Strategies for Accelerating Translation of Research Findings into Cancer Prevention that Works

NAACCR St Louis 2016

Graham A Colditz, MD DrPH
Niess-Gain Professor
Department of Surgery
Division of Public Health Sciences
Conflict of interest

I have no financial relationships to disclose

I will not discuss off-label use and or investigational use in my presentation
Current situation

We are not implementing proven cancer prevention and screening interventions.

Instead we allow millions of people to develop and die from highly preventable forms of cancer.

By not implementing these interventions in ways that reach populations with greatest need, we are permitting disparities to persist.
Outline

Build on potential for prevention and barriers to progress

Issues:

- Improving cancer prevention,
- Implementing what we know,
- Identifying what needs to be done to achieve desired effects

Shared understanding of what implementation science is and the role of cancer registries could become
When and How Do We Bridge the Gap Between Data and Application?

Evidence synthesis

USPSTF + CDC + WHO Guidelines

Monitoring incidence and mortality

Evidence-based interventions
Why are we not preventing cancer now?

Barriers:

1. Skepticism that cancer can be prevented
2. Short term focus of cancer research
3. Interventions deployed too late in life
4. Research focused on treatment not prevention
5. Debates among scientists
6. Societal factors ignored
7. Lack of transdisciplinary training
8. Complexity of implementation

Colditz et al Sci Transl Med 2012: March 28
Long history of accepting prevention

- Pott P, SCC scrotum in chimney sweeps based on clinic experience 1775
- Cook J. Capt. 1768 -1780
  - 3 voyages, 3 men lost to scurvy cf standard 50%
  - British navy adopted citrus in 1795
- Smoking cessation reduces cancer, heart disease
- Given this type of evidence why do we still take so long to get from discovery to delivery?

We must speed up implementing prevention
Trends in smoking and lung cancer, USA

Cigarette consumption

Lung cancer

Men

Lung cancer

Women
US cancer mortality 1950-2010 attributed to smoking, or not:
Rates & 35-yr % risk at ages 35-69 (left – male, right – female)


Norheim et al Lancet 2015
## Smoking attributable mortality adults 35+ USA 2005-09

<table>
<thead>
<tr>
<th>Disease</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Ca</td>
<td>74,300</td>
<td>53,400</td>
<td>127,700</td>
</tr>
<tr>
<td>Other Ca</td>
<td>26,000</td>
<td>10,000</td>
<td>36,000</td>
</tr>
<tr>
<td>Total Cancer</td>
<td>100,300</td>
<td>63,400</td>
<td>163,700</td>
</tr>
<tr>
<td>CVD</td>
<td>95,600</td>
<td>65,000</td>
<td>160,600</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>58,200</td>
<td>54,900</td>
<td>113,100</td>
</tr>
<tr>
<td>All Causes</td>
<td>330,000</td>
<td>225,000</td>
<td>555,800</td>
</tr>
</tbody>
</table>

Source: Surgeon General Report 2014 Table 12.7
Medical interventions proven to prevent cancer: high-income

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Target</th>
<th>Magnitude of reduction</th>
<th>Time (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Colon mortality</td>
<td>40%</td>
<td>20+</td>
</tr>
<tr>
<td>SERMs</td>
<td>Breast incidence</td>
<td>40-50%</td>
<td>5+</td>
</tr>
<tr>
<td>Salpingo oophorectomy</td>
<td>Familial breast cancer</td>
<td>50%</td>
<td>3+</td>
</tr>
<tr>
<td>Screening for colorectal cancer</td>
<td>Colon cancer mortality</td>
<td>30-40%</td>
<td>10</td>
</tr>
<tr>
<td>Viruses - HPV</td>
<td>Cervical cancer incidence</td>
<td>50-100%</td>
<td>20+</td>
</tr>
<tr>
<td>- Hep B</td>
<td>Liver cancer incidence</td>
<td>70-100%</td>
<td>20+</td>
</tr>
<tr>
<td>Mammography</td>
<td>Breast cancer mortality</td>
<td>30%</td>
<td>10-20</td>
</tr>
</tbody>
</table>

Colditz et al, Sci Transl Med 2012
Histologically confirmed cervical abnormalities, Vic, Australia

CIN2, CIN3

Brotherton et al MJA 2016
The Value of Childhood Vaccination:
Benefits Accrue across Time

- **Health gains**: Reduction in morbidity and mortality
- **Health care cost savings**: Savings of medical expenditures because illness is prevented
- **Care-related productivity gains**: Parents’ productivity increases because need to take care of sick child is avoided
- **Outcome-related productivity gains**: Increased productivity due to improved cognition, physical strength, and school attainment
- **Behavior-related productivity gains**: Improvement of child health and survival changes household behavior
- **Community externalities**: Improved outcomes in unvaccinated community members

### Risk factor prevalence, High, Low state, USA, 2013-2014

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>National average</th>
<th>Highest prevalence state</th>
<th>Lowest prevalence state</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap Test</td>
<td>82.6%</td>
<td>88% Massachusetts</td>
<td>76.2% Idaho</td>
</tr>
<tr>
<td>HPV Vaccination (&gt;1 dose)</td>
<td>39.7% Girls</td>
<td>76% RI</td>
<td>38.3% Kansas</td>
</tr>
<tr>
<td></td>
<td>21.6% Goys</td>
<td>76% RI</td>
<td>23.2% Indiana</td>
</tr>
</tbody>
</table>

Reagan-Steiner MMWR 2015
## Lifestyle: high income countries

<table>
<thead>
<tr>
<th>Cause</th>
<th>% cancer caused</th>
<th>Magnitude possible reduction</th>
<th>Time (yrs)</th>
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<tbody>
<tr>
<td>Smoking</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight/obesity</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of exercise</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viruses</td>
<td>5-7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UV/ionizing radiation</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pollution</td>
<td>3</td>
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<tr>
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</table>
**Infections**

- Helicobacter pylori
- HPV
- Hepatitis B & C
- Epstein-Barr virus
- HTLV
- Human herpes virus 8
- *Schistosoma haematobium*
- *Opisthorchis viverrini*

- High income countries 7.4%
- Low and middle income countries 23% of cancer
- 2 million cases/yr (16%)

de Martel et al, Lancet Oncology, 2012
What works: beyond smoking cessation and vaccines?

- ACS guidelines NPA: not overweight, eat a plant based diet, limit alcohol, be active

- Avoid alcohol between adolescence and first birth

Reduced cancer incidence:
- Breast 22%
- Colon 52%

Reduced mortality
- Thomson et al 2014

Reduce premalignant and invasive breast cancer
Definition – implementation science

Scientific study of how to move evidence-based interventions into practice and policy

Demands innovative approaches to identifying, understanding, and developing strategies for overcoming barriers to the adoption, adaptation, integration, scale-up and sustainability of evidence-based interventions, tools, policies, and guidelines.

Includes study of how to sustain changes to improve population health

**PAR13-055; and 16-238**
Where do we focus?
Estimated new cancer cases, World, 1975 to 2050: Region

- 1975: 5.9 million
- 1990: 8.1 million
- 2002: 10.9 million
- Projected 2020: 16.5 million
- Projected 2050: 27.0 million

- Developed regions
- Developing regions

- 2012 – 14 M cases
- 1.7 M breast

Bray and Moller Nat Rev Cancer 2006
WHO priorities: population-wide interventions

- Reducing tobacco use (a best buy)
- Promoting physical activity
- Reducing harmful alcohol use
- Promoting healthy diets
- Cancer specific strategies
  - Hepatitis B vaccine (a best buy)
  - HPV vaccine
  - Cervical cancer screening
  - Not currently recommended in low income countries – CRC screening

WHO: Global status report on non-communicable diseases, 2010
Best buys for 4 risk factors

- **Tobacco use:**
  - Protect from exposure
  - Warning dangers
  - Enforce bans on advertising
  - Raise taxes
- **Harmful alcohol:**
- **Unhealthy diet:**
- **Physical inactivity:**
Best buys for 4 risk factors

- **Tobacco use:**
- **Harmful alcohol:**
  - Restrict access to retailed alcohol
  - Enforce restrictions
  - Ban alcohol advertising
  - Raise taxes
- **Unhealthy diet:**
- **Physical inactivity:**
Best buys for 4 risk factors

- Tobacco use:
- Harmful alcohol:
- **Unhealthy diet:**
  - Reduce salt/sodium in food
  - Replacing trans-fat with unsaturated fatty acids
  - Reduce saturated fats
  - Reduce content of free sugars in food and drinks
  - Promote public awareness about diet
- Physical inactivity:
Best buys for 4 risk factors

- Tobacco use:
- Harmful alcohol:
- Unhealthy diet:
- **Physical inactivity:**
  - Promote physical activity through mass media
WHO Guidelines 2007 - 2015

123 mention implementation techniques

- Passive strategies 21%
- General policy strategies 62%
- Evidence based active implementation methods ignored

“We need more detail on implementation considerations, help with contextualizing interventions, adapting guideless, and provides specific options and strategies”

Wang, Norris, Bero 2016
Dissemination

• Passive dissemination of information is generally ineffective
• It seems necessary to use specific strategies to encourage implementation of research based recommendations and to ensure changes in practice

The Next Inning: Topics in colorectal cancer

NAACCR 2005
<table>
<thead>
<tr>
<th>Level</th>
<th>Barriers/Incentives</th>
</tr>
</thead>
<tbody>
<tr>
<td>Innovation</td>
<td>Advantages in practice, feasibility, credibility, accessibility, attractiveness</td>
</tr>
<tr>
<td>Individual professional</td>
<td>Awareness, knowledge, attitude, motivation to change, behavioral routines</td>
</tr>
<tr>
<td>Patient</td>
<td>Knowledge, skills, attitude, compliance</td>
</tr>
<tr>
<td>Social Context</td>
<td>Opinion of colleagues, culture of the network, collaboration, leadership</td>
</tr>
<tr>
<td>Organizational Context</td>
<td>Organisation of care processes, staff, capacities, resources, structures</td>
</tr>
<tr>
<td>Economic and political context</td>
<td>Financial arrangements, regulations, policies</td>
</tr>
</tbody>
</table>

Grol and Wensing. MJA, 2004
Barriers to Change

Patient

- Embarrassment - beliefs
- Lack of awareness
- Time/Inconvenience
- Cost
- Lack of interest
- Lack of physician recommendation

Barriers to Change

Providers / Individual Professional

- Patient characteristics (e.g. compliance)
- Failure to identify patients due for prevention
- Think the test/vaccine/lifestyle change is ineffective
- Avoid patient inconvenience/discomfort
- Lack of time & cost

Incentives for Change

Knowledge

Patient
- Mass media campaigns
- Spokespersons

Provider
- Residency programs
- Professional societies
- Champions
Incentives for Change

Economic and political context

Health care system (reimbursements)

Organizational approach, individual professional behavioral routines
  – Office systems approach (reminder systems, chart flags, checklists etc.)
Implementation research studies...

Key variables:

- behavior of healthcare professionals and support staff
- healthcare organizations: culture, context, infrastructure
- healthcare consumers and family members: acceptance, demands
- policy: incentives, financial structures

Key outcomes:

- sustainable adoption, implementation and uptake of evidence-based interventions
Sustaining social change

Common agenda
Shared measurement system
Mutually reinforcing activities
Continuous communication and
A backbone support organization

Kania et al 2011 Stanford Social Innovation Review
Conceptual Model: Implementation Research

What? Evidence Based Practices

How? Implementation Strategies

Implementation Outcomes
- Feasibility
- Fidelity
- Penetration
- Acceptability
- Sustainability
- Uptake
- Costs

Service Outcomes*
- Efficiency
- Safety
- Effectiveness
- Equity
- Patient-centeredness
- Timeliness

Patient Outcomes
- Clinical/health status
- Symptoms
- Function
- Satisfaction

* IOM Standards of Care

Proctor et al 2009 Admin. & Pol. Mental Health Services

Implementation Research Methods
Implementation science, Closing the Research-to-Practice Gap

• Maximize access to effective interventions for populations that will benefit most
• Integrate service delivery across organizations to support cancer prevention and control
• Broaden and deepen understanding of community and organizational characteristics that influence use of effective interventions
• Learn about the generalizability of discovery research to different settings and populations
Cancer registry key role (and growing): patient reported outcomes

Physical function
Symptoms
Utilities
Goals of care/preferences
Financial concerns
Physical function

• This could be measured by the PROMIS item Global 06,
• Or by the first 5 items in the EORTC QLQ-C30, which renders a single physical functioning score, and is commonly used in trials.
Symptoms

- These could be measured by the NCI’s PRO-CTCAE, for the “core” symptoms found across cancer types as published in an NCI consensus conference paper:
  - Fatigue, insomnia, pain, anorexia (appetite loss), dyspnea, cognitive problems, anxiety (includes worry), nausea, depression (includes sadness), sensory neuropathy, constipation, and diarrhea.
Utilities

- These can be assessed with the 5-item EuroQoL EQ-5D (commonly used in clinical trials for cost-effectiveness analyses).
- This would be a big step to help assessing value of care.
Goals of care – preferences

Financial concerns
Behavioral interventions

Community guide

Implementation

Cancer registry

Guidelines: USPSTF/CDC professional orgs

Cancer Prevention researchers

Social media
Stack the deck for prevention

Our challenge now is to act on this knowledge, avoiding long delays from discovery to translating knowledge to practice. As a society, we need to avoid procrastination induced by thoughts that chance drives all cancer risk, or that new medical discoveries are needed to make major gains against cancer.

Instead, we must embrace the opportunity to reduce our collective cancer toll by implementing effective prevention strategies and changing the way we live.

It is these efforts that will be our fastest return on past investments in cancer research.  

Colditz & Sutcliffe, 2016
8IGHT WAYS TO PREVENT CANCER
Very long term prevention action:

“In the beginning of every enterprise we should know, as distinctly as possible, what we propose to do, and the means of doing it... We desire to lay the foundation and to mature some parts of the plan. Those who come after us must finish the work.”

William Greenleaf Eliot, co-founder
Washington University in St. Louis
1854
Public health benefits

1. Lie in the future
2. Beneficiaries generally unknown
3. Public has no idea what public health programs do. Thus, when people benefit from prevention they don’t recognize they have been helped
4. Opposition to public health approaches that require societal change

Hemenway D. Why we don’t spend enough on public health. NEJM 2010