	0.15 (-0.28 to 0.58)	0.69	0.49
Kjaergaard et al., 2012 (29)	0.01 (-0.25 to 0.27)	0.09	0.93
Random-effects model for subgroup	**-0.04 (-0.20 to 0.12)**	**-0.51**	**0.61**
Depressed			
Mozaffari-Khosravi et al., 2013 (18)	-0.35 (-0.76 to 0.06)	-1.68	0.09
Khoraminya et al., 2012 (26)	-0.96 (-1.62 to -0.31)	-2.89	0.00
Random-effects model for subgroup	**-0.60 (-1.19 to -0.01)**	**-1.99**	**0.046**
Sufficient Vitamin D			
Dean et al., 2011 (28)	-0.12 (-0.46 to 0.23)	-0.66	0.51
Bertone-Johnson et al., 2012 (27)	0.06 (-0.02 to 0.14)	1.37	0.17
Jorde et al., 2008 (14)	-0.29 (-0.52 to -0.06)	-2.51	0.01
Khoraminya et al., 2012 (26)	-0.96 (-1.62 to -0.31)	-2.89	0.00
Random-effects model for subgroup	**-0.22 (-0.53 to 0.08)**	**-1.43**	**0.15**
Insufficient Vitamin D			
Hogie-Lorenzen et al., 2003 (15)	0.15 (-0.28 to 0.58)	0.69	0.49
Kjaergaard et al., 2012 (29)	0.01 (-0.25 to 0.27)	0.09	0.93
Mozaffari-Khosravi et al., 2013(18)	-0.35 (-0.76 to 0.06)	-1.68	0.09
Random-effects model for subgroup	**-0.05 (-0.31 to 0.20)**	**-0.40**	**0.69**

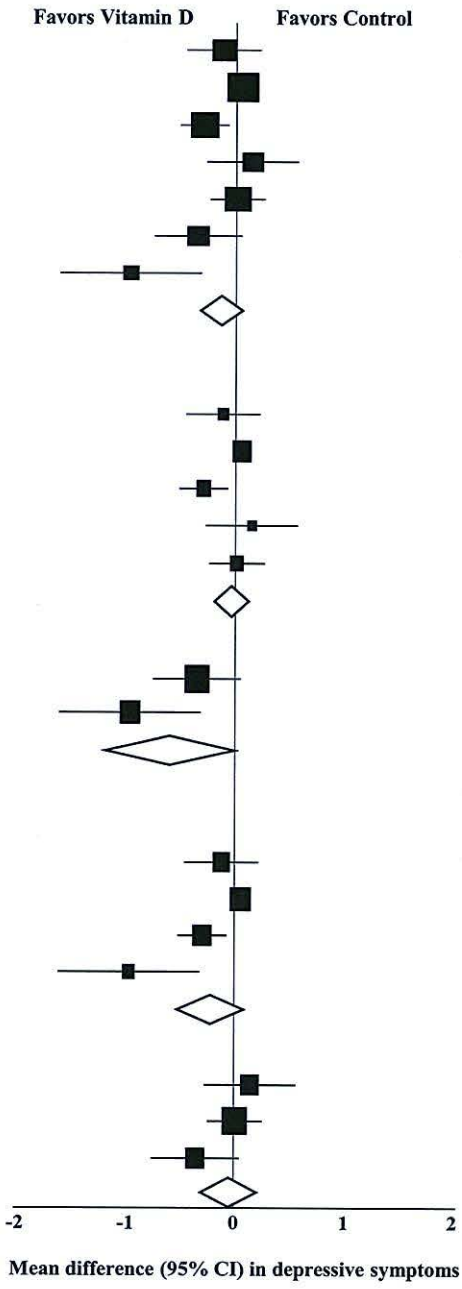

Figure 1.

Forest plots of randomized controlled trials investigating the effect of vitamin D supplementation on depressive symptoms, overall and by depression and vitamin D status. Five weighted pooled intervention effect estimates (diamonds) are shown: one for the full set of 7 trials (overall) and one each for nondepressed participants, depressed participants, participants with sufficient vitamin D, and participants with insufficient vitamin D. Data are expressed as standardized mean differences with 95% CI, using the inverse-variance method and random-effects models. Trials categorized as "nondepressed" did not specifically recruit participants with depression or included participants whose baseline depressive symptom scores were indicative of no or mild depression; trials categorized as "depressed" included participants with clinically significant depressive symptoms and/or major

depressive disorder. Categorization of trials as "sufficient vitamin D" or "insufficient vitamin D" was based on participants' baseline concentrations of 25-hydroxyvitamin D and established cutpoints for interpreting these concentrations (7).

Table 1

Participant and Study Characteristics of Randomized Controlled Trials Investigating the Effect of Vitamin D Supplementation on Depressive Symptoms

Study, Year (Reference)	Participants	Country	Intervention, N	Control, N	Age, y	Study Design
Hogie-Lorenzen, 2003 (15)	Community members	United States	31 (19 F, 12 M)	67 (39 F, 28 M)	>60	Three-arm RCT with pre-post assessment
Jorde et al, 2008 (14)	Community members and outpatients with overweight or obesity	Norway	222 (135 F, 87)	112 (71 F, 41 M)	21-70	Three-arm RCT with pre-post assessment
Dean et al, 2011 (28)	Healthy volunteers	Australia	63 (39 F, 24 M)	65 (34 F, 31 M)	18-30	Two-arm RCT with pre-post assessment
Bertone-Johnson et al, 2012 (27)	Postmenopausal women	United States	1109 (1109 F, 0 M)	1143 (1143 F, 0 M)	50-79	Two-arm RCT with pre-post assessment
Kjaergaard et al, 2012 (29)	Community members with low 25(OH)D level	Norway	120 (66 F, 54 M)	110 (63 F, 47 M)	30-75	Two-arm RCT with pre-post assessment
Khoraminya et al, 2012 (26)	Psychiatric outpatients with MDD and elevated depressive symptoms	Iran	20 (17 F, 3 M)	20 (17 F, 3 M)	18-65	Two-arm RCT with repeated assessments
Mozaffari-Khosravi et al, 2013 (18)	Psychiatric outpatients with elevated depressive symptoms and low vitamin D levels	Iran	75 (52 F, 23 M)	34 (26 F, 8 M)	20-60	Three-arm RCT with pre-post assessment

Abbreviations: 25(OH)D, 25-dihydroxyvitamin D; RCT, randomized controlled trial; MDD, major depressive disorder.

Table 2

Depression and Vitamin D Trial Entry Criteria in Randomized Controlled Trials Investigating the Effect of Vitamin D Supplementation on Depressive Symptoms

Study, Year (Reference)	Depression Entry Criteria	Depression Measure	Baseline Depression Score, Mean (SD)	Vitamin D Entry Criteria	Baseline 25(OH)D Concentration, Mean (SD), nmol/L
Hogie-Lorenzen, 2003 (15)	None reported	GDS	3.3 (3.0)	None reported	8.2 (3.0)
Jorde et al,2008 (14)	Current antidepressant use excluded	BDI	4.8 (4.3)	None reported	53.1 (14.3)
Dean et al, 2011 (28)	Current mood disorder excluded	BDI	6.5 (6.7)	None reported	76.6 (19.9)
Bertone-Johnson et al, 2012 (27)	Diagnosed mental disorder excluded	Burnam scale	Not reported	None reported	Not reported
Kjaergaard et al, 2012 (29)	Elevated depressive symptoms (BDI >29, MADRS >34) or depression diagnosis excluded	BDI	4.0 (6.8)	25(OH)D <55 nmol/L	47.5 (15.7)
Khoraminya et al, 2012 (26)	Diagnosis of MDD and a HDRS score ≥15 included; recent, non-study antidepressant use excluded	HDRS	32.1 (7.3)	None reported	58.2 (10.7)
Mozaffari-Khosravi et al, 2013 (18)	BDI-II scores ≥17 included; current antidepressant use excluded	BDI-II	26.9 (7.2)	25(OH)D <40 nmol/L	Not reported

Abbreviations: 25(OH)D, 25-dihydroxyvitamin D; BDI, Beck Depression Inventory, CES-D, Center for Epidemiologic Studies Depression scale; GDS, Geriatric Depression Scale; HDRS, Hamilton Depression Rating Scale; MADRS, Montgomery-Ashburg Depression Rating Scale; MDD, major depressive disorder.

Table 3

Characteristics of Vitamin D Supplementation in Randomized Controlled Trials Investigating the Effect of Vitamin D Supplementation on Depressive Symptoms

Study, Year (Reference)	Amount of Vitamin D	Frequency	Duration	Mode of Delivery	Type of Vitamin D	Control Type(s)	Nonstudy Vitamin D Use
Hogie-Lorenzen, 2003 (15)	600 IU	Daily	8 weeks	Fortified cheese	D_3	Nonfortified cheese or no cheese	Routine use excluded (>2 days per week)
Jorde et al, 2008 (14)	20,000 or 40,000 IU	Weekly	1 year	Capsule	D_3 with calcium	Identical-appearing placebo capsule	Not allowed per exclusion
Dean et al, 2011 (28)	5000 IU	Daily	6 weeks	Capsule	D_3	Identical-appearing placebo capsule with lactose	Not allowed per exclusion
Bertone-Johnson et al, 2012 (27)	400 IU	Daily	2 years	Not reported	D_3 with calcium	Identical-appearing placebo	<1000IU/d allowed
Kjaergaard et al, 2012 (29)	20,000 IU	Weekly	6 months	Capsule	D_3	Identical-appearing placebo capsule	Not allowed per exclusion
Khoraminya et al, 2012 (26)	1500 IU	Daily	8 weeks	Capsule	D_3 adjunctive to fluoxetine	Identical-appearing placebo capsule with starch	Not allowed per exclusion
Mozaffari-Khosravi et al, 2013 (18)	150,000 or 300,000 IU	Once	NA	IM injection	Not reported	No injection	Not allowed per exclusion

Abbreviations: IM, intramuscular; NA, not applicable; D3, cholecalciferol

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Review

Vitamin D supplementation to reduce depression in adults: Meta-analysis of randomized controlled trials

Usha Gowda M.H.N. [a], Mutsa P. Mutowo M.P.H. [a], Ben J. Smith Ph.D. [a], Anita E. Wluka Ph.D. [b], Andre M.N. Renzaho Ph.D. [a,c,d,*]

[a] Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia
[b] Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Melbourne, Victoria, Australia
[c] Centre for International Health, Burnet Institute, Melbourne, Victoria, Australia
[d] School of Social Sciences and Psychology, University of Western Sydney, Sydney, New South Wales, Australia

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ABSTRACT

Objectives: The aim of this study was to estimate the weighted mean effect of vitamin D supplementation in reducing depressive symptoms among individuals aged ≥18 y diagnosed with depression or depressive symptoms.
Methods: A meta-analysis of randomized controlled trials (RCTs) in which vitamin D supplementation was used to reduce depression or depressive symptoms was conducted. Databases MEDLINE, EMBASE, psych INFO, CINAHL plus, and the Cochrane library were searched from inception to August 2013 for all publications on vitamin D and depression regardless of language. The search was further updated to May 2014 to include newer studies being published. Studies involving individuals aged ≥18 y who were diagnosed with depressive disorder based on both the Diagnostic and Statistical Manual of Mental Disorders or other symptom checklist for depression were included. Meta-analysis was performed using random effects model due to differences between the individual RCTs.
Results: The analysis included nine trials with a total of 4923 participants. No significant reduction in depression was seen after vitamin D supplementation (standardized mean difference = 0.28; 95% confidence interval, −0.14 to 0.69; $P = 0.19$); however, most of the studies focused on individuals with low levels of depression and sufficient serum vitamin D at baseline. The studies included used different vitamin D doses with a varying degree of intervention duration.
Conclusions: Future RCTs examining the effect of vitamin D supplementation among individuals who are both depressed and vitamin D deficient are needed.

Introduction

Mental health disorders are the leading cause of disability-adjusted life years (DALYs) in Australia and worldwide, accounting for 13% of all DALYs [1,2]. Among mental health disorders, depression remains the leading cause of disability worldwide, and contributes significantly to the global burden of disease [3]. Depression is estimated to affect 350 million individuals and imposes a significant economic burden, not just on individuals with the disorder, but also on their families, communities, employers, and health care systems [3].

In addition to genetic, biological, environmental, and psychological factors, nutritional deficiency is reported to be an important factor contributing to depression [4]. Recent discovery that the brain possesses vitamin D receptors [5] suggests the possibility that mood and depressive disorders may be related to vitamin D deficiency and insufficiency [6]. Vitamin D is a unique neurosteroid hormone [5,7] and is involved in numerous brain processes including neuroimmunomodulation, neuroprotection, and brain development [8]. Several studies also have evaluated the relationship for vitamin D and other affective disorders such

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* Corresponding author. Tel.: +61 39 903 0802; fax: +61 39 903 0556.
E-mail address: andre.renzaho@monash.edu (A. M. N. Renzaho).

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0899-9007/

as seasonal affective disorder (SAD), premenstrual syndrome, and fibromyalgia [6].

Results from small randomized trials, however, are inconsistent and provide modest support for a possible effect of vitamin D on mood [9–12]. Although evidence suggests that vitamin D is likely to have important functions in the human brain [5,7], whether or not these functions relate to the occurrence of major depression is unclear [6]. Some observational studies have suggested that there is an association between vitamin D deficiency and major depressive disorder [13], whereas others have found no such association [14]. Notwithstanding these contradictory findings, pooled effects from a recent meta-analysis of cross-sectional and cohort studies found an association between depression and low vitamin D levels [15]. The observational nature of these studies means that it is difficult to ascertain a cause and effect. However, recent meta-analyses [16,17] of randomized controlled trials (RCTs) to assess the efficacy of vitamin D supplementation on depression in adults did not show any significant effect on depression. The studies included in both the reviews varied considerably. Although one study included seven trials and the other six, only three studies were included in both the reviews [16,17]. Moreover, neither of these reviews included trials that investigated the effect of vitamin D supplementation on SAD. Over the past 2 decades, small randomized trials have provided mixed evidence that vitamin D supplementation significantly improves symptoms of SAD [10,12].

In view of the discrepancies in the included studies, and also to include the studies on SAD, our current meta-analysis is an update of the existing reviews. In light of current evidence, this study will make a valuable addition to the current findings on the efficacy of vitamin D supplementation on depression.

Methods

Search strategy

We searched, without language restriction, for all publications on vitamin D and depression. MEDLINE, EMBASE, psych INFO, CINAHL plus, and Cochrane library (up to August 2013) databases were used with separate comprehensive search strategies developed in consultation with an experienced medical librarian. The search was further updated to May 2014 to include newer studies being published. The clinical trials registries clinicaltrials.gov and current controlled trials (controlled-trials.com) were searched for any ongoing trials. Additional publications were hand searched from the reference lists of every primary study.

The following MeSH search terms were adapted: "Vitamin D," "25-HydroxyvitaminD_2," "25 Hydroxyvitamin D_3," and "depression," and "randomized controlled trial." This search strategy was adapted for all other databases modifying as per compatibility of the database. The search strategy for MEDLINE is presented in Table 1.

Inclusion/exclusion criteria

This study included trials involving individuals aged ≥18 y whose primary diagnosis was depressive disorder based on Diagnostic and Statistical Manual of Mental Disorders criteria or other symptoms checklist for depression. Trials in which the primary focus was on a major psychiatric condition like bipolar disorder or schizoaffective disorder were excluded. Studies in which participants experienced depressive symptoms due to a medical condition were included.

RCTs that compared vitamin D supplement only or vitamin D combined with other vitamins or antidepressants, with a placebo were included. Oral, parenteral, intramuscular, and intravenous vitamin D administration were all considered and included in the present study. Studies in which control participants were exposed to light therapy or used different doses of vitamin D were excluded. The primary outcome measure included the measure of depression or depressive mood either as a continuous measure (depression symptom scale) or as a dichotomous outcome (proportion of patients with depressive symptoms) compared with placebo. Secondary outcome measure included change in quality of life.

Table 1
Database: Ovid MEDLINE 1946 to Daily update

Vitamin D supplementation	Depression	Randomized controlled trials
1. exp Vitamin D/	26. Depression/	32. randomized controlled trial.pt.
2. 25-Hydroxyvitamin D 2/	27. Depressive Disorder/	33. controlled clinical trial.pt.
3. 25 hydroxyvitamin D.mp.	28. dysthymia.mp.	34. randomized .ab.
4. vitamin D2.mp.	29. exp Mood Disorders/	35. placebo.ab.
5. vitamin d3.mp.	30. depress*.mp.	36. drug therapy.fs.
6. 25 hydroxyvitamin d3.mp.	31. mood disorder*.mp.	37. randomly.ab.
7. 25 OH VIt D.mp.		38. trial.ab.
8. 1,25 dihydroxyvitamin D3.mp.		39. groups.ab.
9. 1,25-dihydroxyvitamin D3.mp.		40. 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39
10. 1-alpha hydroxyvitamin D3.mp.		41. exp animals /not humans.sh.
11. 25 hydroxycalciferol*.mp.		42. 40 not 41
12. hydroxycholecalciferol*.mp.		43. or/1-25
13. 1,25 dihydroxycholecalciferol.mp.		44. or/26-31
14. 1,25-dihydroxycholecalciferol.mp.		45. 43 and 44
15. calcifediol.mp.		46. 42 and 45
16. calciferol.mp.		
17. calcitriol.mp.		
18. calcidiol.mp.		
19. 24,25 dihydroxyvitamin D3.mp.		
20. 25 hydroxycholecalciferol*.mp.		
21. 25 dihydroxycholecalciferol*.mp.		
22. cholecalciferol*.mp.		
23. Vitamin D.mp.		
24. 25-Hydroxyvitamin D 2.mp.		
25. ergocalciferol*.mp.		

Study selection and data extraction

Selection of studies and data extraction followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The titles and abstracts identified by the search were reviewed independently by two of the authors (UG and MM). Articles were screened and selected for full-text review if they met the selection criteria. Any disagreements were resolved by discussion between the two reviewers. If consensus could not be reached, other co-authors were available to determine the eligibility and to approve the final list of retained studies. Two reviewers (UG and MM) extracted data separately using a standard form that recorded study year, study participants, sample size, sex and age characteristics, vitamin D supplementation dose and duration, serum 25-hydroxyvitamin (OH)D at baseline and post-treatment, primary, and secondary outcomes. Study authors were contacted to obtain missing data for the analysis.

Quality and risk for bias of included studies

Using the Jadad scale [19,20] with allocation concealment added as an additional quality criterion [15], two reviewers assessed the quality of the study. The risk for bias was assessed for each study that is included in the analysis using the Cochrane Collaboration Risk of Bias tool [21]. This tool includes random-sequence generation, allocation concealment, blinding of the participants and personnel, incomplete outcome data, selective outcome reporting, and other bias.

Statistical analysis

Data were analyzed using Review Manager (RevMan) version 5.2 for windows. Meta-analysis was performed using random effects due to differences between the individual RCTs. To enable the analysis of both continuous and dichotomous outcomes, the generic inverse variance outcome was used. Heterogeneity between included studies was assessed using both χ^2 test and the I^2 statistic, with I^2 >50% suggesting substantial heterogeneity and 75% to 100% as considerable heterogeneity [21]. Standardized mean difference (SMD) was calculated for both continuous and dichotomous outcomes for the post-intervention changes for depression scores. As baseline and final score were reported for a different number of participants due to missed study or withdrawal, we calculated the SMD for post-intervention changes rather than change from baseline [21]. SMD was calculated for the mean and SD of the scores. For those studies reporting median and range, mean and SD were calculated using a formula that used the values of median and range for estimation [22]. If the study had more than one intervention arm, effect sizes were calculated separately for each group. We were unable to perform meta-analysis on the secondary outcome due to the small number of studies. Only two studies reported measures of well-being [23,24].

Because it takes up to 8 wk for serum levels of 25(OH)D to plateau [25], subgroup analysis was performed for studies of shorter (<8 wk) and longer duration (>8 wk). Subgroup analysis was also performed to assess whether the effect of vitamin D supplementation varied according to vitamin D levels at baseline, based on the cutoff values recommended by the Institute of Medicine for serum 25(OH)D sufficiency ≥50 nmol/L [26]. Further subgroup analyses were undertaken to examine the effect of vitamin D doses of >4000 IU/d or <4000 IU/d based on recommended tolerable upper-level intake of 4000 IU/d [27]. To assess the efficacy of vitamin D supplementation alone, sensitivity analysis was undertaken by excluding studies that had supplemented vitamin D along with other supplements or antidepressants.

Results

The initial search yielded 2195 articles, 217 of which were duplicates. After removal of duplicates and other nonrelevant studies, 74 articles were assessed for eligibility. After reading the full text, 9 studies met inclusion criteria and were included in the final analysis. The screening and selection of the studies are presented in the PRISMA flowchart shown in Figure 1.

Characteristics of the included studies

Table 2 summarizes the retained studies, which were from Australia, Norway, the United States, Iran, and Turkey. All the studies compared vitamin D with active placebo. Two studies had two intervention groups that tested the effects of different doses of vitamin D [12,28]. In two of the studies, vitamin D intervention was supplemented by calcium [28,29]. In one study, some participants (13% at the beginning of the study) were taking antidepressants [29]. Another study [30] involved depressed participants who were taking fluoxetine (antidepressant). The minimum dose of vitamin D used in the studies was 400 IU/d [12] and the maximum dose of calcitrol was 2 million IU (0.25 g)/d [31]. Minimum duration of the intervention was 5 d [12]; maximum duration was 5 y [29]. A continuous outcome score for depressive symptoms was used in all but one study. The exception was a study in which participants were characterized as depressed or not depressed post-intervention [23].

Inclusion and exclusion of studies compared with the other reviews

The studies included in our review varied compared with the previous reviews [16,17]. Our objective to include the study on SAD allowed us to include another study [12] that was excluded in both the reviews. On the other hand, we excluded one study [4] because it did not administer placebo in the control group. Participants in the intervention arm were given intramuscular injection, whereas the control group received no injection in this study. In addition, only published and peer-reviewed studies were included in our meta-analysis. Hence, one unpublished work [32], which was included in another study [16], was excluded.

Risk for bias in the included studies

Figure 2 shows the risk for bias. Two studies [12,24] that did not mention the method of random-sequence generation were considered as having unclear risk for bias for randomization. Five studies [12,24,28,29,31] had high risk for bias for allocation concealment. Blinding of participants and research personnel was either high or unclear in five studies [12,28–31]. Publication bias was assessed using funnel plots from RevMan (Fig. 3). Visual examination of the funnel plots shows the funnel plot not being symmetrical with effect estimates from a smaller study being scattered to the left bottom of the plot. This may indicate the negative findings from the smaller study being unpublished or the study may be of lesser quality, especially failing to conceal allocation [33]. Because the overall

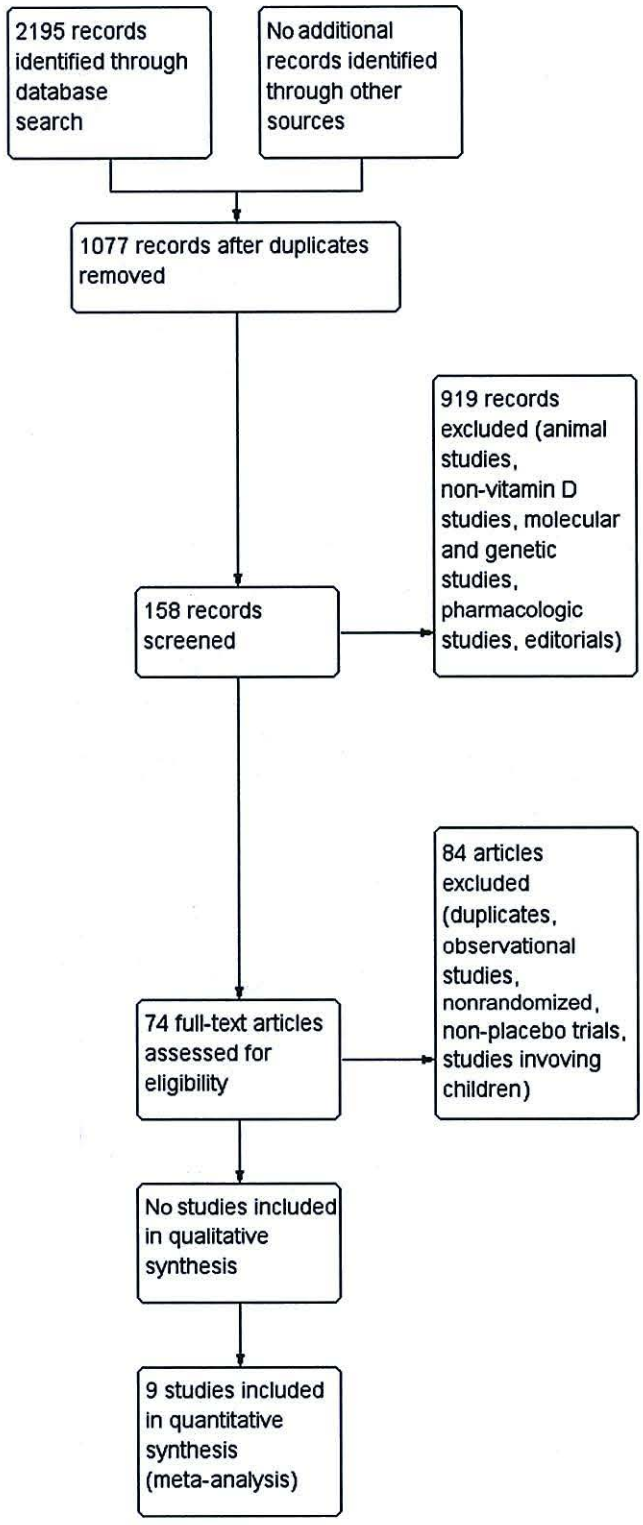

Fig. 1. Diagram of the study selection.

Table 2
Characteristics of the included study

Study	Year	Country	Total	Mean age (y)	Participants	Baseline serum 25 (OH)D (nmol/L)	Treatment	Dose	Duration	Outcomes	Assessment scale used	Study quality
Lansdowne et al. [12]	1998	Australia	44	22	Male and female students	Not measured	Vitamin D_3	400 and 800 IU/d	5 d	Seasonal Affective disorder	PANAS	Unclear randomization; placebo-controlled
Jorde et al. [28]	2008	Norway	440	47	Obese men and women from out-patient clinic	Median: 52.6	Vitamin D + calcium	20 000 IU 40 000 IU/wk	1 y	Depression	BDI	Unclear randomization; placebo-controlled
Arvold et al. [24]	2009	US	100	58	Mild to moderate vitamin D-deficient adult primary care patients	Mean: 44.67 ± 3.5	Vitamin D	50 000 IU/wk	8 wk	Symptoms in Fibromyalgia patients	FIQ	Randomization by compounding pharmacy; placebo-controlled
Dean et al. [34]	2011	Australia	128	21.75	Male and female university volunteers	Mean: 76.2 ± 2.6	Vitamin D	5000 IU/d	6 wk	Depression Anxiety	BDI State-Trait Anxiety Inventory	Varying block randomization; placebo-controlled
Sanders et al. [23]	2011	Australia	1434	75	Community-dwelling older women	Median 53	Vitamin D_3	500 000 IU/y	3–5 y	Depression and well-being	GHQ WHO well-being index SF-12	Computer randomization; placebo-controlled
Bertone et al. [29]	2012	US	2252	22	Women from calcium and vitamin D trial	Mean: 52.9 ± 21.1	Vitamin D + calcium + antidepressants	400 IU/d	2 y	Depression	Burnam scale	Permuted block algorithm randomization; placebo-controlled
Kjaergaard et al. [35]	2012	Norway	237	53.3	Adults from TROMSO study	Mean: 47.4 ± 15.8	Vitamin D	40 000 IU/wk	6 mo	Depression	BDI	Central randomization unit; placebo-controlled
Yalamanchili et al. [31]	2012	US	246	71.4	Older postmenopausal women	Mean: 76.3 ± 9.4	Calcitriol	0.25 g bid (2 million IU)	36 mo	Depression	GDS	Computer-generated randomization; placebo-controlled
Khoraminya et al. [30]	2013	Iran	42	Vitamin D 38.1 ± 10.07 Placebo 39.65 ± 8.27	Depressed adults	Vitamin D 58.78 ± 10.05 Placebo 57.53 ± 11.03	Vitamin D_3	1500 IU/d	8 wk	Depression	HDRS	Unclear randomization; placebo-controlled

BDI, Beck Depression Inventory; bid, twice daily; FIQ, Fibromyalgia Impact Questionnaire; GDS, Geriatric Depression Scale; GHQ, General Health Questionnaire; HDRS, Hamilton Depression Rating Scale; PANAS, Positive and Negative Affect Schedule; SF, short form; WHO, World Health Organization

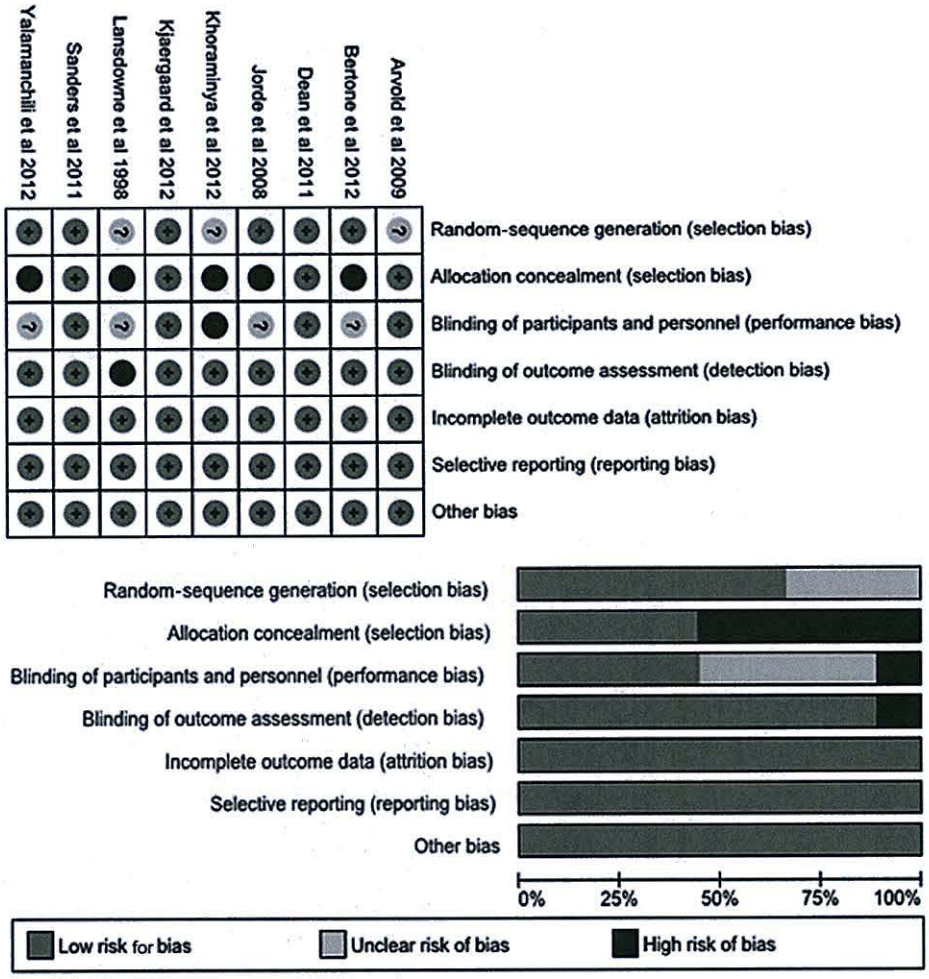

Fig. 2. Risk for bias for individual and across studies.

effect of the vitamin D supplementation was nonsignificant in the current review, publication bias may not have influenced our findings.

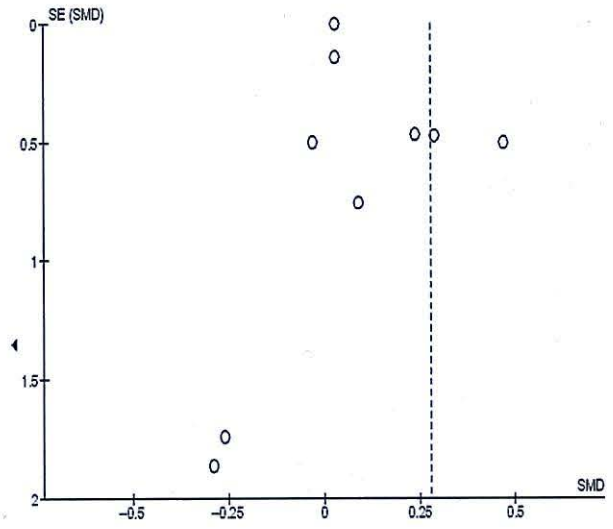

Fig. 3. Funnel plot for the publication bias for vitamin D supplementation and depressive symptoms.

Effects of intervention

The analysis included nine trials involving 4923 participants. Combining effect sizes from nine trials for depression as an outcome found a pooled effect of SMD = 0.28 (95% confidence interval [CI], −0.14 to 0.69; $P = 0.19$) (Fig. 4) favoring the placebo, which was statistically nonsignificant. However, we found a high degree of heterogeneity ($\chi^2 = 65.27$; $df = 10$; $P < 0.05$; $I^2 = 85\%$). Inspection of the results showed the study by Dean et al. [34] vas the likely source of heterogeneity. Exclusion of this study significantly reduced the heterogeneity, which favored the placebo (SMD = 0.03; 95% CI, 0.02–0.04; $P < 0.05$) and was statistically significant.

Subgroup analysis

Subgroup analysis for baseline cutoff points on serum 25(OH)D levels

Combining the studies for those participants with serum 25(OH)D levels ≥50 nmol/L at baseline, the treatment favoured the placebo group, however, the effect was statistically nonsignificant (SMD = 0.30; 95% CI, −0.18 to 0.78; $P = 0.22$).

Similarly, analysis of the outcome among participants with serum levels <50 nmol/L at baseline found effects that favored the placebo but were statistically nonsignificant (SMD = 0.23; 95% CI, −0.55 to 1.02; $P = 0.56$) (Fig. 5).

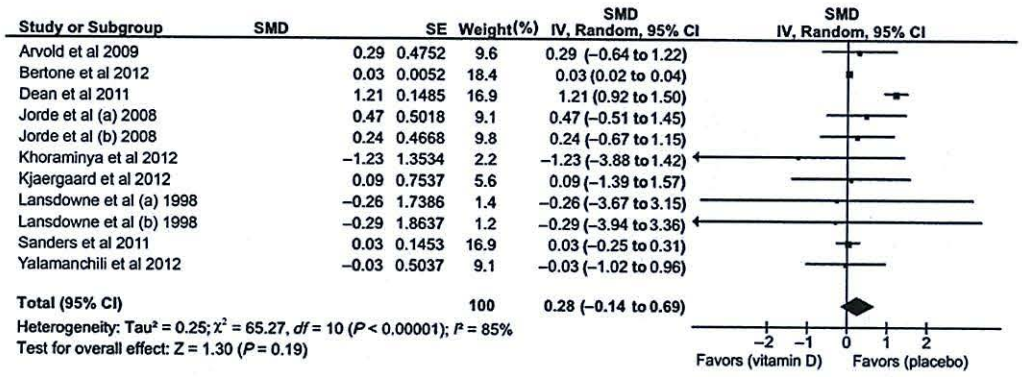

Fig. 4. Forest plot comparing the vitamin D and placebo for depression (includes all eight studies). SMD, standard mean difference. Jorde et al (a) 2008, the effect of 20,000 IU/wk; Jorde et al (b) 2008, the effect of 40,000 IU/wk; Lansdowne et al (a) 1998, the effect of a dose of 400 IU/d; Lansdowne et al (b) 1998, the effect of a dose of 800 IU/d.

Subgroup analysis for the duration of intervention

Analysis of the effects of vitamin D supplementation for shorter (<8 wk) and longer duration (>8 wk) favored placebo, and were statistically significant (SMD = 1.19; 95% CI, 0.90–1.48; $P < 0.05$ and 0.03; 95% CI, −0.02 to 0.04; $P < 0.05$, respectively). (Fig. 6).

Subgroup analysis for high and low dose of vitamin D

Combining studies where the dose of vitamin D was <4000 IU/d found an effect size that favored the placebo, and was statistically significant (SMD = 0.03; 95% CI, 0.02–0.04; $P < 0.05$). A slightly improved intervention effect was found in studies where vitamin D dose was >4000 IU/d, but this was not statistically greater than the placebo (SMD = 0.52; 95% CI, −0.19 to 1.23; $P = 0.15$) (Fig. 7).

Sensitivity analysis

Sensitivity analysis was conducted by excluding studies that tested the effect of vitamin D supplementation together with other supplements, or antidepressants; no statistically significant effect was found of vitamin D supplementation alone on depression (SMD = 0.34; 95% CI, −0.34 to 1.01; $P = 0.33$) (Fig. 8).

Discussion

The current analysis was an update of the existing meta-analyses of RCTs for the efficacy of vitamin D supplementation on depression. One study that examined the effect of vitamin D on SAD was an addition in our meta-analysis, which was excluded in both the reviews [16,17]. To eliminate the possibility of detection bias, we excluded the studies that did not administer placebo to the control group. Congruent with the previous two meta-analyses [16,17], the pooled analysis undertaken here did not find any significant reduction in depressive symptoms after vitamin D supplementation. Our sensitivity analysis, which excluded studies that administered vitamin D supplementation along with other supplements or antidepressants, did not find any effect on the symptoms of depression. The possible influence that various methodological attributes of the included studies had on this finding deserve consideration. First, participants in most of the studies had low depression levels at baseline [34] and very few were diagnosed as clinically depressed [30,31,35]. It is postulated that vitamin D is clinically beneficial for individuals who are depressed, but not in healthy participants [31].

Second, longitudinal studies have shown that low vitamin D status at baseline is associated with the development of

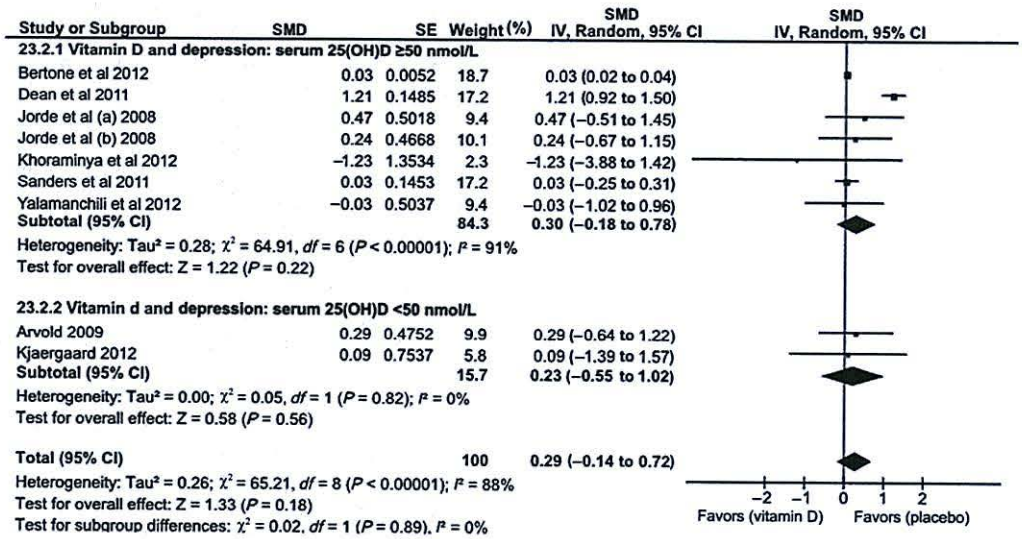

Fig. 5. Forest plot for studies comparing vitamin D and placebo for depression for the participants cutoff serum 25(OH)D > 50 nmol/L and <50 nmol/L at baseline. SMD, standard mean difference. Jorde et al (a) 2008, the effect of 20,000 IU/wk; Jorde et al (b) 2008, the effect of 40,000 IU/wk.

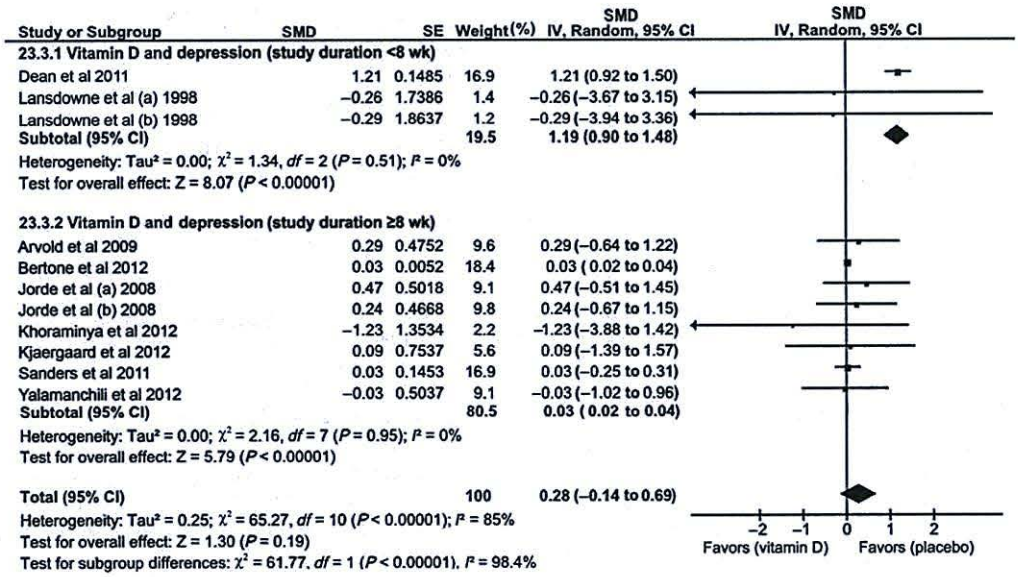

Fig. 6. Forest plot for studies comparing vitamin D and placebo for depression for the duration of study <8 wk and >8 wk. SMD, standard mean difference. Jorde et al (a) 2008, the effect of 20,000 IU/wk; Jorde et al (b) 2008, the effect of 40,000 IU/wk; Lansdowne et al (a) 1998, the effect of a dose of 400 IU/d; Lansdowne et al (b) 1998, the effect of a dose of 800 IU/d.

depression over time [36,37]. A recent meta-analysis of the relationship between serum 25(OH)D levels and risk for depression indicated an inverse association [38]. It has been proposed that depression is associated with increased inflammatory markers [39], whereas vitamin D has been shown to down-regulate inflammatory mediators such as nuclear factor-κB that have been linked to psychosocial stress and depression [40]. Participants with low serum 25(OH)D levels might therefore be expected to show the greatest effect of vitamin D supplementation on depressive symptoms. The present analysis included only two studies [19,30] that had participants with insufficient serum vitamin D levels at baseline.

Third, there was considerable variability in the doses of vitamin D administered in the studies included in our analyses. Some of the studies [23,24,31] used doses higher than the recommended tolerable upper-level intake of 4000 IU/d [27]. Serum levels acquired in some of these studies [23,24] were very high. In contrast, one study [25] used vitamin D 400 IU/d combined with personal intake up to 1000 IU/d. The author stated that the lower dose used in the study may not have been sufficient to affect the occurrence of depression.

Fourth, it may be possible that duration of follow-up in the included studies influenced the findings. Depression is a condition that develops slowly, lasts for several years, and fluctuates over time [30]. Single follow-up assessment points in the current studies may not be sufficient to determine significant changes in the depressive symptoms among intervention recipients.

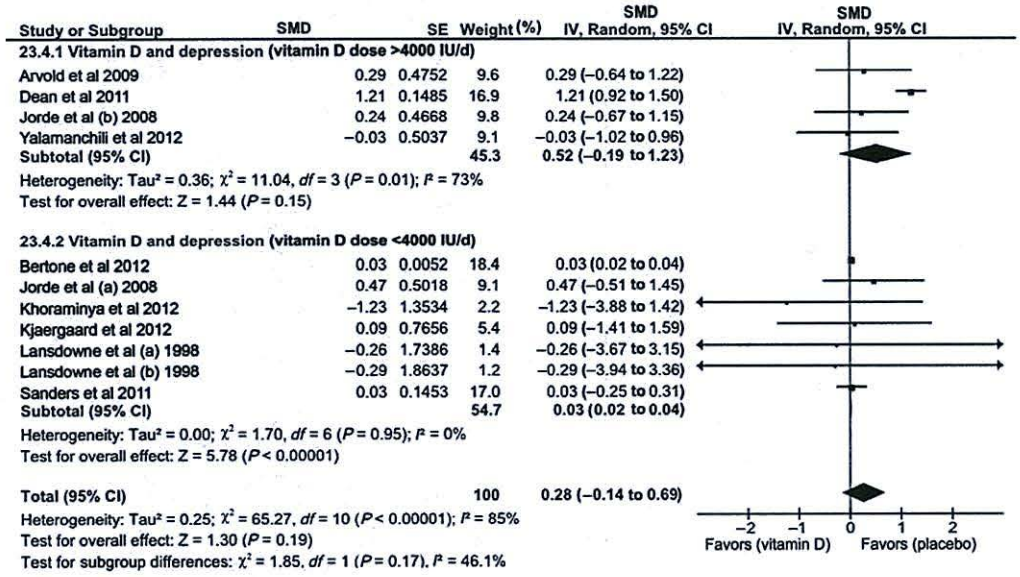

Fig. 7. Forest plot comparing vitamin D and placebo for depression for vitamin D dose <4000 IU and >4000 IU. SMD, standard mean difference. Jorde et al (a) 2008, the effect of 20,000 IU/wk; Jorde et al (b) 2008, the effect of 40,000 IU/wk; Lansdowne et al (a) 1998, the effect of a dose of 400 IU/d; Lansdowne et al (b) 1998, the effect of a dose of 800 IU/d.

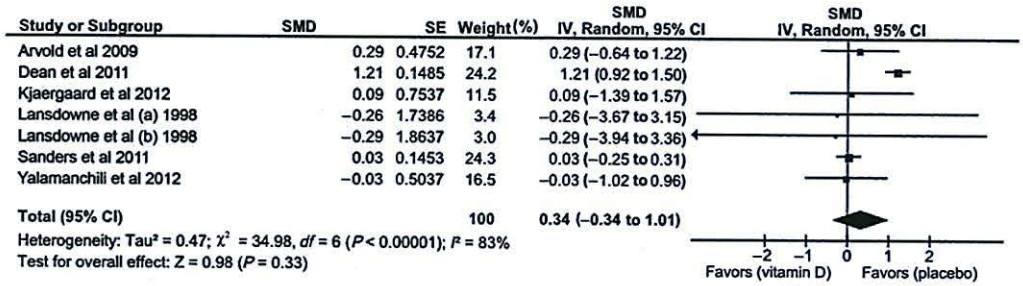

Fig. 8. Forest plot comparing vitamin D and placebo for depression, excluding studies in which participants were supplemented with vitamin D and calcium and antidepressants. SMD, standard mean difference. Lansdowne et al (a) 1998, the effect of a dose of 400 IU/d; Lansdowne et al (b) 1998, the effect of a dose of 800 IU/d.

The studies included employed psychometric measurement scales such as the Beck Depression Inventory, the Global Depression Scale, the General Health Questionnaire-12, the Hamilton Depression Rating Scale, and the Burnam scale, which are found to be valid for the assessment of depression [41–45] One study [24] that used the Fibromyalgia Impact Questionnaire (FIQ) on older patients is not specifically meant to measure depression. The FIQ is used to assess symptoms and functional status in patients with fibromyalgia [46], with self-reported severity of depressed mood included as a subscale. Similarly, one study [12] used the Positive and Negative Affect Schedule, which is intended to differentiate between positive and negative mood states [47]. Sensitivity analysis excluding these two studies did not have any significant changes in the pooled estimate (SMD = 0.29; 95% CI, −0.17 to 0.75; $P = 0.22$).

Vitamin D deficiency is common in the elderly, adolescents, obese individuals, people who are homebound and have limited sun exposure, and those with chronic illness [48]. Interestingly, these groups have been reported to be at risk for depression [49–51] and might benefit from vitamin D supplementation if it is found to be efficacious for the prevention and treatment of depression.

Limitations and strengths

There were certain limitations to our study. There were potential biases across few study designs. Two studies [16,25] had a high risk for bias due to uncertain allocation concealment and lack of blinding of the participants. There was a significant heterogeneity across the studies. The exclusion of the trial that was the source of significant heterogeneity, however, did not show any significant effect of vitamin D supplementation on depression [31].

The main strength of our study was the fact that we used comprehensive search methods to identify all potential studies for inclusion. Additional information required for the analysis was obtained from the study authors, thus enabling us to include all the studies. All the studies were assessed rigorously for their eligibility and assessed for the risk for bias across all studies. We were able to account for the variability of the outcome measures by using random effect method in our analysis.

Conclusion

In the current meta-analysis, our study did not support the evidence for the efficacy of vitamin D in improving depression among adults. Future RCTs that include individuals who are depressed and have low serum vitamin D levels are needed to determine the efficacy of vitamin D in the treatment of depression.

Acknowledgments

The authors acknowledge Lorena Romero and Birgit Spethmann librarians, Alfred Health, for their assistance in developing the search strategy. The authors also acknowledge Matthew Page and Sharon Kramer, Australasian Cochrane Centre, for their guidance in the data analysis. AR is supported by an ARC future fellowship and AW is supported by an NHMRC CDF level 2 Clinical (1063574).

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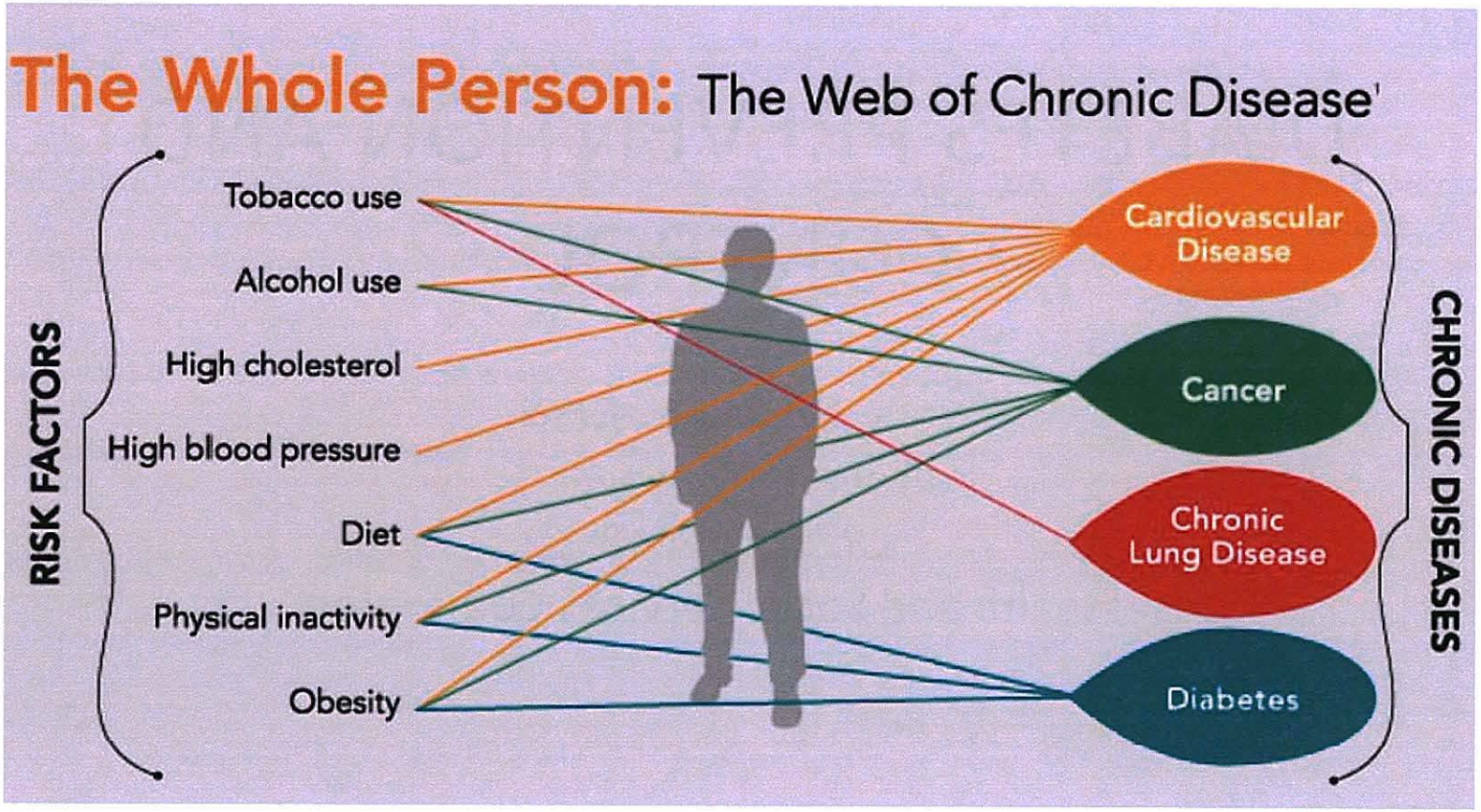
DIABETES PREVENTION AND CONTROL

Nelly Ayala, RN, MSN
Program Manager
October 2015
House Health and Social Services Committee

Chronic Disease Prevention & Health Promotion

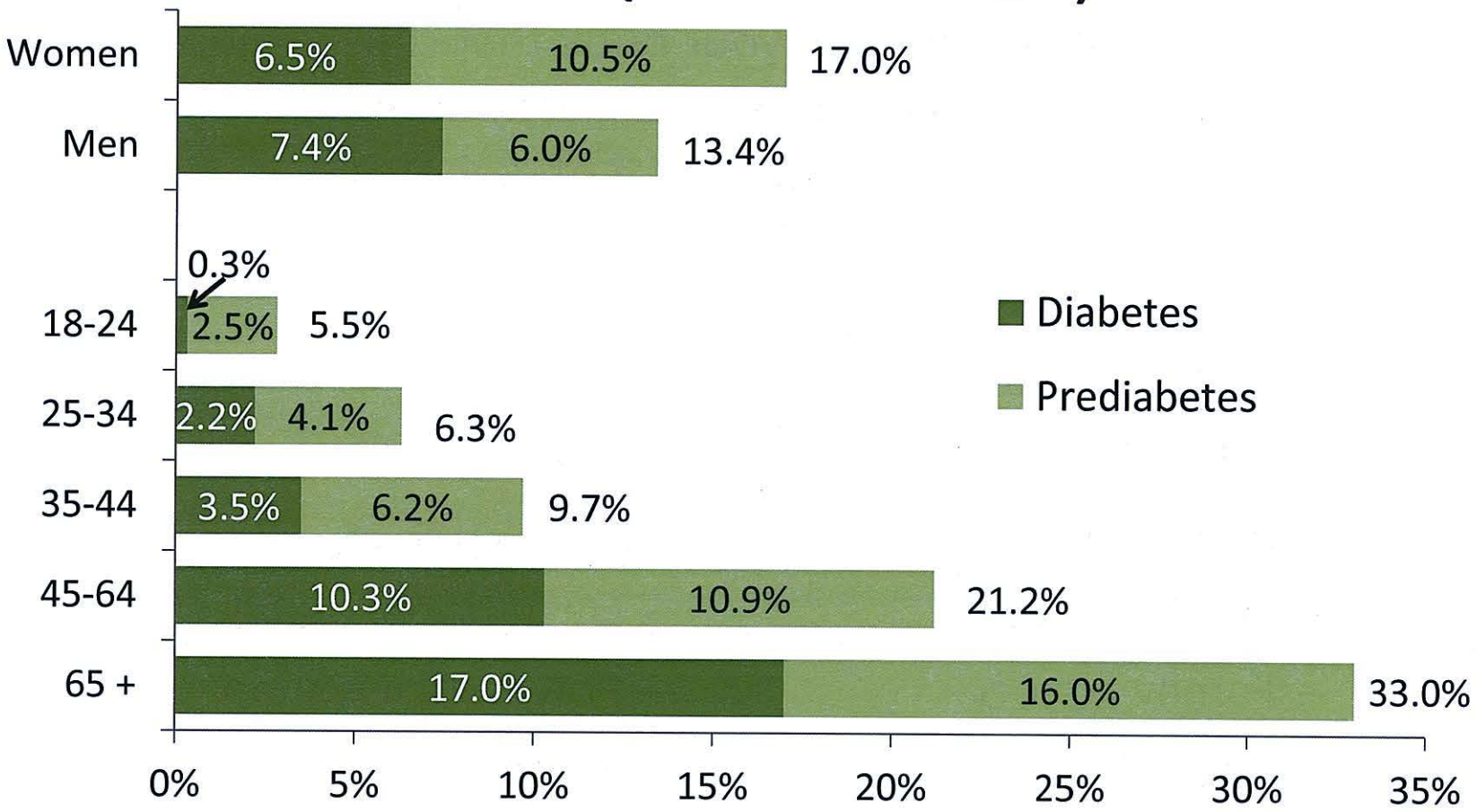


What is Diabetes?

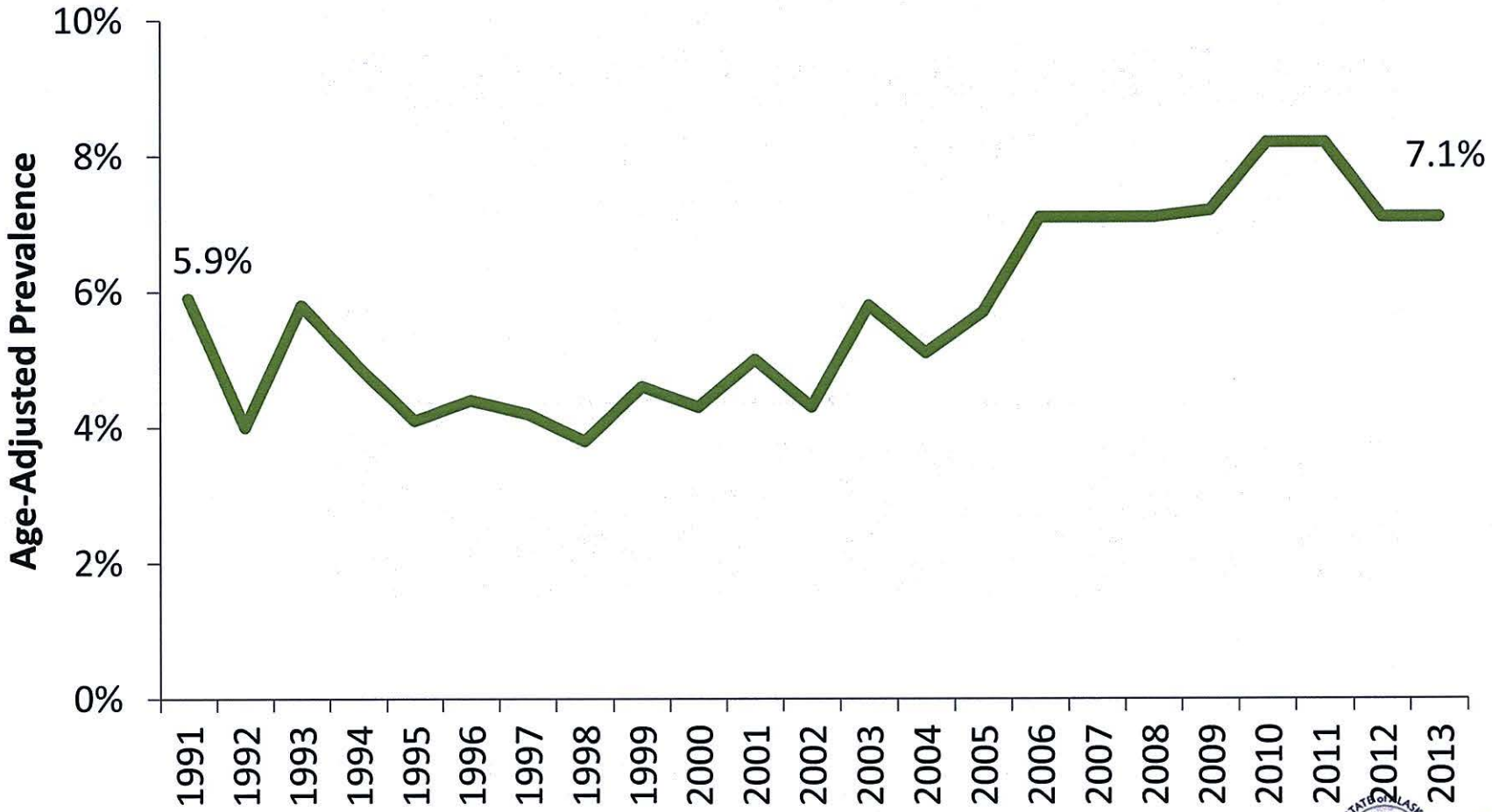
- Diabetes is a problem with your body that causes blood glucose (sugar) to raise higher than normal. Type 2 diabetes is the most common form of diabetes.

- Risk factors:
  - Weight
  - Inactivity
  - Fat distribution
  - Family history
  - Age
  - Race
  - Pre-diabetes
  - Gestational diabetes
  - Polycystic Ovarian Syndrome

Diabetes and Prediabetes Prevalence in Alaska (BRFSS 2013)



Age-Adjusted Diabetes Prevalence in Adults, Alaska (BRFSS)



Cost of Diabetes

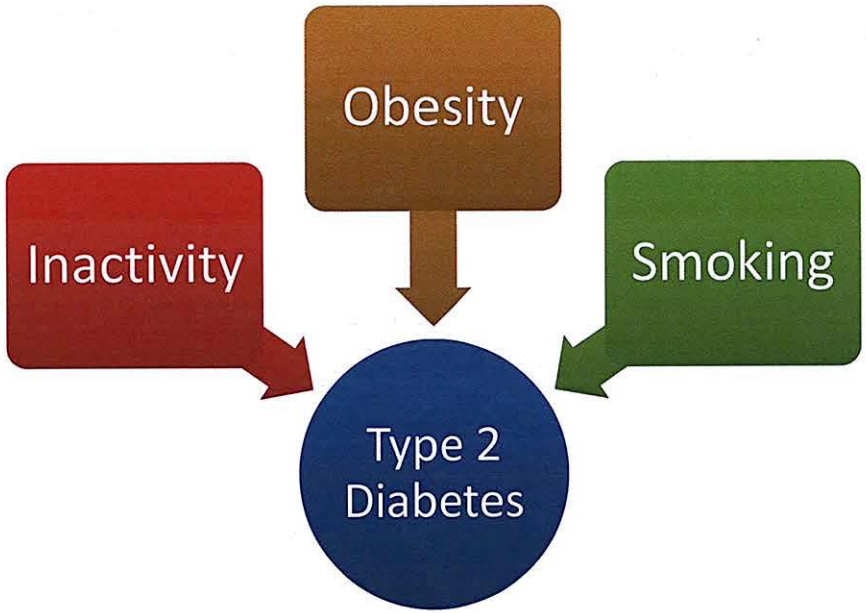
Table 1. The annual cost of care for adults

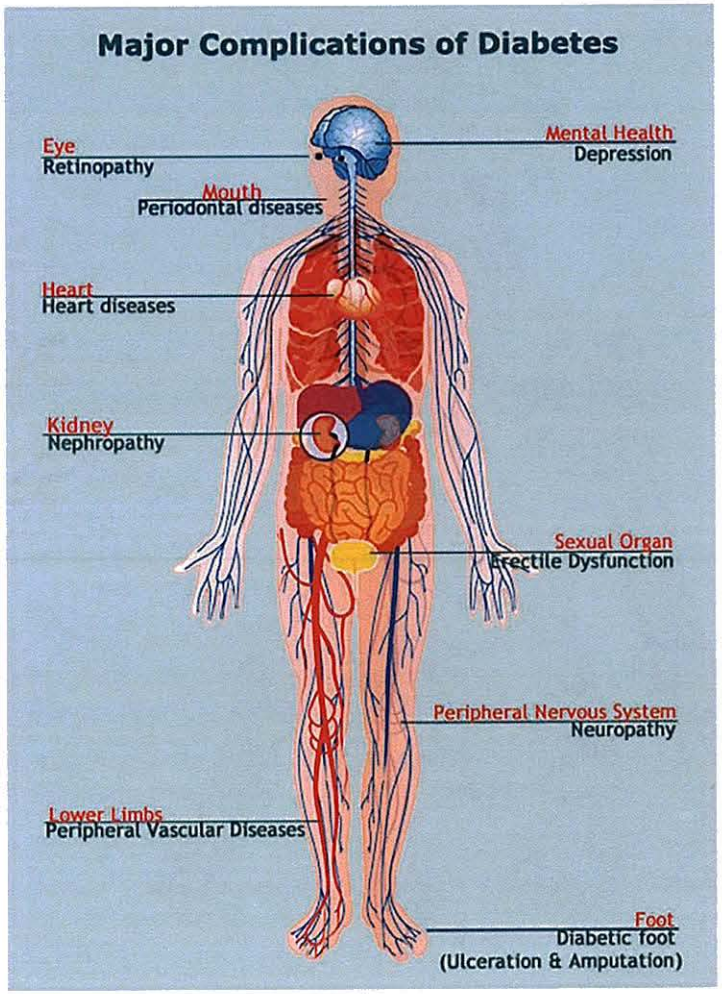
Year	Group	Diabetic	Non-Diabetic
2010	US Medicaid	$14,229	$4,568
2012	US Population	$13,741	$5,853

Table 2. Incurred cost of Medicaid beneficiaries 20 years and older in AK

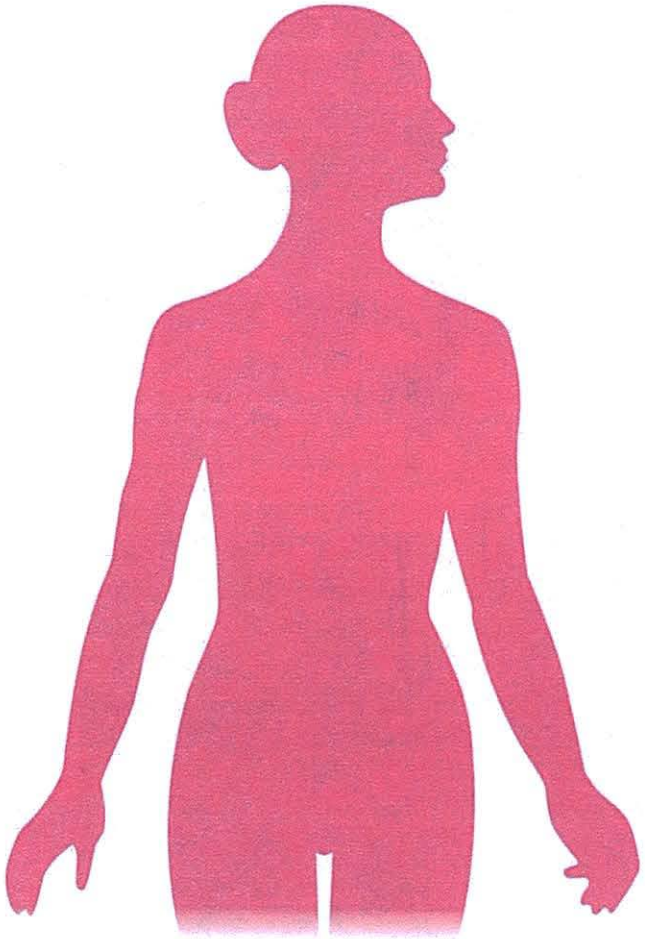
Fiscal Year	Beneficiaries with Diabetes	Incurred cost per diabetic beneficiary	Total cost of diabetic beneficiary
2012	5,938	$26,468	$157,167,553
2013	6,078	$25,940	$157,670,122
2014	6,296	$26,310	$165,655,028

The Key is Prevention





Among Alaska Adults with Diabetes…

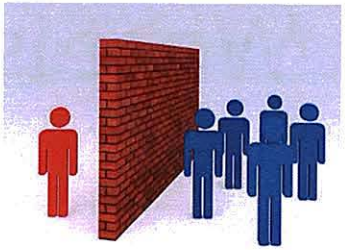


- **19%** smoke
- **30%** are inactive
- **59%** are obese

What is the Diabetes Prevention and Control Program?

- We are a program housed by the Chronic Disease Prevention & Health Promotion Division
- We work alongside the Obesity, Tobacco, Cancer, and Cardiovascular Disease Prevention and Stroke Programs
- The Diabetes Prevention and Control Program focuses on:
  - Type 2 diabetes
  - Adults
  - Access to resources for those who are affected by Type 2 diabetes

Barriers



- Access to healthcare
  - Continuity of care
  - Referrals to community resources
  - Case management at a community level
- Financial barriers
  - Insurance coverage
  - Staffing in programs
  - Cost of implementation, evaluation, and follow-through in programs
  - Cost of effective health communication plans
- Knowledge on impact of chronic disease on overall health
  - A person may have more than one chronic disease
  - The direct relationship between tuberculosis and diabetes, obesity and diabetes, smoking and diabetes
- Education on chronic disease
  - Education on how to self-manage a disease
  - Lack of information on chronic disease

Community-Based Approaches

- Get more people ***screened*** for Diabetes
  - Increasing screening via partnerships with local organizations, including:
    - Alaska Health Fairs Inc. to provide free HbA1C tests
    - Diabetes Lipid Clinic provide free HbA1C tests
    - Providence Outreach Center to inform the public about Alaska Health Fairs
    - YMCA to inform the public about Alaska Health Fairs and provide paper screening tests
    - Alaska Commercial to provide the public with paper screening tests in their store
    - Anchorage Neighborhood Health Centers to include information about screenings in their website and Facebook page
    - American Diabetes Association to get more paper screening tests throughout Alaska and generate more health fairs at new locations

Community-Based Approaches

- Increase ***awareness*** about Diabetes
  - Work with local organizations to spread the word about diabetes, including:
    - American Diabetes Association
    - Alaska Commercial Stores
    - Alaska Public Media
    - ANTHC Special Diabetes Program for Indians
    - YMCA
    - Faith-based organizations
    - Alaska Primary Care Associates
    - Providence Hospital – Alaska, Oregon, Washington
    - Alaska Regional
    - Migrant Clinic Network
    - Mountain Pacific Quality Health, etc.

Programmatic Approaches

- Self-Management Programs
  - Target audience: Adults who **have or care for someone with a chronic disease**, or want to get informed
  - 6-week programs, meet once a week, in a group setting (10 people or more)
  - Evidenced-based, recommended by 2015 ADA clinical guidelines
  - Goal: To teach individuals the goals necessary to adopt healthy habits
  - Two flavors:
    - Chronic Disease Self-Management Program (CDSMP)
    - Diabetes Self-Management Program (DSME)

Programmatic Approaches

- National Diabetes Prevention Program
  - Target audience: Adults who are **pre-diabetic or at-risk** of diabetes
  - Starting with 16 weeks of weekly meetings, then monthly meetings for up to a year, small group setting (six people or more and up to 13 people), using the online program for support as well as monthly support group meetings
  - On-site: Anchorage, Juneau, Fairbanks and in the near future Seward
  - Online program available

Benefits of DSME

- DSME reduces health complications including: heart disease, stroke, kidney disease, nerve damage, pregnancy complications and eye diseases.
- DSME can sustain successful long-term self-management with ongoing follow-up and support.
- DSME can lower hospitalization rates by 34%.
- DSME has been included in the American Diabetes Association's Standards of Medical Care in Diabetes and Clinical Practice Recommendations, it is noted as a best practice program.

Economic Savings of DSME

- For each diabetic Medicaid beneficiary in Alaska the cost is estimated to be approximately $26,300.
- If every Medicaid enrolled diabetic in Alaska took at least 1 DSME class, we would have an estimated Medicaid cost savings of **approximately $6.9 - $36 million per year**
  - A net $4 return-on-investment for every $1 spent.

Pre-Diabetes

NATIONAL DIABETES PREVENTION PROGRAM

TURN AROUND YOUR HEALTH

You CAN Prevent Diabetes

Did you know that in 2013, 8.2% of Alaskans were prediabetic? Among Alaska Natives, the prediabetes rate was 10.5%. The number of ALL people affected by prediabetes in Alaska is growing. The rate for ALL Alaskans ages 23-34 in 2013 was 4.1%, for those ages 35-44 was 6.2%, those ages 45-64 was 10.9%, and those over 65 years of age had a rate of 16%. The numbers are growing and it is our time to do something about it. We need to:

Turn Around Our Health! Take Initiative and ACT TODAY!

Sign up for an on-line program to help you change your life, increase your physical activity, and improve your healthy habits. Small changes can have big rewards.

IT IS YOUR LIFE! TURN AROUND YOUR HEALTH!

JOIN THE FIRST AUTOMATED INTERVENTION PROGRAM WITH PROVEN RESULTS!

AVAILABLE TO YOU

FREE OF CHARGE!

ACT TODAY!

SIGN UP TO: alive.turnaroundhealth.com

PROMO CODE: Alaska2015

This is brought to you by the State of Alaska Diabetes Prevention and Control Program in collaboration with Alaska Health Fairs, Inc.

3601 "C" Street. Suite 722.
Anchorage, AK 99503

Phone: 907-269-8035
Phone: 907-278-0234
E-mail: diabetes@alaska.gov

Summary Slide

- Self-management programs help empower people and provide them with the tools necessary to take care of their health. The total annual cost of Alaskan diabetic Medicaid beneficiaries is $165.7 million.
- Diabetes prevention is needed. CDC estimates that by 2050, 1 out of 3 people in the United States will have diabetes.
- People enjoy these services and learn from them. A person from Ketchikan who took a self-management class stated: *"I thoroughly enjoyed participating in this course and came away with a treasure trove of useful information that will serve me in the future."*

Resources

Alaska Diabetes Prevention and Control Program

Chronic Disease Prevention and Health Promotion

Nelly.Ayala@Alaska.gov or diabetes@alaska.gov

To stay informed on diabetes join our listserv: Visit Http://list.state.ak.us and Join "AKDiabetes"

American Diabetes Association
www.diabetes.org

National Diabetes Education Program
www.ndep.nih.gov

National Diabetes Information Clearinghouse (NDIC)
National Institute of Diabetes and Digestive and Kidney Diseases
www.diabetes.niddk.nih.gov

National Institute on Aging and Information Center
www.nia.nih.gov
www.nia.nih.gov/espanol

ALASKA STATE LEGISLATURE

REPRESENTATIVE GERAN TARR

Understanding and Reducing Adverse Childhood Experiences in Alaska

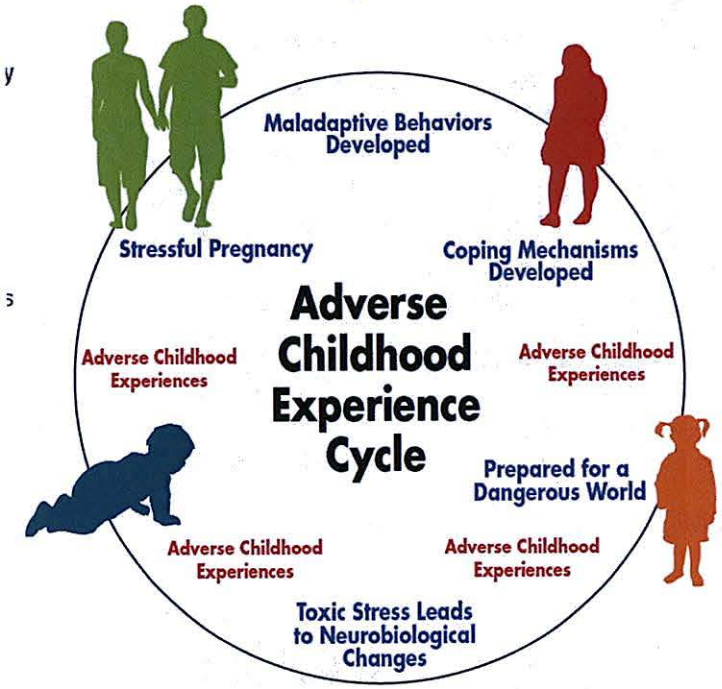
- Preventing Adverse Childhood Experiences (ACES) and supporting those who have experienced childhood trauma will save the State of Alaska significant health care costs.
- Adverse Childhood Experiences include physical, sexual and emotional abuse as well as dysfunction in a child's household. Dysfunction can include living with someone with mental illness, who abuses substances and or has spent time in prison. Adverse experiences also include living through a divorce and witnessing domestic violence.
- Compared with other with five other states (Arkansas, Louisiana, New Mexico, Tennessee and Washington) studied by the Center for Disease Control Alaska had the ACES rates in half of the categories.
- Adverse Childhood Experiences contribute to social, emotional and cognitive impairment, adoption of health-risk behaviors, disease, disability and social problems and early death.
- The State of Alaska Department of Health and Social Services provides resources and information on ways to prevent ACES.
- It is important to provide children who have experienced trauma with adequate medical care to help prevent the occurrence of additional traumatic events.
- Trauma informed practices can be incorporated into our education system to improve student outcomes.

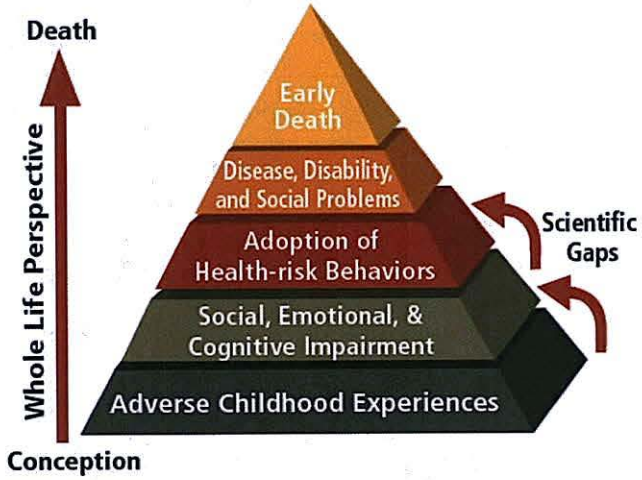
January-May: State Capitol • Juneau, AK 99801-1182 • (907) 465-3424 • Fax (907) 465-3793
June-December: 716 W. 4th Avenue • Anchorage, AK 99501• (907) 269-0144• Fax (907) 269-0148
Rep.Geran.Tarr@akleg.gov

The eight most commonly measured* traumas are in two general categories:

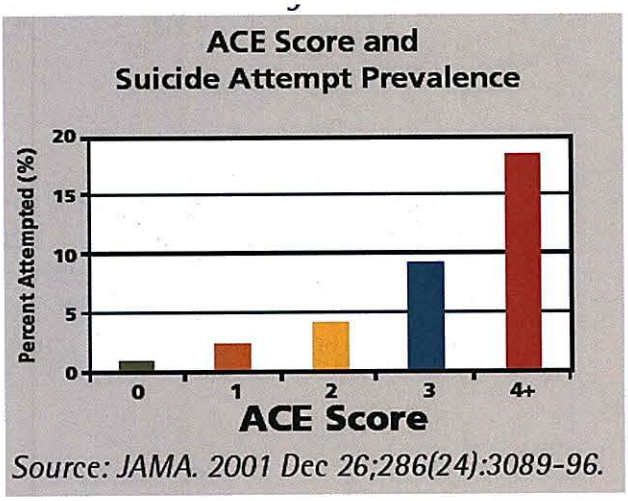
Table 1

Abuse	Household Dysfunction
1. Physical 2. Sexual 3. Emotional	4. Living with Someone with Mental Illness 5. Living with Someone with Substance Abuse 6. Separation or Divorce 7. Living with Someone who went to Jail or Prison 8. Witnessing Domestic Violence





ACE Score	Prevalence
0	33%
1	26%
2	16%
3	10%
4 +	16%



Source: *Adverse Childhood Experiences: Overcoming ACES IN Alaska*, State of Alaska, Department of Health and Social Services

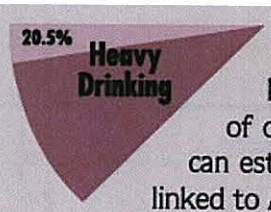
From the office of Rep. Tarr

ACE Rates in Six States						
Adverse Childhood Experience	Alaska	Arkansas	Louisana	New Mexico	Tennessee	Washington
Year study released	2013	2009				
ABUSE						
Verbal/Emotional	31.0%	24.3%	21.1%	28.1%	19.2%	**34.9%**
Physical	19.1%	14.1%	10.5%	**19.5%**	12.9%	18.1%
Sexual	**14.8%**	10.9%	9.9%	12.9%	12.7%	13.5%
HOUSEHOLD DYSFUNCTION						
Mental Illness in the Home	21.9%	17.0%	16.6%	19.4%	17.1%	**24.3%**
Incarcerated Family Member	**11.5%**	5.5%	7.2%	7.1%	8.6%	6.6%
Substance Abuse in Home	**33.8%**	25.5%	26.6%	29.9%	28.3%	32.7%
Separation or Divorce	**31.7%**	23.3%	27.1%	24.4%	29.1%	26.0%
Witnessed Domestic Violence	18.7%	15.1%	14.5%	**18.9%**	17.1%	16.6%

Alaska's 2013 Behavioral Risk Factor Surveillance Survey ACEs data compared to the CDC's five-state study in 2009 using the same BRFSS module. Numbers in red indicate the highest percentage of the problem of the states reviewed.
Source: CDC Morbidity and Mortality Weekly Report, Vol. 59, No. 49 Dec. 10, 2010; Alaska BRFSS, 2014

The Alaska ACE research indicates that, of adult smokers in 2013, the smoking of 32 percent could be linked back to ACEs. If we reduced the estimated $576 million smoking cost for our state by 32 percent by eliminating ACEs, we could see a potential savings of $186 million.

The COST



The Alaska research suggests that 20.5% of adult heavy drinking is linked back to ACEs. If 20 percent of other substance abuse is also tied to ACEs (a conservative estimate), then we can estimate that $350 million in annual costs due to substance abuse in Alaska are linked to ACES.

The COST

Source: *Adverse Childhood Experiences: Overcoming ACES IN Alaska*, State of Alaska, Department of Health and Social Services

From the office of Rep. Tarr

Adverse Childhood Experiences – Supporting Documents
For House Health and Social Services meeting Nov 3, 2015.

From the office of:
Patrick Sidmore, MSW
Planner
Alaska Mental Health Board
Advisory Board on Alcoholism & Drug Abuse
431 N. Franklin St. 201
Juneau, Alaska 99801
(907) 465-3072

Adverse Childhood Experiences *Overcoming ACEs in Alask*
This document gives an overview of the initial results of the ACE study here in Alaska: http://dhss.alaska.gov/abada/ace-ak/Documents/ACEsReportAlaska.pdf

Economic Costs of Adverse Childhood Experiences in Alaska
DHSS recently released this document which explores some saving which might have occurred in six health outcomes if the state had moderately lowered levels of ACEs: http://dhss.alaska.gov/abada/ace-ak/Documents/ACEsEconomicCosts-AK.pdf .

Dept. of Health and Social Services ACEs Website
http://dhss.alaska.gov/abada/ace-ak/Pages/default.aspx . DHSS has developed several Powerpoint slides highlighting the data from various sources which underscore the issues for Alaska.

Adverse Childhood Experiences

Overcoming ACEs in Alaska

State of Alaska
Department of Health and Social Services
Governor, Bill Walker
Commissioner, Valerie Davidson

Advisory Board on Alcoholism and Drug Abuse

abada amhb

Alaska Mental Health Board

The high cost of childhood trauma

An opportunity for change

In the past two decades, we've learned two key things about Alaskans' health:

- Childhood trauma is far more common than previously realized; and
- The impact of this trauma affects individuals over a lifetime and societies over generations.

A keystone 1998 study asked middle class Americans how many traumas they had experienced as a child. Traumas included physical abuse, witnessing domestic violence and having a parent in jail. Researchers then developed an 'adverse childhood experiences' (ACE) score — the more traumas, the higher the ACE score.

Researchers compared scores to measures of adult health and well-being, and found strong links with poor health, social challenges and low earning power. If children experience trauma, this undermines their ability to learn and cope, which in turn undermines their health and ability to earn a living.

Stress from trauma shows up at the cellular level, follow-up studies found, and its influence can be passed on genetically from one generation to the next. This relates directly to many of the health and social problems we wrestle with in Alaska.

This information is incredibly important for Alaska, where rates of child abuse and domestic violence are so high. No nationwide ACE study has been done, but Alaska's first measured rates, in 2013, were higher than those of an earlier five-state study by the U.S. Centers for Disease Control and Prevention.

From low income to lung cancer, the likelihood of a host of problems rise along with trauma scores. Not surprisingly, so does Medicaid participation. The good news is that, if children have positive influences in their lives, they can overcome trauma. The catch phrase among those who support them and their families is, "Resilience trumps ACEs!"

Many of us — individuals, groups, communities, and government agencies — are already working to break the cycle of childhood trauma. We can use ACE data to guide our efforts to reduce human suffering, activate human potential, and save a significant amount of public money.

Together, we can meet this challenge and make Alaska communities even better places to grow up.

Alaskans can follow efforts across the state to prevent and mitigate the impact of ACEs on the "Overcoming ACEs in Alaska" website: dhss.alaska.gov/abada/ace-ak

Table of Contents

Adverse childhood experiences

What are ACEs?

In the late 1990s, the Centers for Disease Control and Prevention and Kaiser Permanente (a health care plan group provider network) asked more than 17,000 members of a Kaiser Health Maintenance Organization in San Diego whether they had experienced various kinds of trauma before age 18. The unexpected and striking results of this Adverse Childhood Experiences Study served as the basis for more than 80 peer-reviewed journal articles and statewide ACE studies.

The eight most commonly measured* traumas are in two general categories:

Table 1

Abuse	Household Dysfunction
1. Physical 2. Sexual 3. Emotional	4. Living with Someone with Mental Illness 5. Living with Someone with Substance Abuse 6. Separation or Divorce 7. Living with Someone who went to Jail or Prison 8. Witnessing Domestic Violence

**The original study also asked about physical and emotional neglect. Several states, including Alaska, did not include neglect data resulting a shorter survey.*

Researchers created a scoring method to determine the "dose" of each study participant's exposure to each type of "adverse childhood experiences," or ACEs.

A person who reported no exposure to any of the adverse experience categories would have an ACE score of zero. A person who reported exposure to all eight categories of trauma would have an ACE score of eight.

ACEs are common, linked with health outcomes

The researchers were surprised at the high number of ACEs reported by their middle-class subjects. Two thirds of adults studied had experienced at least one adverse childhood experience. (Table 2)

Researchers found striking correlations between childhood trauma and a wide range of long-term health and economic outcomes. The higher the ACEs score, the higher the incidence of disease, risky behaviors and negative social outcomes. It is clear that ACEs have a big impact on many of the difficult and entrenched health problems that Alaska faces.

Table 2

ACE Score	Prevalence
0	33%
1	26%
2	16%
3	10%
4 +	16%

These graphs are representative of many ACE studies exploring the relationships between the dose of childhood trauma and the likelihood of poor health / behavior outcomes, perhaps the most striking is the suicide link, (Fig. 1).

As the number of ACEs went up so did the likelihood that those surveyed had experienced poor social, economic or health outcome, (Fig. 2).

Researchers have also found links between ACEs and these health and social outcomes:

• Asthma • Depression • Drug abuse • Fetal death • Frequent headaches • Hallucinations • Health-related quality of life • Insufficient sleep • Intimate partner violence • Liver disease • Sexual assault • Teen pregnancy • Low yearly income • Medicaid participation • Home ownership • Separation and divorce

It is important to remember that the ACE studies and Alaska's ACE analyses are population-based studies and are not predictions of outcomes for individuals. Indeed, some of the people who are able to overcome ACEs can be our best teachers about resiliency in the face of adversity.

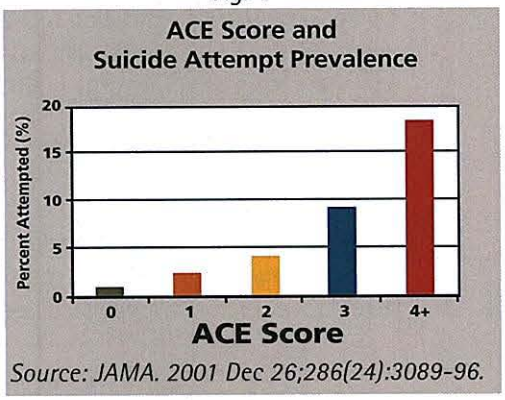
Stress and the developing brain

The initial ACE study was designed by researchers who were not sure what the mechanism for these poor outcomes was. It was clear that ACEs led to negative results (Fig. 3) but just how they did was unclear. Researchers developed the pyramid model, to the right, to explain what they were seeing. When the ACE researchers and brain researchers collaborated, a much clearer picture began to emerge.

The Center for the Developing Child at Harvard University reports that, "It's important to distinguish among three kinds of responses to stress: positive, tolerable, and toxic. As described below, these three terms refer to the stress response system's effects on the body, not to the stressful event or experience itself.

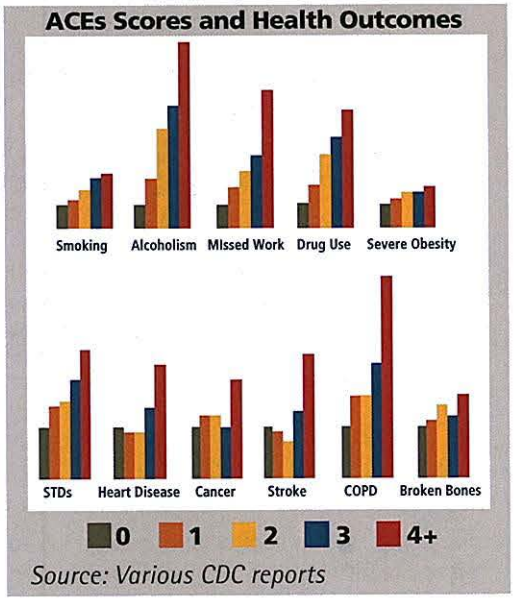
- Positive stress response is a normal and essential part of healthy development, characterized by brief increases in heart rate and mild elevations in hormone levels. Some situations that might trigger a positive stress response are the first day with a new caregiver or receiving an injected immunization.

Fig. 1



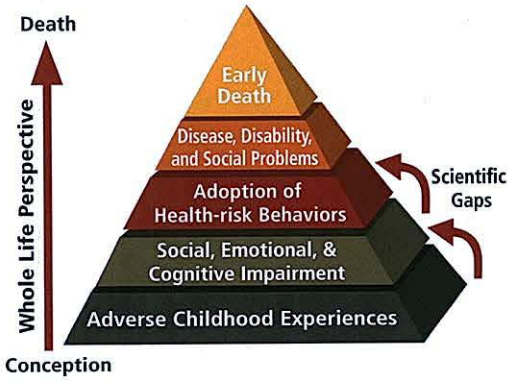
Source: JAMA. 2001 Dec 26;286(24):3089-96.

Fig. 2



Source: Various CDC reports

Fig. 3



- Tolerable stress response activates the body's alert systems to a greater degree as a result of more severe, longer-lasting difficulties, such as the loss of a loved one, a natural disaster, or a frightening injury. If the activation is time-limited and buffered by relationships with adults who help the child adapt, the brain and other organs recover from what might otherwise be damaging effects.

- Toxic stress response can occur when a child experiences strong, frequent, and/or prolonged adversity — such as physical or emotional abuse, chronic neglect, caregiver substance abuse or mental illness, exposure to violence, and/or the accumulated burdens of family economic hardship — without adequate adult support. This kind of prolonged activation of the stress response systems can disrupt the development of brain architecture and other organ systems, and increase the risk for stress-related disease and cognitive impairment, well into the adult years.

Toxic stress affects the brain and the body and has implications for a child as he or she develops. The first steps in brain development are the most basic, and focus on survival. The next steps involve crucial social and intellectual building blocks such as bonding with parents, learning to talk, and learning to get along with others. Those are children's most important lessons in terms of building a foundation for success for the rest of their lives."

When young children feel safe and nurtured, they are calm. This frees their brains, at a neurological level, to develop these more advanced skills.

Children who experience early trauma — toxic stress — are often in a chronic state of crisis. Because they feel unsafe or threatened, their brains spend more time in basic, survival-oriented stages of development. They are too busy trying to cope, trying to feel OK, to focus on more complex learning. These children are often easily overwhelmed by minor stressors such as a change in their schedule or routine. They are used to trauma, expect it at every turn, and so are always ready to react. Small disruptions feel as if they are major. They have difficulty soothing or calming themselves without a reliable and consistent caregiver. This compromises their ability to learn. In seriously stressed children, researchers have observed:

- Less development of the upper brain;
- Smaller brain size; and
- Fewer brain connections.

This brain research is vital for Alaska schools. A child coming to school from a toxic home environment or having experienced toxic stress earlier in life may react quite differently than a child coming from a secure home. The ability to learn is impaired and the pathways in the brain may need to be rewired.

Many schools around Alaska are using this science to help all children be more ready to learn and grow when they are in school.

Generational impacts

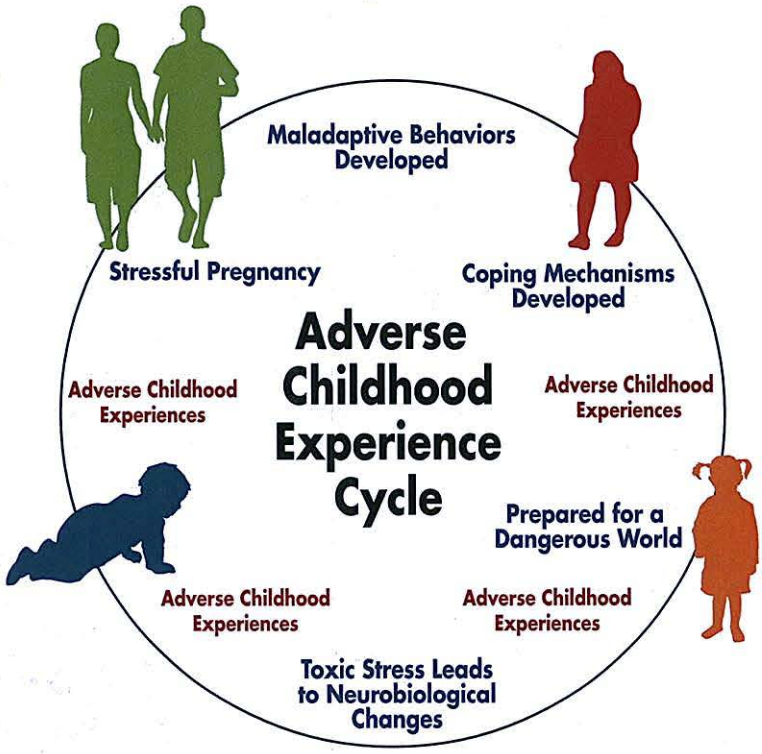
The impacts of overwhelming stress on the brain's development naturally continue into adulthood. As Alaskans exposed to this degree of stress grow up, they may start using drugs as a way to cope with their damaged stress responses. This in turn could lead to prison. If they start families of their own, these become ACEs for another generation. These are examples of behavioral influence — positive or negative habits that parents pass on to their children by example. Positive habits children may pick up from their parents include reading and exercising. Negative habits include smoking and responding to challenges with violence.

Recent research has shown that childhood experiences also have a genetic influence. Physical changes in our genes, triggered by trauma, get passed to our offspring. A study of Swedes over three generations found connections between men going hungry during their youth and rates of cardiovascular disease and diabetes among their children and grandchildren. In some ways, we inherit the experiences of our parents and grandparents as well as their physical characteristics.

Historical trauma

Epigenetics, the science that looks at how people's genes are affected by their environment, is beginning to show how historical traumas continue to affect the children of survivors in biological ways at the cellular level, as well as in behavioral ways. The good news coming from this emerging science is that **we can change our biology, and our lives, for the better.**

Fig. 4



Adverse Childhood Experience Cycle

Source: The Alaska Mental Health Board / Advisory Board on Alcoholism and Drug Abuse

A 2013 article on epigenetics in Discover magazine used these analogies:

> "You might have inherited not just your grandmother's knobby knees, but also her predisposition toward depression caused by the neglect she suffered as a newborn.
>
> Or not. If your grandmother was adopted by nurturing parents, you might be enjoying the boost she received thanks to their love and support. The mechanisms of behavioral epigenetics underlie not only deficits and weaknesses but strengths and resiliencies, too. And for those unlucky enough to descend from miserable or withholding grandparents, emerging drug treatments could reset not just mood, but the epigenetic changes themselves. Like grandmother's vintage dress, you could wear it or have it altered. The genome has long been known as the blueprint of life, but the epigenome is life's Etch-A-Sketch: shake it hard enough, and you can wipe clean the family curse."

This is particularly important in Alaska, which has seen historical traumas such as rural outbreaks of disease that killed nearly entire communities. We also have groups of people born in Alaska or in other parts of the world who have experienced trauma from outside the home. Wars, racism, displacement from a homeland, and loss of culture have been shown to lead to poor health and economic outcomes. Alaskans have experienced all of these things.

Alaska ACE findings

Behavioral Risk Factor Surveillance Survey: ACEs questions

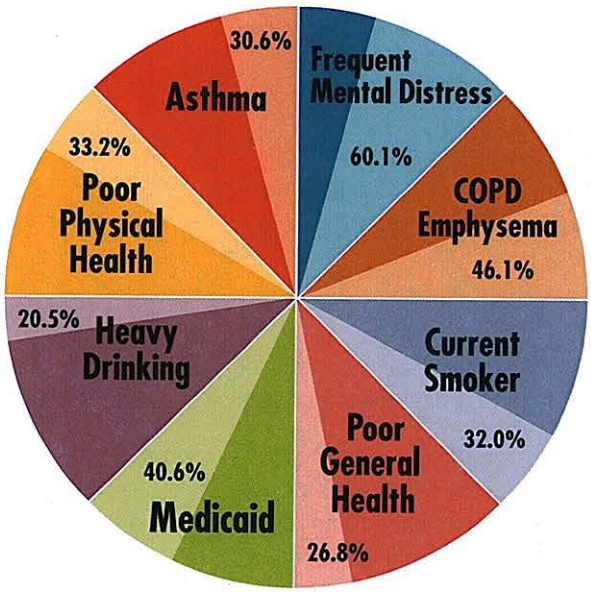
The Behavioral Risk Factor Surveillance Survey (BRFSS) is a public health phone survey of adults, developed by the U.S. Centers for Disease Control and Prevention (CDC), conducted in all states and territories nationwide. To better understand childhood trauma, the CDC developed a set of ACEs questions that states could add to their BRFS surveys starting in 2009. Alaska became the 20th state to do so this in 2013.

The Alaska Division of Public Health surveyed more than 4,000 Alaskans 18 years and older for 2013's BRFSS. The responses give us insight into the relationship between ACEs and chronic disease in Alaska, and how our ACE rates compare with other states.

Alaska population attributable risks

The graphic to the right shows the degree to which childhood trauma contributes to poor health in Alaska. The paler areas represent the proportion of each outcome which can be linked back to ACEs. For example, studies suggest that 32 percent of current smokers would not be smoking if we did away with all of the adverse childhood experiences we measured.

Fig. 5



This linkage, known as population attributable risk, is basically how often something happens in a group of people that have been exposed to something, compared to how often it happens in a group without exposure. For example, how often does chronic obstructive pulmonary disease happen among Alaskans who had childhood trauma, compared to Alaskans who didn't? Looking at the high population attributable risks for these outcomes and ACEs, the potential savings in human and economic costs from reducing childhood trauma is astounding.

Watch for details on costs associated with ACEs in information boxes throughout this report.

The CO$T

Comparison to other states

One of the best ways to gauge the results of the Alaska ACE survey is to compare them with other states. There are no national statistics on ACE scores available, however in 2009 the CDC released a study comparing ACE data from five states (Arkansas, Louisiana, Tennessee, New Mexico, Washington) that used the BRFSS ACE module. This analysis covered more than 23 million people (2010 Census), with direct surveys of more than 26,000 respondents.

Once Alaska added the ACE module to our 2013 risk factor survey, we could compare our data with the CDC's five-state study. Generally Alaska had higher ACE scores.

Table 2

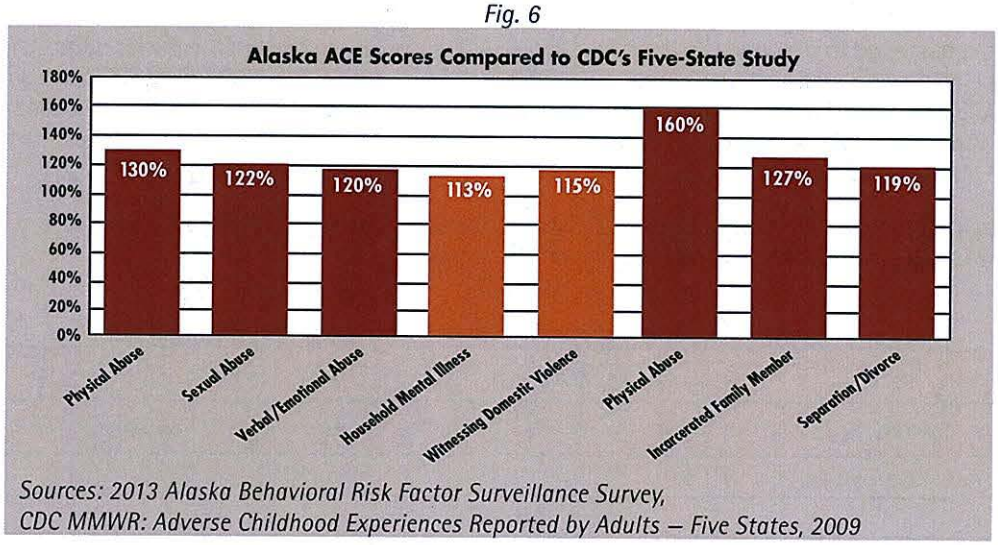
ACE Rates in Six States						
Adverse Childhood Experience	Alaska	Arkansas	Louisana	New Mexico	Tennessee	Washington
Year study released	2013	2009				
ABUSE						
Verbal/Emotional	31.0%	24.3%	21.1%	28.1%	19.2%	**34.9%**
Physical	19.1%	14.1%	10.5%	**19.5%**	12.9%	18.1%
Sexual	**14.8%**	10.9%	9.9%	12.9%	12.7%	13.5%
HOUSEHOLD DYSFUNCTION						
Mental Illness in the Home	21.9%	17.0%	16.6%	19.4%	17.1%	**24.3%**
Incarcerated Family Member	**11.5%**	5.5%	7.2%	7.1%	8.6%	6.6%
Substance Abuse in Home	**33.8%**	25.5%	26.6%	29.9%	28.3%	32.7%
Separation or Divorce	**31.7%**	23.3%	27.1%	24.4%	29.1%	26.0%
Witnessed Domestic Violence	18.7%	15.1%	14.5%	**18.9%**	17.1%	16.6%

Alaska's 2013 Behavioral Risk Factor Surveillance Survey ACEs data compared to the CDC's five-state study in 2009 using the same BRFSS module. Numbers in red indicate the highest percentage of the problem of the states reviewed.
Source: CDC Morbidity and Mortality Weekly Report, Vol. 59, No. 49 Dec. 10, 2010; Alaska BRFSS, 2014

The rates reported by Alaska adults for each category of adverse experiences were higher than the five-state study's average rates. In all but two of the categories, these higher rates were statistically significant given the two studies' sample sizes. The three categories of adverse experiences with significantly higher rates among adults in Alaska — incarcerated family member, household substance abuse and separation and divorce — were also found to be significantly higher in a sample of Alaska children when compared with a national rate.

Figure 6 shows that Alaska 2013 BRFSS ACE scores as a percentage of the mean ACE rates in the CDC's 2009 five-state study. A percentage of 100 percent would mean Alaska's rate was equal to the five-state average. Gold bars indicate the difference between Alaska's rate and the five-state average is not statistically significant.

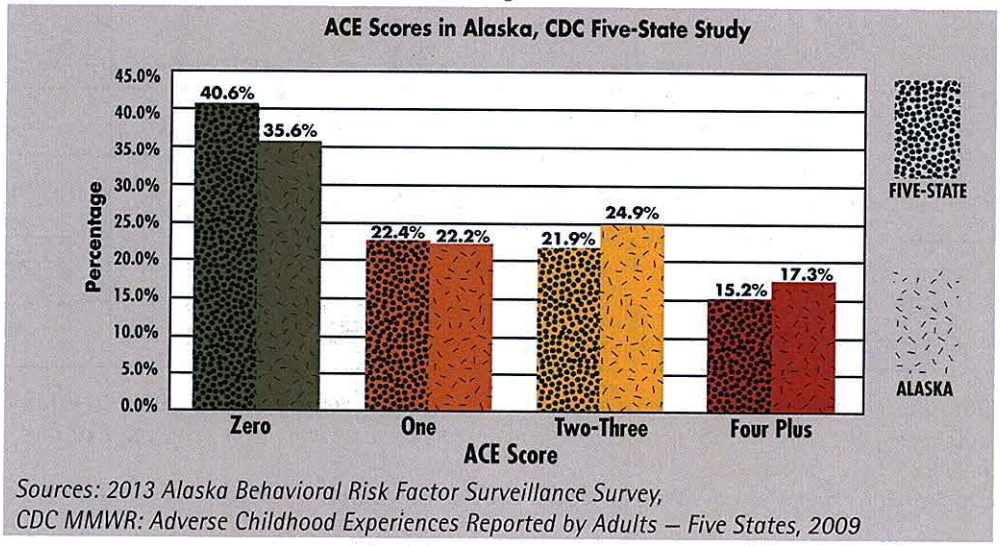
Fig. 6



Sources: 2013 Alaska Behavioral Risk Factor Surveillance Survey, CDC MMWR: Adverse Childhood Experiences Reported by Adults – Five States, 2009

While the rates in different categories are important for those Alaskans who work to prevent those traumas, the overall statewide ACE score or "dose" of ACEs sheds light on the general health outcome at a population level. (Again, individuals may have widely different outcomes depending on their unique personalities, experiences and the protective factors they have.) Alaska's ACE score results are higher than five-state averages.

Fig. 7



Sources: 2013 Alaska Behavioral Risk Factor Surveillance Survey, CDC MMWR: Adverse Childhood Experiences Reported by Adults – Five States, 2009

The Alaska Department of Labor and Workforce Development estimated that there were approximately 550,000 Alaskans aged 18 and older in 2013. What does the five-point difference between the five-state average of 40.6 percent of residents with an ACE score of zero to Alaska's 35.6 percent mean? If Alaska were to improve to the level of the five states, approximately **27,500 more adults would have zero ACEs.** If Alaska could reduce the percentage of people with four or more ACEs to the level of the five states, then **more than 11,500 Alaskans would have a lower ACE score**. Changing an ACE score for 11,500 people may not seem significant but evidence suggests it would have a great impact on many health, economic, and social outcomes.

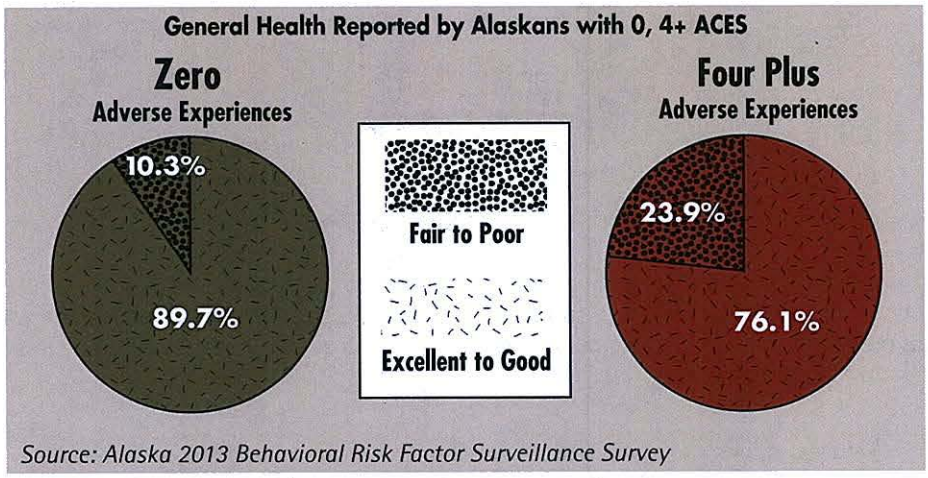
Health and economic costs for Alaska

Alaska's results are similar to those of other ACE studies have found. The more ACEs a person has, the more likely he or she is to experience poor health, both self-reported and measured.

Health outcomes

An analysis of Alaskans' general health shows that people with four or more ACEs reported that their general health was "fair to poor" at more than twice the rate compared to those with zero ACEs, (Fig. 8).

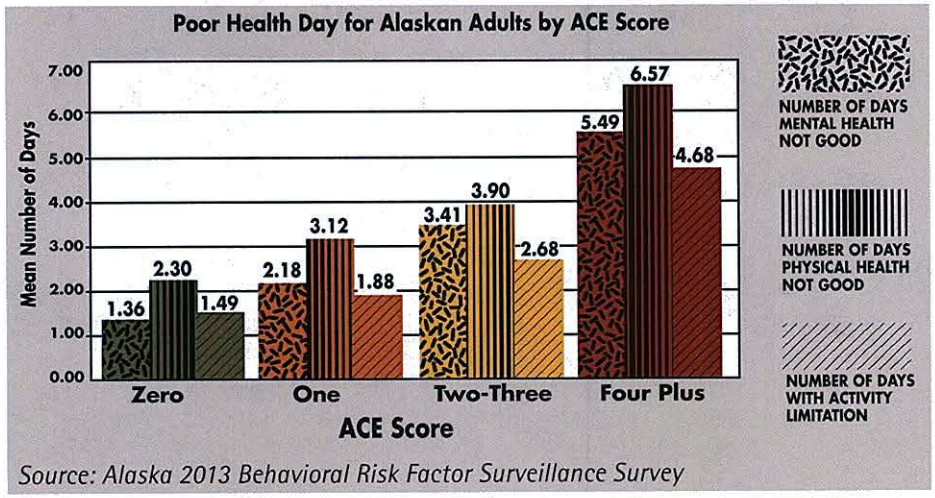
Fig. 8



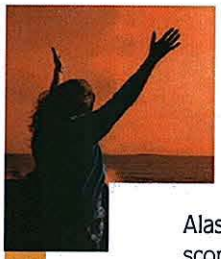
Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey

Alaskans were asked the number of days of poor mental and physical health outcomes during the previous month they experienced. The average number of days in that month this led to limited activities was reported as well. The results are shown in Figure 9 and demonstrated that the more ACEs Alaskans had the higher average number of days impacted per month.

Fig. 9

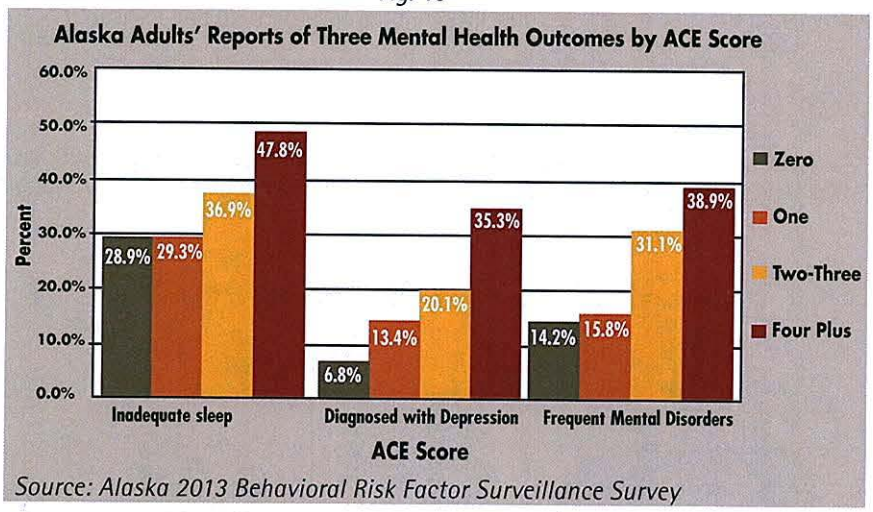


Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey



Alaskans reported increasing difficulty with sleep, depression and frequent mental distress as their ACE scores rose. Figure ten displays these results. For example Alaskans with four or more ACEs were more than 5 times more likely to report having ever been diagnosed with depression than their peers with zero ACEs.

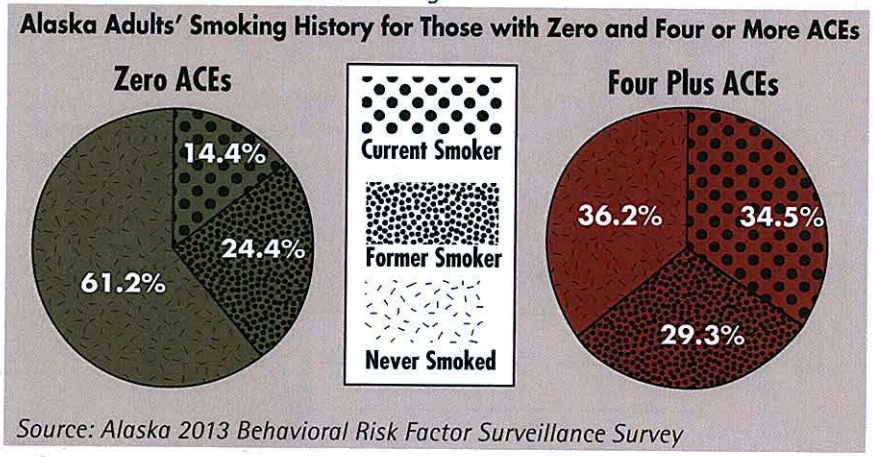
Fig. 10



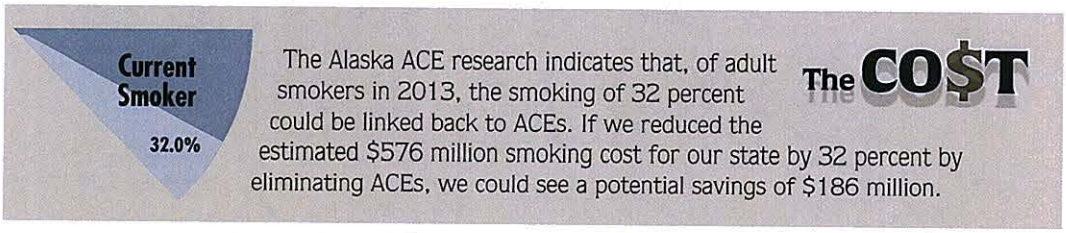
Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey

Smoking in Alaska costs $576 million annually. While rates are improving, it remains a large and costly health problem. The likelihood of being a current smoker is 240 percent higher for an Alaskan with four or more ACEs compared with zero ACEs. Additionally, Alaskans with zero ACEs are significantly less likely to have ever smoked in their lifetimes. (Fig. 11)

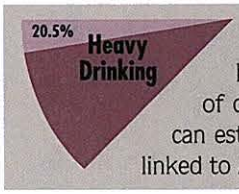
Fig. 11



Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey



Substance abuse in Alaska has been estimated to cost the state $1.2 billion dollars annually in direct and indirect costs. The original ACE research found multiple connections between ACEs and substance abuse, from intravenous drug use to alcoholism. The Alaska BRFSS asks questions about alcohol but not prescription or illicit drug abuse. Looking at the CDC research and other states' data, though, we can estimate that a significant amount of drug abuse in Alaska is linked to ACEs.



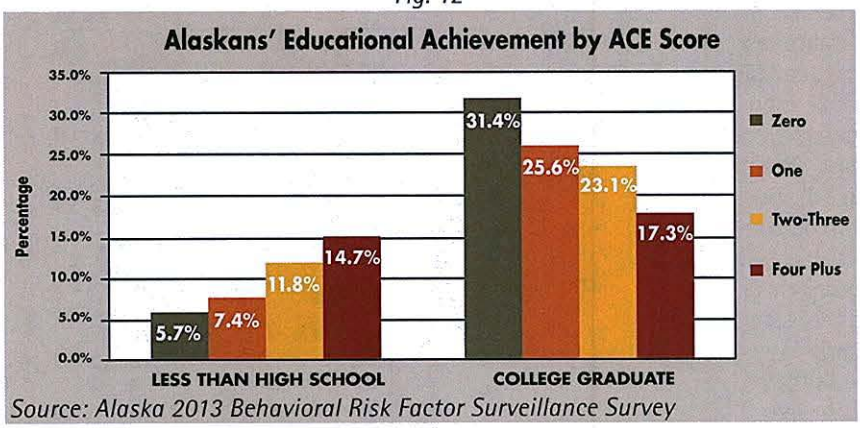
The Alaska research suggests that 20.5% of adult heavy drinking is linked back to ACEs. If 20 percent of other substance abuse is also tied to ACEs (a conservative estimate), then we can estimate that $350 million in annual costs due to substance abuse in Alaska are linked to ACES.

The CO$T

Economic and educational impacts

Childhood trauma can reduce Alaskans' ability to earn a good living. The impact starts early by undermining educational achievement. Alaskan adults with four or more ACEs are more than 250% less likely to have graduated from high school than those with zero ACEs. Graduation rates for college show that having zero ACEs almost doubles an Alaskan's chance of having a four year degree than those with four or more ACEs, (Fig. 12).

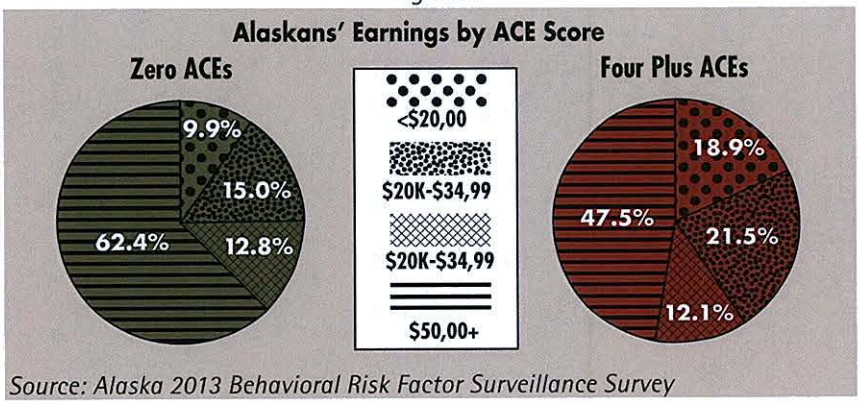
Fig. 12



Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey

Figure 13 graphs the annual income reported by Alaskan adults with zero and four or more ACEs. Having a ACE free childhood is linked with higher annual income.

Fig. 13



Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey

Health care access and Medicaid enrollment

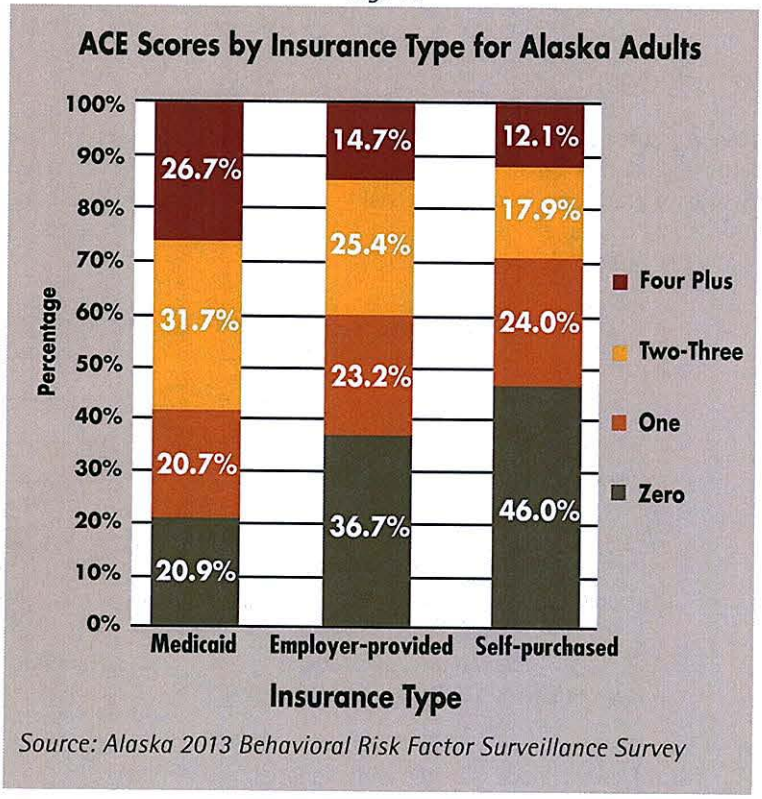
Medicaid eligibility for adults is related to financial hardship, poor health or a combination of both. As a result, it is not surprising that people using Medicaid as their health insurance have higher ACE scores than those in the private health insurance market, given what we have seen above when it comes to poor economic and health outcomes for Alaskans with higher ACE scores.

There has been considerable attention paid to the costs of Medicaid and ways to contain and improve this large system. Much of this discussion is related to care delivery and payment reforms. Bringing the prevention and mitigation of ACEs into the equation has the potential to pay large dividends.

In 2012, Alaska Medicaid spent $1.38 billion to provide care for 146,476 Alaskans' health care. Of these Alaskans served, 53,794 were adults age 20 or older at a cost of $860 million, or 62.1 percent of the total.

Alaskans who report Medicaid as their source of health insurance report significantly higher ACE scores than those who report employer provided or self-purchased health insurance (fig 14). Due to the poor health outcomes associated with high ACE scores this means that Medicaid has enrollees with significantly worse health prospects than other insurance types. This disparity leads to higher treatment costs and a higher burden on government resources.

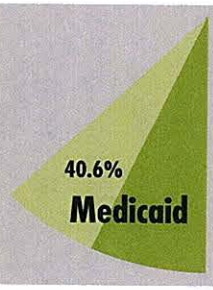
Fig. 14



Source: Alaska 2013 Behavioral Risk Factor Surveillance Survey

The COST

Alaska research suggests that 40.6% of the state's Adult Medicaid enrollment is linked back to ACEs. In 2012, that means that approximately $350 million of Adult Medicaid (age 20+) costs in Alaska could have been prevented by the elimination of ACEs.



Conclusion

Our brains can recover from trauma, but it is a challenging process. It is more cost-effective, in human and financial terms, for children to grow and develop in a healthy environment than to try to help them heal from toxic stress later. This means interrupting the ACE cycle. Fortunately, there are many opportunities to do so.

Alaska has many groups working on mitigating ACEs, trauma prevention, and community resilience & wellness. For more information on this and other resources, and updates on what is happening around the state, visit the **"Overcoming ACEs in Alaska"** website, dhss.alaska.gov/abada/ace-ak.

Building resilience and preventing ACEs

Across Alaska, people are working in large and small ways to prevent childhood trauma and ease the effects of damage already done. Here are a few examples (as of early 2015):

- Statewide, teachers and public health nurses provide teens with information on healthy relationship and life skills. They have partnered with the Alaska Departments of Health and Social Services and Education and Early Development, the Council on Domestic Violence and Sexual Assault, and the Alaska Network on Domestic Violence and Sexual Assault on a 7th, 8th and 9th grade, evidenced-based curriculum for the 7th-9th grade called "the Fourth R for Healthy Relationships."

- A statewide webinar series on trauma-informed schools was completed in January 2015. Hundreds of educators and school staff participated. The series will be offered again in 2015-16 and can be accessed online at no cost

- The Division of Public Health partnered with the Alaska Native Tribal Health Consortium and the Alaska Family Violence Prevention Project to develop a teen safety card, a gender-neutral resource developed for Alaska teens with guidance from Alaska teens. The card provides information about healthy and unhealthy relationships characteristics, what consent looks and sounds like, and where to get help if needed. Another safety card was designed specifically for women.

- The Division of Behavioral Health has promoted trauma informed care for several years. Efforts include development of "Trauma 101" and "Trauma 201" curriculum for behavioral helath providers, used around the state.

- Teens Acting Against Violence (TAAV) is a violence-prevention and youth-empowerment program at the Tundra Women's Coalition for teenagers living in Bethel. Participation is voluntary and open for any interested teens age 12–18.

- The Alaska Mental Health Board and Advisory Board on Alcoholism and Drug Abuse have coordinated the efforts of many organizations to gather Alaska specific ACE data. The Boards have focused since 2008 on community wellness and personal resilience.

- Donlin Gold – a corporation doing business in Alaska - has embraced community wellness as part of their mission. In 2013 it won the Workforce Association's National Employer of the Year Award. Donlin Gold has seen that a healthy workforce helps everyone.

- The Association of Alaska School Boards, through its Initiative for Community Engagement (ICE), has been working for nearly two decades with schools and communities to create healthier school and community climates to support youth resilience.

- The Council on Domestic Violence and Sexual Assault and Green Dot, etc., are developing an Alaska-specific teaching tool on how to intervene in potentially dangerous everyday situations — like calling a cab for someone who has been drinking, or offering the number for the local women's shelter to someone experiencing domestic violence. The Green Dot curriculum is being implemented in Anchorage, Bethel, Homer, Kenai and Prince of Wales.

- In Homer, teens lead ACE awareness sessions that focus on resilience-building strategies. They are working on training that emphasizes how to build resilience and will share this resource at a national conference in Oregon spring 2015.

- People in Kodiak and Kotzebue are focusing on how ACEs affect their communities and how to make positive changes for all their residents.

- The Mat-Su Borough held an ACEs Summit and has created a broad range of work groups to identify strategies to address ACEs as a way to improve the schools, reduce substance abuse, and improve the health of its residents.

- Yakutat decided the best way to prevent substance abuse is to tackle ACEs. They developed public service announcements to educate their community about the connection between ACEs, binge drinking, and alcohol abuse.

Next Steps

We've learned that many Alaskans have experienced ACEs. We now understand that when we break the cycle of trauma and toxic stress, our efforts pay off in many ways.

From the highest level of political power in Alaska to homes where family members care for our youngest and most vulnerable citizens, we all have a role in making our communities places where adults can overcome a rough start and thrive, and where the next generation is raised in a healthier, more supportive environment.

Alaskans can follow efforts across the state to prevent and mitigate the impact of ACEs on the "Overcoming ACEs in Alaska" website: dhss.alaska.gov/abada/ace-ak

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In this podcast, childhood trauma expert Dr. Robert Anda describes the Centers for Disease Control Adverse Childhood Experiences (ACE) Study. David Driscoll offers an Alaska perspective on childhood trauma; Elizabeth Ripley discusses what grantmakers are willing to fund; and Bill Hogan of the UAA College of Health opens the sessions and facilitates audience questions and answers. Recorded Oct. 23, 2012. http://greenandgold.uaa.alaska.edu/podcasts/index.php?id=724

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Notes

Advisory Board on Alcoholism and Drug Abuse

abada

amhb

Alaska Mental Health Board

State of Alaska
Department of Health and Social Services
ABADA/AMHB

Governor, Bill Walker
Commissioner, Valerie Davidson

January 2015

Adverse Childhood Experiences

What is ACES?

- 1998 study asked middle class Americans about traumas experienced as a child
- Traumas include physical abuse, sexual abuse, domestic violence, having a parent in jail
- Developed as ACE score based on answers
- Score can be 0-10

What is your ACES Score?

- Group exercise to take the test and produce your own score
- Can be found online at http://www.npr.org/sections/health-shots/2015/03/02/387007941/take-the-ace-quiz-and-learn-what-it-does-and-doesnt-mean

ACES Studies in Alaska

- 2 Key Findings
  - Childhood trauma is far more common than previously realized
  - The impact of this trauma affects individuals over a lifetime and societies over generations

ACES Scores in Alaska

ACES Score	Prevalence
0	33%
1	26%
2	16%
3	10%
4+	16%

Select Negative Health Outcomes

- Medicaid
  - 40.6%
- Current Smoker
  - 32%
- Heavy Drinking
  - 20.5%
- Poor Physical Health
  - 33.2%

Costs Associated with ACES

- Reduce smoking cost of $576 million by 32% = $186 million in savings
- Reduce substance abuse by 20% = $350 million in savings
- Reduce Medicaid costs by 40.6% = $350 million in savings
  - **Total = $886 million in annual savings by preventing ACES**

Opportunities for Prevention

- Trauma-informed health care
- Trauma informed curriculum
- Raise awareness by distributing information related to ACES to state and local entities
- Increase community's ability to respond to, prevent, and address ACES
- Pilot programs to conduct Alaska based research

Economic Costs of Adverse Childhood Experiences in Alaska

The Price of Not Intervening

Before Trauma Occurs

This document and other information related to Adverse Childhood Experiences in Alaska can be accessed at http://dhss.alaska.gov/abada/ace-ak/Pages/default.aspx

Advisory Board on Alcoholism and Drug Abuse
abada
amhb
Alaska Mental Health Board

Prepared for the Alaska Mental Health Board and the Advisory Board on Alcoholism and Drug Abuse by Patrick Sidmore, MSW

Child Adversity and State Fiscal Health

In Alaska, Adverse Childhood Experiences (ACEs) have been a frequently discussed subject in the fields of behavioral health and child development over the past 5-10 years. This paper will take the discussion in a different direction in light of the recent survey of Alaskan adults - asking them about their own experiences with adverse childhood experiences or ACEs. Links to numerous poor health, economic and social outcomes have been found for adults who experienced ACEs.[i] Subsequent to the dozens of ACE studies from all over the U.S and around the world since the original data first became available, research in the fields of neuroscience and epigenetics have sharpened the picture of the mechanisms that lead from child trauma to negative outcomes, often years later.

As the funding of state government changes from a tax base linked almost entirely to resource extraction[ii] to one which is derived from broad-based taxes on citizens, the economic health of Alaska will be tied more than ever to its workforce. Since the building of the pipeline, Alaska has invested heavily in its people through social and health programs offered by the state. There is evidence that these investments have paid dividends which have been largely unrecognized due to the current budgeting and tax processes. In the past, the majority of successful government spending was not tied to increased state revenue because the tax base was reliant primarily on one or two industries. This is changing.

What follows is a unique way to look at the issues of child maltreatment and other adverse childhood experiences. Policymakers see the costs when a child is taken into custody but rarely connect the expenses incurred thirty years later. This discussion will explore those economic impacts to which a concentrated effort to reduce child trauma might lead, using the Alaska 2013 Behavioral Risk Factor Surveillance System[iii] (BRFSS) survey data. A model will be explored where a change in the ACE scores of Alaskan adults will be overlaid with outcome data to see if there would be a reduction in the number of adults who experience certain chronic health conditions. Added to that will be an analysis of costs that are currently associated with these chronic health issues and how these expenditures might have looked with a change in ACE scores.

The main focus of this analysis will be on the long term costs of ACEs – specifically the costs Alaska pays for adults who experienced ACEs. **It is important to remember that costs associated with child trauma, however, begin in childhood.** A recent report from the Centers for Disease Control and Prevention estimating lifetime costs of child maltreatment, an especially high level of adverse childhood experience, are seen below.

Key findings:[iv]

The estimated average lifetime cost per victim of nonfatal child maltreatment includes:

$32,648 in childhood health care costs

+ $7,728 in child welfare costs

+ $7,999 in special education costs

$48,375 Total Childhood Costs of Maltreatment

What Are The Recent Child Abuse Numbers in Alaska?

First-Time Child Abuse Victims in Alaska[v]
Average Annual Number 2009 - 2013
1705

Applying the **$48,375** cost estimate for childhood expenses to the average number of Alaskan children who had a substantiated report of harm over the past several years (1,705) the financial liability anticipated is large each year. It can be estimated that Alaska takes on the burden of approximately $82 million in current and projected costs each year on average.

Why Are Adverse Childhood Experiences So Important to Alaska?
The Intersection of Economics and Childhood Development

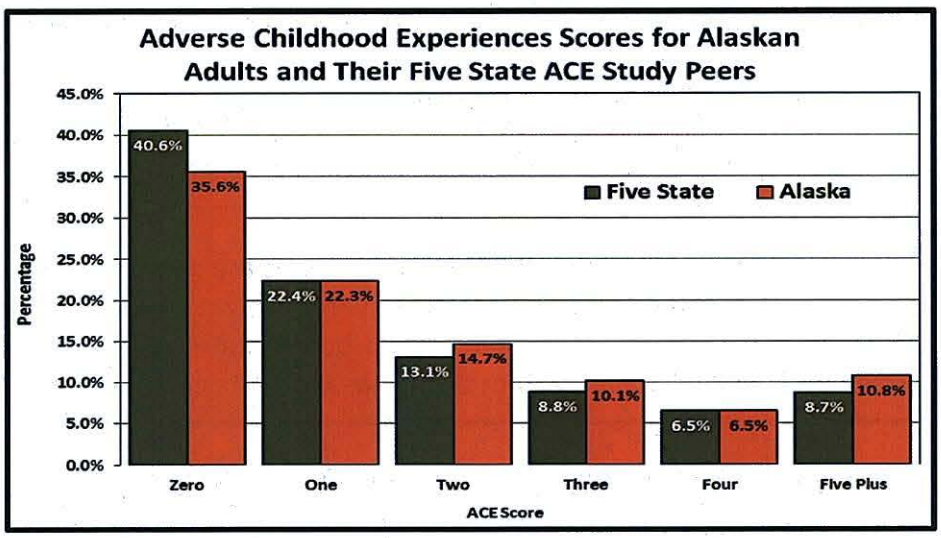
The fields of economics and business have discovered that child development has a profound impact on the economic health of a community. Groups and individuals like the Rand Corporation,[vi] The Federal Reserve Bank,[vii] the Upjohn Institute,[viii] and Nobel Laureate (Economics 2000) James Heckman[ix] from the University of Chicago have explored the importance of the earliest years of an individual's life to his or her later economic success. The idea that **"skills beget skills"** in child development leads to the very real cost benefit analysis that clearly demonstrates the need to get the early years of children's lives right. Alaskan professionals can and do repair damage caused to the developing brains of young children through their exposure to trauma - but it is costly.

In Alaska's state government there is, of course, considerable work being done with children who have been traumatized. The Office of Children's Services and the Divisions of Behavioral Health, Public Health and Juvenile Justice as well as the Department of Education and Early Development primarily do the work of helping to repair the damage caused by trauma. **Yet, is Alaska optimizing its chances to reduce social and economic costs when it comes to child maltreatment?**

The Alaskan ACE Study – What the Numbers Show

Alaska surveyed more than 4,000 adults in the 2013 Behavioral Risk Factor Surveillance System (BRFSS) to determine the extent of their ACEs experienced prior to age 18. The results, shown below in **Figure 1**, were compared to a sample of five states[x] which had been combined by the Centers for Disease Control and Prevention using a questionnaire identical to Alaska's study. The results of these states' statistically significant assessment of 23,000 residents represent one of the largest population bases of ACE questions asked of Americans (more than 20 million residents live in the five states sampled).

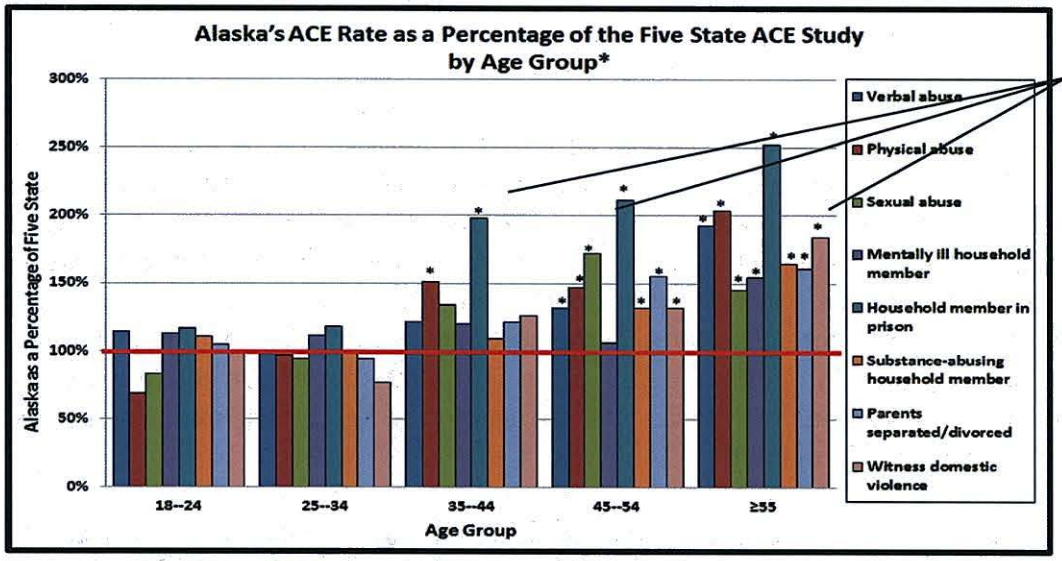
Figure 1[xi]



Alaska clearly has higher rates of ACEs than the average of the five states surveyed. As Alaska's Health and Social Services staff explored the data more fully, they uncovered an interesting finding. When comparing Alaska's ACE prevalence to the five states (Washington, Louisiana, Tennessee, Arkansas, and New Mexico) by age groups, it appears that the higher ACE scores in Alaska are held in the older generations. Below, **Figure 2** compares Alaska's rate for each ACE as a percentage of the five states' rate. For example if Alaska had exactly the same rate for an adverse experience it would register as 100% (red horizontal line).

What accounts for this leveling when compared to age cohorts in other states? Is it the flow of oil and the better jobs it created? Is it a result of immigration that has occurred since then? Can it be linked to significant spending on health and social programs? The answer probably includes all of these and others. These figures show that relative to peer groups in the five state sample, Alaska's younger adults are more in line with ACE levels elsewhere. The ACE research shows that these changes will have considerable health, social and economic benefits moving forward.

Figure 2[xii]



Alaska's older generations have higher rates of ACEs than their peers in the five states. The rates are similar for the younger generations.

Now is a pivotal time as Alaska confronts a budget crisis and moves to a broader based funding structure. The impact of investments provided from state coffers in preventing and mitigating the results of ACEs must not be lost as budgets are cut. ***To lose ground leads not only to increased future costs, but given the new reality, most likely decreased future revenues as well.*** Alaskans with high ACE scores make less money, are less likely to own their own homes and are more likely to be unable to work[xiii]. ACE awareness is even more important now.

There have been great strides in the past few years increasing Alaskans' knowledge of domestic violence, with primary prevention efforts taken to scale across the state.[xiv] Though there are agencies and groups working on the issue – **a comprehensive primary prevention effort to prevent child abuse and neglect doesn't exist in Alaska.** Could more be done to prevent ACEs?

Three Levels of Prevention[xv]

Public Health offers a model of prevention which is pertinent for a discussion of ACE prevention and mitigation.

In the field of Public Health, three levels of prevention are observed:

- **Primary Prevention** - aims to prevent disease or injury before it ever occurs.
- **Secondary Prevention** - aims to reduce the impact of a disease or injury that has already occurred.
- **Tertiary Prevention** - aims to soften the impact of an ongoing illness or injury that has lasting effects

The three tables joined below illustrate how the problem of ACEs in Alaska could be viewed. In this example, the data refer to the level of current smoking by Alaskan adults and their ACE scores.

An Example

Table 1 represents the estimated number of Alaskan adults who experience four levels of ACE scores. These figures were derived from using the 2013 Department of Labor and Workforce Developments' population estimate and the 2013 BRFSS ACE Survey percentages as reported by Alaskan adults. If impacts were made upon ACE rates at this level in the Alaskan population - **that would be an example of primary prevention**. Prevention at that level (moving people to lower ACE scores) would save the costs associated with child maltreatment cited above and pay dividends into adulthood by reducing the number of current smokers. As this table demonstrates – Alaskans with lower ACE scores tend to be current smokers at lower rates (See explanation of Table 2 below).

Table 1		Table 2	Table 3	
ACE Scores of 2013 Adult Alaska Population		Current Smoking	**Current Smoking Estimate Adult Alaska Population**	
Zero	**194,275**	14.4%	**Zero**	**27,901**
One	**121,950**	18.3%	**One**	**22,298**
Two - Three	**135,398**	24.1%	**Two - Three**	**32,564**
Four Plus	**94,134**	34.5%	**Four Plus**	**32,481**
Total	**545,757**	21.1%	**Total**	**115,244**

The black box above **(Table 2)** displays the results from the 2013 Alaskan ACE research demonstrating the percentage, by each ACE score level, of those who are currently smoking. For example, 14.4% of Alaskan adults with zero ACEs currently smoke and 34.5% of those with four or more ACEs do. Lowering these percentages for people with high ACE scores by providing trauma informed behavioral health treatment, for example, would teach Alaskans coping skills other than using nicotine to deal with stress. That would be an instance of **secondary prevention**.

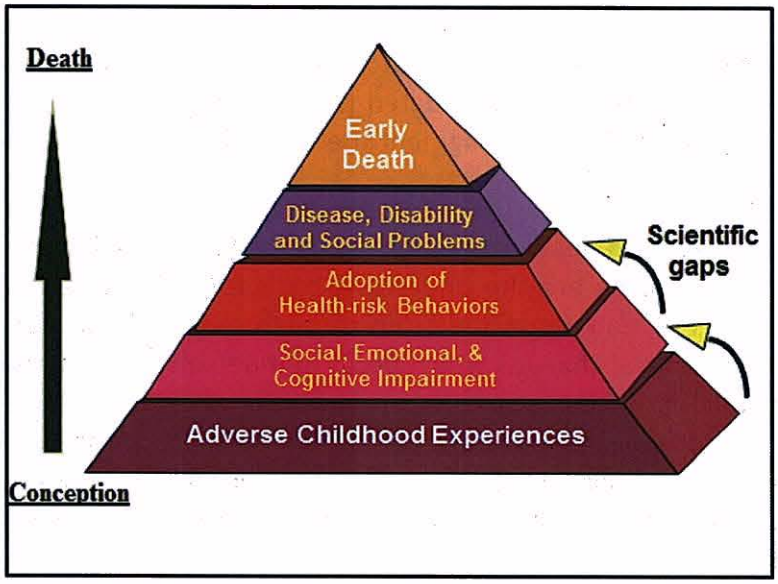
Table 3 represents the estimated current level of smokers in Alaska using the 2013 BRFSS survey results. It is derived from applying the percentages in the black box **(Table 2)** to the population based ACE estimates from **Table 1**. Working at this end of the continuum would, for example, include providing tobacco cessation programs to those Alaskans currently smoking. In terms of trauma and smoking reduction this is an example of **tertiary prevention,** as it is a way to mitigate somewhat the results of trauma (i.e. smoking). Primary, secondary and tertiary levels of prevention all have potential to improve the outcomes for Alaskans. Of course, primary prevention allows for fewer costs associated with "fixing" already damaging conditions or habits.

The Initial Paradigm

When the original ACEs studies were released, the researchers developed a graphic (**Figure 3**) to explain what they had been observing from their results. Five levels or tiers were observed throughout a person's life course if they experienced ACEs:

1. **ACEs occurred,** which led through an unknown mechanism to
2. **Social, emotional and cognitive impairments,** which led through an unknown mechanism to
3. **Adoption of high risk health behaviors ,**
4. **High rates of disease, disability and social problems, and**
5. **Early death**

Figure 3[xvi]



Subsequently, the researchers began to explore other fields of science doing complementary work. The synthesis of these fields with the ACE epidemiological work shed more light on this original paradigm.

Causation

Neurobiology & Epidemiology

Approximately eight years after the original ACE studies began to appear, the two original ACE researchers, Dr. Robert Anda and Dr. Vincent Felitti, with other scientists wrote a journal article[xvii] making the case that the links between ACEs and other health outcomes were more than correlations. In a well-reasoned argument they proposed that ACEs cause many of the outcomes linked with them. They made their case using both the original ACE epidemiology work, and new findings in neurobiology which had for years been exploring changes in the brain as a result of traumatic experiences in childhood. In this journal article, the authors cover nine points (**Figure 4**) establishing an argument for causation.

Figure 4

Sir Bradford Hill's - 9 criteria for establishing an argument for causation[xviii]

1. Demonstration of a strong association between causative agent and outcome
2. Consistency of findings across research sites and methods
3. Specificity
4. Temporal sequence
5. Biological gradient
6. Biological plausibility
7. Coherence
8. Experiential evidence
9. Analogous evidence

The understanding that ACEs lead to costly outcomes is key to achieving savings through ACE reduction efforts. The commentary, while dated (2005), if rewritten, could further expand on the neurobiological research cited and augment the case for causation, with research from the field of epigenetics.

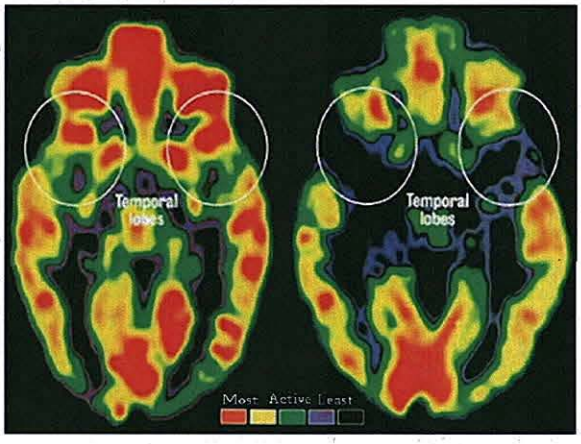
The changes in the brain and gene expression (epigenetics)[xix] of individuals who experience emotional and physical trauma are the underlying basis for these arguments. Scientists can show the consequences of trauma on the brain through new technologies. Research studies show that there are structural changes which occur in a person's brain and body as a result of trauma. This material provides new opportunities to alter poor outcomes as a better understanding of the mechanisms of the impacts of trauma exposure are understood. The well-known graphic comparing brain scans of a Romanian orphan who was severely neglected compared with a normally developing child is shown in **Figure 5** below and illustrates the impacts of trauma.

Figure 5[xx]

PET SCANS

Healthy Brain **Abused Brain**

The brain of a normal child shows regions of high (red) and low (blue and balck) activity. At birth, only primitive structures such as the brain stem (center) are fully functional: in regions like the tompral lobes (top) early childhood experiences wire the circuits.



The brain of a Romanian orphan, who was institutionalized shortly after birth, shows the effect of extreme deprivationin infancy. The temporal lobes (top), which regulate emotions andreceive input from the senses, are nearly quiescent. Such children suffer emotional and cognitive problems

Population Attributable Risk[xxi]

Population attributable risk is a well-established method in epidemiology of determining the percentage of an outcome which is linked back to a precursor – in this case - ACEs. **Table 4** below represents the calculations of population attributable risks associated with a number of economic, social and health outcomes as reported by Alaskan adults. For example, if all ACEs could be eliminate then it would be expected that 40% fewer Alaskan adults would be enrolled in Medicaid or there would be 32% percent fewer smokers. This table begins to hint at the potential savings available to Alaskans with a successful ACE prevention program in place.

The items in **Table 4** are from Alaska-specific research. Additional studies in various populations explored other health links to ACEs which were not studied in Alaska suggest population attributable risks which further bolster the argument for primary ACE prevention in Alaska and in other populations. For example, the population attributable risk for adolescent suicide attempts as a result of ACEs was 80% while in adults 68% in one study[xxii].

Eliminating all ACEs is not a realistic goal for a policy discussion. However, the research offers some guidelines which may be especially helpful in developing a coordinated approach to effective service arrays, prevention and intervention efforts.

Table 4

Health Behavior or Outcome	PAR%*
Frequent Mental Distress	60.1%
Chronic Obstructive Pulmonary Disease, Emphysema or Chronic Bronchitis	46.1%
Health Insurance: Medicaid	40.6%
Physical Health Not Good 14+ Days	33.2%
Current Smoker	32.0%
Current or Former Asthma	30.6%
General Health	26.8%
Non-Gestational Diabetes	23.7%
Activity Limitation 14+ Days	23.7%
Heavy Alcohol Consumption	20.5%
Ever Smoker	19.3%
Told Have Arthritis	15.8%
Insufficient Sleep	15.5%
Obesity	14.3%
Separated or Divorced	13.2%
Binge Drinking Risk Factor	11.0%
No Leisure Time Physical Activity	10.2%

A Caution for Individuals & Policy Makers

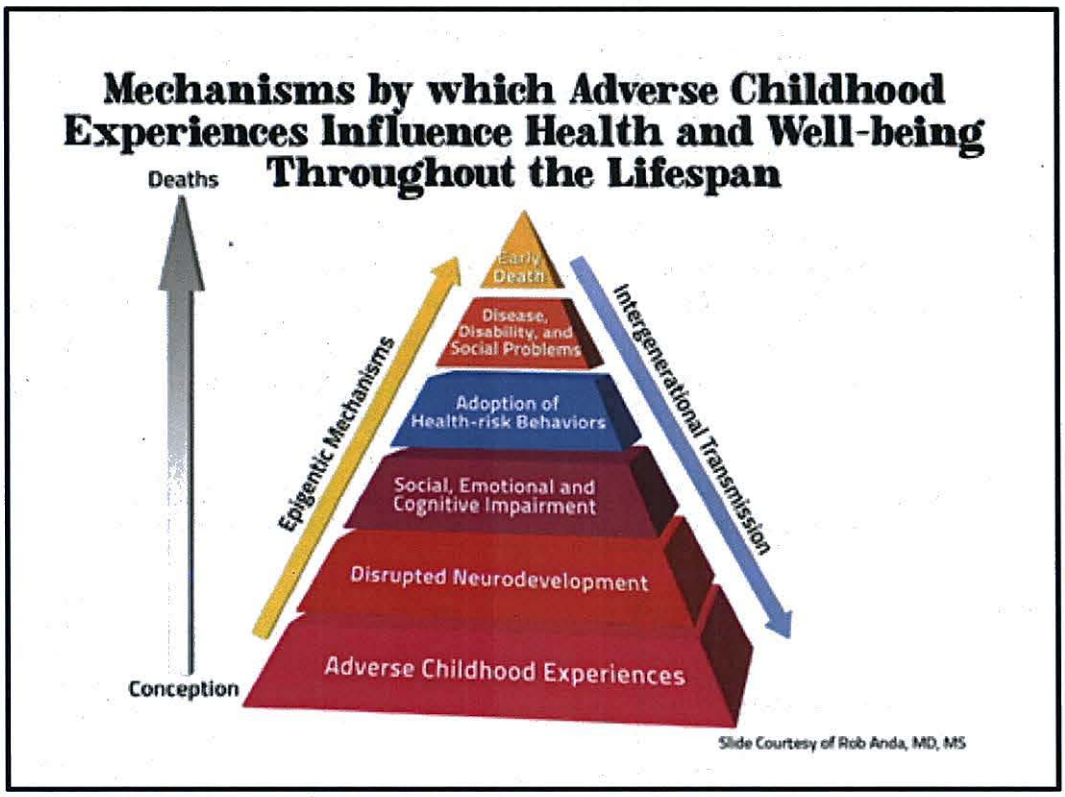
ACE research shows powerful relationships between exposure to ACEs and poor outcomes. These are important findings, but they do not predict specific outcomes for **individuals**. A person may be exposed to several ACEs and not experience the negative effects linked to ACEs. Conversely a person with no ACE exposure may develop some of the negative health outcomes associated with early trauma exposure. Because of unique biological or environmental conditions, some people are able to avoid poor outcomes (just like a person may develop lung cancer having never smoked or a person who smoked for 60 years does not develop lung cancer). Thus, ACEs research is most useful at the population level.

Policy makers must understand that while individual differences occur, these differences in outcomes should not be used to discount the overwhelming evidence and costs associated with ACEs. The strength of ACE study data is that it is **best suited** to inform how to effectively allocate resources. While individuals may vary in results - changing the ACEs for a population will pay dividends as shown below.

A New Paradigm

Recently, Dr. Rob Anda released a new ACE pyramid graphic (**Figure 6**). This representation of the ACE progression removes the "scientific gaps" seen in Figure 3 above. With the addition of research results from neurobiology and epigenetics, the mechanisms which lead from ACEs to poor health outcomes are better understood – and expanding rapidly. This graphic also brings into the discussion the idea of intergenerational transmission of ACEs. Some of the poor outcomes associated with ACEs, such as substance abuse and depression, can, if untreated, become ACEs for the next generation.

Figure 6



This new paradigm may lead in a different direction. Given what is known about the impact of trauma on developing brains and the physiological resources (**Figure 7**, below) needed to "rewire" them if damaged by toxic levels of stress, a different approach is warranted. James Heckman and others have shown that it is not just high levels of physiological resources which need to be used to fix trauma – it is also economic resources.[xxiii] **What would a primary prevention effort do for Alaskans, both economically and socially?** Alaska expends significant resources on corrections ($278 million in unrestricted general funds in 2016[xxiv]), substance abuse ($1.2 billion annually of public and private costs[xxv]), chronic health conditions (see below) and other issues related to ACEs.

Figure 7[xxvi]

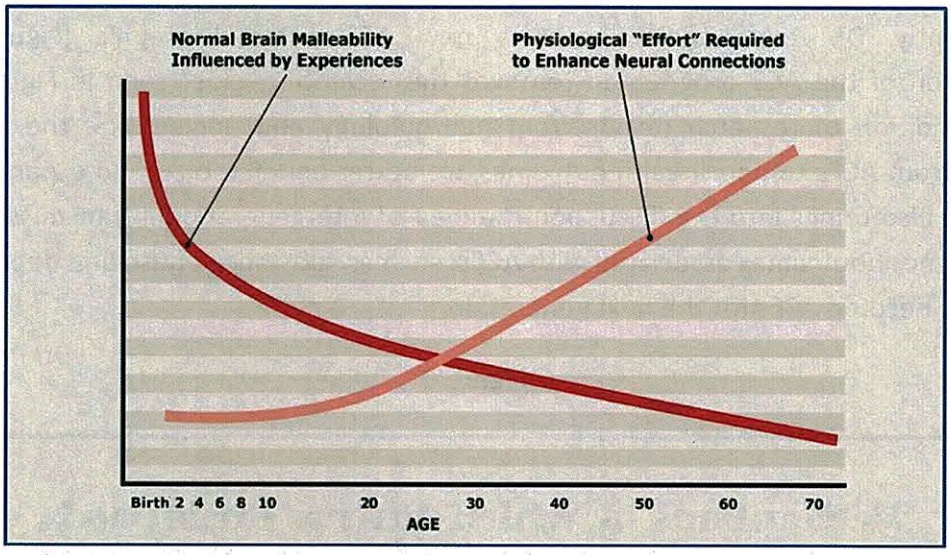


Figure 7 also gives insight into the time which is most productive to intervene if ACEs have occurred. Infants and young children require fewer physiological and economic resources to support their brains after trauma. Yet, they are the most susceptible to its effects. While intervening at any age can be effective, the younger the person is when treated after trauma the better the likelihood that the outcome will be positive with fewer resources needed.

Figure 8[xxvii]

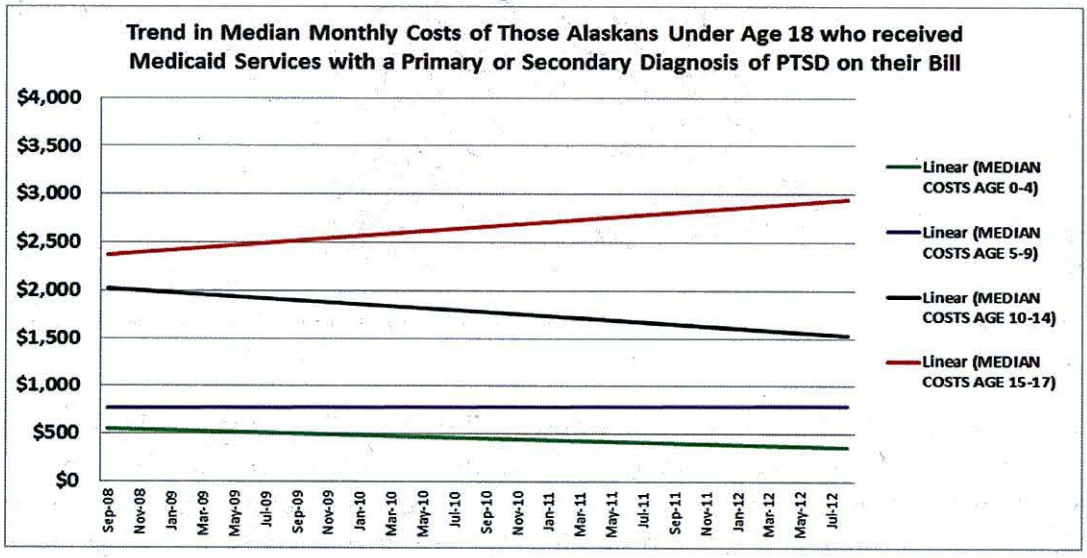


Figure 8 shows an analysis of Medicaid costs for children and youth with a PTSD diagnosis conducted by the Alaska Mental Health Board staff. It shows that treating younger children with this trauma condition is significantly cheaper than treating it later in life. Even waiting until adolescence has additional costs associated with it.

Establishing a Goal for Primary Prevention of ACEs in Alaska

Because many states (**Figure 9**) which have conducted the same ACE survey of their adult population that Alaska has, there is a rich data source from which to draw. Choosing a state or two that have a better rate of ACEs than Alaska seems a sensible place to start when developing a target for ACE prevention.

After examining the data, Vermont and Arkansas have ACE scores that are better than Alaska's. Since they have already achieved a lower level of ACE scores, it is plausible that another state can do the same.

Figure 9[xxviii]

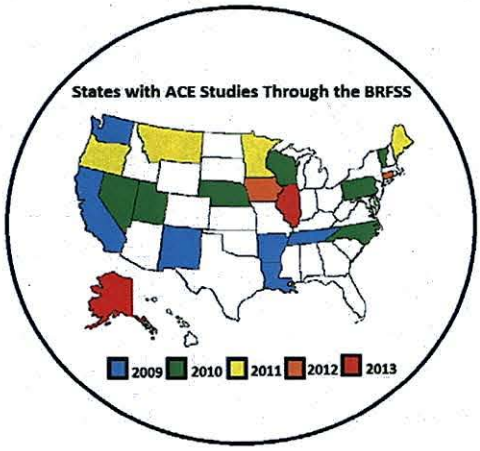
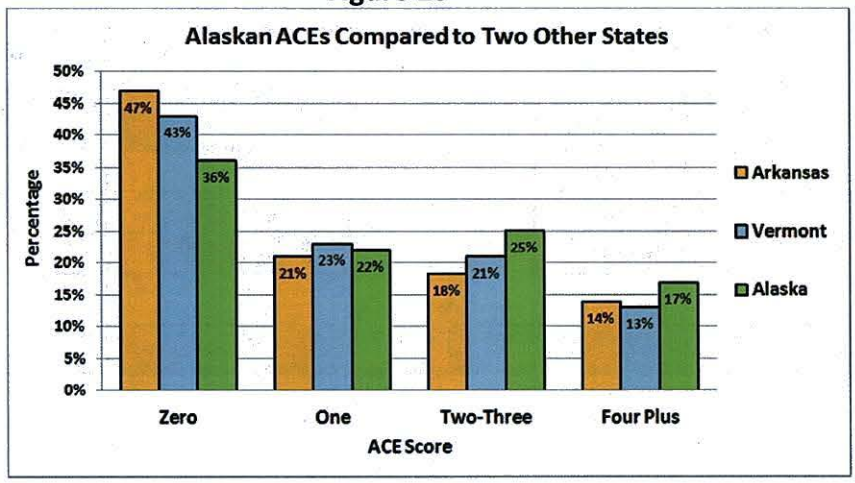


Figure 10 displays Alaska's rate of ACEs compared to Arkansas and Vermont, two states with relatively good ACE scores. The Zero ACE category is higher for the other two states. What would it take to get Alaska to the level of ACEs similar to Arkansas or Vermont?

Figure 10[xxix] [xxx]



To search the possibilities for ACE reduction the staff of the Alaska Mental Health Board and Advisory Board on Alcoholism and Drug Abuse explored several scenarios with population

based reductions in ACEs. A one ACE reduction for any Alaskan who had one was first examined, but proved too ambitious. Modeling a reduction of one ACE for half of the individuals at each level of ACE score was done. For example, if half the people with one ACE dropped to no ACEs while the other half remained at one and if half the Alaskans with two ACEs dropped to one ACE and the other half stayed at two, etc. (**Table 5**).

Table 5

ACE Score	2013 Adult Alaska Population	%	ACE Score Target Reduction	%
Zero	194,275	35.6%	255,250	46.8%
One	121,950	22.3%	101,002	18.5%
Two	80,053	14.7%	67,699	12.4%
Three	55,345	10.1%	45,382	8.3%
Four	35,419	6.5%	30,554	5.6%
Five	25,689	4.7%	20,428	3.7%
Six	15,166	2.8%	14,324	2.6%
Seven	13,482	2.5%	8,930	1.6%
Eight	4,378	0.8%	2,189	0.4%
	545,757	100.0%	545,757	100.0%

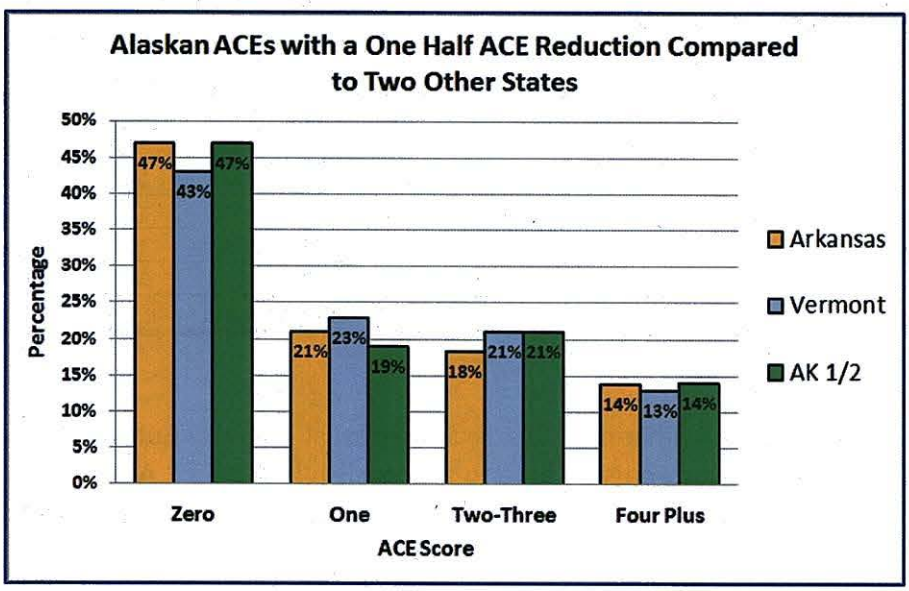
Table Six simplifies Table Five into a more manageable format and groups the higher ACE scores together. This allows for a simpler format and is in line with how most ACE data are presented across the many studies.

Table 6

ACE Scores of 2013 Adult Alaska Population			ACE Scores of 2013 Adult Alaska Population with Reduction	
Zero	194,275		Zero	255,250
One	121,950		One	101,002
Two - Three	135,398		Two - Three	113,081
Four Plus	94,134		Four Plus	76,425
Total	545,757		Total	545,757

The results of that analysis generated **Figure 11** below, which would move Alaska into the realm of the other two states.

Figure 11



The changes necessary to achieve the level of the other two states are ambitious, but Alaska has some momentum in this area already. When comparing Alaska's ACE scores to a five state average, Alaska's younger generations compare more favorably, whether this is due to in-migration, better services, or an improved economy based on oil wealth. Compared to their peers in other states Alaskan elders had much rougher childhoods.

Current Costs and Potential Savings

In **Table 7** below, categories of five costly health conditions and adult use of Medicaid are outlined in terms of their estimated annual costs to Alaska. These costs are incurred by both the public and private sectors. For each one of these categories, a population attributable risk was calculated using the 2013 BRFSS data as they related to adverse childhood experiences. Those rates are shown and in the final column those rates are applied to the estimated annual costs to determine the expenditures associated for those categories linked with ACEs, In simple terms, if all ACEs were eliminated nearly $800 million dollars of annual costs would be eliminated from Alaska's expense column for these six health measures.

Table 7*

Population Attributable Risk for ACEs			
Health Behavior or Outcome	**Estimated Annual Costs***	**Percentage of Population Attributable Risk****	**Estimated Annual Costs Linked to ACEs*****
Adult Medicaid (Age 20+)	$ 860,000,000	40.6%	$ 349,160,000
Current Smoker	$ 579,000,000	32.0%	$ 185,280,000
Non-Gestational Diabetes	$ 450,000,000	23.7%	$ 106,650,000
Binge Drinking	$ 545,000,000	11.0%	$ 59,950,000
Arthritis	$ 274,000,000	15.8%	$ 43,292,000
Obesity	$ 219,000,000	14.3%	$ 31,317,000
Total	**$ 2,927,000,000**		**$ 775,649,000**

Again, completely eliminating ACEs is an unrealistic goal. But what might a primary prevention effort with realistic goals be able to accomplish in Alaska? A change in rates of ACEs in Alaskan adults which moves the state to similar rates achieved in Arkansas and Vermont will be explored below.

* For the source of each health behavior or outcomes costs see the individual analysis of the individual items below.

** These population attributable risks were calculated for this report by the Alaska Department of Health and Social Services, Division of Public Health, Section of Chronic Disease Prevention and Health Promotion from the Alaska ACE data captured in the 2013 BRFSS

*** These cost were calculated by multiplying the two adjacent columns

Creating an ACEs Ledger

In order to answer the questions about how a reduction in ACEs in the past might have impacted Alaska today, an ACE Ledger was developed (**Table 8**). The **first column** describes several health outcomes linked to ACEs for which there is Alaska-specific annual costs data available. Additionally Alaskan adults were asked about these conditions in the 2013 BRFSS and their answers can be cross-tabbed with their ACEs scores.

The **second column** will show an estimated number of Alaskans who experience each condition based on the 2013 BRFSS and 2013 Census estimate of Alaskan adults. The **third column** will be filled out using cost estimates for Alaska of these specific health issues as calculated by various academic and government agencies.

The **fourth column** will be calculated by dividing column three by column two to estimate an annual per person cost of each health issue. The **fifth column** will be based on overlaying the reduction of one ACE for one half of the Alaskan adult population on top of the 2013 BRFSS results. This number will be the estimated number of fewer Alaskan who would be experiencing each health measure if ACE scores had been lower. Finally, an estimated saving will be calculated by multiplying columns 4 and 5 in **column six**.

This ledger below will be completed to demonstrate estimated cost savings with a realistic reduction in ACE scores.

Table 8

One	Two	Three	Four	Five	Six
Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	**Estimated Savings**
Medicaid	**0**	**$0**	**$0**	**0**	$0
Current Smoking	**0**	**$0**	**$0**	**0**	$0
Diabetes	**0**	**$0**	**$0**	**0**	$0
Binge Drinking	**0**	**$0**	**$0**	**0**	$0
Arthritis	**0**	**$0**	**$0**	**0**	$0
Obesity	**0**	**$0**	**$0**	**0**	$0

Alaskan Adults Who Use Medicaid

According to the Alaska Department of Health and Social Services $860 million was spent on Alaskan adults aged 20 or older in 2012 in the Medicaid program.[xxxi] These costs were spread over approximately 53,800 Alaskans. When dividing those two figures, an annual per person cost of nearly $16,000 is calculated. Because of the nature of the 2013 BRFSS survey (which does not survey people who are institutionalized and which is conducted in a way that makes surveying people in home and community based services more difficult), the survey results only estimated the adults using Medicaid at approximately 34,500. The following estimates will be based on these lower figures to keep them in the conservative range.

Tables 9, 10, and 11, below display the results of the 2013 BRFSS survey in combination with the 2013 Census estimates for Alaska. **Table 9** is the current estimated ACE levels for adults and the goal estimate of ACEs with successful primary prevention. **Table 10** is the percentage of the Alaskans who reported using Medicaid by ACE score. **Table 11** is calculated by multiplying Table 9 and Table 10's current estimates by goal estimates respectively.

Table 9			Table 10	Table 11	
ACE Score	Population		Adult Medicaid	Medicaid Recipients	
	Current Estimate	Goal Estimate		Current Estimate	Goal Estimate
Zero	194,275	255,250	3.8%	7,382	9,700
One	121,950	101,002	5.9%	7,195	5,959
Two-Three	135,398	113,081	8.0%	10,832	9,046
Four Plus	94,134	76,425	9.7%	9,131	7,413
Total	545,757	545,758		34,540	32,118

The resulting estimated reduction in the number of Alaskans who use Medicaid is 2,422 people if ACE scores were lower. This represents approximately a 7% reduction. Putting these calculations into the ACE Ledger below, the annual savings which Alaska could realize if it had levels of ACE scores like Vermont or Arkansas would be approximately $39 million.

Table 12

Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	Estimated Savings
Medicaid	53,800	$860,000,000	$15,985	2,422	$38,715,670

Alaskan Adults who Currently Smoke

According to the State of Alaska publication Alaska Tobacco Facts 2012,[xxxii] $576 million was spent on Alaskans as a result of tobacco use. A choice was made to use the current smoking figure in this calculation because the 2013 BRFSS data show that not only are people with higher ACE scores at greater risk for ever smoking they are also less likely to have quit if they ever started. These costs were spread over approximately 115,200 Alaskans. When dividing those two figures, an annual per person cost of approximately $5,000 was calculated.

Tables 13, 14, and 15, below display the results of the 2013 BRFSS survey in combination with the 2013 Census estimates for Alaska. **Table 13** is the current estimated ACE levels for adults and the goal estimate of ACEs with successful primary prevention. **Table 14** is the percentage of the Alaskans who reported being current smokers by ACE score. **Table 15** is calculated by multiplying Table 13 and Table 14's current estimates by goal estimates respectively.

Table 13			Table 14	Table 15	
ACE Score	Population		Current Smoking	Currently Smoke	
	Current Estimate	Goal Estimate		Current Estimate	Goal Estimate
Zero	194,275	255,250	14.4%	27,901	36,658
One	121,950	101,002	18.3%	22,298	18,468
Two-Three	135,398	113,081	24.1%	32,564	27,196
Four Plus	94,134	76,425	34.5%	32,481	26,371
Total	545,757	545,758		115,244	108,693

By changing the base rate of the ACEs in **Table 13** and leaving **Table 14** as it is - then **Table 15** is determined by multiplying Table 13 and Table 14. The results show a reduction of those currently smoking by 6,551 people

Adding these calculations into the ACE Ledger below (**Table 16**) the annual savings which Alaska could realize if it had levels of ACE scores like Vermont or Arkansas is approximately $33 million.

Table 16

Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	Estimated Savings
Current Smoking	115,244	$579,000,000	$5,024	6,551	$32,912,224

In order to calculate a total using the first two measures there is a need to eliminate "double counting" of costs. For example, some of the costs associated with current smokers are accounted for by people who are on Medicaid and currently smoke. By leaving the Medicaid calculation intact and removing the people who are on Medicaid from those Alaskans who currently smoke a **net potential savings of $69,558,006** between these **two categories is calculated**, as seen in **Table 17** below.

Table 17

Issue	Total 2013 BRFSS	With Reduction of ACEs	Percentage Unduplicated	Number of Alaskans Unduplicated*	Total Costs of Unduplicated Alaskans**	Average Annual Costs***	Target Reduction Unduplicated*	Estimated Savings*
Medicaid	**53,800**	**51,378**	**100.0%**	**51,378**	**$821,277,330**	**$15,985**	**2,422**	$38,715,670
Current Smoking	**115,244**	**108,693**	**93.7%**	**101,893**	**$511,910,432**	**$5,024**	**6,139**	$30,842,336

Unduplicated **$69,558,006**

*93.7% of people who reported currently smoking were not using Medicaid. These starred items were reduced by multiplying by the 93.7% figure in the "Percentage Unduplicated" column.

** Total costs of unduplicated Alaskans includes the reduction in ACES and the percentage unduplicated

*** Average annual per person costs remained the same for this analysis

Alaskan Adults Who Have Ever Been Diagnosed With Diabetes

According to an article in the journal Diabetes Care, *The Economic Costs of Diabetes in the U.S. 2012,*[xxxiii] the annual cost of Alaskans with diabetes is $450 million. Using the 2013 BRFSS an estimated 41,160 Alaskan adults had ever been diagnosed with diabetes. The average annual cost per person therefore is estimated at just under $11,000 ($450 Million/41,160).

Tables 18, 19, and 20, below display the results of the 2013 BRFSS survey in combination with the 2013 Census estimates for Alaska. **Table 18** is the current estimated ACE levels for adults and the goal estimate of ACEs with successful primary prevention. **Table 19** is the percentage of the Alaskans who reported being ever diagnosed with diabetes by ACE score. **Table 20** is calculated by multiplying Table 18 and Table 19's current estimates by goal estimates respectively.

Table 18			Table 19	Table 20	
ACE Score	Population		Diabetes	Diabetes	
	Current Estimate	Goal Estimate		Current Estimate	Goal Estimate
Zero	194,275	255,250	5.9%	11,522	15,139
One	121,950	101,002	6.7%	8,124	6,728
Two-Three	135,398	113,081	10.1%	13,725	11,506
Four Plus	94,134	76,425	8.3%	7,789	6,441
Total	545,757	545,758		41,160	39,814

By changing the base rate of the ACEs in **Table 18** and leaving **Table 19** as it is - then **Table 20** is determined by multiplying Table 18 and Table 19. The results show a reduction of those with diabetes by 1,346 Alaskans.

The ACE Ledger below (**Table 21**) displays the annual savings which Alaska could realize if it had levels of ACE scores like Vermont or Arkansas is approximately $14.7 million.

Table 21

Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	Estimated Savings
Diabetes	**41,160**	**$450,000,000**	**$10,933**	**1,346**	$14,715,743

Again, there is a need to eliminate "multiple counting" of costs. For example, some of the costs associated with diabetes are accounted for by people who are on Medicaid and/or currently smoking. By leaving the Medicaid calculation intact and removing the people who are current smokers from those Alaskans who receive Medicaid and then again removing those people with diabetes who fall into either category a **net potential savings of $78,938,520** between these **three categories is calculated**, as seen in **Table 22** below.

Table 22

Issue	Total 2013 BRFSS	With Reduction of ACEs	Percentage Unduplicated	Number of Alaskans Unduplicated*	Total Costs of Unduplicated Alaskans**	Average Annual Costs***	Target Reduction Unduplicated*	Estimated Savings*
Medicaid	**53,800**	**51,378**	**100.0%**	**51,378**	**$821,277,330**	**$15,985**	**2,422**	$38,715,670
Current Smoking	**115,244**	**108,693**	**93.7%**	**101,893**	**$511,910,432**	**$5,024**	**6,139**	$30,842,336
Diabetes	**41,160**	**39,814**	**63.7%**	**25,376**	**$277,435,808**	**$10,933**	**858**	$9,380,514

Unduplicated **$78,938,520**

*63.7% of people who reported diabetes were not currently smoking or using Medicaid. These starred items were reduced by multiplying by the figure in the respective "Percentage Unduplicated" column.

** Total costs of unduplicated Alaskans includes the reduction in ACES and the percentage unduplicated

*** Average annual per person costs remained the same for this analysis

Alaskan Adults who Binge Drink

In an article in The Journal of Preventative Medicine titled *State Costs of Excessive Alcohol Consumption*[xxxiv] the annual cost of Alaskans who binge drink is $545 million. Using the 2013 BRFSS an estimated 98,152 Alaskan adults binge drink. The average annual cost per person is estimated at just over $5,500.

Tables 23, 24, and 25, below display the results of the 2013 BRFSS survey in combination with the 2013 Census estimates for Alaska. **Table 23** is the current estimated ACE levels for adults and the goal estimate of ACEs with successful primary prevention. **Table 24** is the percentage of the Alaskans who reported binge drinking by ACE score. **Table 25** is calculated by multiplying Table 23 and Table 24's current estimates by goal estimates respectively.

Table 23			Table 24	Table 25	
ACE Score	Population		Binge Drinking	Binge Drinking	
	Current Estimate	Goal Estimate		Current Estimate	Goal Estimate
Zero	194,275	255,250	16.0%	31,105	40,868
One	121,950	101,002	17.1%	20,880	17,294
Two-Three	135,398	113,081	19.6%	26,507	22,138
Four Plus	94,134	76,425	20.9%	19,659	15,961
Total	545,757	545,758		98,152	96,260

By changing the base rate of the ACEs in **Table 23** and leaving **Table 24** as it is - then **Table 25** is determined by multiplying Table 23 and Table 24. The results show a reduction of those binge drinking by 1,892 Alaskans.

The ACE Ledger below (**Table 26**) displays the annual savings which Alaska could realize if it had levels of ACE scores like Vermont or Arkansas is approximately $10.5 million.

Table 26

Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	Estimated Savings
Binge Drinking	**98,150**	**$545,000,000**	**$5,553**	**1,892**	$10,505,796

In order to calculate a total using these four measures there is a need to eliminate "multiple counting" of costs. A **net potential savings of $85,291,152** between these **four categories** can be calculated, as seen in **Table 27** below.

Table 27

Issue	Total 2013 BRFSS	With Reduction of ACEs	Percentage Unduplicated	Number of Alaskans Unduplicated*	Total Costs of Unduplicated Alaskans**	Average Annual Costs***	Target Reduction Unduplicated*	Estimated Savings*
Medicaid	53,800	51,378	100.0%	51,378	$821,277,330	$15,985	2,422	$38,715,670
Current Smoking	115,244	108,693	93.7%	101,893	$511,910,432	$5,024	6,139	$30,842,336
Diabetes	41,160	39,814	63.7%	25,376	$277,435,808	$10,933	858	$9,380,514
Binge Drinking	98,152	96,260	60.5%	58,219	$323,290,107	$5,553	1,144	$6,352,632

Unduplicated **$85,291,152**

*60.5% of people who reported binge drinking were not diabetic, currently smoking or using Medicaid. These starred items were reduced by multiplying by the figure in the respective "Percentage Unduplicated" column.

** Total costs of unduplicated Alaskans includes the reduction in ACES and the percentage unduplicated

*** Average annual per person costs remained the same for this analysis

Alaskan Adults Who Have Arthritis

According to **National and State Medical Expenditures and Lost Earnings Attributable to Arthritis and Other Rheumatic Conditions U.S. 2003**[xxxv] the annual costs of arthritis in Alaska is an estimated $274.7 million. While the figure is clearly dated, it gives a conservative estimate of today's costs for this common malady. Using the 2013 BRFSS an estimated 132,136 Alaskan adults have arthritis. The average annual cost per person is estimated at $2,453.

Tables 28, 29, and 30, below display the results of the 2013 BRFSS survey in combination with the 2013 Census estimates for Alaska. **Table 28** is the current estimated ACE levels for adults and the goal estimate of ACEs with successful primary prevention. **Table 29** is the percentage of the Alaskans who reported having arthritis by ACE score. **Table 30** is calculated by multiplying Table 28 and Table 29's current estimates by goal estimates respectively.

Table 28			Table 29	Table 30	
ACE Score	Population		Arthritis	Arthritis	
	Current Estimate	Goal Estimate		Current Estimate	Goal Estimate
Zero	194,275	255,250	20.4%	39,610	52,041
One	121,950	101,002	22.4%	27,280	22,594
Two-Three	135,398	113,081	25.9%	35,122	29,333
Four Plus	94,134	76,425	32.0%	30,125	24,457
Total	545,757	545,758		132,136	128,425

By changing the base rate of the ACEs in **Table 28** and leaving **Table 29** as it is - then **Table 30** is determined by multiplying Table 28 and Table 29. The results show a reduction of those with arthritis by 3,711 Alaskans.

The ACE Ledger below (**Table 31**) displays the annual savings which Alaska could realize if it had levels of ACE scores like Vermont or Arkansas is approximately $9.1 million.

Table 31

Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	Estimated Savings
Arthritis	132,136	$274,700,000	$2,453	3,711	$9,101,890

In order to calculate a total using these five measures there is a need to eliminate "multiple counting" of costs. A **net potential savings of $89,946,946** between these **five categories** can be calculated, as seen in **Table 32** below.

Table 32

Issue	Total 2013 BRFSS	With Reduction of ACEs	Percentage Unduplicated	Number of Alaskans Unduplicated*	Total Costs of Unduplicated Alaskans**	Average Annual Costs***	Target Reduction Unduplicated*	Estimated Savings*
Medicaid	**53,800**	**51,378**	**100.0%**	**51,378**	**$821,277,330**	**$15,985**	**2,422**	$38,715,670
Current Smoking	**115,244**	**108,693**	**93.7%**	**101,893**	**$511,910,432**	**$5,024**	**6,139**	$30,842,336
Diabetes	**41,160**	**39,814**	**63.7%**	**25,376**	**$277,435,808**	**$10,933**	**858**	$9,380,514
Binge Drinking	**98,152**	**96,260**	**60.5%**	**58,219**	**$323,290,107**	**$5,553**	**1,144**	$6,352,632
Arthritis	**132,136**	**128,425**	**51.1%**	**65,674**	**$161,098,322**	**$2,453**	**1,898**	$4,655,794

Unduplicated **$89,946,946**

*51.1% of people who reported having arthritis were not binge drinking, diabetic, currently smoking or using Medicaid. These starred items were reduced by multiplying by the figure in the respective "Percentage Unduplicated" column.

** Total costs of unduplicated Alaskans includes the reduction in ACES and the percentage unduplicated

*** Average annual per person costs remained the same for this analysis

Alaskan Adults who are Obese

The Institute for Social and Economic Research published a study in 2014 that estimated annual costs of adult obesity in Alaska were $219 million.[xxxvi] Using the 2013 BRFSS, an estimated 156,656 Alaskan adults are obese. The average annual cost per person is estimated at $1,398.

Tables 33, 34, and 35, below display the results of the 2013 BRFSS survey in combination with the 2013 Census estimates for Alaska. **Table 33** is the current estimated ACE levels for adults and the goal estimate of ACEs with successful primary prevention. **Table 34** is the percentage of the Alaskans who reported being obese by ACE score. **Table 35** is calculated by multiplying Table 33 and Table 34's current estimates by goal estimates respectively.

Table 33			Table 34	Table 35	
ACE Score	Population		Obesity	Obesity	
	Current Estimate	Goal Estimate		Current Estimate	Goal Estimate
Zero	194,275	255,250	24.6%	47,818	62,826
One	121,950	101,002	26.9%	32,835	27,195
Two-Three	135,398	113,081	32.9%	44,521	37,183
Four Plus	94,134	76,425	33.4%	31,482	25,559
Total	545,757	545,758		156,656	152,763

By changing the base rate of the ACEs in **Table 33** and leaving **Table 34** as it is - then **Table 35** is determined by multiplying Table 33 and Table 34. The results show a reduction of those who are obese by 3,893 Alaskans.

The ACE Ledger below (**Table 36**) displays the annual savings which Alaska could realize if it had levels of ACE scores like Vermont or Arkansas is approximately $5.4 million.

Table 36

Issue	Number of Alaskans	Total Costs	Average Annual Costs	Target Reduction	Estimated Savings
Obesity	156,656	$219,000,000	$1,398	3,893	$5,442,288

In order to calculate a total using these six measures there is a need to eliminate "multiple counting" of costs. A **net potential savings of $91,936,300** between these **six categories** can be calculated, as seen in **Table 37** below.

Table 37

Issue	Total 2013 BRFSS	With Reduction of ACEs	Percentage Unduplicated	Number of Alaskans Unduplicated*	Total Costs of Unduplicated Alaskans**	Average Annual Costs***	Target Reduction Unduplicated*	Estimated Savings*
Medicaid	53,800	51,378	100.0%	51,378	$821,277,330	$15,985	2,422	$38,715,670
Current Smoking	115,244	108,693	93.7%	101,893	$511,910,432	$5,024	6,139	$30,842,336
Diabetes	41,160	39,814	63.7%	25,376	$277,435,808	$10,933	858	$9,380,514
Binge Drinking	98,152	96,260	60.5%	58,219	$323,290,107	$5,553	1,144	$6,352,632
Arthritis	132,136	128,425	51.1%	65,674	$161,098,322	$2,453	1,898	$4,655,794
Obesity	156,656	152,763	36.6%	55,845	$78,071,310	$1,398	1,423	$1,989,354

Unduplicated **$91,936,300**

*36.6% of people who reported being obese were not arthritic, binge drinking, diabetic, currently smoking or using Medicaid. These starred items were reduced by multiplying by the figure in the respective "Percentage Unduplicated" column.

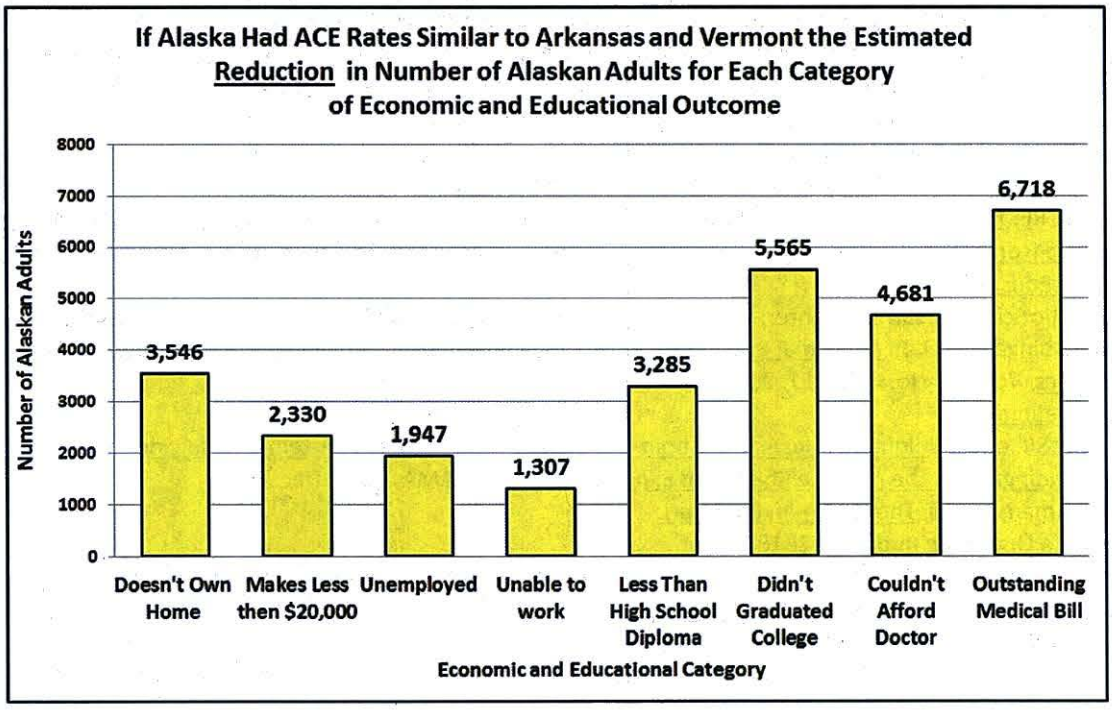
** Total costs of unduplicated Alaskans includes the reduction in ACES and the percentage unduplicated

*** Average annual per person costs remained the same for this analysis

ACEs are Costly

Whether it is the $82 million dollars estimated annual burden Alaskans take on each year for the costs during childhood of child abuse or the nearly $91 million Alaskans are paying now because Alaska's adults faced more adversity than some other Americans, ACEs are costly. These data demonstrate that a modest reduction of ACEs would have a profound impact on Alaska's government and private sector costs. While the six items explored in this document are high costs items, they don't begin to capture the many other poor outcomes associated with ACEs. **Cancer, suicide, heart disease, asthma, COPD** have all been linked to ACEs[xxxvii]. More potential areas for savings and increased economic contributions available, if ACEs are reduced, are outlined in **Figure 12** below.

Figure 12



The next steps are to explore those efforts around the state that prevent and mitigate the effects of ACEs and then take them to scale. There is solid evidence that various programs and ideas work[xxxviii]. Whether it be through faith-based organizations, community health efforts, government programs and services, or private employers – we can avoid many of the costs of social and economic issues Alaskans pay every day. **In times such as these - saving such as these - are hard to ignore.**

End Notes

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[i] Centers for Disease Control and Prevention website, ACE Publications by Health Outcomes
[ii] Knapp, G., An Introduction to Alaska Fiscal Facts and Choices, UAA Institute for Social and Economic Research
[iii] Division of Public Health, Behavioral Risk Factor Surveillance System website
[iv] Centers for Disease Control and Prevention, Child Abuse and Neglect Costs the United States $124 Billion, February 1, 2012
[v] U.S. Department of Health & Human Services, Administration for Children and Families, Child Maltreatment 2013, Children's Bureau, Page 50
[vi] See Rand Corporation website, Children and Families section
[vii] See Federal Reserve Bank of Minneapolis website, Special Studies, Early Childhood Development
[viii] See The Upjohn Institute for Employment Research, Early Childhood section
[ix] See the Heckman Equation website
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