National Cancer Institute

CENTER FOR GLOBAL HEALTH

Master Course: Cancer Control Planning and Implementation

Webinar #6

The Role of Research in National Cancer Control Planning and Implementation

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Webinar 6 Overview

1. *Why should you care about research?*
   - *What does everyone need to know about health research?*
2. *The role of dissemination and implementation research*
3. *Translating research into policy and practice*

Why should you care about research?

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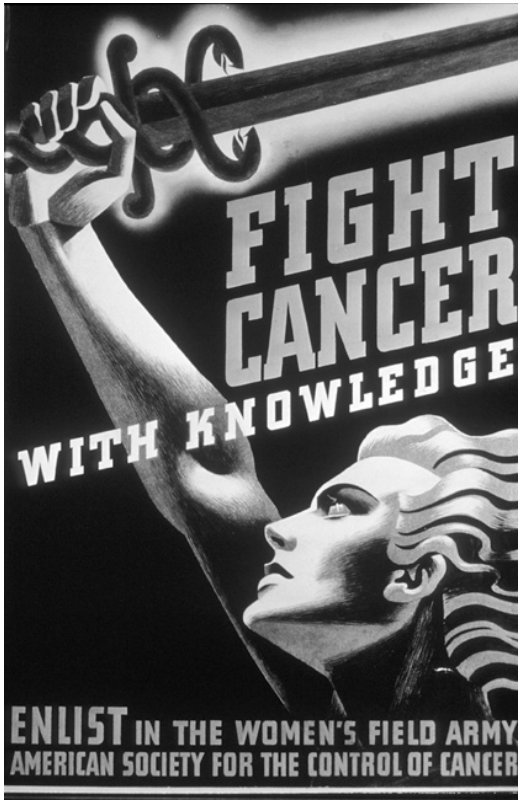

"Research and innovation have been and will be increasingly essential to find solutions to health problems, address predictable and unpredictable threats to human security, alleviate poverty, and accelerate development"

-*The Bamako Call to Action on Research for Health, 2008 WHO*

http://www.who.int/rpc/news/BAMAKOCALLTOACTIONFinalNov24.pdf

The Bamako Call to Action

- **Greater equity** in research for health is needed
- Need to **mobilize all relevant sectors** (public, private, civil society)

"Funding for research for health, especially in low- and middle-income countries, is difficult to secure, but there are considerable societal returns available as a result of that investment."

WHO Task Force on Scaling Up Research

Recommendations

1. Mobilize around a high-profile agenda of research and learning to improve the performance of health systems
2. Engage policy makers and practitioners in shaping the research agenda, and using evidence to inform decision-making
3. Strengthen country capacity for health systems research backed up by effective regional and global support
4. Increase financing for health systems research and learning

http://www.who.int/rpc/publications/scaling_up_research.pdf

Who should care about research?

Stakeholders

- Researchers
- Public health policymakers
  - Ministries of health, regional departments of health
- Civil society
- Care providers
- Patients and families
- Other ministries and organizations

The National Cancer Institute's role

NCI

- Is the U.S. government's principle agency for research on cancer;
- Supports and coordinates research conducted by universities, hospitals, research foundations, and businesses throughout the U.S. and around the world mainly through research grants;
- Conducts research in its own laboratories and clinics;
- Supports cancer research education and training.

*****NCI's focus on research results in a strong motivation for ensuring cancer control interventions are evidence-based*****

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What does everyone need to know about health research?

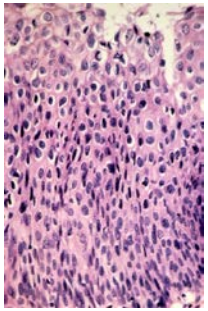
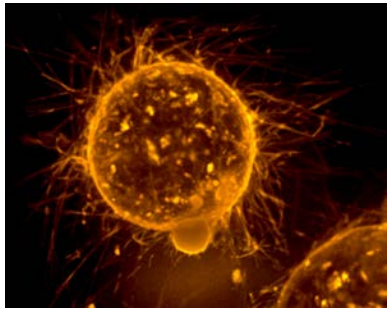
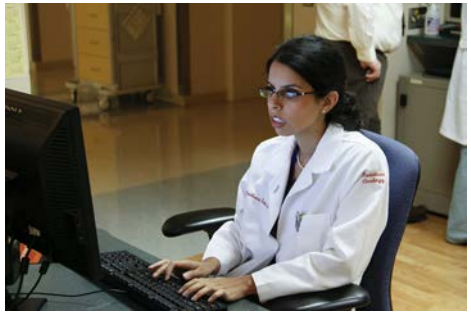
What is research?

Research consists of

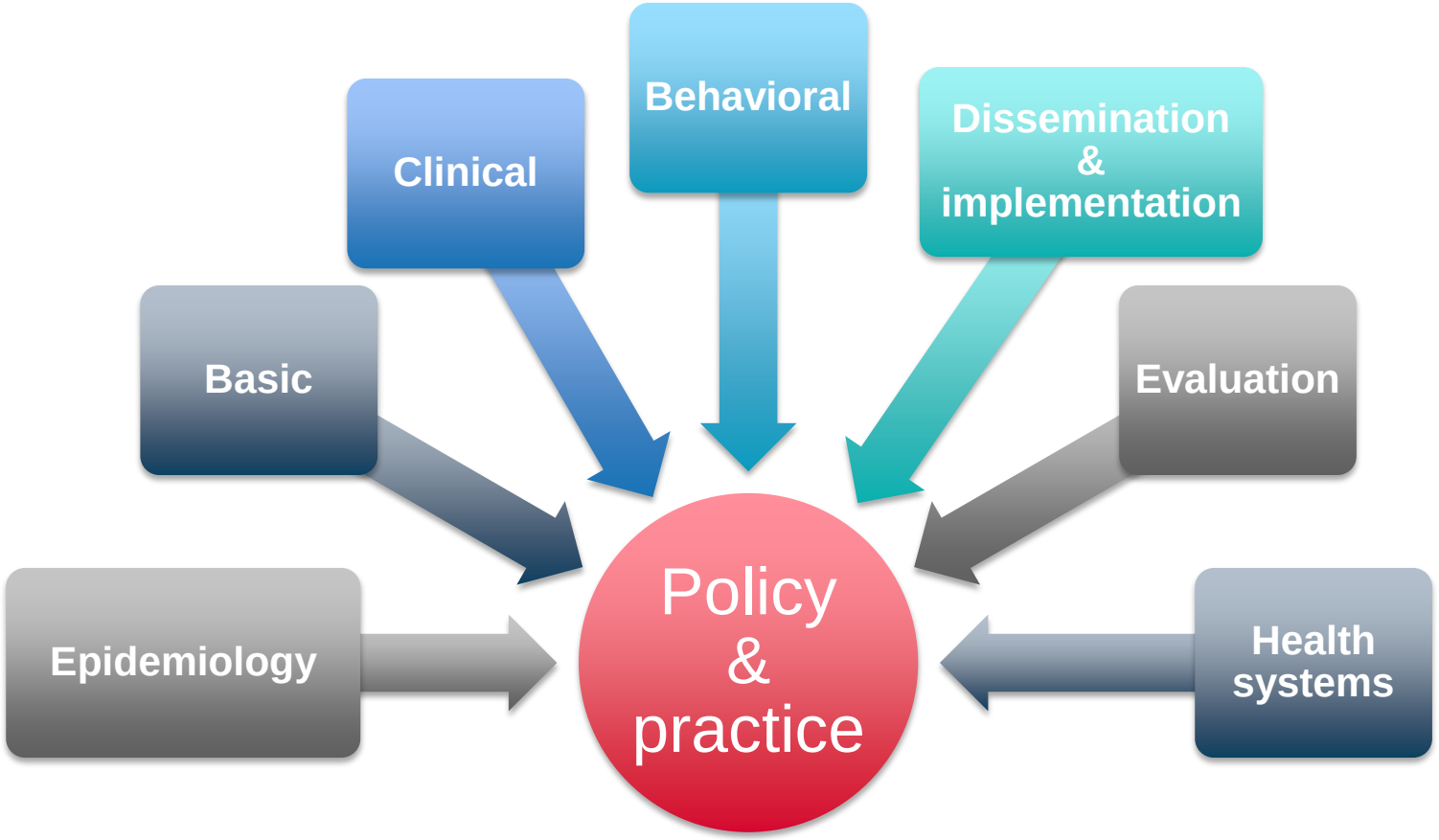
- Asking a question
- Posing a hypothesis
- Collecting data
- Analyzing the data
- Drawing conclusions
- Communicating the results

Is it right?

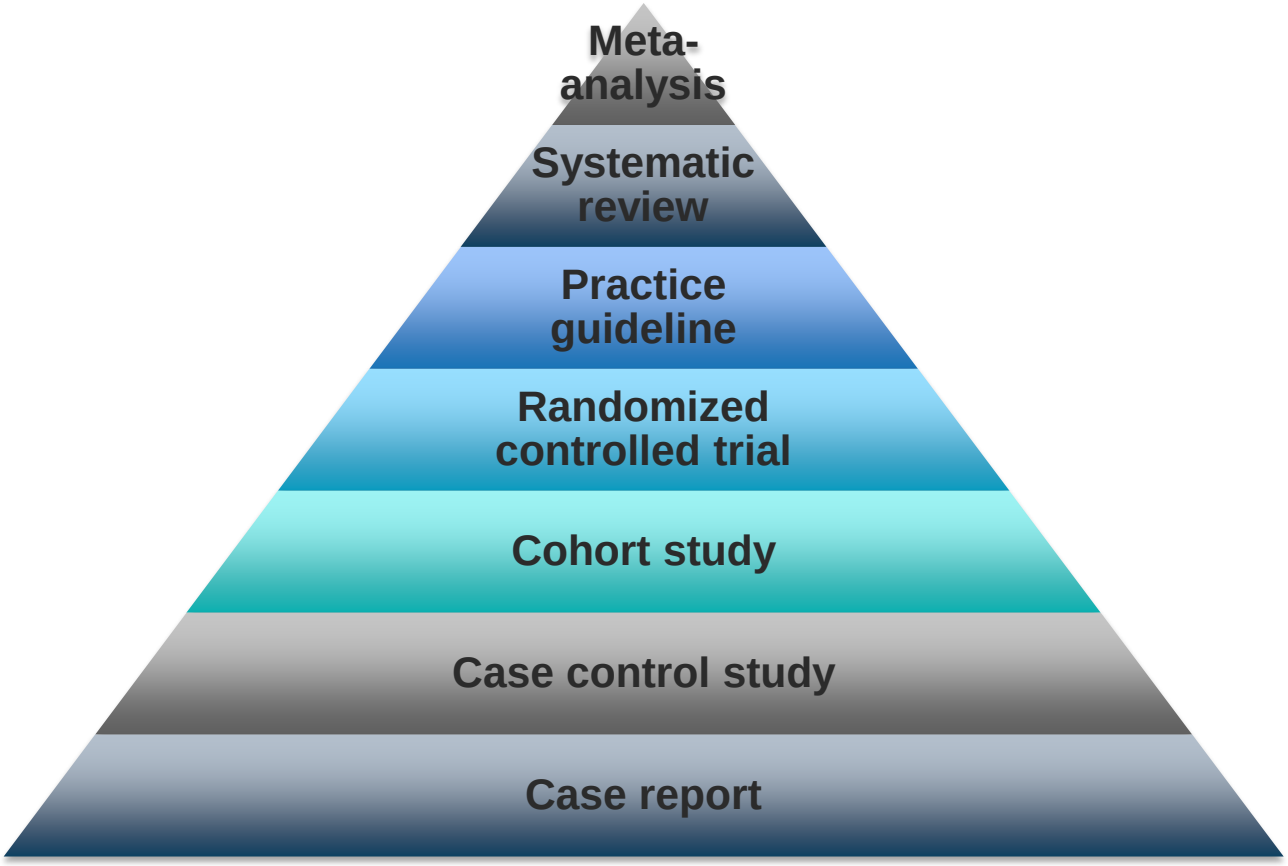
- Validity of measurements
- Quality and reliability of data
- Logic used to draw conclusions
  - Correlation/association vs causation
  - Absence of evidence vs evidence of absence
  - Reproducibility

What fields of research are relevant?



How is evidence collected, analyzed and used?



Adapted from Study Design 101 – Himmelfarb Health Sciences Library
George Washington University
https://himmelfarb.gwu.edu/tutorials/studydesign101/index.html

Case report

Definition	• Describes and interprets and individual case
Advantages	• Can help communicate new observations and rare occurrences
Disadvantages	• Not generalizable • Not useful for public health purposes

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/casereports.html

Case control study

Definition	• Study that compares patients who have a disease or outcome of interest (cases) with patients who do not (control) and looks back retrospectively to compare how frequently the exposure to a risk factor is present in each group
Advantages	• Good for studying rare conditions or diseases • Less time to conduct the study • Simultaneously look at multiple risk factors • Initial establishment of an association
Disadvantages	• May have data quality problems because they rely on memory and recall bias • Can be difficult to find a suitable control group

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/casecontrols.html

Cohort study

Definition	• Study that usually looks forward (prospective) and observes a large cohort of people over time, collecting data that may be relevant to a specific disease or outcome
Advantages	• Allows calculation of incidence, absolute & relative risk • Facilitate study of rare exposures • Can provide strong evidence of association between risk factor and disease or outcome
Disadvantages	• Less suited to study of rare diseases • Takes time (years-decades) and can be expensive

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/corhorts.html

Randomized controlled trial

Definition

- Study that randomly assigns participants into either a group that receives a new intervention or into a control group that receives a standard treatment or placebo. The difference in outcome between the two groups is then measured.

Advantages

- Randomization helps ensure both groups are similar in all respects except the intervention
- Blinding (when neither the provider nor patient knows which group the patient is in) is often possible and helps reduce bias

Disadvantages

- Expensive and time consuming
- The population that volunteers may not be representative of the whole population
- The context of the trial may not be easily reproduced in a larger population

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/rcts.html

Practice guideline

Definition

- Statement produced by a panel of experts after extensive review of the literature that outlines current best practice to inform clinical decisions.

Advantages

- Practical guidance for clinicians
- Informed by systematic reviews
- An evidence-based resource

Disadvantages

- Slow to change and be updated
- May not address controversial topics
- Can be time-consuming to produce
- May be affected by the type of organization creating it

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/practiceguidelines.html

Systematic review

Definition	• Scientific investigation that summarizes the findings of similar, but separate studies on a specific health-related topic.
Advantages	• Extensive review of current literature and other sources • Results can be generalized and extrapolated into the general population more broadly than individual studies • Considered an evidence-based resource
Disadvantages	• May not be easy to combine studies • Can be time-consuming to produce

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/systematicreviews.html

Meta-analysis

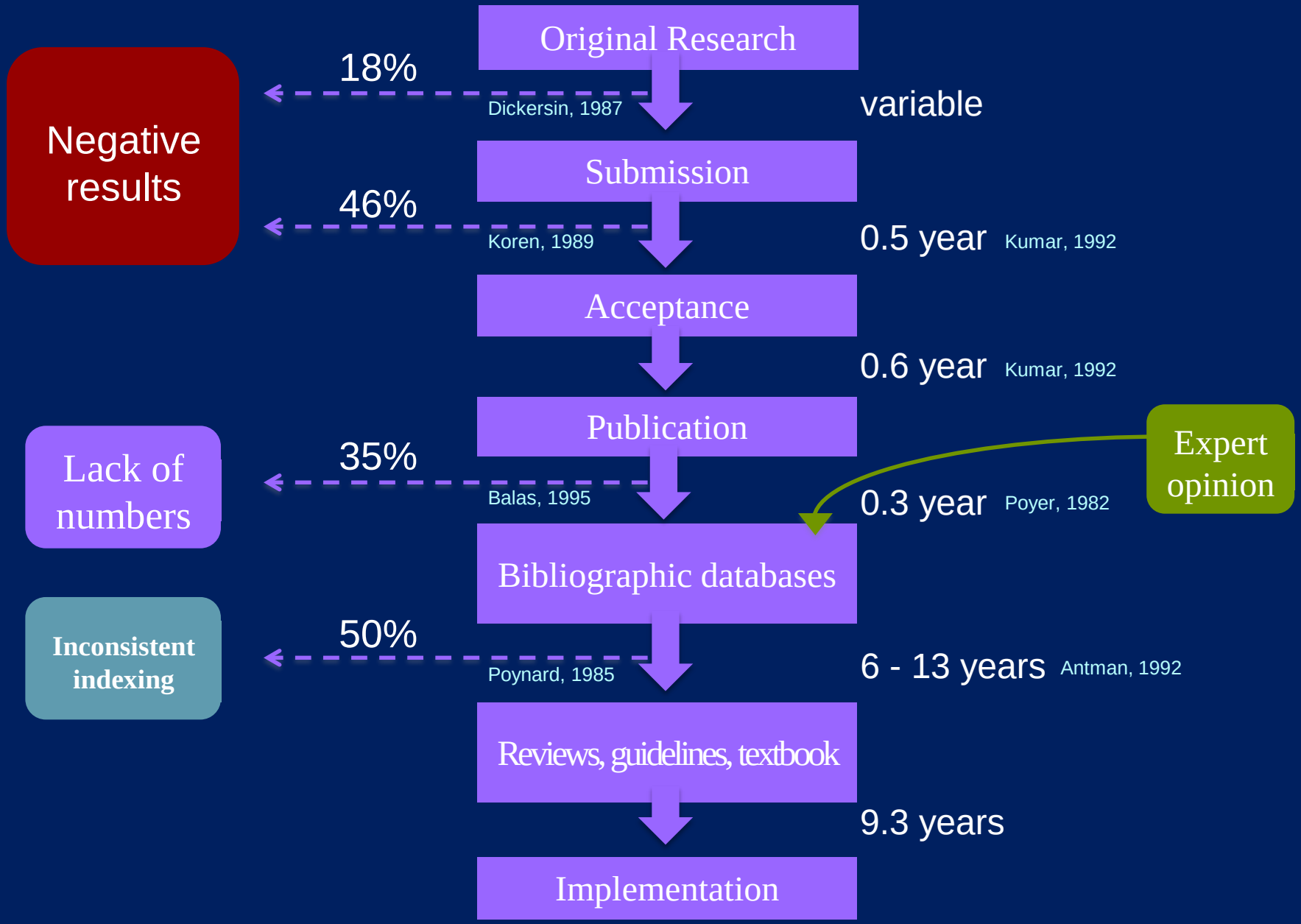
Definition	• A method for systematically combining qualitative and quantitative study data from several selected studies to develop a single conclusion that has greater statistical power than a single study
Advantages	Increased number and greater diversity of subjects Greater ability to extrapolate to general population An evidence-based resource
Disadvantages	• Difficult and time consuming • Not all studies provide adequate data for inclusion • Requires advanced statistical techniques • Heterogeneity of study popluations

Adapted from https://himmelfarb.gwu.edu/tutorials/studydesign101/metaanalyses.html

The role of dissemination & implementation research

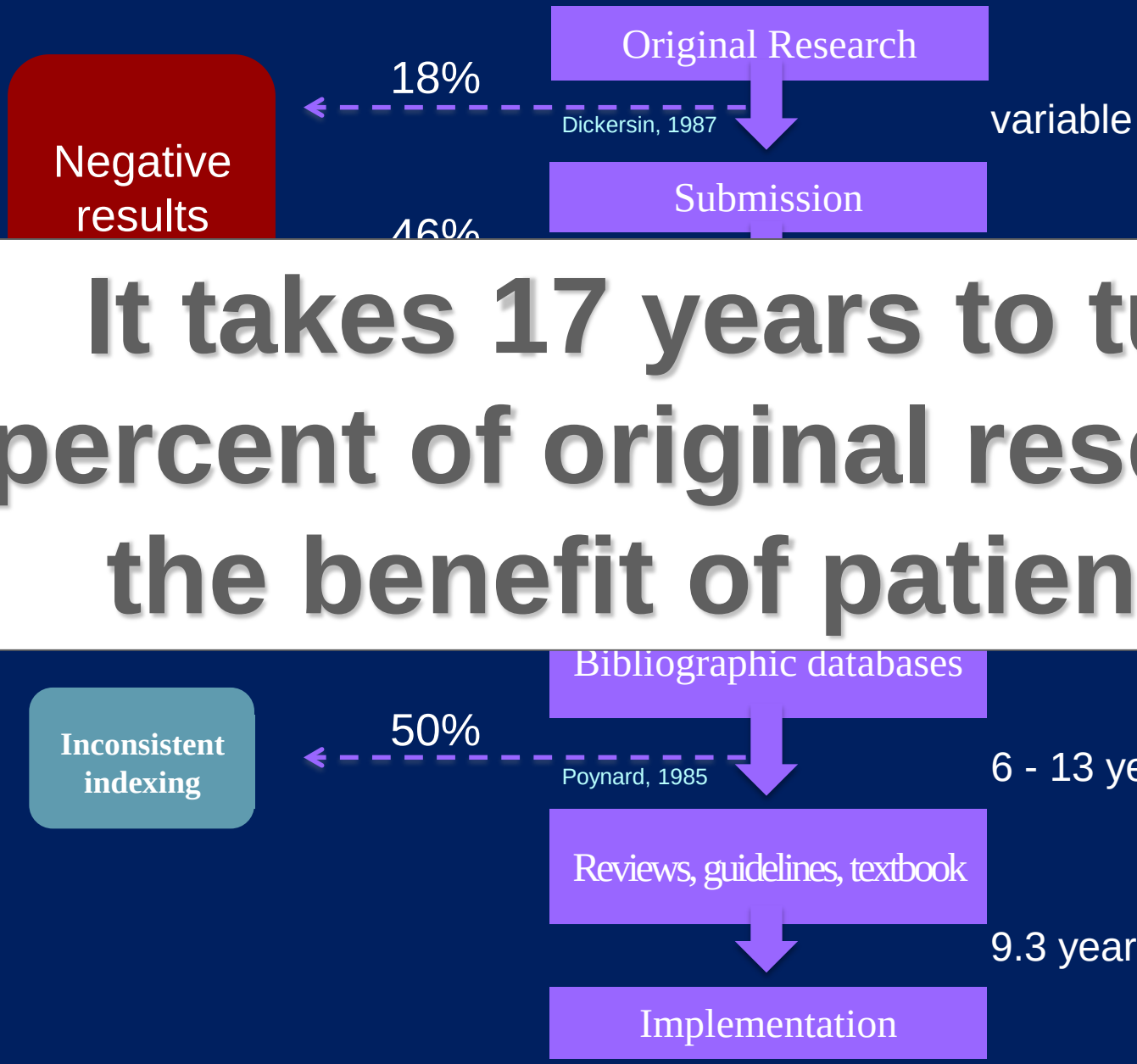
"PUBLICATION PATHWAY"

Balas & Boren, 2000



“PUBLICATION PATHWAY”

Balas & Boren, 2000



It takes 17 years to turn 14 percent of original research to the benefit of patient care

Definitions

"Dissemination is the targeted distribution of information and intervention materials to a specific public health or clinical practice audience. The intent is to spread knowledge and the associated evidence-based interventions."

"Implementation is the use of strategies to adopt and integrate evidence-based health interventions and change practice patterns within specific

Program Announcement (PA) Number: PAR-13-055

Definitions D&I Research

- **Evidence-based intervention:** The objects of dissemination and implementation are interventions with proven efficacy and effectiveness.
- **Knowledge translation (Canada):** A dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge.
  - Strong linkage between researchers and users of knowledge
- **Translational research (CDC):** The sequence of events (i.e., process) in which a proven scientific discovery (i.e., evidence based public health intervention) is successfully institutionalized (i.e., seamlessly integrated into established practice and policy).
  - Comprised of implementation, dissemination, and diffusion research
  - Includes research on replication

*Also see Chapter 2 in "Dissemination and Implementation Research in Health"

What's different about D&I research?

D&I research may differ in:

- Origin of the research question
- Involvement of end users in the research process

The differences stem from the need:

- To study strategies to better inform healthcare service and quality improvement efforts
- To facilitate uptake (healthcare and patients/public)
- To generate generalizable knowledge; applied across multiple settings and contexts
- Involves multiple disciplines—including epidemiology, social scientists, and health economics
- To develop policy recommendations and practical solutions based on empirical research findings

Possible dissemination research topics

- Analysis of factors influencing the **creation, packaging, transmission** and **reception** of valid health research knowledge
- Experimental studies to test the **effectiveness** of individual and systemic **dissemination strategies**, focusing on relevant outcomes (e.g., acquisition of new knowledge, maintenance of knowledge, attitudes about the dissemination strategies, use of knowledge in practice decision-making)
- Studies testing the utility of alternative **dissemination strategies for service delivery systems** targeting rural, minority, and/or other underserved populations
- Studies on how **target audiences** are defined, and how evidence is packaged for specific target audiences

Possible implementation research topics

- Studies of efforts to **implement** prevention, early detection, and diagnostic **interventions**, as well as **treatments** or clinical **procedures** of demonstrated efficacy **into existing care systems** to measure the extent to which such procedures are utilized, and adhered to, by providers and consumers
- Studies on the **fidelity of implementation** efforts, including the identification of components of implementation that will enable fidelity to be assessed meaningfully
- Longitudinal and follow-up studies on the **factors** that contribute to the **sustainability** of research-based improvements in public health and clinical practice

Possible Dissemination and Implementation research topics

- Studies of the **capacity of specific care delivery settings** (e.g., primary care, schools, community health settings) to incorporate D&I efforts within current organizational forms
- Studies that focus on the **development and testing of theoretical models** for D&I processes
- Development of **outcome measures** and suitable **methodologies** for D&I approaches that accurately assess the success of an approach to move evidence into practice (i.e., not just clinical outcomes)

D&I training opportunities

Global health D&I resources

- Cancer Control P.L.A.N.E.T.
  - http://cancercontrolplanet.cancer.gov/
- Dissemination and Implementation Research in Health PAR
  - http://cancercontrol.cancer.gov/funding_apply.html#is

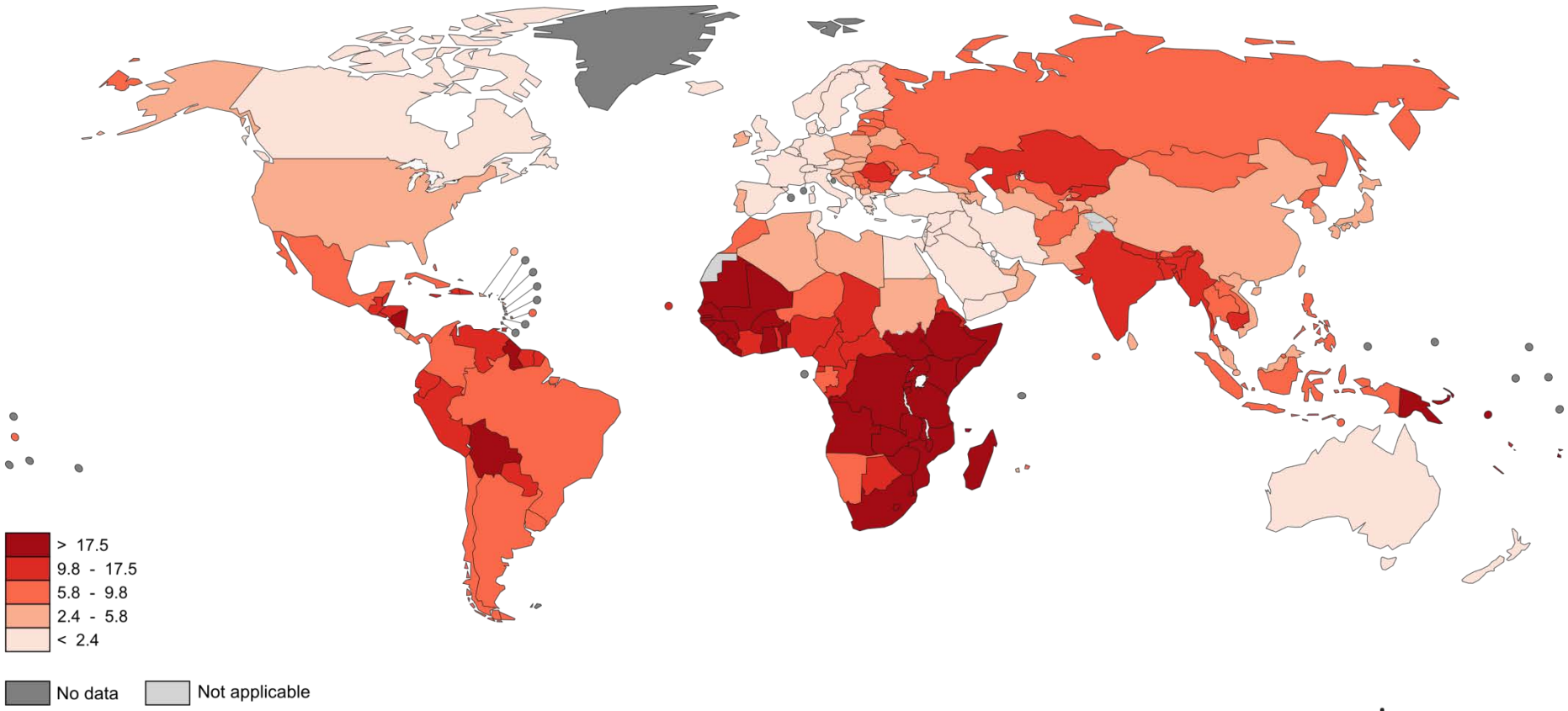
Other Organization Websites:

- Partners in Health - http://www.pih.org/
- Earth Institute - http://www.earth.columbia.edu/
- Millennium Villages - http://www.millenniumvillages.org/
- WHO TDR - http://apps.who.int/tdr/
- KT Canada - http://ktclearinghouse.ca/ktcanada

Translating research into policy and practice

Case Study: *Cervical Cancer Prevention and Control*

Death from Cervical Cancer

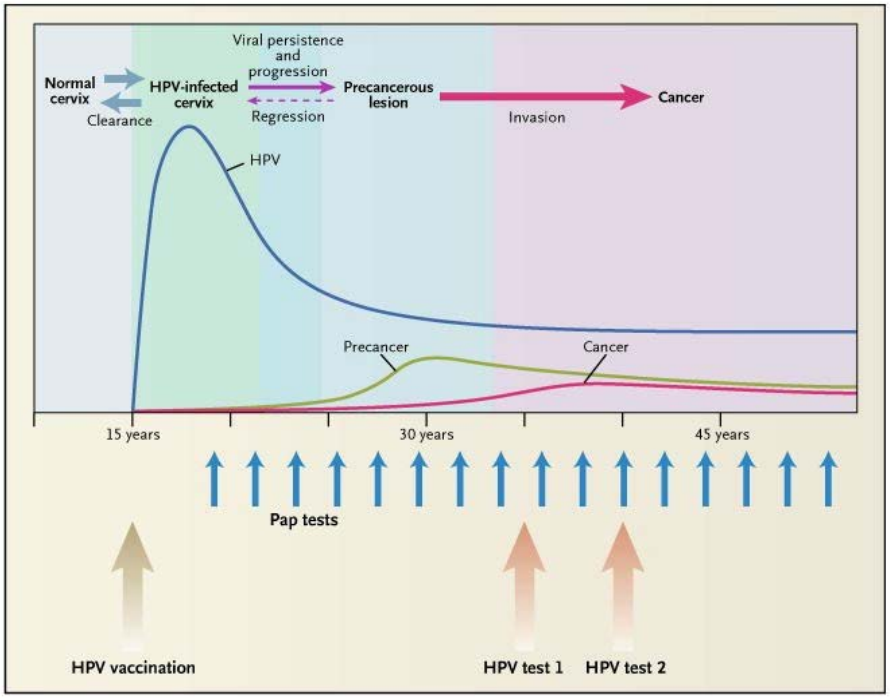


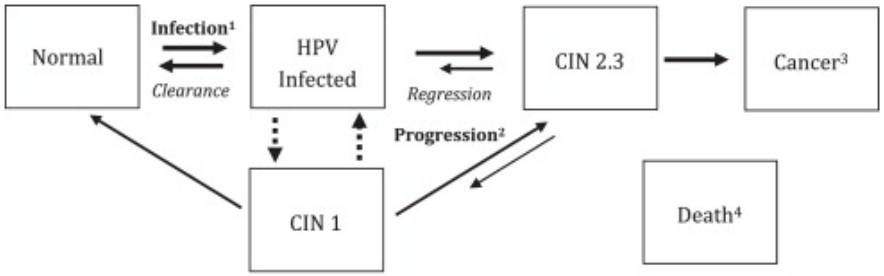
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data source: GLOBOCAN 2012
Map production: IARC
World Health Organization

World Health Organization

The Natural History of Cervical Cancer & Intervention Points





1. Incidence of infection depends on age, HPV type, prior infection, and type-specific immunity.
2. Progression of HPV infection and CIN 1 depends on age and HPV type.
3. Cancer states are stratefied by stage (local, regional, distant) and detection status (undetected, symptom-detected, screen-detected).
4. Death can occur from all-cause mortality from every health state and excess cancer-specific mortality from cancer states.

Image (top) from Schiffman et al., N Engl J Med (2005), (bottom) from Levin et al., Vaccine (2015)

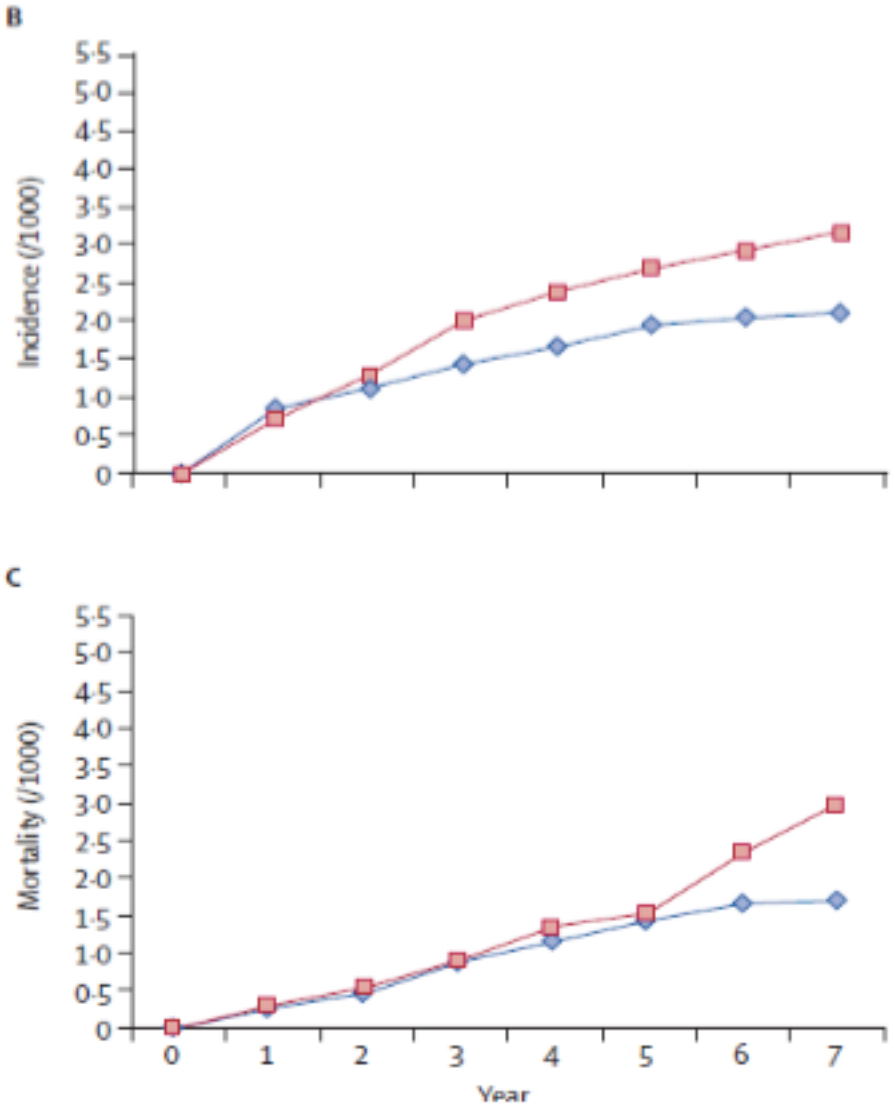
Comparison of Cervical Cancer Screening Tests

	Pap smear (cytology)	VIA	HPV testing
Cost	Moderate ($10-$15/test)	**Low (<$5/test)**	High, but lower in new formats (<$10/test)
Provider	Cytotechnologist and cytopathologist	**Nurses or mid-level providers**	**Lab technician**
Training/QA	++ (Significant)	++ (Significant)	**+ (Limited)**
Sensitivity	60-80%	50-80%	**80-95%**
Specificity	**85-95%**	70-80%	80-90%
Min. # of visits	2	**1**	1-2
Linking screening & treatment	Not possible in same visit	**Immediate treatment possible**	Possible in same visit or on same-day
Home testing	Not possible		**Self sampling possible**
Inter-obs.variation	++ (Significant)		**+ (Minimal)**
Reproducibility	Limited, unless using with digital imaging		**Easily achievable**
Technology	**Open source/public domain**		Proprietary

Sahasrabuddhe et al., Ca Prev Res (2012)

Slide Courtesy of V. Sahasrabuddhe.

Efficacy of Visual Inspection with Acetic Acid



Cluster randomized trial of VIA vs. standard of care in Dindigul district, Tamil Nadu, India

30-59 years
>79,000 participants
114 clusters
7 years follow-up

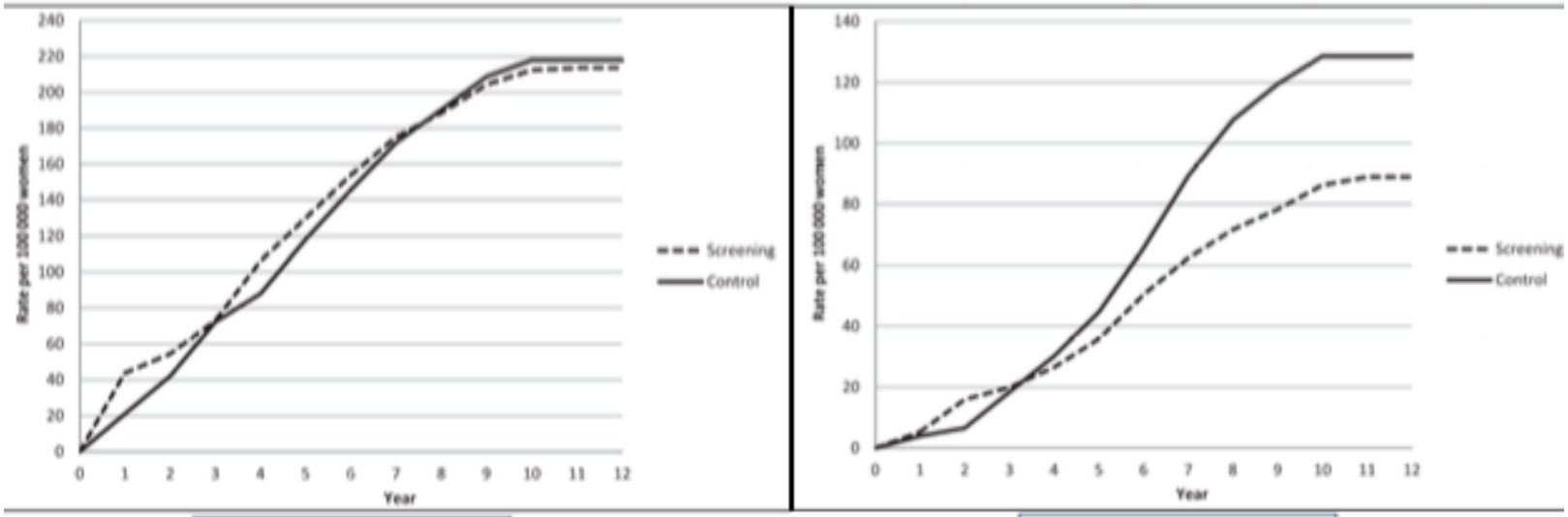
VIA vs. Control
Decline in incidence: 25%
Decline in mortality: 35%

Sankaranarayanan et al 2007 Lancet

Slide Courtesy of V. Sahasrabuddhe.

Efficacy of Visual Inspection with Acetic Acid

Cluster randomized trial of VIA vs. standard of care in Mumbai, India



Cervical Cancer Incidence

Cervical Cancer Mortality

35-64 years
>151,000 participants
20 clusters
12 years follow-up

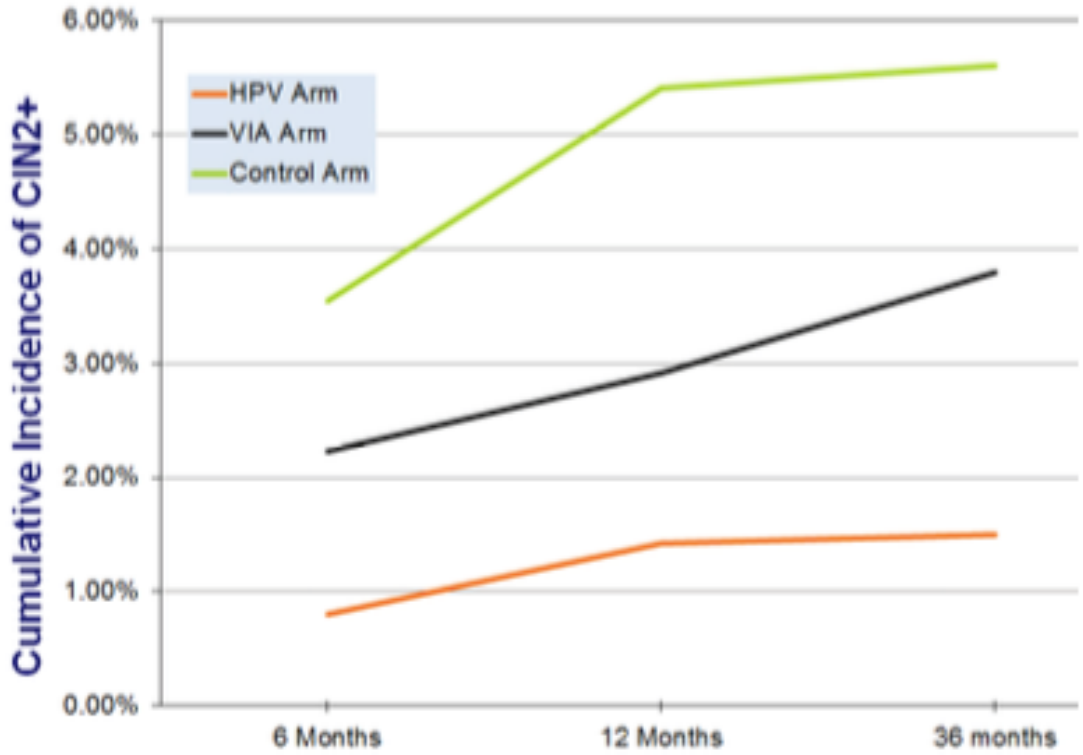
VIA vs. Control
No significant diff in incidence%
Decline in mortality: 31%

Shastri et al 2014 JNCI

Slide Courtesy of V. Sahasrabuddhe.

Added Value of HPV Screening

Individual randomized trial of HPV vs. VIA-based 'Screen-and Treat' in South Africa



35-66 years
~6500 participants
3 years follow-up

HPV vs. Control
73% reduction in CIN2+

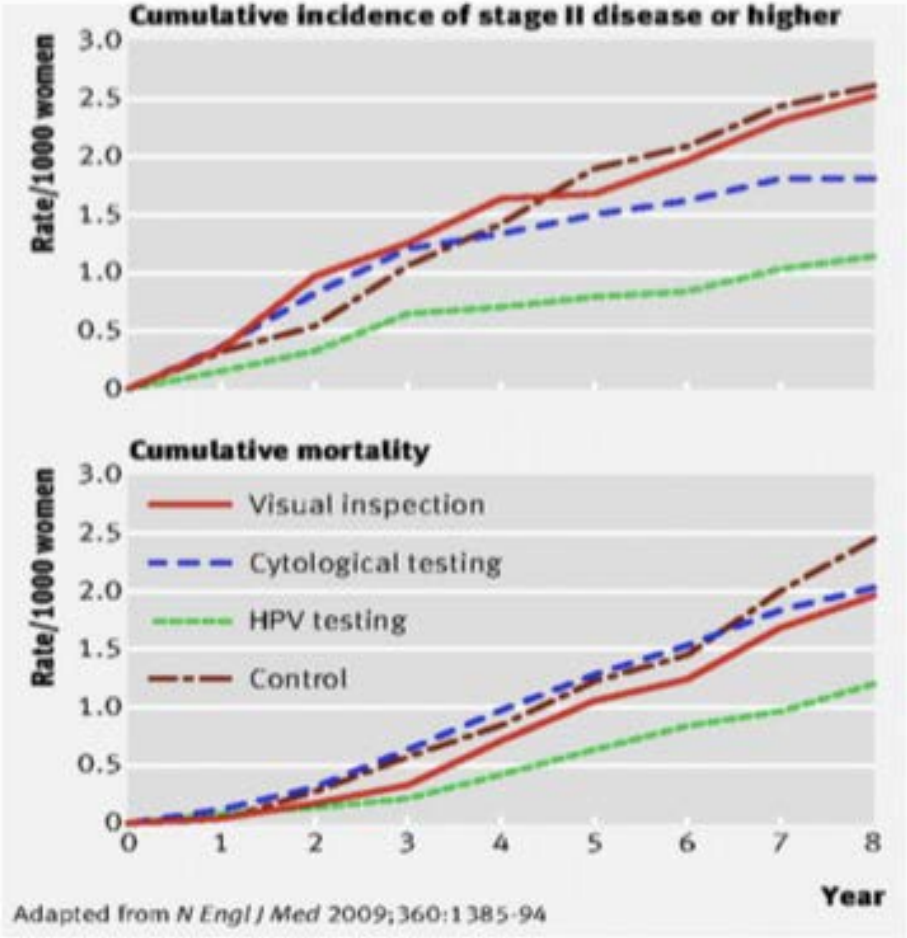
VIA vs. Control
32% reduction in CIN2+

Denny et al., JNCI (2010)

Slide Courtesy of V. Sahasrabuddhe.

Added Value of HPV Screening

Cluster randomized trial of HPV vs. VIA vs. Cytology vs. Standard of Care screening in Rural Maharashtra, India



30-59 years
>131,000 participants
52 clusters
8 years follow-up

HPV vs. Control
Decline in incidence: 53%
Decline in mortality: 48%

VIA/Pap vs. Control
No sig. difference in incidence or mortality

Sankaranarayanan et al., NEJM (2009)

Slide Courtesy of V. Sahasrabuddhe.

Meta-Analysis

Reaching women who do not participate in the regular cervical cancer screening programme by offering self-sampling kits: A systematic review and meta-analysis of randomised trials

Snijders, M. Arbyn

2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors

Massad, L. Stewart MD; Einstein, Mark H. MD; Huh, Warner K. MD; Kat... Hormuzd A. PhD; Kinney, Walter K. MD; Schiffman, Mark MD; Solomon, Diane MD; Wentzensen, Nicolas... the 2012 ASCCP Consensus Guidelines Conference

Self-collected HPV Testing Improves Participation in Cervical Cancer Screening: A Systematic Review and Meta-analysis

C. Sarai Racey, Diana R. Withrow and Dionne Gesink
Canadian Journal of Public Health / Revue Canadienne de Santé Publique
Vol. 104, No. 2 (March/April 2013), pp. e159-e166

Screening for cervical cancer: a s... meta-analysis

Leslea Peirson ✉ , Donna Fitzpatrick-Lewis, Donna Ciliska and Rachel Warren

...-35 | © Peirson et al.; licensee BioMed Central Ltd. 2013

...lished: 24 May 2013

American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer[†‡§]

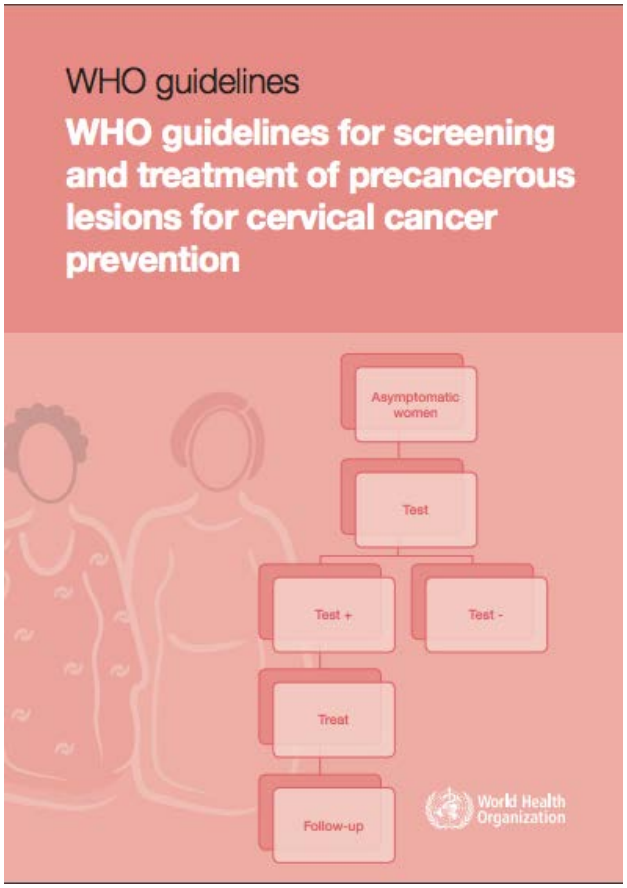
Debbie Saslow PhD ✉, Diane Solomon MD, Herschel W. Lawson MD, Maureen Killackey MD, Shalini L. Kulasingam PhD, Joanna Cain MD, Francisco A. R. Garcia MD, MPH, Ann T. Moriarty MD, Alan G. Waxman MD, MPH, David C. Wilbur MD, Nicolas Wentzensen MD, PhD, MS, Levi S. Downs Jr MD, Mark Spitzer MD, Anna-Barbara Moscicki MD, Eduardo L. Franco DrPH, Mark H. Stoler MD, Mark Schiffman MD, Philip E. Castle PhD, MPH, Evan R. Myers MD, MPH, ACS-ASCCP-ASCP Cervical Cancer Guideline Committee

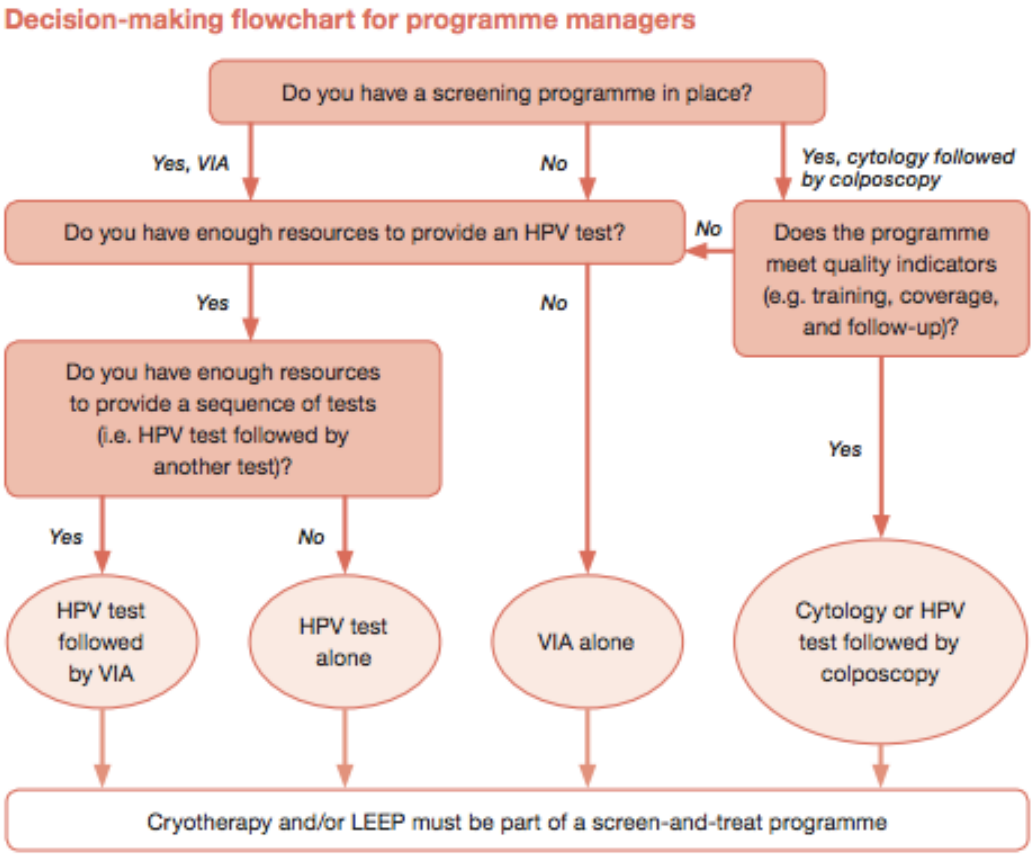
Is HPV DNA testing specificity comparable to that of cytological testing in primary cervical cancer screening? Results of a meta-analysis of randomized controlled trials

Claudia Pileggi, Domenico Flotta, Aida Bianco, Carmelo G.A. Nobile, Maria Pavia ✉

First published: 24 January 2014 Full publication history

Where all of this can get us…





http://apps.who.int/iris/bitstream/10665/94830/1/9789241548694_eng.pdf

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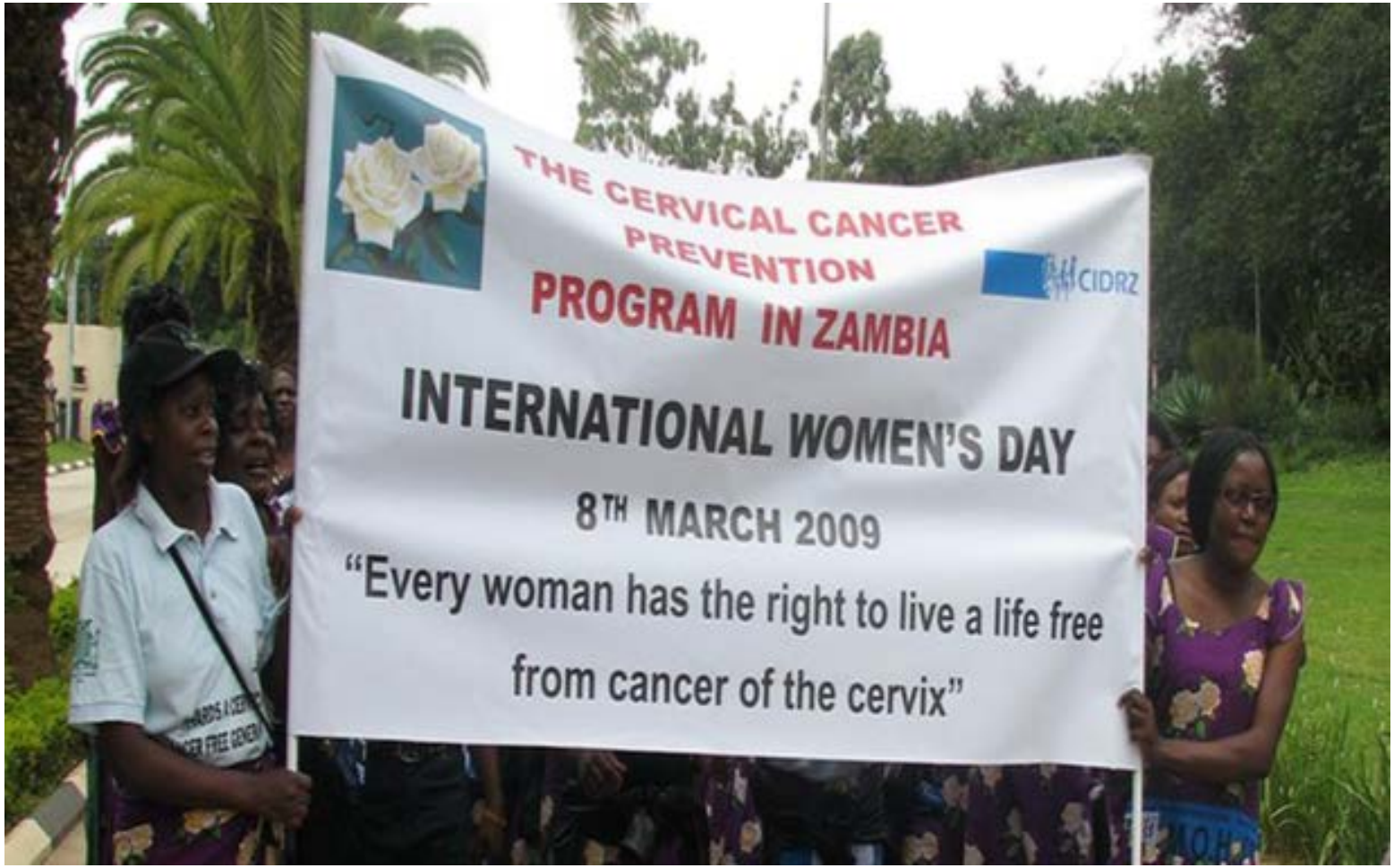
Reproducibility	Limited, unless using with digital imaging		**Easily achievable**
Technology	**Open source/public domain**		Proprietary

Sahasrabuddhe et al., Ca Prev Res (2012)

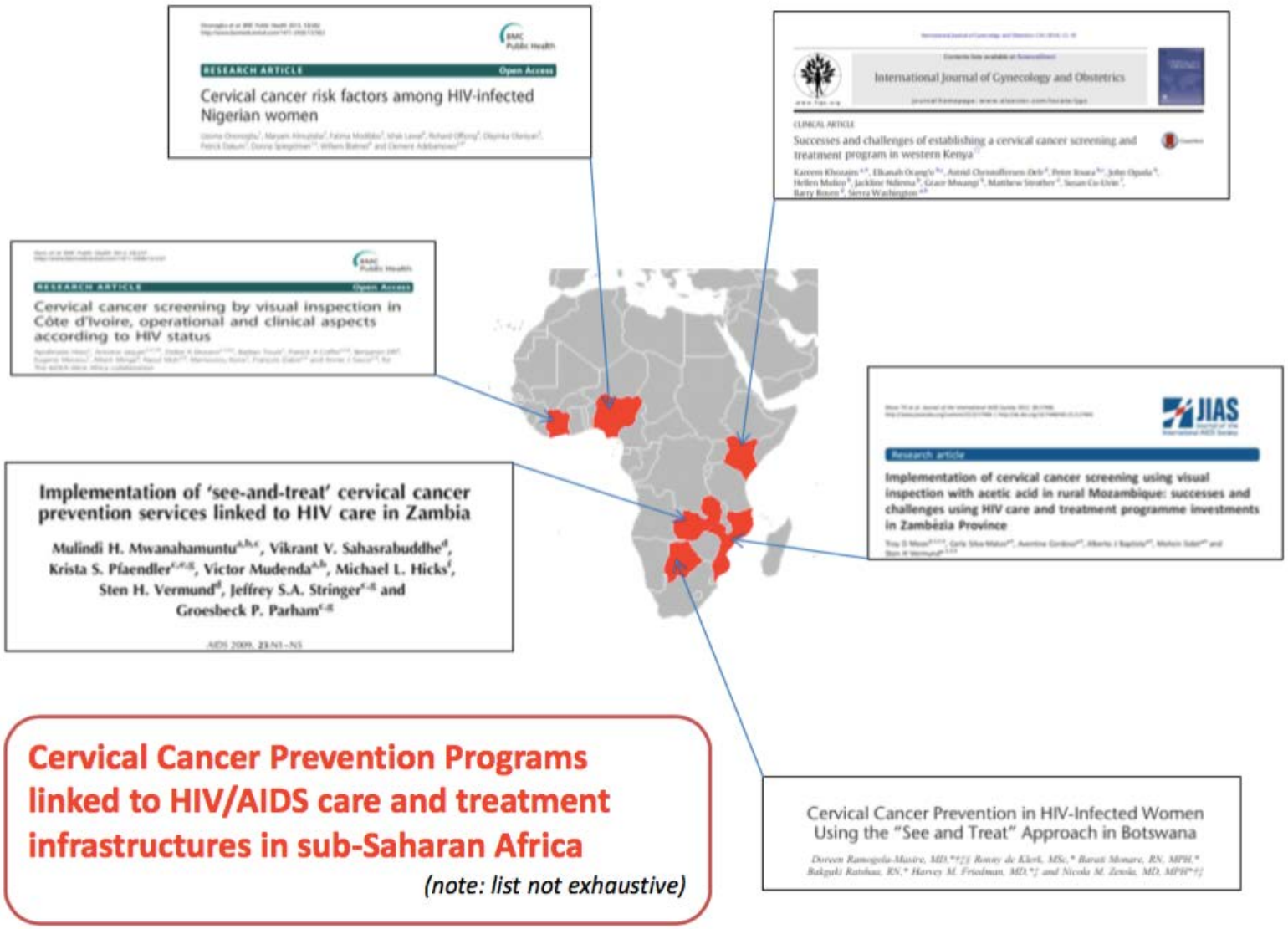
Slide Courtesy of V. Sahasrabuddhe.

Zambia Case Study:
CaCx Screening Linked to HIV/AIDS Programs



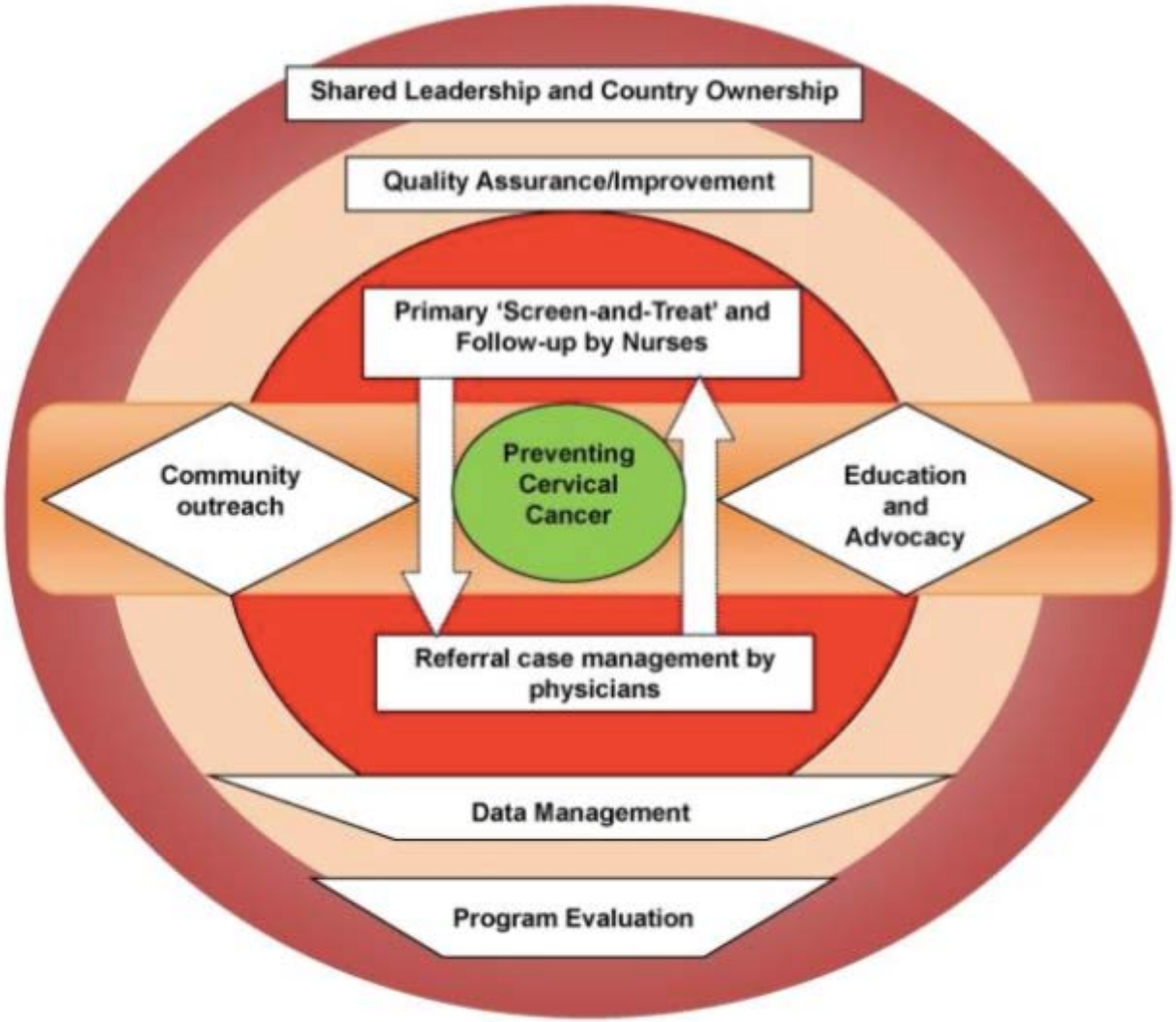
Slide Courtesy of V. Sahasrabuddhe.

Evidence Supporting Individual Programs



Slide Courtesy of V. Sahasrabuddhe.

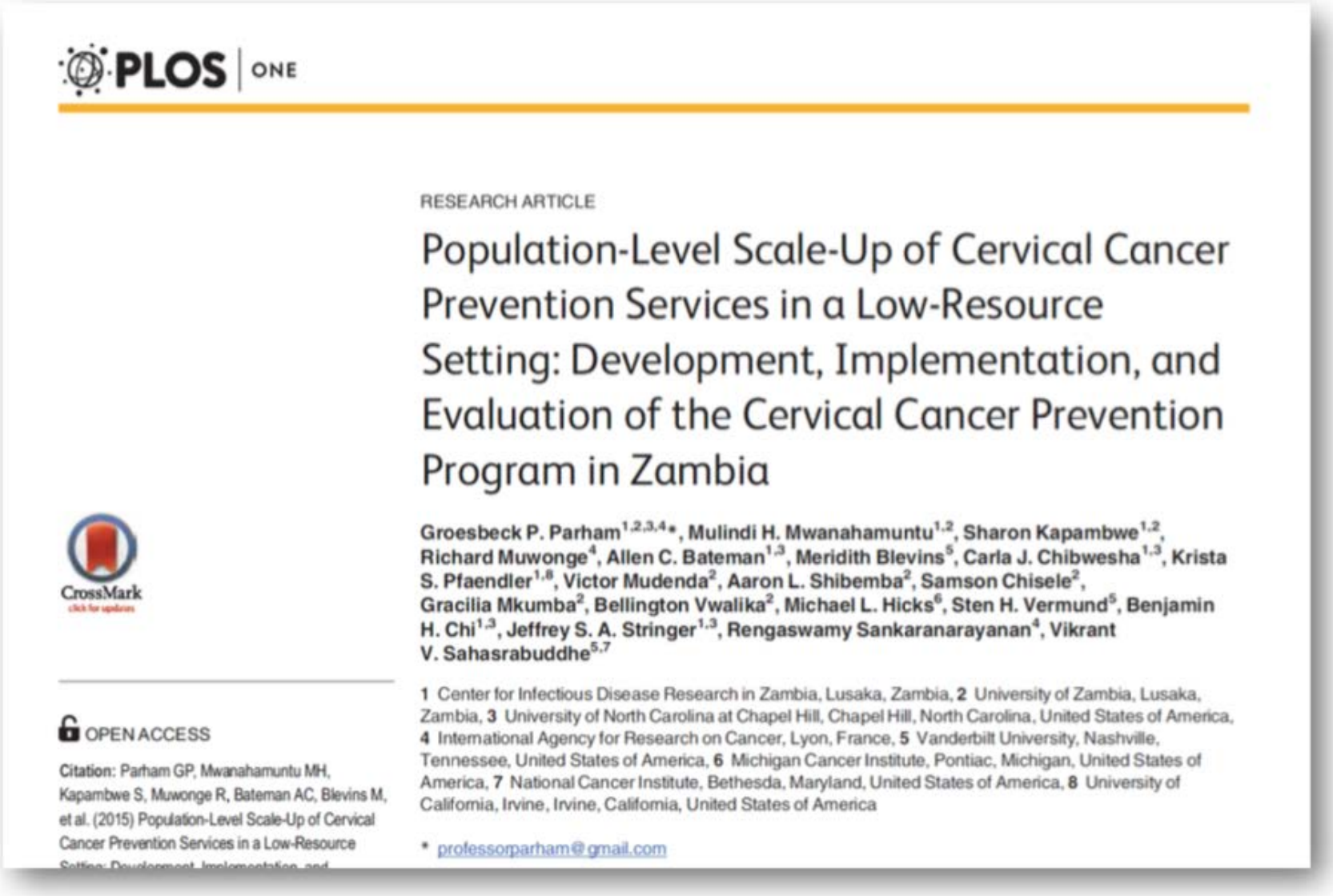
Implementation Model



Mwanahamuntu et al., PLoS Med (2011)

Slide Courtesy of V. Sahasrabuddhe.

Dissemination and Scale-up



PLOS | ONE

RESEARCH ARTICLE

Population-Level Scale-Up of Cervical Cancer Prevention Services in a Low-Resource Setting: Development, Implementation, and Evaluation of the Cervical Cancer Prevention Program in Zambia

Groesbeck P. Parham[1,2,3,4]*, Mulindi H. Mwanahamuntu[1,2], Sharon Kapambwe[1,2], Richard Muwonge[4], Allen C. Bateman[1,3], Meridith Blevins[5], Carla J. Chibwesha[1,3], Krista S. Pfaendler[1,8], Victor Mudenda[2], Aaron L. Shibemba[2], Samson Chisele[2], Gracilia Mkumba[2], Bellington Vwalika[2], Michael L. Hicks[6], Sten H. Vermund[5], Benjamin H. Chi[1,3], Jeffrey S. A. Stringer[1,3], Rengaswamy Sankaranarayanan[4], Vikrant V. Sahasrabuddhe[5,7]

1 Center for Infectious Disease Research in Zambia, Lusaka, Zambia, 2 University of Zambia, Lusaka, Zambia, 3 University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States of America, 4 International Agency for Research on Cancer, Lyon, France, 5 Vanderbilt University, Nashville, Tennessee, United States of America, 6 Michigan Cancer Institute, Pontiac, Michigan, United States of America, 7 National Cancer Institute, Bethesda, Maryland, United States of America, 8 University of California, Irvine, Irvine, California, United States of America

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Citation: Parham GP, Mwanahamuntu MH, Kapambwe S, Muwonge R, Bateman AC, Blevins M, et al. (2015) Population-Level Scale-Up of Cervical Cancer Prevention Services in a Low-Resource Setting: Development, Implementation, and

Slide Courtesy of V. Sahasrabuddhe.

Monitoring and Evaluation

OPEN ACCESS Freely available online

PLOS ONE

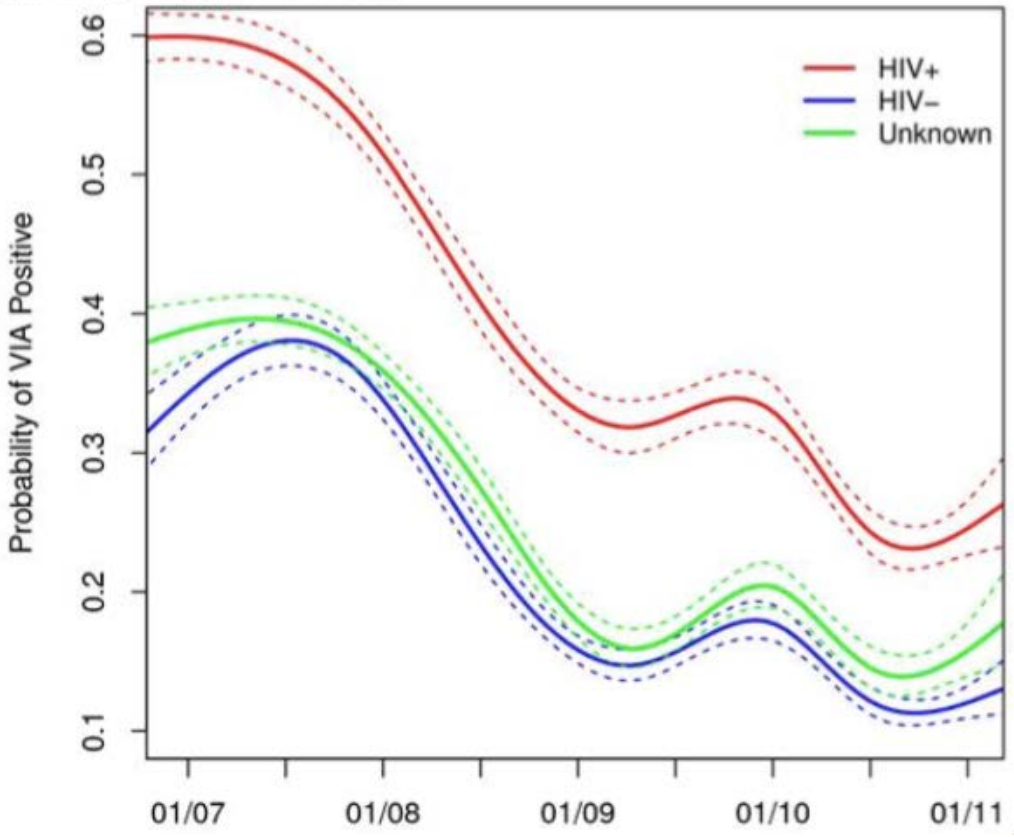
Utilization of Cervical Cancer Screening Services and Trends in Screening Positivity Rates in a 'Screen-And-Treat' Program Integrated with HIV/AIDS Care in Zambia

Mulindi H. Mwanahamuntu[1,2☯], Vikrant V. Sahasrabuddhe[3☯], Meridith Blevins[3☯], Sharon Kapambwe[1], Bryan E. Shepherd[3], Carla Chibwesha[1,4], Krista S. Pfaendler[5], Gracilia Mkumba[2], Belington Vwalika[2], Michael L. Hicks[6], Sten H. Vermund[3], Jeffrey S.A. Stringer[1,2,4], Groesbeck P. Parham[1,2,4*]

Indicators

Decreasing VIA positivity by HIV status (2007-2011)

→reflecting improved training and quality assurance



Slide Courtesy of V. Sahasrabuddhe.

Monitoring and Evaluation

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BRIEF COMMUNICATION

Monitoring the performance of "screen-and-treat" cervical cancer prevention programs

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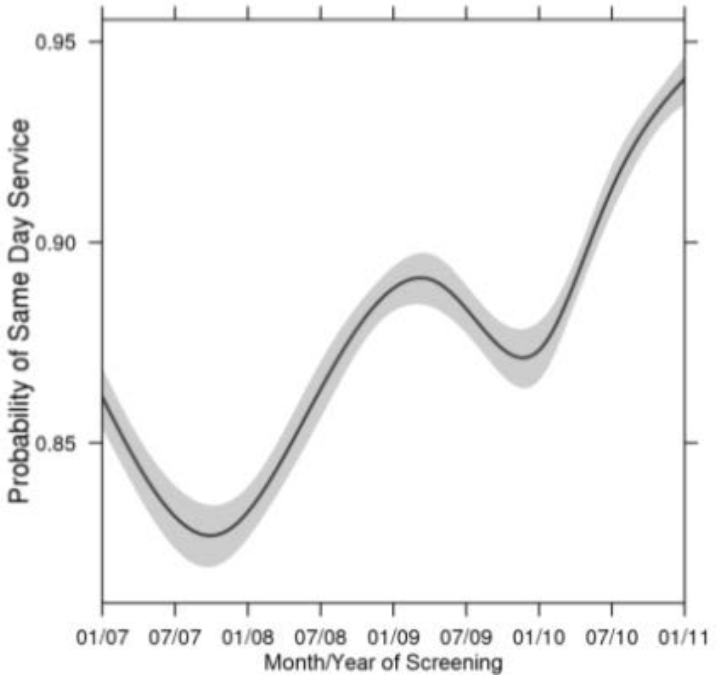
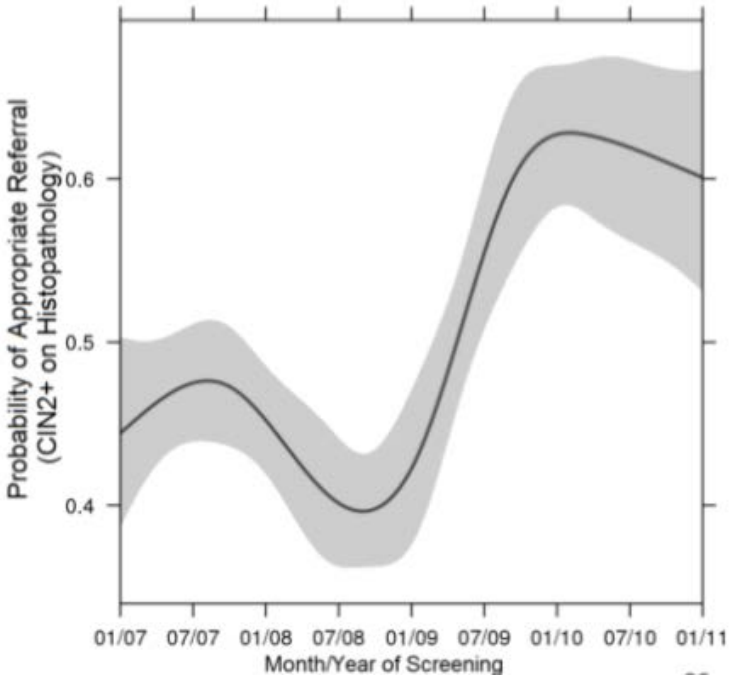
Indicators

'Same Day Services'

'Rate of Appropriate Referral'





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Tying it All Together…