ALASKA HEALTHCARE COSTS
Health-care spending for Alaskans reached about $7.5 billion in 2010. For comparison, that's close to half the wellhead value of all the oil produced in Alaska that year. It's also roughly equal to half the wages Alaskans collected in 2010. The state's health-care spending has been rising fast, tripling since 1990 and jumping 40% just between 2005 and 2010—and at current trends it could double by 2020, reaching more than $14 billion.

Here we report on who's paying the bills, what we're buying, what's contributing to the growth, and other aspects of health-care spending. We conclude with a discussion of how Alaska could get better value for its health-care dollars.

- **Who pays the bills?** Individual Alaskans directly pay about 20%, state and federal programs around 40%, and private and government employers another 40% (Figure 1 and page 2).

- **What's the biggest cost?** Medicaid is the largest single expense, making up nearly 18% of all Alaska health-care spending. But that's down from 20% of total spending in 2005. Why? Because spending for Medicaid didn't grow as fast as other kinds of spending (page 3).

- **Are costs shifting?** Every category of spending increased since 2005—but because spending by individuals and private employers increased faster, their shares of total spending increased (page 4).

- **What are we buying?** Hospitals and doctors account for nearly 60% of total spending—but the next largest cost is the 10% that goes for administering private and government health insurance (page 4).

- **What's driving spending?** Over the past 50 years, technology, income growth, medical-price inflation, changing insurance coverage, and a growing, aging population have driven health-care spending (page 5).

- **How many Alaskans are uninsured?** The answer varies depending on how “uninsured” is measured and when. But recent estimates say about 18% of adults and 9% of children are uninsured. Based on 2010 census figures, that would be about 17,000 children and 94,000 adults (page 6).

- **How many Alaska businesses offer health insurance?** More than 90% of large firms offer insurance, compared with just 30% of small businesses—and that's down from 35% in 2003 (page 7).

- **Are prices higher in Alaska?** Yes. But Alaska's isolation, small markets, and other factors contribute to those higher prices—a day in the hospital costs on average 50% more than in the U.S. as a whole, and costs for common procedures are roughly 35% higher (page 8).

- **How is spending distributed?** Just 10% of Americans are responsible for two-thirds of all health-care spending in an average year (page 9).

- **What about the future?** Expanded insurance coverage; an aging population; and continued growth in technology, incomes, and medical prices will keep driving growth in health-care spending in the coming years. Controlling that growth will be an ongoing challenge (page 11).
How Have Patterns of Spending Changed?
Every category of health-care spending increased between 2005 and 2010, but the shares of spending shifted slightly among the various payers. We don’t have enough information to say exactly what caused this shift—but several things likely contributed, as we describe below.
- Individuals paid 20% of Alaska’s health-care bills in 2010, up from 19% in 2005. As costs of health-care benefits increased rapidly, employers shifted more of those costs to employees (see page 7). Also, prices for policies individuals buy directly increased significantly.
- Private employers’ share of spending increased from 17% to 18%. That increase was in part because private industry added nearly four times more jobs than governments did since 2005—and at least some of that bigger base of employees had health-care coverage.
- Government employers’ share of spending was about the same, at 22%.
- Government health programs accounted for a somewhat smaller share of spending, down from about 41% to 39%.

The federal and state governments have attempted to hold down growth in costs of health programs—but federal programs alone continue to make up nearly a third of all Alaska’s health-care spending. Local government spending for health programs remains small, relative to that of the state and federal governments, and the increase in local spending was smaller as well.

What Do Health-Care Dollars Buy?
Alaska’s $7.5 billion health-care bill includes everything from visits to doctors and dentists to prescriptions and nursing-home care. Figure 7 summarizes what Alaska’s health-care dollars bought in 2010.
- Hospital care was the largest expense, followed closely by payments for doctors and related clinical services—together they accounted for about 60% of Alaska health-care spending in 2010.
- Administering private and public insurance plans cost one of every ten dollars spent for Alaska health care in 2010. That’s more than spending for prescriptions and medical equipment, and nearly twice the spending for dentists.
- Spending for nursing homes and home health care made up only about 3% of total spending, even though spending for home health care has increased rapidly in the past decade. Much of this care is paid for under Medicaid.

How About Health-Care Jobs?
This summary looks at health care from the perspective of spending for care—but it’s important to remember that the spending also supports jobs for Alaskans. As the Alaska Department of Labor and Workforce Development reports in its August 2011 Alaska Economic Trends:
- Health-care spending directly supports 31,800 jobs in Alaska. That’s one in ten of all wage and salary jobs—in hospitals, offices of doctors and other providers, nursing homes, and many other places.
- Many additional jobs related to health care—in government agencies, and among the self-employed—aren’t included in that total.
- Alaska employment in health care has been increasing at an annual rate of 4.3% for the past decade.
Who Pays the Bills?

Individuals, private employers, and governments share the direct costs of health care in Alaska (Figure 1 and Table 1).

Individual Alaskans spent about $1.5 billion for health care in 2010—20% of total spending.

- Alaskans with employer-based insurance—both private and government—paid about $640 million for premiums, and those with individual policies spent $350 million.
- Out-of-pocket costs for Alaskans totaled about $545 million in 2010. That includes deductibles and co-pays—the part of medical bills insurance doesn’t pay. It also includes costs for services not covered by insurance, and money that uninsured Alaskans spent for medical bills.

Private employers spent about $1.4 billion—18% of total spending.

- Alaska businesses spent around $835 million to self-insure in 2010. They set aside money to pay medical bills themselves, rather than pay insurance premiums. They’re betting that the medical bills will be less than the premiums they would have paid—and that their reserves will be enough to cover annual variation in claims. Many self-insured firms carry “stop loss” insurance, to protect them against very large claims. At first only large firms self-insured, but as insurance costs climbed, smaller businesses have also begun self-insuring.
- Businesses spent about $400 million for insurance premiums in 2010. That’s only about half what businesses spent to self-insure, showing how widespread the practice of self-insuring is.
- Medical bills of employees injured at work cost businesses about $150 million in 2010. State law requires employers to pay for such injuries.

Government employers spent $1.6 billion for health benefits in 2010.

- Local government employers—including school districts—spent about $630 million, the federal government nearly $590 million, and the state $410 million.
- Like businesses, many public employers self-insure, rather than pay insurance premiums—but we don’t have enough data to separate out those costs. The federal government also pays medical costs for active-duty and retired military personnel and veterans.

Governments spent nearly $3 billion for health programs in 2010.

- Medicaid spending was nearly $1.3 billion in 2010—$871 million in federal money and $409 million in state money. Medicaid is a federal program, but the state administers it and shares the costs (see page 3).
- Medicare spending was $733 million in 2010, accounting for nearly 10% of all health-care spending. Medicare is a federal program for people 65 and older and those with certain disabilities. Medicare spending is expected to grow rapidly in the next decade, as older Alaskans make up an ever-growing share of the population (see page 5).
- The federal government spent close to $650 million for other health programs in 2010, including the Indian Health Service, which provides medical care for Alaska Natives, and the Veterans Administration, which provides care for military veterans. Spending for these programs depends somewhat on enrollment, but it’s also constrained by Congressional appropriations.
- Besides its share of Medicaid, the state government spent about $260 million for a variety of other programs in 2010, including grants to local governments, the state-operated Pioneer Homes for older Alaskans, and the Alaska Psychiatric Institute.

Table 1. Health-Care Spending in Alaska, 2010 (Total Spending: $7.5 Billion)

<table>
<thead>
<tr>
<th>Category</th>
<th>Spending</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals</td>
<td>$1.529 million</td>
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<td>Employee premiums</td>
<td>$637</td>
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<tr>
<td>Out-of-pocket costs</td>
<td>$544</td>
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<td>Individual policies</td>
<td>$348</td>
</tr>
<tr>
<td>Private Employers*</td>
<td>$1,384 million</td>
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<tr>
<td>Insurance premiums</td>
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<td>Self-insurance costs</td>
<td>$836</td>
</tr>
<tr>
<td>Workers’ compensation medical</td>
<td>$153</td>
</tr>
<tr>
<td>Government Employers*</td>
<td>$1,625 million</td>
</tr>
<tr>
<td>Federal</td>
<td>$586</td>
</tr>
<tr>
<td>State</td>
<td>$408</td>
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<tr>
<td>Local</td>
<td>$631</td>
</tr>
<tr>
<td>Federal Health Programs</td>
<td>$2,250 million</td>
</tr>
<tr>
<td>Medicare</td>
<td>$733</td>
</tr>
<tr>
<td>Medicaid</td>
<td>$871</td>
</tr>
<tr>
<td>IHS, VA, Community Health Centers, public health, K-12 health</td>
<td>$646</td>
</tr>
<tr>
<td>State Health Programs</td>
<td>$670 million</td>
</tr>
<tr>
<td>Medicaid</td>
<td>$409</td>
</tr>
<tr>
<td>Local grants, API, Pioneer Homes, K-12 health, WAMI, Department of Corrections</td>
<td>$261</td>
</tr>
<tr>
<td>Local Health Programs</td>
<td>$45 million</td>
</tr>
<tr>
<td>Hospital and health program support</td>
<td>$40</td>
</tr>
<tr>
<td>Other local</td>
<td>$5</td>
</tr>
</tbody>
</table>

*includes coverage for current and retired employees. Source: Authors’ estimates. See page 12 for a description of what’s included in health-care costs.

- Local health programs are much smaller, at around $45 million in 2010, largely support for hospitals and health programs.

And finally, keep in mind that even though governments and businesses pay most of the direct costs of health care, individual Alaskans and other Americans indirectly pay all the costs of health care—because they buy goods and services, own businesses, and pay taxes.
ALASKA ACTIVE AND RETIREE HEALTH PLAN DATA
### Aggregate Risk Profile

**ACTIVE PLAN**

<table>
<thead>
<tr>
<th>Member Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Member Count</strong></td>
<td>17338</td>
</tr>
<tr>
<td><strong>Avg Age</strong></td>
<td>35</td>
</tr>
<tr>
<td><strong>Percent Female</strong></td>
<td>51%</td>
</tr>
<tr>
<td><strong>Avg Months Enrolled</strong></td>
<td>11</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aggregate Risk Summary</th>
<th># Members</th>
<th>Avg Risk Contribution</th>
<th>Contribution to Forecast</th>
<th>Risk Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>17338</td>
<td>SENIORS SKIN, FRACTURES, FALLS</td>
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<td>$5,987,784</td>
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<td>Acute Respiratory Disorders</td>
<td>2880</td>
<td>TUBERCULOSIS</td>
<td>$1,125</td>
<td>$3,251,578</td>
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<tr>
<td>Arrhythmia Disorders</td>
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<td>CHRONIC HEART FAILURE</td>
<td>$3,181</td>
<td>$2,140,732</td>
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<td>CHF Conditions</td>
<td>673</td>
<td>$4,192</td>
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<td>UPPER RESPIRATORY TRACT</td>
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<td>$4,005,542</td>
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<td>CORONARY HEART DISEASE</td>
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<td>Coronary Artery Related Conditions</td>
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<td>TYPE 1 AND TYPE 2</td>
<td>$5,932</td>
<td>$5,231,938</td>
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<td>Diabetic Disorders</td>
<td>882</td>
<td>$2,510</td>
<td>$856,045</td>
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<tr>
<td>Female Reproductive Conditions</td>
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<td>PRETERM BIRTHS</td>
<td>$5,628</td>
<td>$1,013,046</td>
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<tr>
<td>Gastrointestinal Disorders</td>
<td>2351</td>
<td>COLORECTAL CANCER</td>
<td>$2,011</td>
<td>$4,728,854</td>
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<tr>
<td>Heart Related Conditions</td>
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<td>$1,982</td>
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<tr>
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<td>$2,070</td>
<td>$3,937,924</td>
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<td>Hypotensive Drugs</td>
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<td>MRSA</td>
<td>$2,023</td>
<td>$5,968,497</td>
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<tr>
<td>Major Infection Related Conditions</td>
<td>2950</td>
<td>FIBROMYALGIA</td>
<td>$2,680</td>
<td>$8,247,421</td>
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<tr>
<td>Metabolic Conditions</td>
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<td>$1,340</td>
<td>$4,965,037</td>
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<tr>
<td>Minor Infection Related Conditions</td>
<td>3704</td>
<td>$2,303</td>
<td>$10,940,626</td>
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<td>INFANT MUSCLE, SENIOR FALLS</td>
<td>$2,206</td>
<td>$11,409,047</td>
</tr>
<tr>
<td>Myocardial Infarction Related Conditions</td>
<td>2271</td>
<td>AUTISM, HEART PROGRAMMING</td>
<td>$2,763,900</td>
<td>2.39%</td>
</tr>
<tr>
<td>Neonatal Issues</td>
<td>255</td>
<td>$935</td>
<td>$238,289</td>
<td>0.72%</td>
</tr>
<tr>
<td>Neoplastic Related Conditions</td>
<td>638</td>
<td>$4,332</td>
<td>$2,763,900</td>
<td>2.39%</td>
</tr>
<tr>
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<td>$1,435</td>
<td>$5,409,047</td>
<td>4.68%</td>
</tr>
<tr>
<td>Non-specific condition</td>
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<td>$780,877</td>
<td>0.68%</td>
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<tr>
<td>Pneumonia</td>
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<td>UPPER RESPIRATORY TRACT</td>
<td>$3,822</td>
<td>$298,744</td>
</tr>
<tr>
<td>Psychological Disorder</td>
<td>2688</td>
<td>S.A.D. AND DEPRESSION</td>
<td>$2,771</td>
<td>$7,447,883</td>
</tr>
<tr>
<td>Renal Disorders</td>
<td>309</td>
<td>$15,145</td>
<td>$4,679,794</td>
<td>4.05%</td>
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<td>1822</td>
<td>TRAUMATIC BRAIN INJURY</td>
<td>$1,459</td>
<td>$2,651,019</td>
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<td>Urinary Disorders</td>
<td>1381</td>
<td>$2,170</td>
<td>$2,996,360</td>
<td>2.59%</td>
</tr>
</tbody>
</table>

% total diseases directly related to Vitamin D status = 66.08%

Notes in red by office of Rep. Seaton
### Aggregate Risk Profile

#### Member Information

- **Member Count**: 65376
- **Avg Age**: 63
- **Percent Female**: 54%
- **Avg Months Enrolled**: 12
- **Avg Total Cost**: $17,726
- **Avg Forecasted Cost**: $15,666
- **% w/ Acute Impact Score >= 95**: 5.47%
- **% w/ Chronic Impact Score >= 95**: 16.63%
- **% w/ Motivation Rank >= 95**: 9.70%
- **Avg Forecasted Risk Index**: 2.56

#### Aggregate Risk Summary

<table>
<thead>
<tr>
<th>Risk Drivers</th>
<th># Members</th>
<th>Avg Risk Contribution</th>
<th>Contribution to Forecast</th>
<th>Risk Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>65376</td>
<td>SENIORS SKIN, FRACTURES, FALLS $454</td>
<td>$29,702,943</td>
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<td>9520</td>
<td>TUBERCULOSIS $1,669</td>
<td>$15,893,121</td>
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<td>Arrhythmia Disorders</td>
<td>5170</td>
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<td>CHRONIC HEART FAILURE $2,758</td>
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<td>Cerebral Vascular Disorder</td>
<td>5021</td>
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<td>$18,710,595</td>
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<td>11241</td>
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<td>15979</td>
<td>$1,958</td>
<td>$31,281,265</td>
<td>3.05%</td>
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<tr>
<td>Diabetic Disorders</td>
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<td>TYPE 1 AND TYPE 2 $5,966</td>
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<td>6.23%</td>
</tr>
<tr>
<td>Female Reproductive Conditions</td>
<td>18753</td>
<td>PRETERM BIRTHS $1,489</td>
<td>$153,413</td>
<td>0.01%</td>
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<tr>
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<td>COLORECTAL CANCER $2,146</td>
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<td>Heart Related Conditions</td>
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<td>Hypertension</td>
<td>21822</td>
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<td>$39,772,355</td>
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<td>Hypotensive Drugs</td>
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<td>FIBROMYALGIA $2,545</td>
<td>$73,213,862</td>
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<td>$1,726</td>
<td>$24,754,410</td>
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<td>$2,498</td>
<td>$82,154,255</td>
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<td>$3,424</td>
<td>$19,844,208</td>
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<td>AUTISM, HEART PROGRAMMING $1,504</td>
<td>$94,751</td>
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<td>$3,928</td>
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<td>12687</td>
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<td>Pneumonia</td>
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<td>UPPER RESPIRATORY TRACT $5,098</td>
<td>$8,254,358</td>
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<td>S.A.D. AND DEPRESSION $2,659</td>
<td>$42,623,390</td>
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<td>Urinary Disorders</td>
<td>11515</td>
<td>$2,504</td>
<td>$26,836,425</td>
<td>2.82%</td>
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</tbody>
</table>

% total diseases directly related to Vitamin D status = 61.16%

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Notes in red by office of Rep. Seaton
DIABETES COST
Research Brief

TO: Representative Paul Seaton
FROM: Tim Spengler, Legislative Analyst
DATE: February 28, 2014
RE: Average Annual Cost Estimates Related to Diabetes and Cancer
LRS Report 14.251

You asked for estimates on the average annual medical costs for individuals with diabetes and cancer. You requested estimates that consider a number of factors including doctor visits, equipment, and expected procedures, if available.¹

Diabetes Cost Estimates

According to a major research study released in March 2013 commissioned by the American Diabetes Association (ADA), the estimated total costs of diagnosed diabetes nationwide have risen by 41 percent from 2007 to 2012.² Nationwide, costs associated with diabetes have increased from $174 to $245 billion during this time period. Most of these costs pertain to medical expenses although a portion relates to reduced productivity of diagnosed individuals. This in-depth study addresses the increased financial burden, health resources used, and lost productivity associated with diabetes.³

As for annual costs, the study concludes that people with diagnosed diabetes incur average medical expenditures directly attributable to the condition of around $7,900. The largest medical expenditures are

- hospital inpatient care (43 percent of total medical cost);
- prescription medications (18 percent);
- anti-diabetic agents and diabetic supplies (12 percent);
- physician office visits (9 percent); and
- nursing/residential facility stays (8 percent).

Indirect costs of the disease pertain to the reduced productively of those with diabetes. Such costs include increased absenteeism, reduced productively in the workplace, inability to work as a result of disease-related disability, and lost productive capacity due to early mortality. Such costs exist, but were not calculated on a per person average.

The ADA-commissioned study also relates that people with diagnosed diabetes, on the average, have medical expenditures approximately 2.3 times higher than what expenditures would be in the absence of diabetes. Additionally, more than one in ten health care dollars spent in the United States is spent directly on diabetes and its related complications.

¹ You were also interested in the prevalence of diabetes and cancer among active and retired State of Alaska employees. We looked, but found no such data.

² You were particularly interested in costs for type 2 diabetes. While the study does not disaggregate by type, around 95 percent of diabetes cases are of the type 2 variety.

According to the ADA, in 2012 there were around 22.3 million people—about seven percent of the U.S. population—with diagnosed diabetes. As many as seven million more people, by some estimates, likely have the disease but are, as of yet, unaware of it. Should current trends continue, by 2050, up to one in three American may have diabetes.

Cancer Cost Estimates

We identified the cancer cost estimates in this section from a 2013 study funded by the Centers for Disease Control (CDC) and published by American Cancer Society. The study’s findings are presented in a June 2013 original article entitled “State-Level Cancer Treatment Costs,” which we include as Attachment A. According to the authors it is the first time state-level estimates of cancer treatment costs have been published.

The study, which looked at cancer care costs across the nation during 2004 to 2008, concludes that expenditures for cancer treatment were substantial in all states and accounted for a sizable fraction of medical expenditures for all payers: Medicare, Medicaid, and private insurance. The high financial costs that cancer imposes on society underscore the importance of preventing and controlling cancer as one approach to managing state-level costs, according to the article. This is in addition to, of course, the terrible human costs that the disease causes.

The estimated average annual cancer cost per person in Alaska during 2004 to 2008 was right around $10,000 a year. This is slightly less than the $11,100 average for all states. Treatment costs were highest in Michigan at around $12,600 per year, while Arizona and California were the least expensive at around $9,600. The study did not disaggregate costs by particular types of cancer. The article includes a great deal of additional information that you may find of interest. For example, Table 1 estimates the average annual cancer prevalence rates for each state. Alaska’s rate for all residents was 3.3 percent compared to the median national average of 4.2 percent.

Another document that you may find illuminating is the American Cancer Society’s “Cancer Facts and Figures, 2014.” The document estimates that in 2014 about 1,665,540 new cancer cases are expected to be diagnosed across the country. Of these diagnoses, it is estimated that 3,750 will occur in Alaska.7 It also disaggregates the estimated cancers by type; in Alaska, the most commonly diagnosed cancers are predicted to be prostate, breast, lung, and colon in that order.

Finally, you may wish to peruse the CDC’s “Cancer Rates by States” (http://www.cdc.gov/cancer/dcpc/data/state.htm). The site includes both incident and death rates for cancer disaggregated by state and type of cancer. The prevalence rates in Alaska appear to be generally on the middle or lower end of the nationwide spectrum.

We hope this is helpful. If you have questions or need additional information, please let us know.

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4 An "original" research article is a detailed account of research activity written by the scientists who did the research—not by someone else who is reporting on the research: it is considered a primary resource.

5 Considering inflation, $10,000 in 2008 would be equivalent to around $11,000 in 2014.

6 Another resource is the CDC’s "cost calculator" for various chronic diseases, including cancer. The calculator must be downloaded but worked well for us. The calculator estimates the cost per person to treat cancer in Alaska to be nearly $10,000, the same cost as "State-Level Cancer Treatment Costs," which the CDC was also involved with.

7 This document can be accessed at http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-041770.pdf. Information on rates by state can be found on pages five through eight.
Diabetes Incidence: Comparing NHANES and D*action (18+ years)

In a comparison of data from the National Health and Nutrition Examination Survey (NHANES), 2005-2006, and GrassrootsHealth D*action participants in the United States, we found the following:

Incidence of Diabetes:

NHANES: 8.5/1,000 person-years
D*action: 0.9/1,000 person-years

A full 90% reduction in incidence - before adjusting for co-factors.

(Both groups had a similar average BMI, within 3 points.)

Rate Ratio = 9.7 (P=0.0002)

Chart Date: 8/6/13

Blood 25-Hydroxy Vitamin D Levels and Incident Type 2 Diabetes

A meta-analysis of prospective studies

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3. Anastassios G. Pittas, MD, MS, 2
4. Liana C. Del Gobbo, PHD, 3
5. Cuilin Zhang, MD, PHD, 5
6. JoAnn E. Manson, MD, DRPH, 6, and
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Abstract

OBJECTIVE To quantitatively assess the strength and shape of the association between blood 25-hydroxy vitamin D [25(OH)D] levels and incident risk of type 2 diabetes.

RESEARCH DESIGN AND METHODS A systematic search of the MEDLINE and Embase databases and a hand search of references from original reports were conducted up to 31 October 2012. Prospective observational studies that assessed the association between blood levels of 25(OH)D and risk of incident type 2 diabetes were included for meta-analysis. DerSimonian and Laird's random-effects model was used. A quadratic spline regression analysis was used to examine the shape of the association with a generalized least-squares trend test performed for the dose-response relation.

RESULTS A total of 21 prospective studies involving 76,220 participants and 4,996 incident type 2 diabetes cases were included for meta-analysis. Comparing the highest to the lowest category of 25(OH)D levels, the summary relative risk for type 2 diabetes was 0.62 (95% CI 0.54–0.70). A spline regression model showed that higher 25(OH)D
Active State Of Alaska employees, Retirees and dependents – 83,000

Employees, Retirees and dependents minus those with Diabetes already – 71,143

New incidences of diabetes per year – 8.5 per 1,000 per year (.0085)

Average cost of annual medical expenditures directly attributable to diabetes – $7,900

Current Diabetes Cost per year = $4,777,252

Per year Savings at 90% reduction = $4,299,527

(GrassrootsHealth D*Action study)

Per year Savings at 38% reduction = $1,815,356

(Meta-analysis of prospective studies - Song et.al.)
COLORECTAL CANCER
Association Between Vitamin D and Risk of Colorectal Cancer: A Systematic Review of Prospective Studies

Yanlei Ma, Peng Zhang, Feng Wang, Jianjun Yang, Zhihua Liu, and Huanlong Qin

ABSTRACT

Purpose
To conduct a systematic review of prospective studies assessing the association of vitamin D intake or blood levels of 25-hydroxyvitamin D [25(OH)D] with the risk of colorectal cancer using meta-analysis.

Methods
Relevant studies were identified by a search of MEDLINE and EMBASE databases before October 2010 with no restrictions. We included prospective studies that reported relative risk (RR) estimates with 95% CIs for the association between vitamin D intake or blood 25(OH)D levels and the risk of colorectal, colon, or rectal cancer. Approximately 1,000,000 participants from several countries were included in this analysis.

Results
Nine studies on vitamin D intake and nine studies on blood 25(OH)D levels were included in the meta-analysis. The pooled RRs of colorectal cancer for the highest versus lowest categories of vitamin D intake and blood 25(OH)D levels were 0.88 (95% CI, 0.80 to 0.96) and 0.67 (95% CI, 0.54 to 0.80), respectively. There was no heterogeneity among studies of vitamin D intake (P = .19) or among studies of blood 25(OH)D levels (P = .96). A 10 ng/mL increment in blood 25(OH)D level conferred an RR of 0.74 (95% CI, 0.63 to 0.89).

Conclusion
Vitamin D intake and blood 25(OH)D levels were inversely associated with the risk of colorectal cancer in this meta-analysis.

J Clin Oncol 29:3775-3782. © 2011 by American Society of Clinical Oncology

25-hydroxyvitamin D [25(OH)D] is the precursor of the physiologically active form of vitamin D. The serum level of 25(OH)D is a result of exposure of the skin to sunlight, total vitamin D intake, and other factors such as age and skin pigmentation. Vitamin D has the ability to inhibit cell proliferation and increase apoptosis in vitro, and several tissues can locally produce the physiologically active form of vitamin D, which has anticarcinogenic properties. In addition, many cell types, including colorectal epithelial cells, contain vitamin D receptors. These cells are able to convert the circulating 25(OH)D into active 1 to 25(OH)D metabolites, which in turn bind to the cells' own vitamin D receptors to produce an autocrine effect by inducing cell differentiation and inhibiting proliferation, invasiveness, angiogenesis, and metastatic potential. Therefore, low vitamin D levels may increase the risk of colorectal cancer through the above potential mechanism. Currently, vitamin D deficiency is an important health problem in the industrial world in the United States, 25% to 58% of adolescents and adults are deficient in vitamin D.

The results from prospective studies that have examined the association between vitamin D intake or 25(OH)D levels in the blood and the risk of colorectal cancer have been inconsistent. The aim of this review was to evaluate the evidence from prospective studies on vitamin D intake or blood levels of 25(OH)D and the risk of colorectal cancer by summarizing it quantitatively with a meta-analysis approach.

SEARCH STRATEGY
The literature search was conducted before October 2010 in the MEDLINE and EMBASE databases without restrictions and included articles ahead of publication. The following keywords were used in searching: "vitamin D or 25(OH)D" and "colorectal cancer or colon cancer or rectal cancer." Moreover, we searched...
Figure 1. Dose–response gradient for colorectal cancer according to serum 25(OH)D concentration, all five studies combined. The five points are the odds ratios for each quintile of 25(OH)D based on combined data from the five studies.
Active State Of Alaska employees, Retirees and dependents – 83,000

Incidence of Colorectal Cancer per year in AK - **43 per 100,000 (.0043)**

Average cost of annual medical expenditures directly attributable to Colon Cancer – **$11,000**

= **$1,962,950**

AK State Cost for Colorectal Cancer per year $**3,925,900**

50% per year savings with vitamin D

(meta-analysis Gorham et. al.)
BREAST CANCER
Dose–response gradient of risk of breast cancer according to serum 25-hydroxyvitamin D concentration, pooled analysis.
Active State Of Alaska employees, Retirees and dependents – 83,000

Female percentage of AK employees and retirees: 53% = 43,990

Incidence of Breast Cancer per year in AK - 125 per 100,000 (.0125)

Average cost of annual medical expenditures directly attributable to Breast Cancer – $11,000

= 

Per year AK State Cost for Breast Cancer: $6,048,625

50% reduction with vitamin D

Per Year Savings with vitamin D: $3,024,312
PRETERM BIRTHS
Alaska

Find maternal and infant health data on a state level, or by county or city. Narrow your results or compare with another region.

Location: Alaska
Topic: Preterm by race/ethnicity
Format: Bar Graph

Preterm by race/ethnicity: Alaska, 2009-2011 Average

Percent of live births

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Hollis/Wagner Results</th>
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<tbody>
<tr>
<td>Hispanic</td>
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</tr>
<tr>
<td>White</td>
<td>7%</td>
</tr>
<tr>
<td>Black</td>
<td>11.2%</td>
</tr>
<tr>
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</tr>
<tr>
<td>Asian</td>
<td>N/A</td>
</tr>
<tr>
<td>Total</td>
<td>7%</td>
</tr>
</tbody>
</table>

Potential REDUCTIONS

32% from 10.3% births
24% from 9.2% births
Protect Our Children NOW!

A community outreach program to reduce the incidence of preterm births quickly, easily, and safely by attending to solving the vitamin D deficiency epidemic through the engagement of pregnant women in a value changing program of Good Health vs ‘Treating Illness’

Approximately 1300 infants will be born prematurely in Alaska in 2014 per the March of Dimes. Fully 25-50% of these in the state, 325-650 babies and their families, could possibly have this trauma prevented with vitamin D supplementation to the pregnant mother. Premature births are closely associated with cerebral palsy, mental impairment and permanent hearing loss among other deficiencies.

The March of Dimes estimates that the cost of each premature infant is $55,000, adding up to a total annual cost of $72MM of which $18-36MM could likely be saved (on an annual basis). Data from randomized trials and others works from Dr. Wagner et al. showed a potential reduction of 50% in preterm births and significant reductions in preeclampsia and gestational diabetes as well as other complications of pregnancy. The problem now is getting the results into practice quickly vs waiting the standard 15-25 years.

Solving this problem requires nothing less than Changing Cultural Values, from ‘Early Detection’ to ‘Primary Prevention’; from ‘Affordable Care’ to ‘Good Health’; from individuals ‘Taking Advice’ of physicians to ‘Consultation’ with them. In order to accomplish this, the timing is perfect to link a new, highly accepted technology (internet application) to the new value of HEALTH through the environment of ‘MyOWNHealth™’ which captures all the essential ingredients of change: the science, the proven recommendations for pregnancy, clear methods for setting priorities for the individual, personal feedback and rewards for performance, a process for total engagement from learning through personal reward systems. This is a personal portal for the patient.

Behind the scenes, information is tracked by the system to provide information to the providers, the insurers, the scientists about what’s working, what needs changing, i.e., a complete feedback loop to perfect the process. This will improve processes as well as strengthen public health.

A full demonstration of this process, to serve as a ‘seed’ for an entire community, has been developed by an international non-profit public health promotion organization, GrassrootsHealth, in conjunction with the leading researcher, Dr. Carol L. Wagner of the Medical University of South Carolina as the Principal Designer/Leader. They have in place not only a vitamin D testing program for the mothers and infants, but all the pieces of the MyOWNHealth™ system: simple, interactive educational programs for participants and physicians, engaging games and reward systems, programs to track the progress of healthy behavioral changes, management feedback to provide ongoing enhancements to the process.

This community project will involve the active participation of about 500 pregnant women. With the 500 women participating, there could be 25 children saved this problem with a potential cost savings of $1,375,000 for this group alone in the first implementation.

Next steps to explore this program would include a meeting with Carole Baggerly, director of GrassrootsHealth and Dr. Wagner to highlight the details of a project plan for the community site.
• Approximate number of births per year in Alaska = 11,000

• Assumption: 500 births per year to State of Alaska Employees, Retirees and Dependents

• For each 500 pregnancies in the Alaska insured and dependent category with vitamin D sufficiency 25 preterm births avoided

**Savings to the state by avoiding 25 preterm births = $1,375,000**
UPPER RESPIRATORY TRACT INFECTIONS
Upper Respiratory Tract Infections

Recently, a study was conducted with seven hundred forty-three children ages 3-15 in a Canadian Hutterite Community. **The findings of the study show that children with higher vitamin D blood levels had a 50% lower relative risk of contracting an Upper Respiratory Tract infection.** Those children at the United States national average of 21 ng/ml vitamin D levels were at a 70% greater risk of contracting respiratory infections. Illnesses such as RTI’s are commonly a factor in children’s absences from school. Making sure your child has sufficient vitamin D will not only increase their health, but will lead to less school absences due to illness.


Prepared by the office of Representative Paul Seaton
Vitamin D₃ supplementation in patients with frequent respiratory tract infections: a randomised and double-blind intervention study

Peter Bergman,¹,²,³ Anna-Carin Norlin,²,⁴ Susanne Hansen,² Rokeya Sultana Rekha,⁵ Birgitta Agerberth,⁵ Linda Björkhem-Bergman,⁵ Lena Ekström,⁶ Jonatan D Lindh,⁶ Jan Andersson³

ABSTRACT

Background: Low serum levels of 25-hydroxyvitamin D₃ are associated with an increased risk of respiratory tract infections (RTIs). Clinical trials with vitamin D₃ against various infections have been carried out but data are so far not conclusive. Thus, there is a need for additional randomised controlled trials of effects of vitamin D₃ on infections.

Objective: To investigate if supplementation with vitamin D₃ could reduce infectious symptoms and antibiotic consumption among patients with antibody deficiency or frequent RTIs.

Design: A double-blind randomised controlled trial.

Setting: Karolinska University Hospital, Huddinge.

Participants: 140 patients with antibody deficiency (selective IgA subclass deficiency, IgG subclass deficiency, common variable immune disorder) and patients with increased susceptibility to RTIs (>4 bacterial RTIs/year) but without immunological diagnosis.

Intervention: Vitamin D₃ (4000 IU) or placebo was given daily for 1 year.

Primary and secondary outcome measures: The primary endpoint was an infectious score based on five parameters: symptoms from respiratory tract, ears and sinuses, malaise and antibiotic consumption. Secondary endpoints were serum levels of 25-hydroxyvitamin D₃, microbiological findings and levels of antimicrobial peptides (LL-37, HNP1–3) in nasal fluid.

Results: The overall infectious score was significantly reduced for patients allocated to the vitamin D₃ group (202 points) compared with the placebo group (249 points; adjusted relative score 0.771, 95% CI 0.604 to 0.985, p=0.04).

Limitations: A single study centre, small sample size and a selected group of patients. The sample size calculation was performed using p=0.02 as the significance level whereas the primary and secondary endpoints were analysed using the conventional p=0.05 as the significance level.

Conclusions: Supplementation with vitamin D₃ may reduce disease burden in patients with frequent RTIs.

ARTICLE SUMMARY

Article focus

- Recent evidence suggests that vitamin D₃ has potent extraskeletal effects, such as suppression of inflammation and strengthening of mucosal immunity by induction of antimicrobial peptides.
- Data from observational studies suggest that low levels of 25-hydroxyvitamin D₃ are associated with an increased risk of respiratory tract infections.
- Results from a limited number of randomised controlled trials on the protective role of vitamin D₃ against respiratory tract infections are inconclusive and thus additional studies are warranted.

Key messages

- Therefore we designed and carried out a randomised controlled trial where a large dose (4000 IU) of vitamin D₃ was given to patients with an increased susceptibility to infections for 1 year.
- The main conclusion is that vitamin D₃ supplementation reduces symptoms and antibiotic consumption among patients with an increased frequency of respiratory tract infections. Thus, vitamin D₃ supplementation may be an alternative strategy to reduce antibiotic use among patients with recurrent respiratory tract infections.

Strengths and limitations of this study

- A high daily dose of vitamin D₃ was used, the study time was a full year covering all seasons and patients with an increased frequency of respiratory tract infections were studied.
- A single study centre, small sample size (n=140) and a selected group of patients.

INTRODUCTION

Vitamin D was discovered when it was noted that rachitic children were improved by exposure to sunlight.¹ It was later shown by Holick et al² that vitamin D₃ is synthesised in the skin under the influence of ultraviolet light. Vitamin D₃ is further hydroxylated in the liver
INFLAMMATION
Inflammatory gum disease

As vitamin D levels go up (bars), inflammation scores go down (lines).

0 IU (placebo) After 3 months
500 IU/day More than 50% reduction
1000 IU/day More than 65% reduction
2000 IU/day More than 80% reduction

MUSCLE FUNCTION
Original Study

Vitamin D and Muscle Function: Is There a Threshold in the Relation?

Hennie C.J.P. Janssen MD a, *, Marielle H. Emmelot-Vonk MD, PhD a, Harald J.J. Verhaar MD, PhD a, Yvonne T. van der Schouw Prof II

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ABSTRACT

Objectives: First, to determine the association between serum 25 hydroxyvitamin D (25OHD) concentration and muscle mass, strength, and performance. Second, to explore if there is a threshold in the association.

Design: Cross-sectional, single-center study.

Setting: The central part of the Netherlands (52° Northern latitude).

Participants: A total of 802 independently living men and postmenopausal women 40 to 80 years of age.

Measurements: Health-related and lifestyle factors, including physical activity, 25OHD concentration, lean mass, handgrip strength, knee extension strength, and physical performance were determined.

Results: Overall, higher 25OHD level was significantly associated with higher lean mass (22.6 g per nmol/L 95% CI 7.3—37.9), handgrip strength (0.020 kg per nmol/L, 95% CI 0.001—0.038), and physical performance (0.006 points per nmol/L 95% CI 0.001—0.012), after adjustment for various confounders. This association was most pronounced below a 25OHD level of 60 nmol/L with lean mass increase 79.6 g per nmol/L (95% CI 40.8—118.4, P < .01), handgrip strength 0.09 kg per nmol/L (95% CI 0.045—0.141, P < .01), and physical performance 0.02 points per nmol/L (95% CI 0.005—0.032, P < .01), and these significant associations attenuated to null above this threshold.

Conclusion: In middle-aged men and (postmenopausal) women, a higher 25OHD level was significantly associated with higher lean mass, muscle strength, and performance. These associations were most pronounced below 60 nmol/L and absent above 60 nmol/L indicating a ceiling effect.

Evidence on the diverse actions of vitamin D has been growing exponentially over the past decades. In addition to its well-known role in bone metabolism, vitamin D involvement has been reported in autoimmune disease, reproductive function, malignancy, mood disorder, the metabolic syndrome, and, recently, even in sleep disorders. One of the major fields of investigation regarding vitamin D has been in the prevention of falls and fractures in the elderly. Several mechanisms have been postulated for a causal role of vitamin D deficiency in falls and fractures. First, vitamin D deficiency may impair bone metabolism and thereby increase proneness to fracture, should a fall occur. Second, vitamin D deficiency may cause muscle weakness, and, finally, it may exert a negative effect on postural stability and body sway. In severe vitamin D deficiency, vitamin D supplementation, with or without calcium, improved muscle function and balance. However, evidence from meta-analyses on falls and fractures is still inconclusive. This may be partly because it is unclear what serum hydroxyvitamin D concentration constitutes adequate vitamin D status with regard to bone health and extraskeletal vitamin D actions. International guidelines advise a serum hydroxyvitamin D concentration of 50 nmol/L and 75 nmol/L as adequate. However, in a meta-analysis on fall prevention in older people, a minimum serum hydroxyvitamin D concentration of 60 nmol/L was necessary requiring medical attention and about 6% experiencing a fracture. This has profound implications on quality of life, and in a US population-based survey, no fewer than 50% of independently living patients with a fall-related injury admitted to hospital were discharged to a nursing home. Several mechanisms have been postulated for a causal role of vitamin D deficiency in falls and fractures. 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A randomized study on the effect of vitamin D₃ supplementation on skeletal muscle morphology and vitamin D receptor concentration in older women

Lisa Ceglia¹,², Sathit Nimiratmahapanya²,³, Mauricio da S. Morais⁴, Donato A. Rivas⁴, Susan S. Harris², Heike Bischoff-Ferrari ²,⁵,⁶, Roger A. Fielding⁴, Bess Dawson-Hughes²

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Context: Studies examining whether vitamin D supplementation increases muscle mass or muscle-specific vitamin D receptor (VDR) concentration are lacking.

Objective: To determine whether vitamin D₃ 4000 IU/d alters muscle fiber cross-sectional area (FCSA) and intramyonuclear VDR concentration over 4 months.

Design and Setting: Randomized, double-blind, placebo-controlled study in a single center.

Participants: 21 mobility-limited women (aged ≥65 years) with serum 25-hydroxyvitamin D (25OHD) levels 22.5—60 nmol/L.

Main Outcome Measures: Baseline and 4-month FCSA and intramyonuclear VDR were measured from vastus lateralis muscle cross-sections probed for muscle fiber type (I/IIa/IIx) and VDR using immunofluorescence.

Results: At baseline, mean (±SD) age was 78±5 years; body mass index (BMI) was 27±5 kg/m²; 25OHD was 46.3±9.5 nmol/L; and a short physical performance battery score was 7.95±1.57 out of 12. At 4 months, 25OHD level was 52.5±17.1 (placebo) vs. 80.0±11.5 nmol/L (VD; P<0.01) and change in 25OHD level was strongly associated with percent change in intramyonuclear VDR concentration independent of group (r=0.87, P<0.001). By treatment group, percent change in intramyonuclear VDR concentration was 7.8±18.2% (placebo) vs. 29.7±11.7% (VD; P=0.03) with a more pronounced group difference in type II vs. I fibers. Percent change in total (type II) FCSA was -7.4±18.9% (placebo) vs. 10.6±20.0% (VD; P=0.048).

Conclusion: Vitamin D₃ supplementation increased intramyonuclear VDR concentration by 30% and increased muscle fiber size by 10% in older, mobility limited, vitamin D insufficient women. Further work is needed to determine whether the observed effect of vitamin D on fiber size is mediated by the VDR and to identify which signaling pathways are involved.

Low vitamin D status has been associated with reduced muscle mass, strength, and performance in older adults (1–5). Several intervention studies have reported that vitamin D supplementation increases appendicular muscle strength and improves physical function particularly in older women with low vitamin D status (6–9).
Maternal Antenatal Vitamin D Status and Offspring Muscle Development: Findings From the Southampton Women’s Survey

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Context: Maternal 25-hydroxyvitamin D [25(OH)D] status in pregnancy has been associated with offspring bone development and adiposity. Vitamin D has also been implicated in postnatal muscle function, but little is known about a role for antenatal 25(OH)D exposure in programming muscle development.

Objective: We investigated the associations between maternal plasma 25(OH)D status at 34 weeks of gestation and offspring lean mass and muscle strength at 4 years of age.

Design and Setting: We studied a prospective UK population-based mother-offspring cohort: the Southampton Women’s Survey (SWS).

Participants: Initially, 12,583 nonpregnant women were recruited into the SWS, of whom 3,159 had singleton pregnancies; 678 mother-child pairs were included in this analysis.

Main Outcomes Measured: At 4 years of age, offspring assessments included hand grip strength and whole-body dual-energy x-ray absorptiometry, yielding lean mass and percent lean mass. Physical activity was assessed by 7-day accelerometry in a subset of children (n = 326).

Results: The maternal serum 25(OH)D concentration in pregnancy was positively associated with offspring height-adjusted hand grip strength (β = 0.10 SD/SD, P = .013), which persisted after adjustment for maternal confounding factors, duration of breastfeeding, and child’s physical activity at 4 years (β = 0.13 SD/SD, P = .014). Maternal 25(OH)D was also positively associated with offspring percent lean mass (β = 0.11 SD/SD, P = .006), but not total lean mass (β = 0.06 SD/SD, P = .15). However, this association did not persist after adjustment for confounding factors (β = 0.09 SD/SD, P = .11).

Conclusions: This observational study suggests that intrauterine exposure to 25(OH)D during late pregnancy might influence offspring muscle development through an effect primarily on muscle strength rather than on muscle mass. (J Clin Endocrinol Metab 99:330–337, 2014)
SENIOR FALLS AND FRACTURES
Vitamin D project helps prevent falls and saves health costs

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Source: New Zealand Government – Press Release/Statement:

Headline: Vitamin D project helps prevent falls and saves health costs

Associate Minister of Health Jo Goodhew says MidCentral DHB’s vitamin D project is a good example of how a simple intervention can improve lives and save health dollars.

In 2010 the DHB, in partnership with ACC, began encouraging health professionals to prescribe vitamin D to residents in aged care facilities. Between March 2010 and June 2012 the uptake of vitamin D by aged care residents increased from 15 to 74 per cent.

“Comparisons from before and after the start of the project show a 32 per cent reduction in aged residential care residents going to the emergency department with falls-related fractures, and a 41 per cent reduction in their hospital admissions due to these fractures.” Mrs Goodhew said.

“The benefits of preventing falls in older people cannot be overstated. Preventing falls enables older people to maintain their independence and confidence.

“Of older people who suffer a hip fracture, nearly 20 per cent will die within a year. Almost half will require long-term care and half will require help at home. Half of those who walked without help before fracturing a hip will be unable to walk without assistance in the year following the fracture.”

The vitamin D project is also estimated to have saved MidCentral DHB more than $540,000 because of fewer people coming to the emergency department and reduced admissions to hospital. Further savings are also likely because of reduced need for clinical support, hospital pharmacy services, and physiotherapy and rehabilitation services.

International evidence shows that taking vitamin D significantly reduces older adults’ risk of falling.

“We know older people are less likely to fall and injure themselves if they keep their muscles and bones in good condition.

Vitamin D has been shown to increase the number and size of type II muscle fibres, which play an important role in balance and mobility. Vitamin D also helps maintain bone strength,” MidCentral DHB pharmacy advisor Andrew Orange says.

The Health Quality & Safety Commission’s national patient safety campaign Open for better care is currently focusing on falls prevention. For more information about the Open campaign, go to www.open.hqsc.govt.nz.
PURPOSE:
To standardize and optimize vitamin D supplementation for people living in Fraser Health (FH) residential care facilities.

BACKGROUND
Vitamin D supplementation has been extensively studied as a treatment to prevent both falls and fractures. Vitamin D is an important nutrient involved in calcium metabolism, bone health, and muscle function, hence its direct beneficial effect on falls and fracture prevention. In addition, prospective epidemiologic studies have suggested that vitamin D may reduce the risk of cardiovascular disease and some forms of cancer, and may have positive effects on immune responses and anti-inflammatory benefits.

Vitamin D deficiency can arise from limited sun exposure, impaired ability of the liver or kidneys to activate vitamin D, limited dietary intake, or poor absorption from the intestine. Vitamin D deficiency can cause osteomalacia (characterized by weakness of the bone and muscle), contribute to the development of osteoporosis, immune system dysfunction, and bone pain and is also associated with an increased risk of falls and higher risk of fractures in older adults.

Despite the evidence that vitamin D is an important treatment for falls and fracture prevention, as well as potential cancer and cardiovascular benefits, vitamin D supplementation is not standard in most residential facilities and the prevalence of vitamin D deficiency is high in institutionalized people.

To address this gap, FH (with funding from the Canadian Institutes of Health Research), brought together a Specialist Advisory Group (see Appendix A) comprised of health professionals, researchers, decision makers, policy makers, and other relevant stakeholders for a series of meetings with the purpose of developing an evidence based, practical and sustainable vitamin D protocol for residents of residential care facilities. The main objective of the group was to develop recommendations to indicate who should and should not be placed on the vitamin D protocol, how much vitamin D is safe and effective, and what the optimum dosing frequency is with minimal impact on staff workload and cost.

According to the recommendation from the Specialist Advisory Group, the adequate safe and effective dosage for older adult residents living in residential care facilities is 20,000 IU weekly of vitamin D₃ (2X 10,000 IU in tablet form). Only residents with hypercalcaemia and/or severe renal...

* The upper level intakes of Vitamin D set by the Institute of Medicine (4,000 IU/day) and the Endocrine Society Clinical Practice Guideline (10,000 IU/day) represent the safe boundary at the high end of the scale and should not be misunderstood as amounts people need or should strive to consume.

* Diagnosing hypercalcaemia should not utilize serum calcium level testing to implement protocol unless physicians have significant evidence to test.
failure (GFR <20 mL/ min) or those who refuse supplementation, should be excluded from the protocol.

DEFINITIONS

**Vitamin D**: is a fat soluble steroid hormone derived from cholesterol. Vitamin D₃ (cholecalciferol) is one form that is synthesized in our skin when exposed to sunlight. Another form of vitamin D, vitamin D₂ (ergocalciferol) can be obtained from certain foods, supplements or by prescription.

**Vitamin D deficiency**: blood serum levels are less than 25 nmol/L

**Vitamin D insufficiency**: blood serum levels are between 25-75 nmol/L

**Vitamin D sufficiency**: blood serum levels are between 75-250 nmol/L

**Vitamin D toxicity**: blood serum levels are above 375 nmol/L

**Tolerable Upper Limit**: is the highest dose a person can chronically consume without risk of adverse effects

RELATED RESOURCES


VII. Hanley DA, Cranney A, Jones G, Whiting SJ, Leslie WD. Vitamin D in adult health and disease: a review and guideline statement from Osteoporosis Canada (summary). *CMAJ*. 2010;182(12):1315-1319
REVIEW OF RECENT EVIDENCE ON VITAMIN D AND HEALTH
Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality—A review of recent evidence

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ABSTRACT
Background: Optimal vitamin D intake and its status are important not only for bone and calcium-phosphate metabolism, but also for overall health and well-being. Vitamin D deficiency and insufficiency as a global health problem are likely to be a risk for a wide spectrum of acute and chronic illnesses.

Methods: A review of randomized controlled trials, meta-analyses, and other evidence of vitamin D action on various health outcomes.

Results: Adequate vitamin D status seems to be protective against musculoskeletal disorders (muscle weakness, falls, fractures), infectious diseases, autoimmune diseases, cardiovascular disease, type 1 and type 2 diabetes mellitus, several types of cancer, neurocognitive dysfunction and mental illness, and other diseases, as well as infertility and adverse pregnancy and birth outcomes. Vitamin D deficiency/insufficiency is associated with all-cause mortality.

Conclusions: Adequate vitamin D supplementation and sensible sunlight exposure to reach optimal vitamin D status are among the front line factors of prophylaxis for the spectrum of disorders. Supplementation guidelines and population strategies for the eradication of vitamin D deficiency must be included in the priorities of physicians, medical professionals and healthcare policy-makers.

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Controversy remains regarding the appropriate adjustment for covariates in observational studies of vitamin D in relation to cognitive decline or dementia. For example, the sources of vitamin D itself (sunlight exposure, dietary intake, fortification and supplementation) are not likely to be confounders, and adjustment for these variables or proxy measures such as time spent outdoors or latitude is likely to represent over adjustment. Even adjustment for age is not without controversy, as human skin is known to become less efficient at vitamin D production with age. Age is therefore related to the synthesis of vitamin D and is not just a proxy measure for possible unmeasured confounding.

Ultimately randomized controlled trials are needed to establish whether vitamin D supplementation has clinical relevance in this context and can be used to prevent, delay or treat dementia. At this point no large well-designed randomized controlled trials have been conducted, and the causal relationship between vitamin D and dementia remains uncertain and caution should be exercised. Existing trials on vitamin D and cognitive decline have produced inconclusive results and had a number of important drawbacks including small sample sizes (<100) [195,196] and the use of low doses of vitamin D (<520 IU/day) with a combination of other nutrients [195,197], making interpretation difficult. However, several large trials are currently underway which will provide important new information. The DOHealth trial is being conducted in around 2000 participants aged 70 years and older across eight European cities. Vitamin D3 supplements (2000 IU/day) are one of the three interventions incorporated and cognitive outcomes will be measured over 3 years. Another key trial is the VITAL study in the US that aims to recruit around 20,000 middle aged and older adults. Again one of the interventions investigated will be vitamin D3 supplements (2000 IU/day), although cognitive outcomes over 4.5 years will only be assessed in a subsample of around 10% of participants. Neither trial targets older adults who are known to have low levels of vitamin D and early cognitive changes indicating that they are at high risk for dementia. If these trials do not produce promising results we may be left wondering if a more targeted approach or a different dose of vitamin D supplementation might be more effective.

11. Conclusion

It is now recognized that vitamin D deficiency and insufficiency are a global health problem [1,5,198-201]. A multitude of studies have suggested that vitamin D deficiency and insufficiency not only have negative consequences on bone health but are also likely to be a risk for many acute and chronic illnesses including infectious diseases, autoimmune diseases, cardiovascular disease, type 1 and type 2 diabetes mellitus, several types of cancer, negligible cognitive dysfunction and mental illness, and other diseases, as well as infertility and adverse pregnancy and birth outcomes [24,26,37,49,55,75-79,85,99-105,117,118,136,141,146,186,187,202,203].

It is interesting that healthy black children in South Africa have blood levels of 25(OH)D of 49 ± 4 ng/mL [204] similar to adult Maasai herders of 47 ± 10 ng/mL [205]. It is well documented that blood levels of 25(OH)D are maximum at the end of the summer and are at their nadir at the end of the winter even in Denmark [206]. Physiological it makes no sense to have wide swings in the circulating levels of 25(OH)D. This is the reason why a three-part strategy to maintain circulating levels of 25(OH)D of at least 30 ng/mL should be encouraged. Sensible sun exposure, which remains the major source of vitamin D for most children and adults [1,207] along with including foods that naturally contain or are fortified with vitamin D [1], and taking a daily supplement of vitamin D should be able to sustain blood levels of 25(OH)D in a range similar to our hunter-gatherer forefathers, i.e. 25(OH)D – 40–50 ng/mL. Since there is no downside to increasing children's and adults' vitamin D status (with the exception of patients with granulomatous disorders) it is reasonable to attain and maintain a circulating level of 25(OH)D of 40–60 ng/mL as recommended by the Endocrine Society Experts or even slightly lower (30–50 ng/mL) as recommended in "Practical guidelines for supplementation of vitamin D and treatment of deficits in Central Europe: Recommended vitamin D intakes in general population and groups at risk of vitamin D deficiency" [208], not only for optimal bone health but also for overall health and well-being.

Take-home messages

- Vitamin D deficiency is a global health problem for children and adults. Vitamin D deficiency is associated with rickets and growth retardation in children and osteoporosis and osteomalacia in adults. Vitamin D deficiency has also been linked to many acute and chronic illnesses including some cancers, autoimmune diseases, cardiovascular disease, type 1 and type 2 diabetes mellitus, infectious diseases and neurocognitive dysfunction and other diseases, as well as infertility and adverse pregnancy and birth outcomes.
- A three-part strategy should be implemented to combat the vitamin D deficiency pandemic which includes:
  - Eating foods that naturally contain vitamin D.
  - Encouraging food fortification with vitamin D in countries that do not practice this fortification and.
  - Providing guidelines for both vitamin D supplementation of general population and for sensible sun exposure as a reliable source of vitamin D.
- Anti-fall and anti-fracture action of vitamin D administration of at least 800 IU/day with at least 24 ng/mL (60 nmol/L) of 25(OH)D serum levels appeared effective and beneficial for musculoskeletal machinery. Vitamin D may be instrumental in the immune system homeostasis, and in preventing autoimmune diseases and lowering risk of infections.
- Vitamin D deficient individuals are at increased cardiovascular risk even after adjustments for common cardiovascular risk factors.
- Risk for breast and colorectal cancer decreases as serum 25(OH)D level increases to 30–40 ng/mL (75–100 nmol/L).
- All-cause mortality risk in general population seems to be the lowest at 25(OH)D levels ranging from 30 to 45 ng/mL (75 to 112.5 nmol/L).
- Vitamin D supplementation up to 4000 IU/day in pregnant woman is safe and effective in achieving sufficiency and improving health not only in the mother but also in the developing fetus. Every 10 ng/mL increase in maternal 25(OH)D at delivery reduces the risk of four main comorbidities of pregnancy by 16%.
- It is reasonable to attain and maintain a circulating level of 25(OH)D of 30–60 ng/mL as recommended by the Endocrine Society or even slightly lower (30–50 ng/mL) as recommended in "Practical guidelines for supplementation of vitamin D and treatment of deficits in Central Europe", not only for optimal bone health but also for overall health and well-being.

References