NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

NNE-CTR EAC Annual Retreat

June 7, 2019

Administrative Core

Clifford Rosen MD

Gary Stein PhD

Maine Medical Center

The University of Vermont

UNIVERSITY OF SOUTHERN MAINE

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ADMINISTRATIVE CORE OBJECTIVES & OPERATING PRINCIPLES

Aim 1. The Administrative Core oversees the infrastructure that provides a foundation to support, sustain and evolve clinical and translational research in Maine, New Hampshire, and Vermont.

Aim 2. Support a transparent organizational structure with uniform policies and procedures to guide and integrate overall NNE-CTR operations.

Aim 3. Respond strategically to performance evaluations to continually realign the NNE-CTR with its mission of enhancing infrastructure and capabilities to capture opportunities that improve the health of the region.

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Invested Year 1 Carry-forward funds ($1.25M) to expand research capacity and capabilities
  - Enhanced research infrastructure (genomics, imaging and proteomics/ lipidomics, computational infrastructure and software)
  - Boot Camp Translation Facilitator training for community engagement
  - Pilot Projects
    - Paul Han (MMC) and Robert Gramling (UVM): Northern New England Palliative Care Teleconsult Research Laboratory
    - Sanchit Maruti (UVM): Emergency Department-Initiated Buprenorphine Intervention for Opioid Use Disorder

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Interactions with other CTRs and CTSAs/CTSIs
  - Sally Hodder accepted invitation to chair the NNE-CTR EAC
  - NNE-CTR PIs joined the Dartmouth SYNERGY CTSI EAC
  - Cliff Rosen appointed to EAC for the Rhode Island Advance CTR
  - Cliff Rosen continued to Chair the Mayo Clinic CTSA EAC
  - Gary Stein participated in Nebraska and Delaware CTR annual meetings
  - Initiated discussions with regional CTSAs for collaborations on shared thematically-aligned objectives
    - Dartmouth Medical School (SYNERGY)
    - UMass Medical School
  - Investigated opportunities for CTR/CTSA and CTR/INBRE initiatives
  - Maine INBRE renewed for 5 years

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Quarterly NNE-CTR Core presentations of progress to NIGMS by videoconference for evaluation and recommendations
- Provided accessible videoconferences and outreach (seminars, conferences, professional development, pilot project progress presentations)
  - Developed a series of interactive web-based sessions focused on applications for recently acquired instrumentation for genomic analysis and cellular imaging

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Promoted mission of NNE-CTR widely at MMC, UVM and other venues
  - Explored opportunities for collaborative initiatives
  - NNE-CTR leadership elected to Dartmouth COOP governing board
  - Participated in Dartmouth COOP annual meeting
  - Investigated collaborative public health-focused research initiatives with Vermont Department of Health leadership
  - Expanded content of the NNE-CTR website, and transferred website maintenance to the UVM Larner College of Medicine Office of Medical Communication
    - Databases, warehouse

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Provided periodic updates and testimony to key thought leaders and lawmakers at VT Statehouse
- Participated in the Maine Alzheimer's Summit, a meeting to engage basic, translational, and clinical researchers, as well as those involved in clinical care and advocacy, in advancing research and funding for Alzheimer's and dementia research in Maine
- Professional Development – mentoring mentors and investigators
- Organized today's External Advisory Committee Retreat
    - Speakers aligned thematically with NNE-CTR initiatives:

      Mark Levine, Commissioner of VT Dept of Health

      Robert Croyle, Director, NCI Cancer Control & Population Sciences

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Attendance/participation at annual meetings of CTRs with complementary programs and upcoming NERIC meeting at Mt. Washington
- Reciprocal working visits and seminar presentations by Pilot awardees
- Round 3 Pilot Projects reviewed by the Scientific Review Committee. Six pilots will be funded, one with Year 2 funds, the others with Year 3 funds. The Year 2 pilot is awaiting approval from NIGMS. The five Year 3 pilots are obtaining regulatory approvals and will be sent shortly to the EAC for evaluation and approval.

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Cancer Working Group - collaborating on initiatives with states and advocacy groups
  - NNE Center for Rural Health & Cancer (shared initiatives: VT, ME, NH)
  - CDC Supplemental Funding (Survivorship Care Plan, Cancer treatment rehabilitation “Steps to Wellness”)
  - HPV Messaging Success & Disparities (NCI Grant R01)
  - Biden Foundation and State Cancer Coalitions
  - Expanded CRDEB support for rural health initiatives
  - Engagement in Women’s and Men’s Health & Cancer Programs
  - Leadership for regional initiatives to collaboratively address the challenges of cancer prevention, early detection, treatment and survivorship in rural norther New England (VT, NH, ME and western MA)

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Addiction Working Group
  - Administrative Supplement awarded September 2018
  - Legislative advocacy to secure state funding for e-cig education
  - Advocacy for successful tobacco control legislation (T21)
  - Support for development of HRSA Center for Excellence for Rural Communities
  - Engagement with city and state programs to address substance abuse
  - Meetings with the Mayor of Burlington and State legislators/staff to identify options and opportunities for addiction interventions

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ADMINISTRATIVE CORE ACTIVITIES HIGHLIGHTS

- Round 3 Pilot Project Proposals:
  - New/Early Investigator 18
  - Rural focus 5
  - Addiction-related 9
  - Cancer 9
  - Cardiovascular 5

By institution:

- MMC 13
- UVM 9
- Joint MMC & UVM 5

- 5 pilot projects will be funded after July 1, 2019, using Year 3 CTR funding

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EAC SUGGESTIONS (from June 2018 Retreat)

- Encourage collaborative (multi-site) Pilots
  - Several multi-site (ME, NH, VT) have been funded. We encourage multi-site submissions when we solicit new pilots.
- Collaborate with Dartmouth CTSA
  - NNE-CTR PIs joined the Dartmouth SYNERGY CTSI EAC
  - Collaborative HEAL Initiative grant submitted
- Develop training modules and studios
  - Developed interactive web-based sessions focused on applications for recently acquired instrumentation for genomic analysis and cellular imaging. Presentations on applications given several times per year by the Translational Technologies Core
- Prioritize community engagement and projects
  - Rural Health Core in both VT and ME are prioritizing community engagement. Boot Camp Translation Facilitator training next week
- Consider “charge-backs” for Core services (i.e., genomics)
  - Maine Translational Technologies Core charges user fees.

VDH's Efforts to Address the Challenges of Health and Health Care in a Rural State
Opportunities for Collaboration with NNE-CTR

Mark A. Levine, MD, Commissioner

VERMONT
DEPARTMENT OF HEALTH

June 7, 2019

Objectives

- Public and population health 101: a vision of health equity
- Priorities from the State Health Assessment and State Health Improvement Strategies
- Potential for ongoing collaboration with academic center-based programs:
  - Survivorship
  - Rurality
  - SUD
- Challenges in cancer prevention and early detection
  - Lung cancer
  - Our State Cancer Plan

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2019-2023 State Health Improvement Plan

State Health Assessment and Plan

State Health Assessment =

What do we know about the health of Vermonters?

State Health Improvement Plan = Priorities for Vermont

What are we going to do about it?

What is the plan for all state partners, public and private, to improve health outcomes?

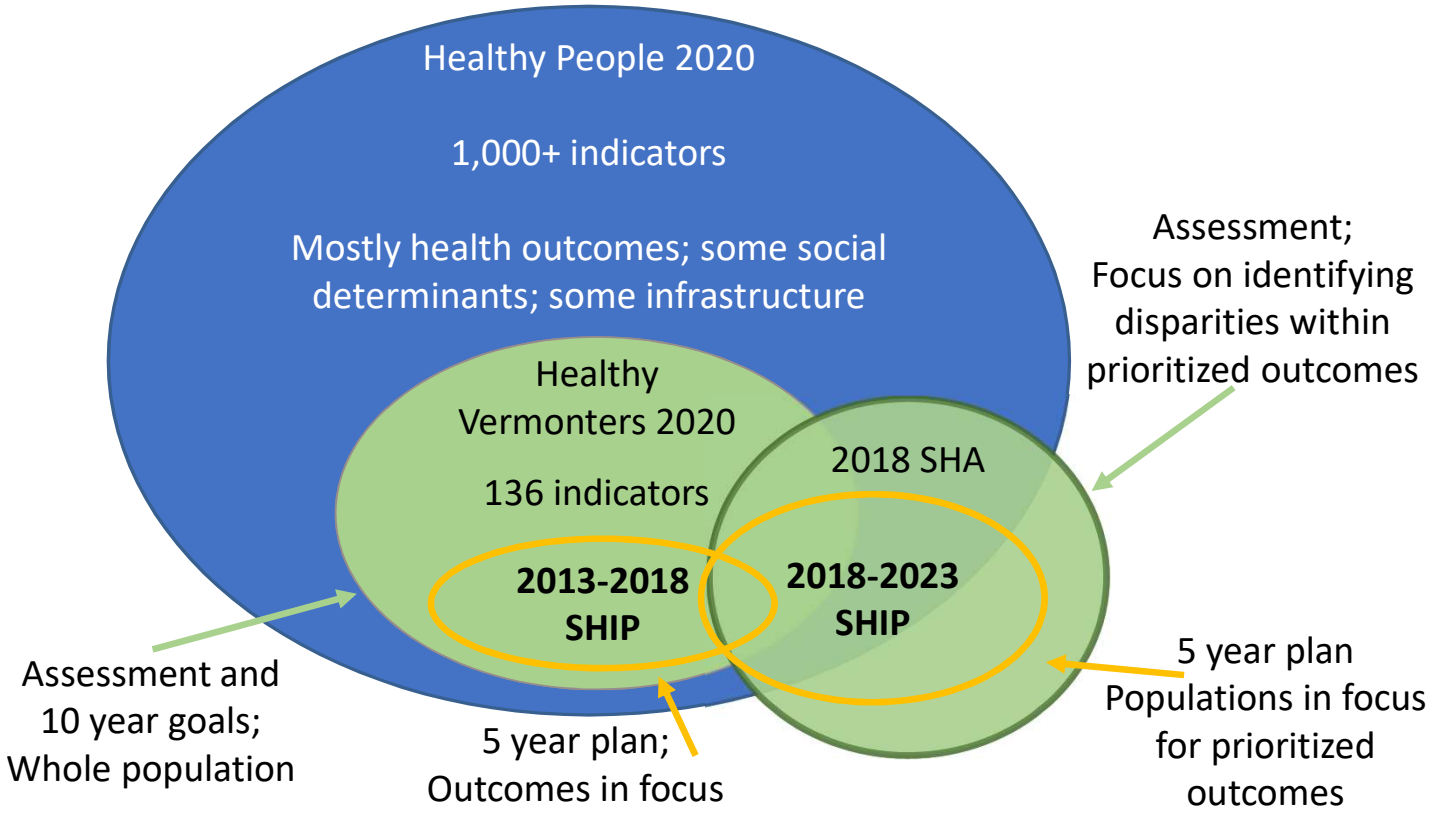
Which populations are most affected?

Disparities: Statistical differences in health that occur among populations defined by specific characteristics (e.g. age, sex) Could be from any cause.

Inequity: Differences in health outcomes that are avoidable, unfair, and shaped by condition of people's lives related to the distribution of money, power and resources.

Often associated with social categories of race, gender, ethnicity, social position, sexual orientation and disability.

SHAs and SHIPs

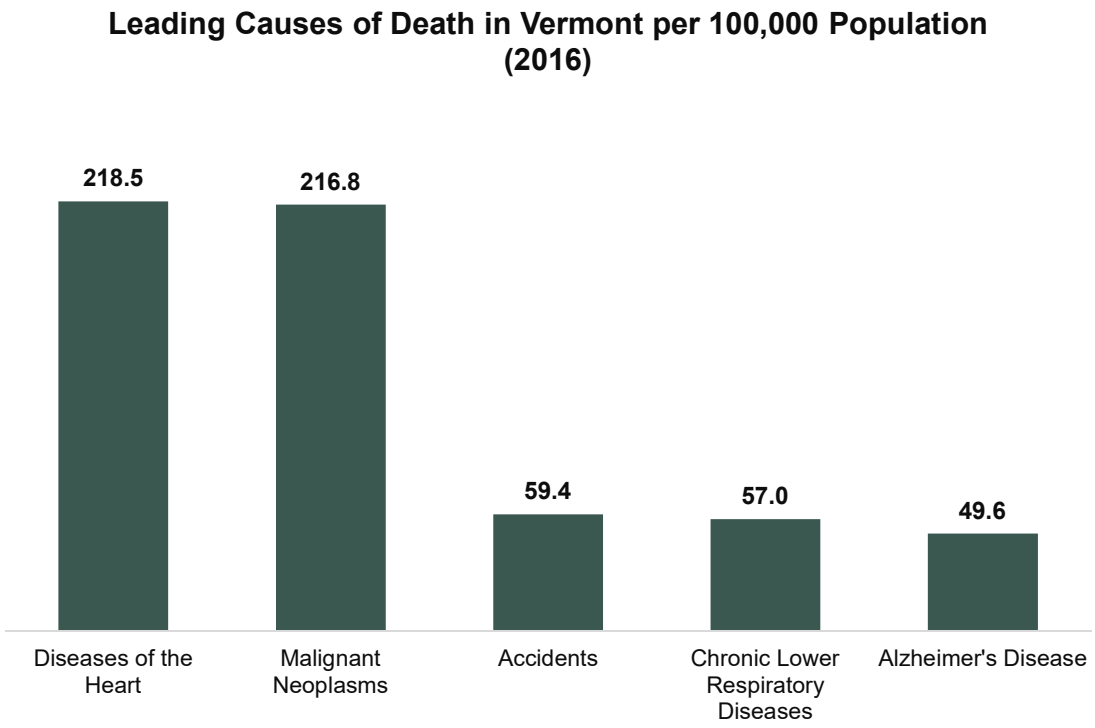


Health Equity

Health equity exists when all people have a fair and just opportunity to be healthy, especially those who have experienced socioeconomic disadvantage, historical injustice and other avoidable inequalities that are often associated with social categories of race, gender, ethnicity, social position, sexual orientation and disability.

What is Health Equity?

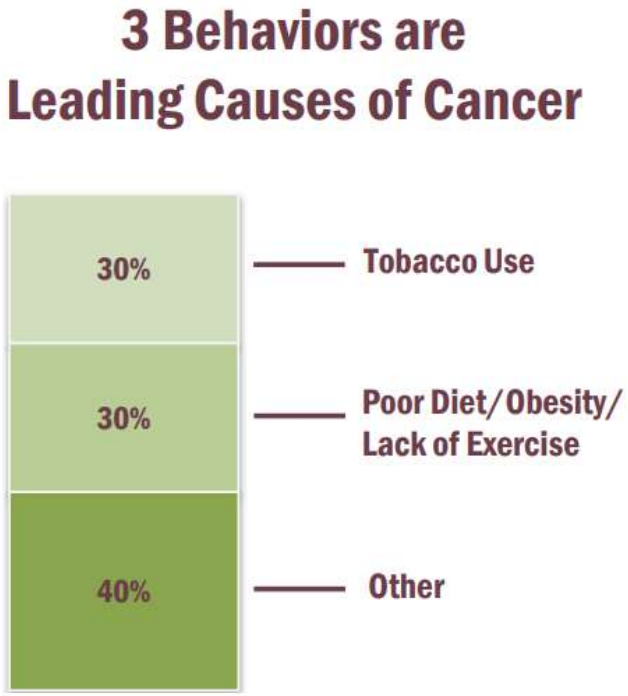
Leading Causes of Death in Vermont



Note: All rates shown are crude rates.

Data Source: VT Vital Statistics 2016

What Causes Cancer?

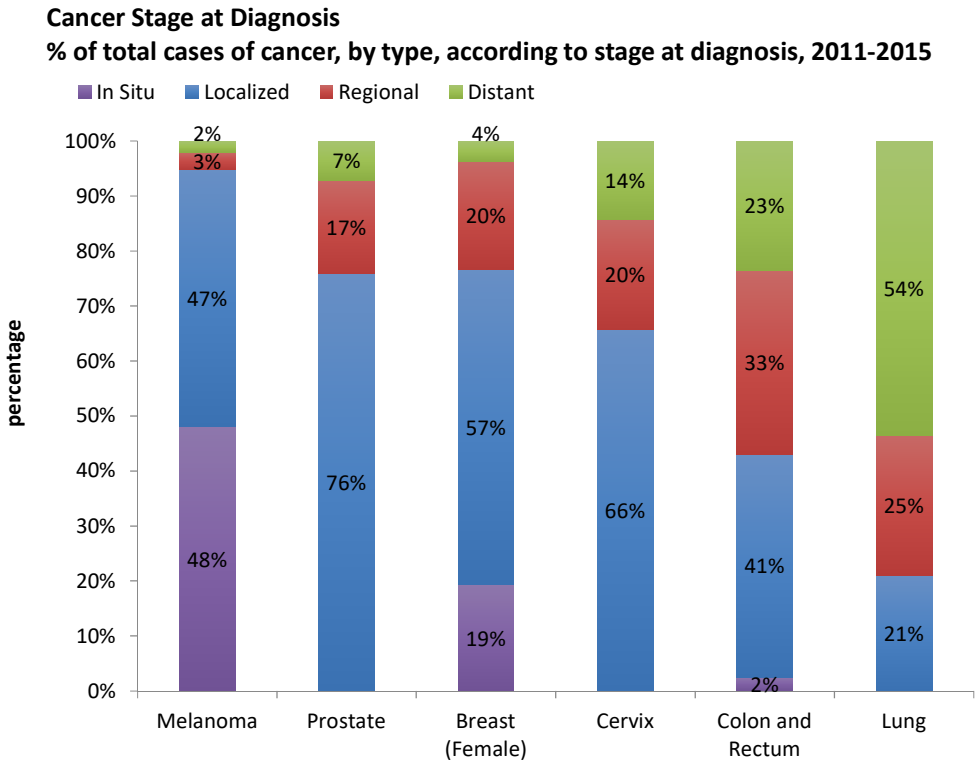


- Other causes of cancer include viruses, family history of cancer, reproductive factors, prescription drugs or medical procedures, and environmental pollution.

3 › 4 › 50
VERMONT

Source: *Cancer Causes Control*. 2012 April; 23(4): 601–608. doi:10.1007/s10552-012-9924-y.

Cancer Stage at Diagnosis



Note: Cervical cancers diagnosed as in situ are not reported to the Cancer Registry and are therefore not included in this chart. Stage of disease at diagnosis is SEER Summary Stage.

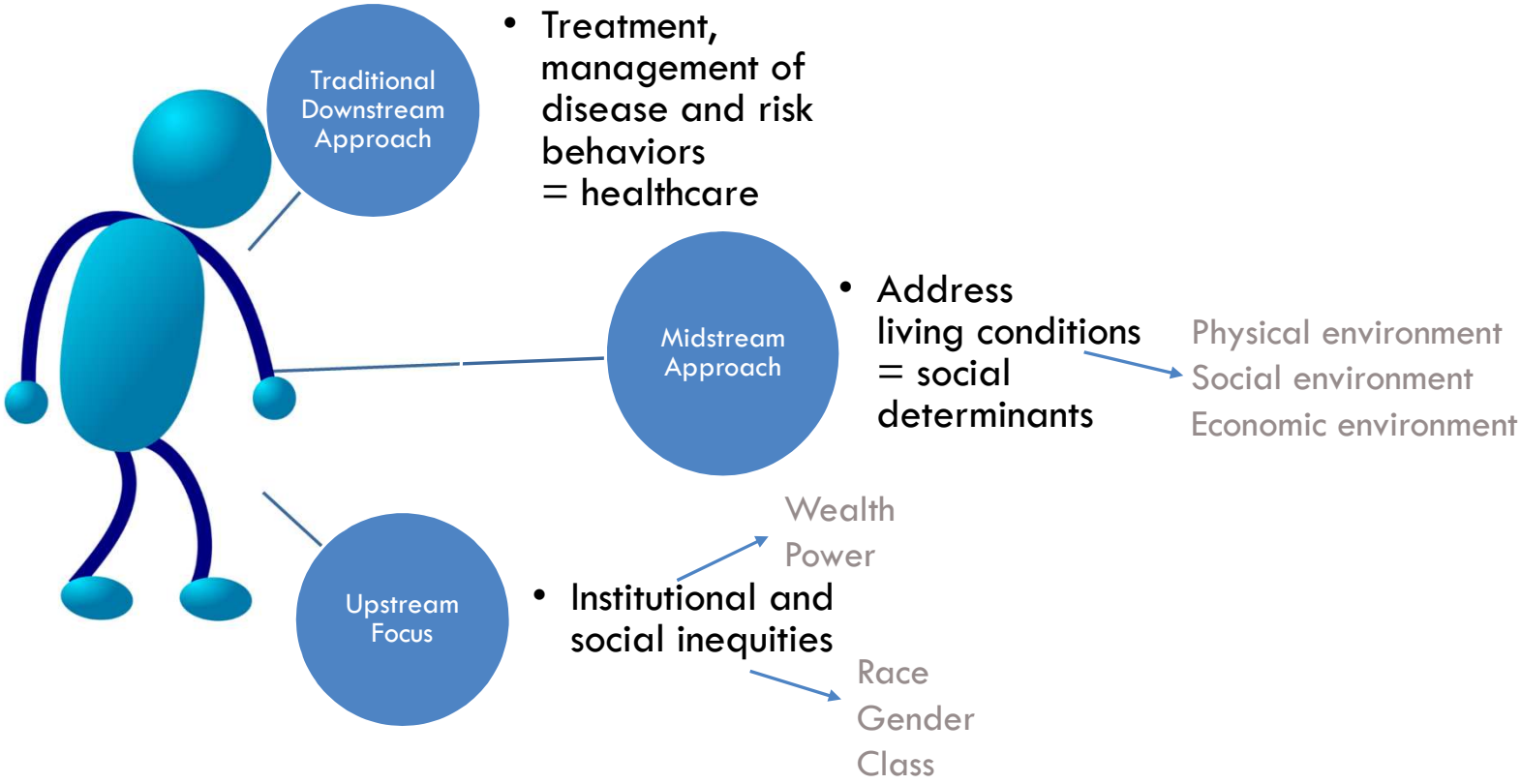
Data Source: VCR 2011-2015

From the What to the

Why to the

How

Public Health Framework for Reducing Health Inequities



In five years, if we have successfully worked towards achieving health equity, what would we have accomplished?

Vision: All people in Vermont have a fair and just opportunity to be healthy and live in healthy communities

- Everyone feels respected, valued, included, and safe to pursue healthy and meaningful lives;
- All ages, all abilities, and all Vermonters have equitable access to the conditions that create health;
- Investments are focused on prevention and the conditions that create positive health outcomes; and
- Services are available, accessible, affordable, coordinated, culturally and linguistically appropriate and offered with cultural humility.

Core Values: Equity • Affordability • Access

Priorities from the State Health Assessment

Health Conditions/Outcomes

- Child Development *(chD)*
- Chronic Disease *(CD)*
- Mental Health *(MH)*
- Oral Health *(OH)*
- Substance Use Disorder *(SU)*

Social Conditions *(SDOH)*

- Housing
- Transportation
- Food
- Income/Economic Stability

http://www.healthvermont.gov/about/reports/state-health-assessment-2018

Each strategy is designed to improve one or more priority health and social conditions (color key below) –

State Health Improvement Strategies

Invest in policies and infrastructure that create healthy communities - page 6.

Implement policies and promote norms that encourage physical activity and healthy eating, and discourage tobacco, alcohol, drug use/misuse.

Use health care reform and regulatory levers to support access to food, housing, transportation.

Expand housing and weatherization programs.

Form partnerships and shared investments to expand transportation services.

Expand community water fluoridation.

Invest in programs that promote resilience, connection and belonging - page 8.

Expand access to home visiting programs.

Promote the *Strengthening Families* system.

Expand opportunities such as mentoring, peer support and after-school programs for youth.

Implement strong school health and wellness plans, policies and programs.

Create community supports for people in recovery.

Implement *Zero Suicide* in health care systems.

Expand access to integrated person-centered care - page 10.

Integrate oral health, mental health, substance use disorder prevention into primary care.

Create a universal system for developmental screening and referrals for children and families.

Implement SBINS* for health behaviors, housing, transportation, food and economic security.

Integrate oral health into health care practice and other settings (nursing homes, schools, etc.).

Promote practice improvements and professional development for early care and learning providers.

* Screening, Brief Intervention & Navigation to Services

Adopt organizational and institutional practices that advance equity - page 12.

Meaningful community engagement • Equitable programs, policies and budgets • Respectful care and services • Informed actions and decisions

KEY – Child Development · Chronic Disease Prevention · Mental Health · Oral Health · Substance Use Prevention · Housing, Transportation, Food & Economic Security

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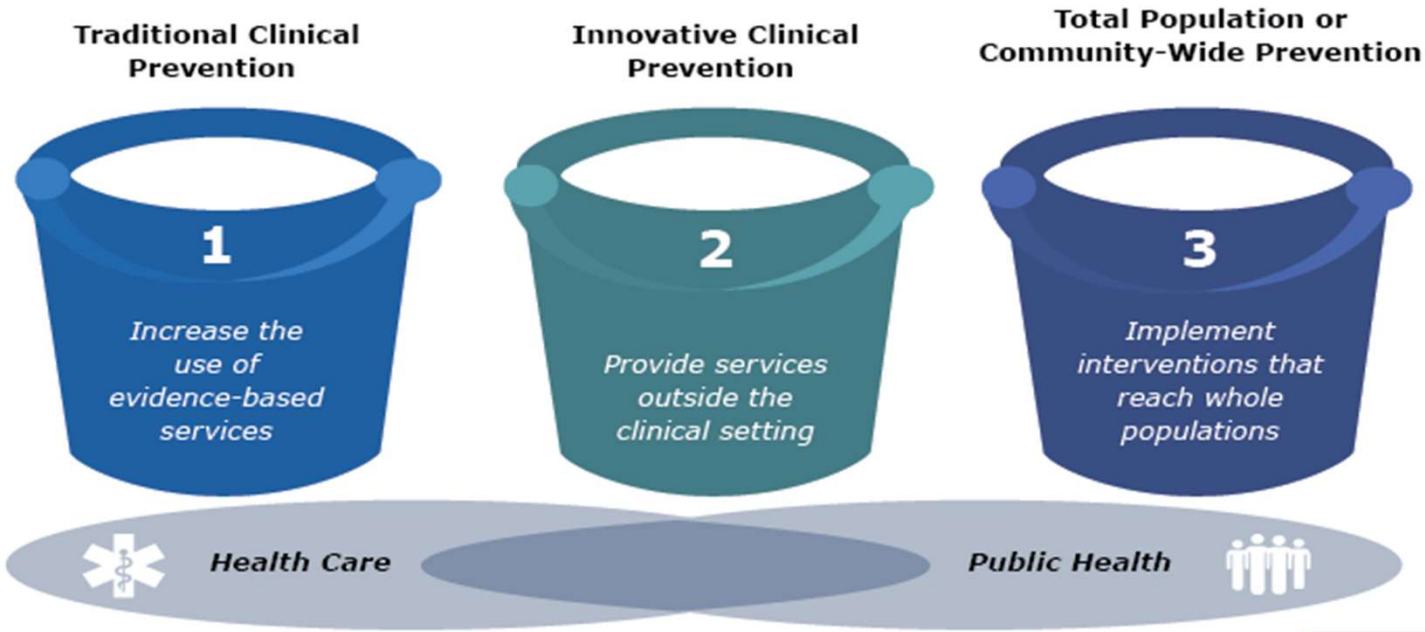
Framework for Strategies with Health Care Partners



To read more: http://journal.lww.com/jphmp/toc/publishahead

Objectives

- Public and population health 101: a vision of health equity
- Priorities from the State Health Assessment and State Health Improvement Strategies
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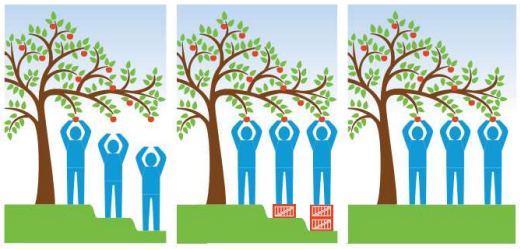
Disparities

Reduce cancer-related disparities in Vermont

- Disparities objectives across the Cancer Continuum
- Priority Populations:
  - Low-Income Vermonters (<250% FPL)
  - Cancer Survivors



Health equity exists when all people have a fair and just opportunity to be healthy – especially those who have experienced socioeconomic disadvantage, historical injustice, and other avoidable systemic inequalities that are often associated with social categories of race, gender, ethnicity, social position, sexual orientation, and disability.

Cancer Survivorship

- Approximately 8% or 39,000 adult Vermonters report having ever been diagnosed with cancer (BRFSS, 2016).
- Several layers of collaboration on work in Vermont related to cancer survivor physical and emotional health
- VTAAC Quality of Life workgroup coordinates, supports and promotes work of many partners addressing cancer survivorship
- Upcoming UVM Cancer Center – Department of Health collaboration CDC Survivorship Supplemental funds
  - Focus: Cancer survivor care and patient navigation

Rurality

- Differences in health equity in rural vs. urban settings.
- Rural communities are hard to define in largely rural states
- Department of Health Rural-Urban Workgroup
  - Looking to identify consistent definitions for use in data analysis across the Department.
  - Exploring use of Rural-Urban Commuting Area (RUCA) to define rurality.

Rurality

Journal of oncology practice
The Authoritative Resource for Practicing Oncology
University of Vermont Medical Center
VERMONT DEPARTMENT OF HEALTH
Vermont Cancer Registry

Access to Care in Vermont: Factors Linked with Time to Chemotherapy for Women with Breast Cancer

Purpose:

In the rural United States, there are multiple potential barriers to the timely initiation of chemotherapy. The goal of this study was to identify factors associated with delays in the time from initial diagnosis to first systemic therapy (TTC) among women with breast cancer in Vermont.

Methods:

Using data from the Vermont Cancer Registry, we explored TTC for 702 female Vermont residents diagnosed with stage I to III breast cancer between 2006 and 2010 who received adjuvant chemotherapy. Multivariable linear regression was used to evaluate the associations between TTC and patient, tumor, treatment, and geographic variables.

Results:

Mean TTC was 10.2 weeks. Longer drive time ($P < .001$), more invasive surgery ($P = .01$), and breast reconstruction ($P < .001$) were each associated with longer TTC. Each additional 15 minutes of drive time was associated with a 0.34-week (95% CI, 0.22 to 0.46 weeks) increase in TTC. Participants age younger than 65 years whose primary payer was Medicare (n = 27) had significantly longer average TTC, by 2.37 weeks ($P = .001$), compared with those with private or military insurance. There was also substantial variation in TTC across hospitals ($P < .001$).

Conclusion:

Most female patients with stage I to III breast cancer in Vermont are receiving adjuvant chemotherapy within the National Comprehensive Cancer Network–recommended timeframe; however, improvements remain needed for certain subgroups. Novel approaches for women with long drive times need to be developed and evaluated in the community. Variation in TTC by hospital, even after adjusting for patient, tumor, and treatment factors, also suggests opportunities for process improvement.

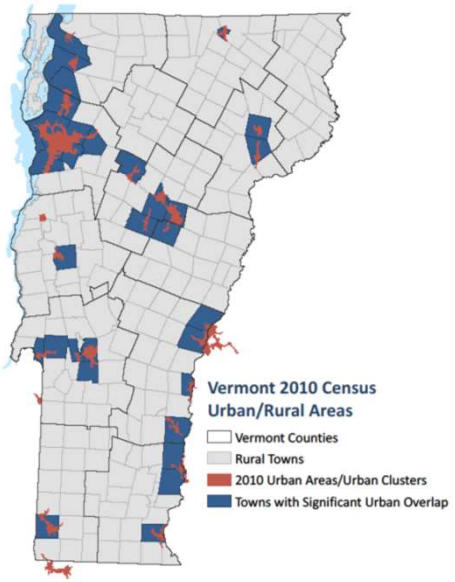


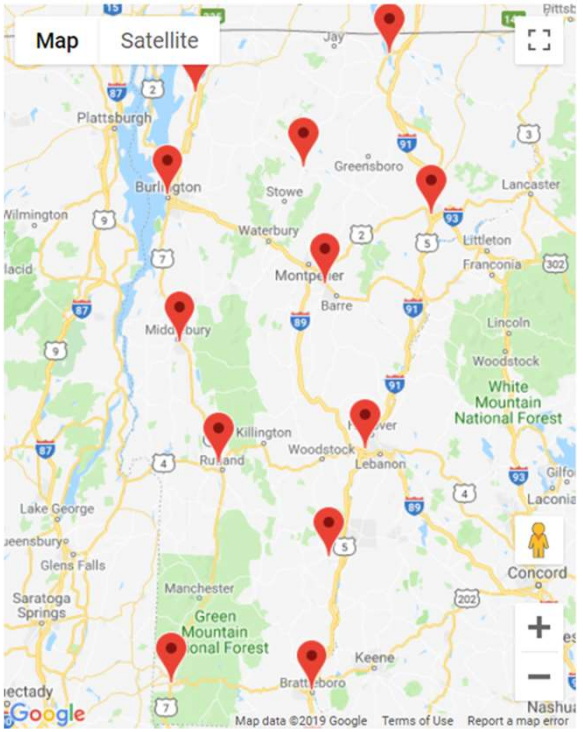
Table 2. Linear Regression Results for Models of TTC As Function of Various Patient, Tumor, Treatment, and Geographic Variables

Variable	Unadjusted Estimated ΔTTC (weeks)	Unadjusted 95% CI	Unadjusted P	Hospital Adjusted Estimated ΔTTC (weeks)	Hospital Adjusted 95% CI	Hospital Adjusted P	Multivariable Adjusted* Estimated ΔTTC (weeks)	Multivariable Adjusted* 95% CI	Multivariable Adjusted* P
Stage			.115			.052			.155
I	Referent			Referent			Referent		
II	−0.32	−0.97 to 0.34	.341	−0.63	−1.24 to −0.03	.041	−0.60	−1.24 to 0.04	.067
III	0.58	−0.31 to 1.47	.202	0.13	−0.70 to 0.95	.760	−0.13	−1.05 to 0.79	.784
Surgery			< .001			.002			.009
Partial mastectomy	Referent			Referent			Referent		
Total mastectomy	1.39	0.71 to 2.08	< .001	1.06	0.42 to1.71	.001	0.64	−0.14 to 1.42	.106
Other mastectomy or unspecified mastectomy	1.84	0.86 to 2.81	< .001	0.54	−0.01 to 1.09	.052	1.56	0.53 to 2.59	.003
Reconstruction			< .001			< .001			< .001
No	Referent			Referent			Referent		
Yes	2.38	1.42 to 3.34	< .001	1.66	0.75 to 2.57	< .001	2.22	1.13 to 3.31	< .001
10-year increase in age	0.02	−0.01 to 0.05	.124	0.16	−0.12 to 0.43	.260	0.30	−0.01 to 0.60	.055
Hospital			< .001						< .001
County			< .001			.100			< .001
Rural or urban (n = 701)†			.061			.802			.068
Rural	Referent			Referent			Referent		
Urban	−0.57	−1.16 to 0.03	.061	0.07	−0.49 to 0.64	.80	−0.54	−1.12 to 0.04	.068
Drive time (n = 699)†			< .001			.207			< .001
15-minute increase	0.37	0.25 to 0.49	< .001	0.09	−0.05 to 0.24	.207	0.34	0.22 to 0.46	< .001

http://www.healthvermont.gov/sites/default/files/documents/2017/02/stat_cancer_JOP.2016.pdf

Local Health Offices – Chronic Disease

- All 12 Local Health Offices addressing chronic disease
- Chronic Disease Designees & other key staff
- Offices engage worksites, schools, providers, municipalities & faith communities to consider policy development and environmental changes that promote health and well being



Local Health Offices – Activities

- Promotion of 3-4-50 in multiple sectors
- Healthy community design
- Tobacco Prevention – working with local coalitions
- Sun safety program local support
- HPV activities with providers & northwestern VT high school clinics
- Cancer screening QI activities with providers
- Many other community-based prevention activities!

Brattleboro OLH Dress in Blue Day for Colorectal Cancer Awareness

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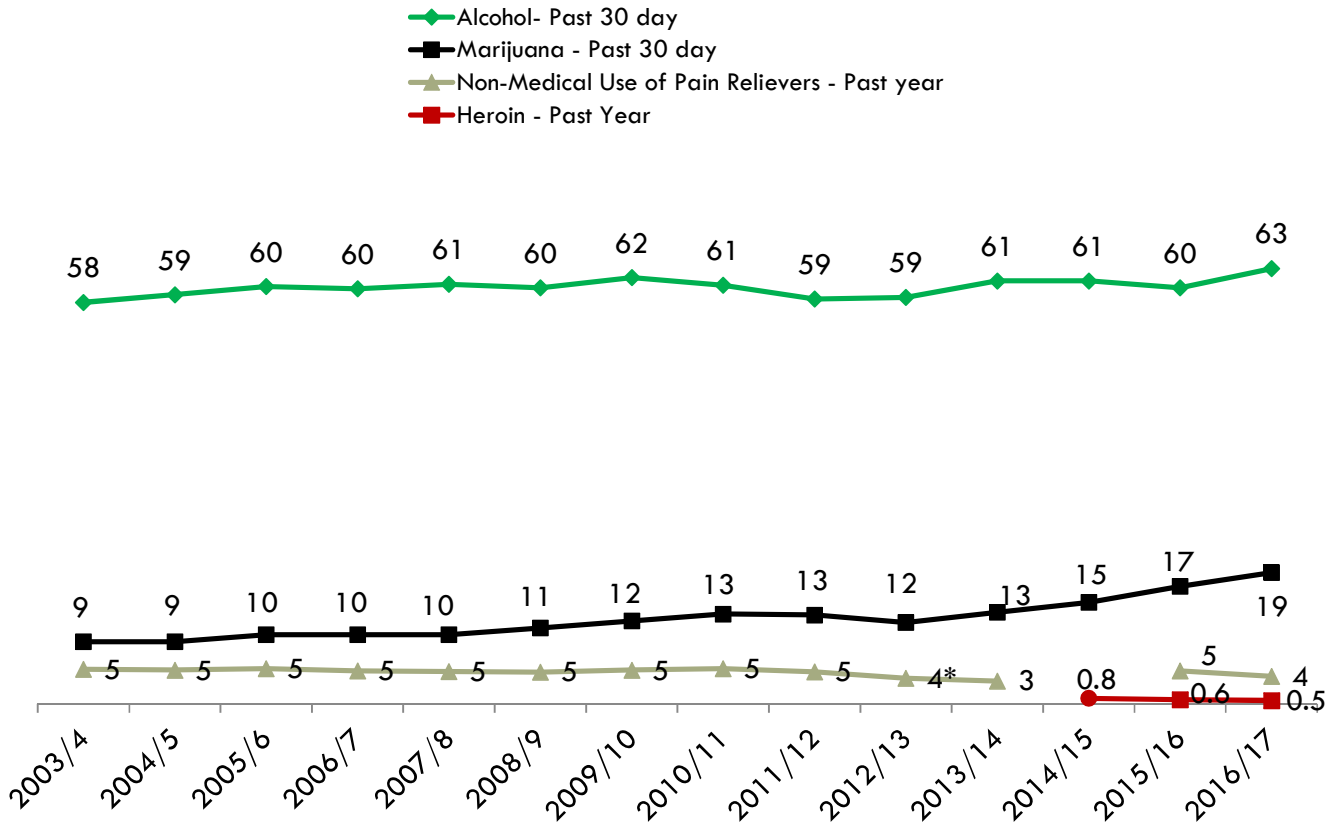
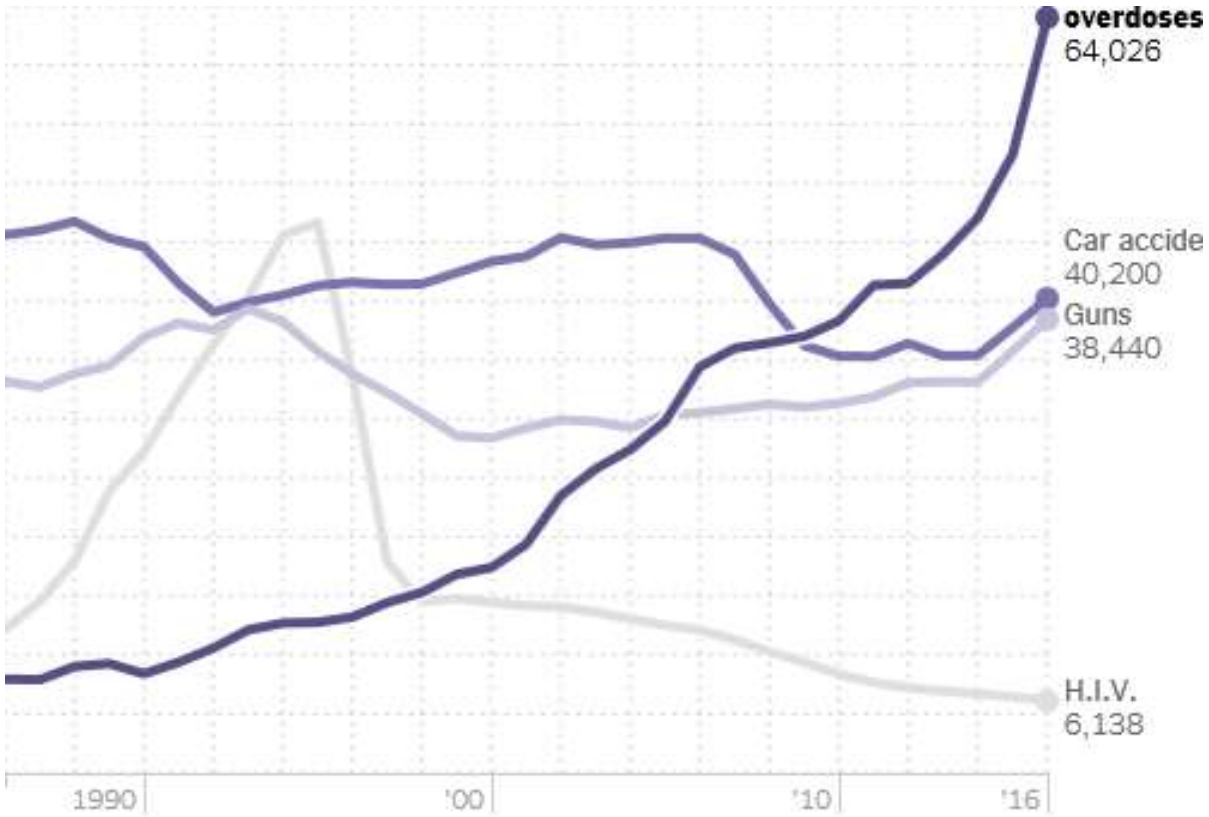
Substances Used by Vermonters ages 12+ by Substance Type

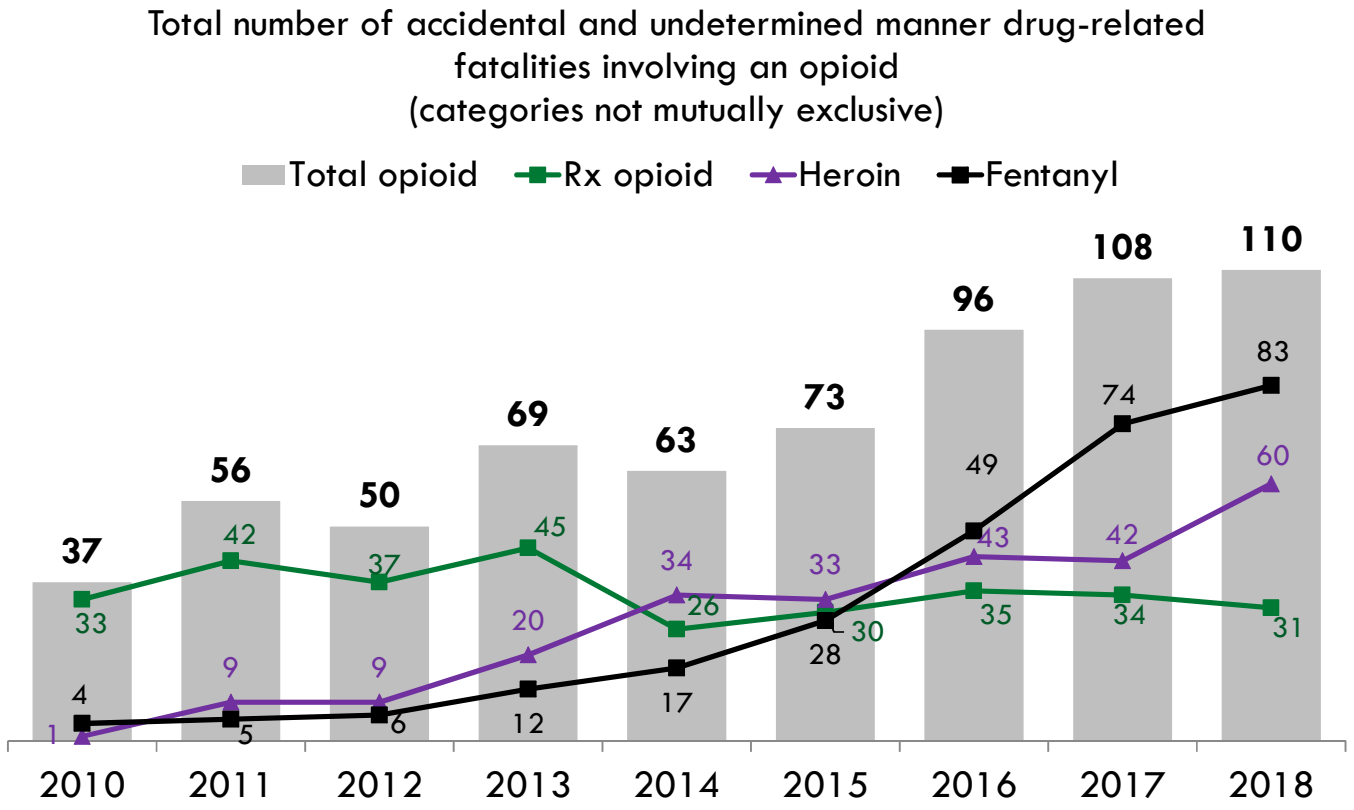


Source: National Survey on Drug Use and Health, 2002-2016. Methodology changes for Rx drug occurred in 2015
Note: * delineates a significant drop since 2011/2012 ($p<0.05$)

US Drug overdoses have overtaken car accidents, guns and HIV as cause of death and are leading cause under age 50

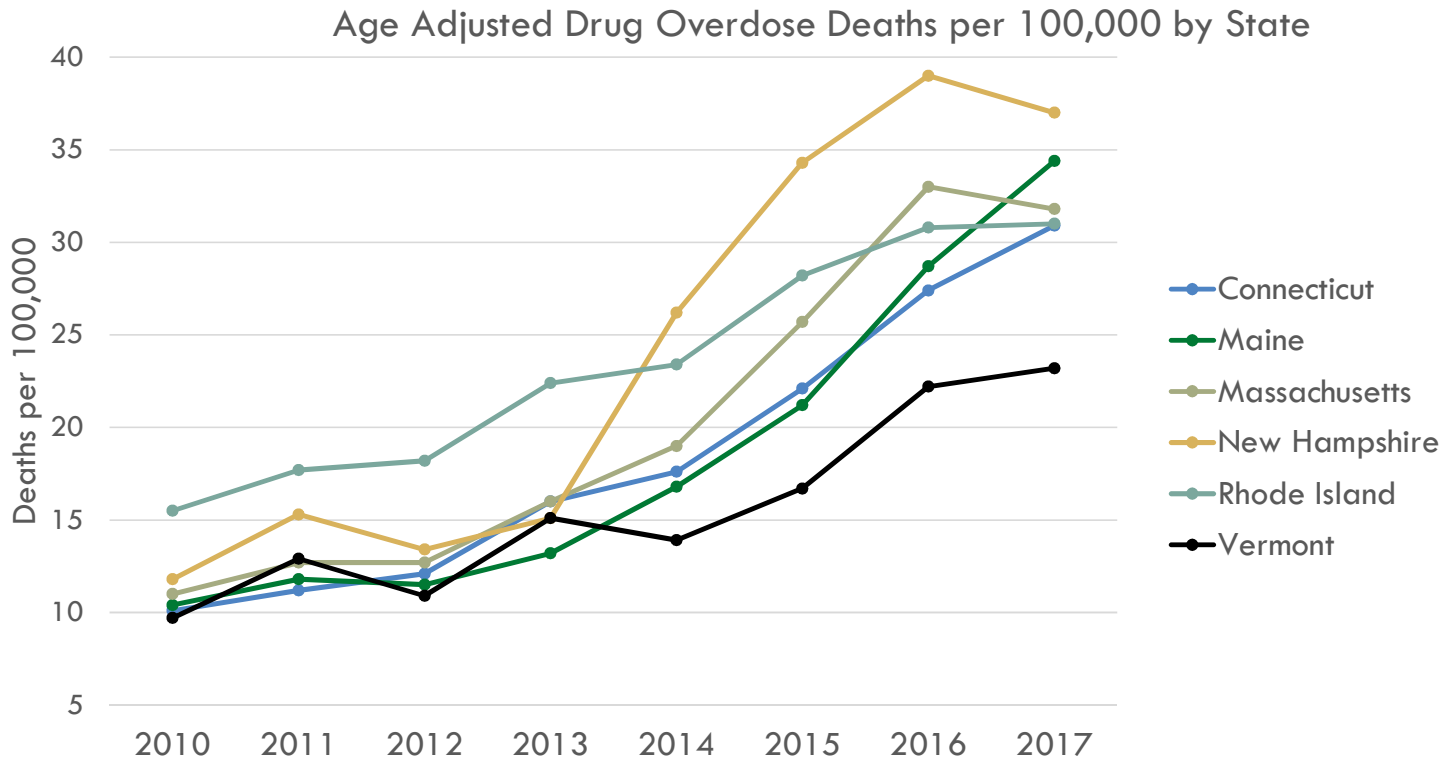


Drug-Related Fatalities Involving Opioids



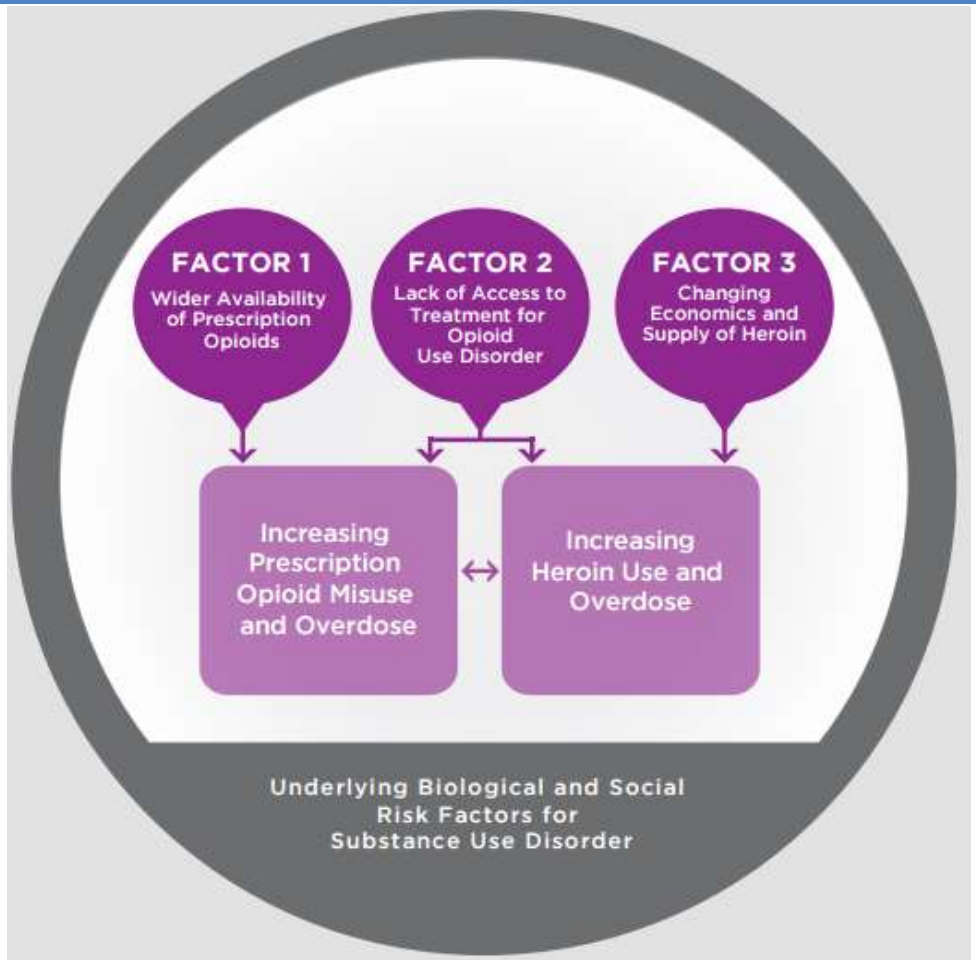
Source: Vermont Department of Health Vital Statistics System

New England - Any Drug Overdose Deaths



Source: CDC/ NCHS

Major Factors Driving the Prescription Opioid and Heroin Epidemic



Source: NGA

The Basic Three Components that any State Must Prioritize

1. Prescriber-focused prevention: decrease circulating supply, develop clinical and surveillance tools.
2. Harm reduction-focused: improve naloxone availability.
3. Treatment-focused: expand access to Medication-Assisted Treatment.

Vermont's Prescriber Rules and PDMP

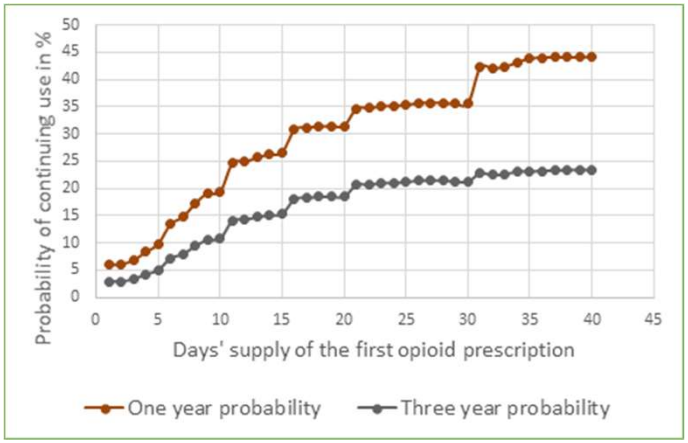
The Problem

- As many as four out of five heroin users begin by abusing prescription drugs
- Of those who abuse prescription opioids, seven out of 10 received these drugs through methods of diversion
- Opioids are overprescribed. They are prescribed:
  - Too often
  - At too high a dose
  - For too long
- Prescribers play a role in the supply and use of opioids in communities.

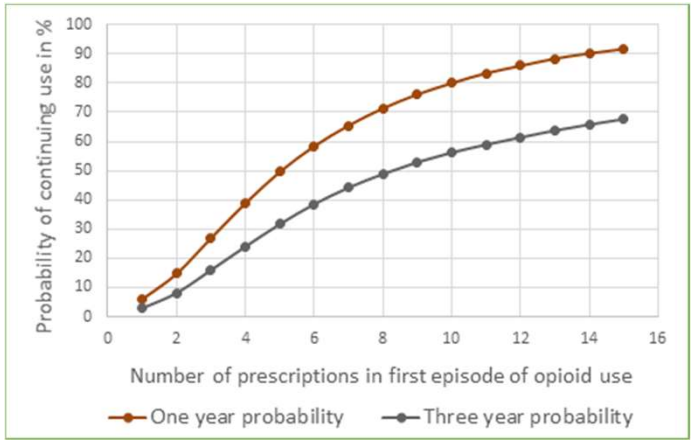
The more opioids prescribed during the first episode of opioid use, the greater the likelihood of continued opioid use

Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015

One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply* of the first opioid prescription — United States, 2006–2015

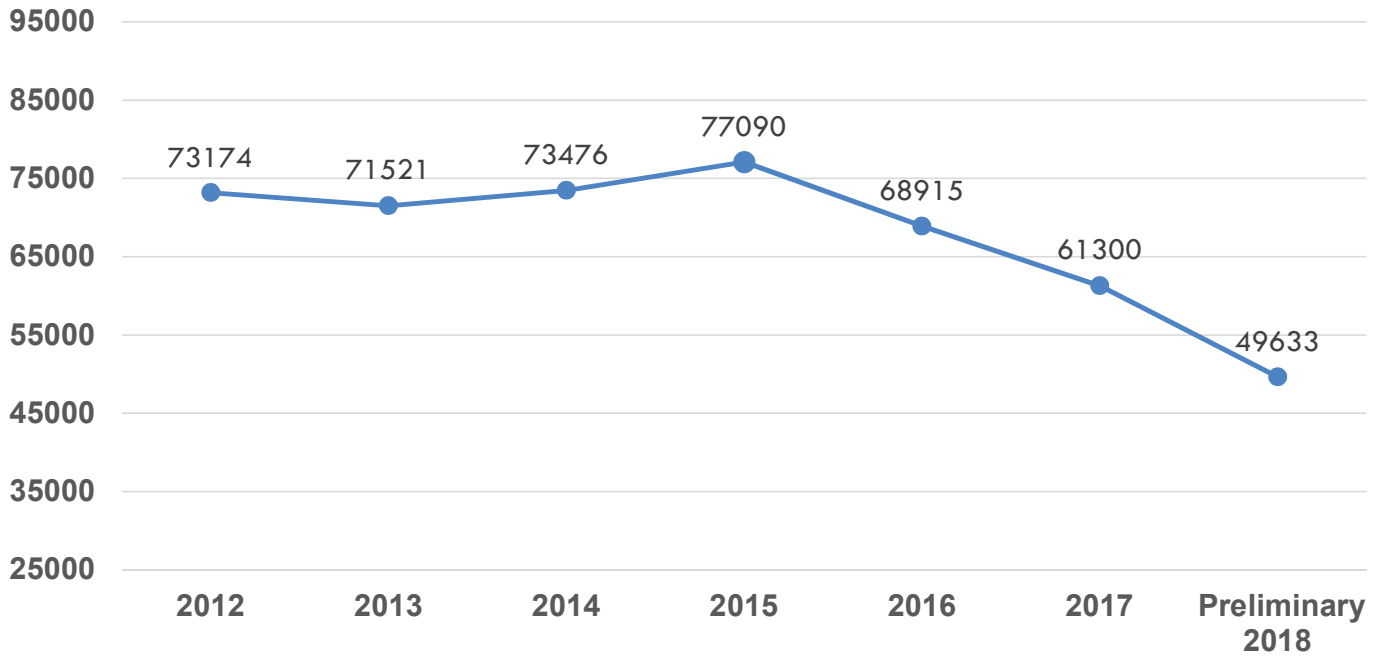


One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of prescriptions* in the first episode of opioid use — United States, 2006–2015



Source: Shah A, Hayes CJ, Martin BC. Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:265–269. DOI: http://dx.doi.org/10.15585/mmwr.mm6610a1.

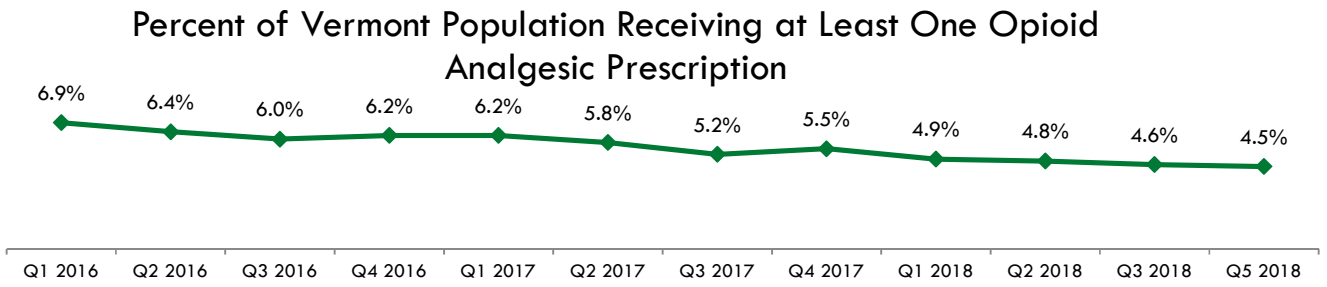
Fewer Opioid Pain Relievers are Being Dispensed in Vermont - Total MME Opioid Analgesics per 100 Residents



Note: Prior to rescheduling tramadol was not reported to VPMS. On August 14, 2014 tramadol was changed from a schedule V to a schedule IV drug. There was a 36% decrease in dispensed opioids between 2015 and 2018, years that include tramadol.

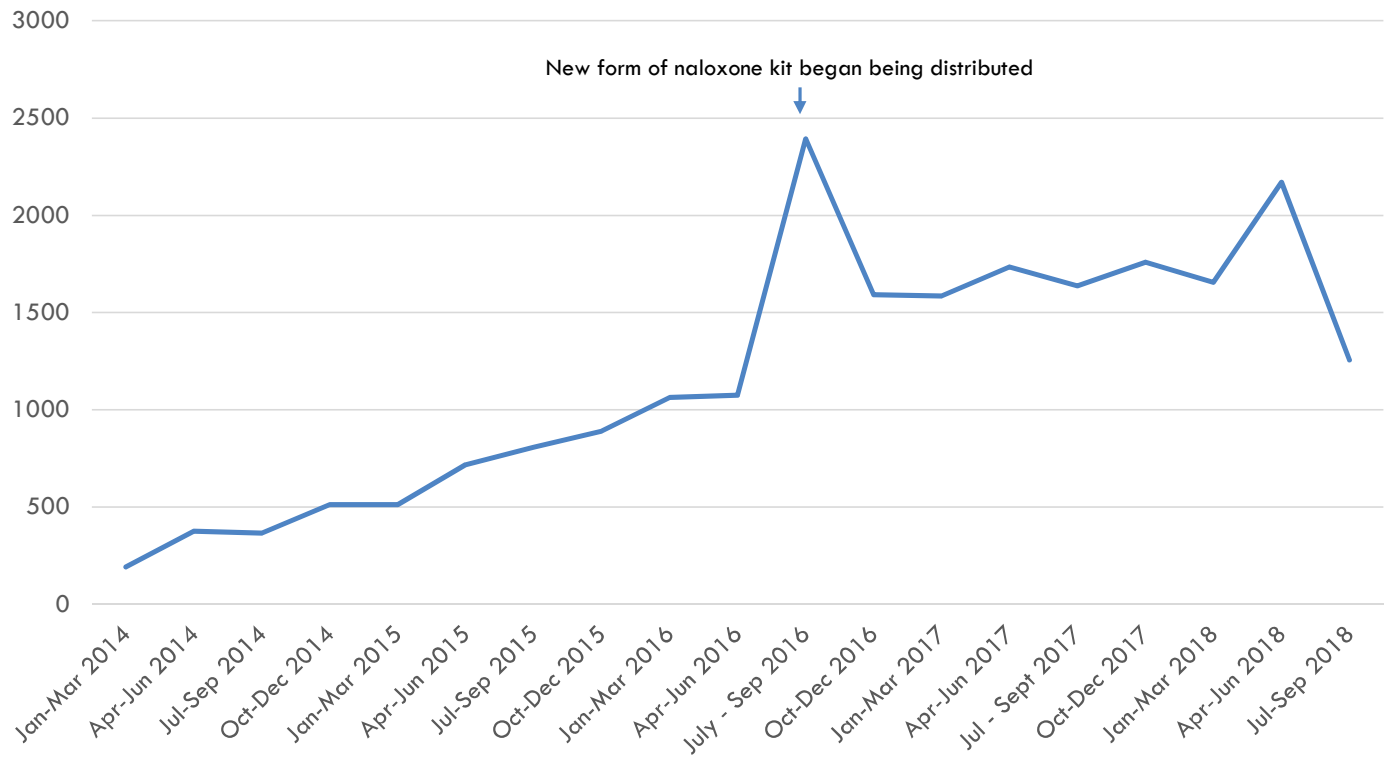
Data Source: VPMS

Statewide VPMS Quarterly Trends

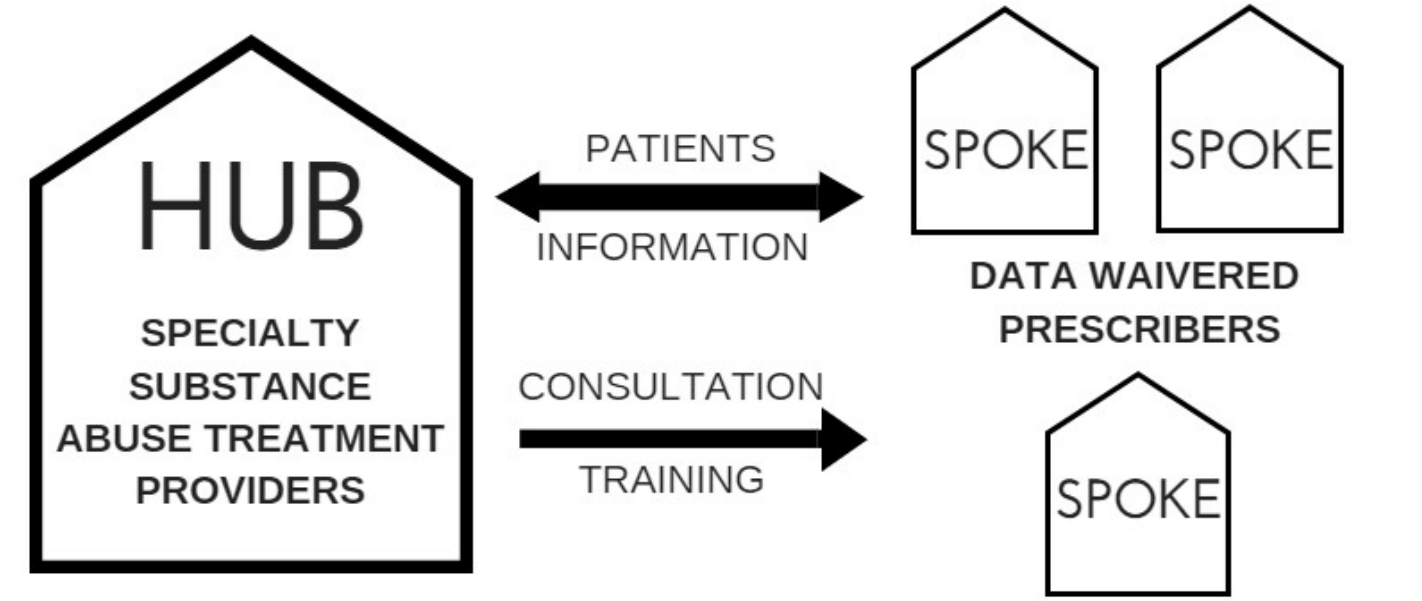


Data Source: VPMS Reports

Number of naloxone kits distributed to community members



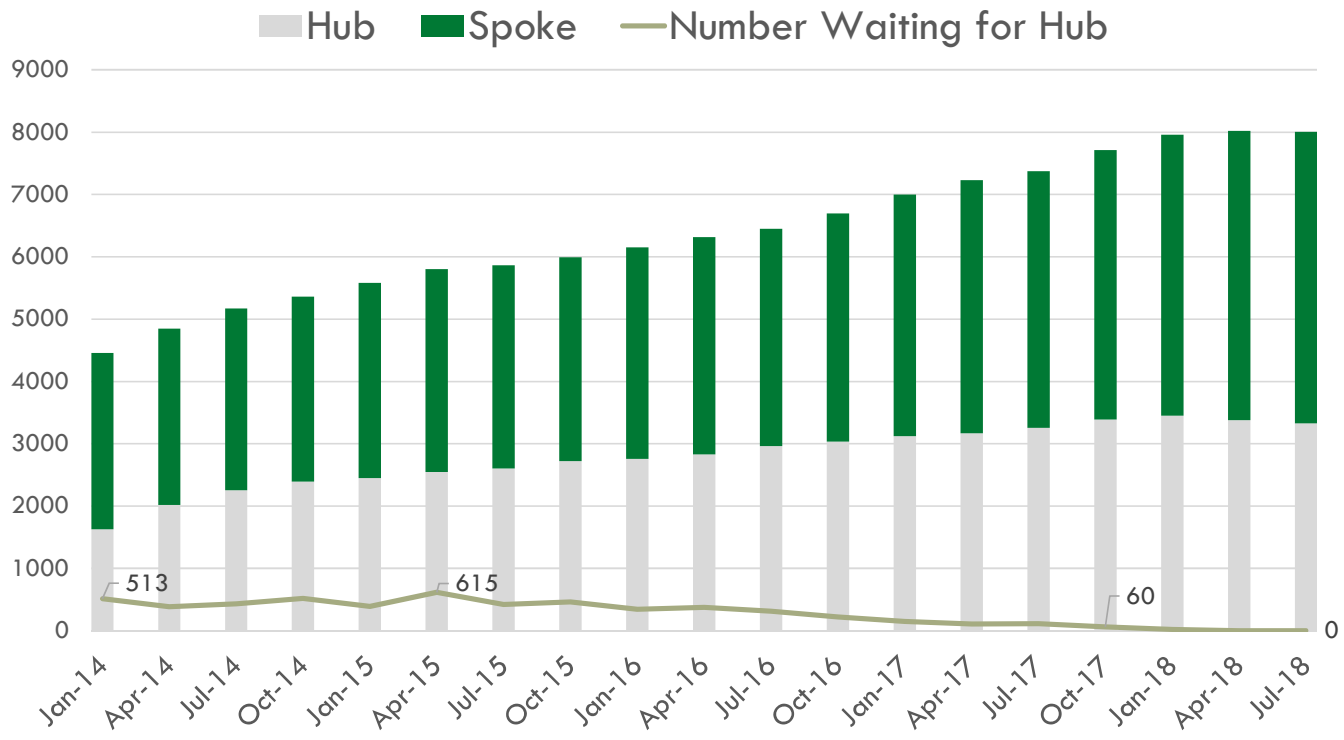
Hub and Spoke



High-intensity MAT
Methadone, buprenorphine, naltrexone
Regional locations

Maintenance MAT
Buprenorphine, naltrexone
Community locations
Prescriber + nurse + licensed counselor

Number of Vermonters Age 18-64 receiving MAT in hubs and spokes and number waiting for services over time



Source: SATIS, Provider Waitlist, VPMS

Our Future is in Prevention-Across the Lifespan

- Messaging campaigns and education to raise awareness, address stigma.
- Evidence-based nurse practitioner home visiting models – ACEs reduction.
- Afterschool curricula and activities for adolescents – the "third space".
- Iceland model – community activation, parental investment, youth voice.
- School-based primary prevention programs.
- Community mobilization – developing and expanding community coalitions.

Objectives

- Challenges in cancer prevention and early detection
  - Lung cancer
  - Our State Cancer Plan

Vermont Cancer Plan and the Continuum of Care

2016 – 2020 VERMONT CANCER PLAN

A FRAMEWORK FOR ACTION

VERMONT
DEPARTMENT OF HEALTH

VTAAC
Vermonters Taking Action Against Cancer

Shared goals, objectives and strategies for reducing the burden of cancer in Vermont

Vermont Cancer Plan Goals

Disparities
Reduce cancer-related disparities in Vermont.

Prevention
Prevent cancer from occurring or recurring.

Early Detection
Detect cancer at its earliest stages.

Cancer Directed Therapy & Supportive Care
Treat cancer with appropriate, quality care.

Survivorship & End-of-Life Care
Assure the highest quality of life possible for cancer survivors.

- ✓ Measurable Objectives
- ✓ Specific Targets
- ✓ Suggested Strategies

Cancer Program Integration

Department of Health Cancer Programs

- Vermont Cancer Registry
- You First
- Comprehensive Cancer Control (CCC)
  - Supports Statewide Coalition VTAAC

YOU FIRST
Screening and support for heart disease, breast and cervical cancer.

VTAAC
Vermonters Taking Action Against Cancer

Interconnected Programs

- Gary Stein Co-Chair of VTAAC
- CCC Coordinator (Sharon Mallory) on Clinical & Translational research cancer working group
- You First Coordinator (Nancy Kaplan) on UVM CC Community Advisory Board

THE University of Vermont CANCER CENTER

Socioeconomic Status

Cervical Cancer Screening**

Women 21 to 65 with some college are significantly less likely to meet cervical cancer screening recommendations than those with more education.

Women 25 to 44 are significantly more likely to meet cervical cancer screening recommendations, in comparison to women in other age groups.

Women 21 to 65 in homes making <$25,000 annually are significantly less likely than those with more income to be screened for cervical cancer.

Breast Cancer Screening

Women 50 to 74 in homes making $75,000+ per year are significantly more likely than those in homes making less than $50,000 annually to have had a mammogram.

Colorectal Cancer Screening

Adults 50 to 74 with a high school education or less are significantly less likely to meet colorectal cancer screening recommendations in comparison to those with a college education or higher.

Adults 50 to 74 with low annual household incomes (<$25,000/year) are significantly less likely than those with incomes of at least $50,000 to meet colorectal cancer screening guidelines.

Note: All data is age adjusted to the U.S. 2000 population, except statistics broken down by age only.
**Usually women who have had a hysterectomy are excluded from cervical cancer screening calculations. In 2016, women 45-65 were not asked whether they've had a hysterectomy, and as such the proportion meeting PAP test screening recommendations is underestimated.

Data Source: Breast, Cervical, Colorectal: BRFSS 2016;
Lung: BRFSS 2017

Example - Lung Cancer

Vermont Cancer Plan

Goal 10. Increase early detection of lung cancer among Vermonters.

	Objectives	Measures: BASELINE (YEAR)	Measures: **TARGET (2020)**
10.1	Decrease rate of lung cancer diagnosed at an advanced stage among adults 55+. (Per 100,000 persons, Data Source: VCR)*	210.0 (2008-2012)	**199.5**
10.2	Decrease % of lung cancers diagnosed at an advanced stage among adults 55+. (Data Source: VCR)	80% (2008-2012)	**76%**
10.2	Increase % of adults age 55-80 who are current or former smokers (quit within 15 years) with no history of cancer who had discussed lung cancer screening with a health care provider. (Data Source: Adult Tobacco Survey)	N/A	**N/A**

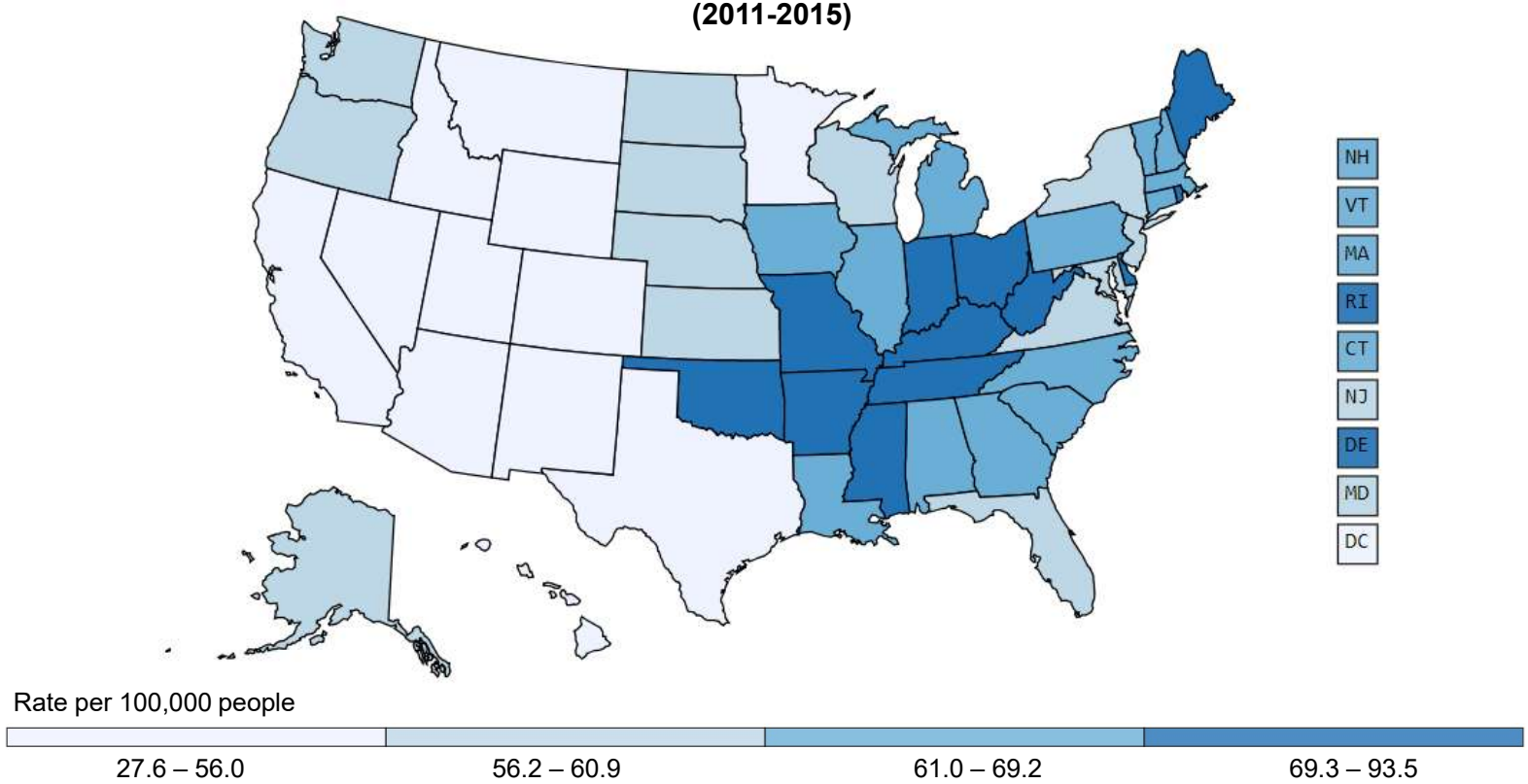
* Measure is age adjusted to the 2000 U.S. standard population.

Strategies

- Promote nationally recognized lung cancer screening guidelines to health care providers and to the public.
- Conduct provider and public education and training to increase awareness of the need for lung cancer screening and the use of risk assessment to determine who should be screened.
- Develop a system for measuring the number of Vermonters receiving lung cancer screening.
- Increase the capacity of hospitals to screen adults for lung cancer.

How do Vermont Lung Cancer Incidence Rates Compare to Other States?

New Cases of Lung and Bronchus Cancers, Rate per 100,000 persons (2011-2015)

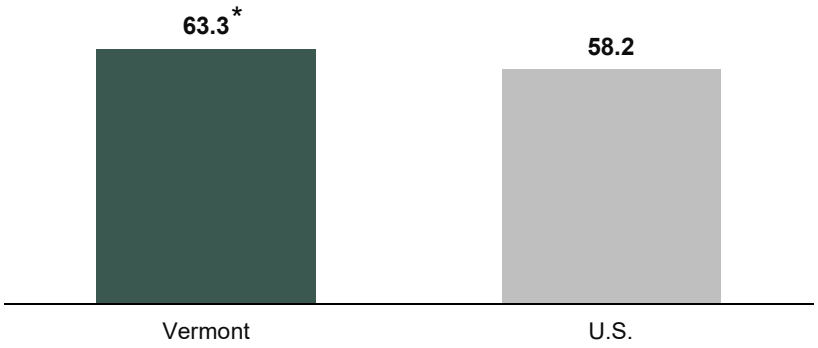


Data Source: U.S. Cancer Statistics 2011-2015

Lung Cancer Incidence

From 2011 to 2015, there were about 522 cases of lung cancer per year in Vermont.

Lung and Bronchus Cancer Incidence in Vermont and U.S., Rates per 100,000 persons, 2011-2015



Note: All rates are age-adjusted to the 2000 U.S. standard population.

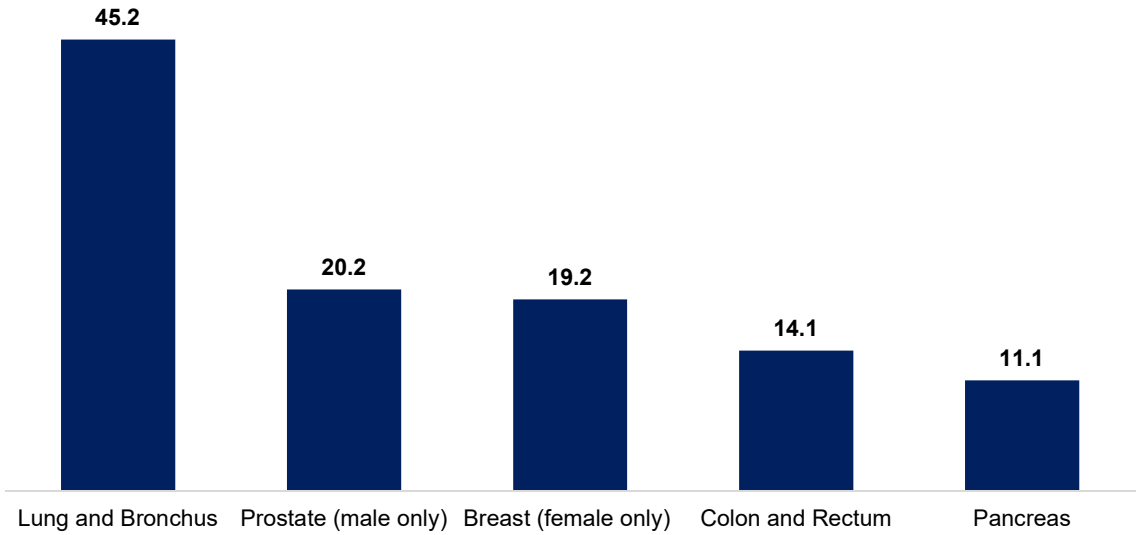
*Statistically higher than the U.S. rate.

Data can be accessed at http://www.healthvermont.gov/health-statistics-vital-records/surveillance-reporting-topic/cancer Under "Age Adjusted Incidence and Mortality Rates".

Data Source: VCR 2011-2015

Lung Cancer Mortality

Top 5 Fatal Cancers in Vermont per 100,000 Population (2011-2015)



Note: All rates are age-adjusted to the 2000 U.S. standard population.

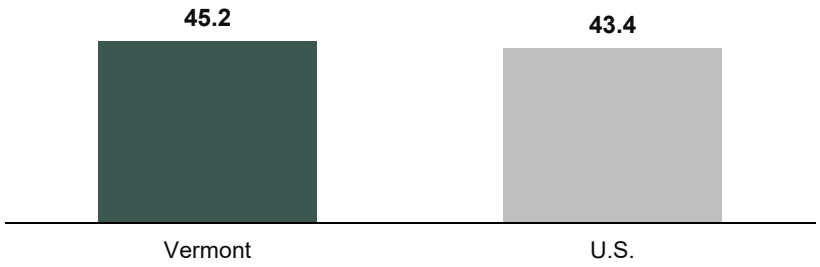
Vermont is ranked 18th lowest in the U.S. for lung cancer mortality.

Data Source: VT Vital Statistics 2011-2015

Lung Cancer Mortality

There is no statistically significant difference in the lung cancer mortality rate between Vermont and the U.S.

Lung and Bronchus Cancer Mortality Rates in Vermont and U.S., Rates per 100,000 persons, 2011-2015



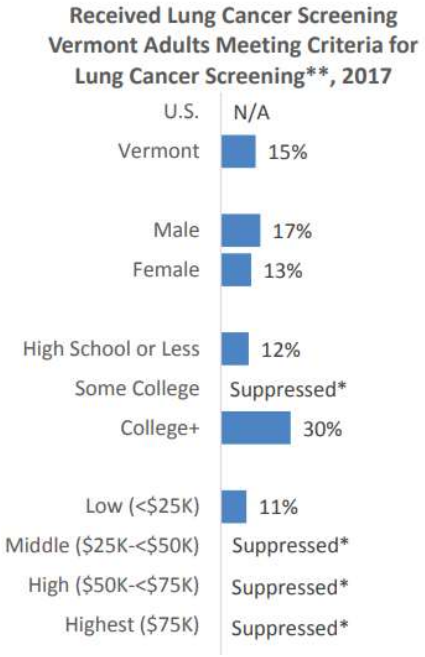
Note: All rates are age-adjusted to the 2000 U.S. standard population.

Data can be accessed at http://www.healthvermont.gov/health-statistics-vital-records/surveillance-reporting-topic/cancer
Under "Age Adjusted Incidence and Mortality Rates".

Data Source: VCR 2011-2015

Lung Cancer Screening in Vermont

15% Of Vermont adults ages 55-80 who are a current or former heavy smoker are up-to-date on lung cancer screening.



*Value suppressed due to sample size too small or relative standard error (RSE) is > 30.
**Lung cancer screening is recommended for adults who are 55-80, have a 30 pack-year smoking history, and are a current smoker or stopped smoking within the last 15 years. Additional information about lung cancer screening recommendations can be found here: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening
Data accessible at http://www.healthvermont.gov/health-statistics-vital-records/population-health-surveys-data/brfss Under "BRFSS Annual Data Summary"

Data Source: BRFSS 2017

Cancer Screening in Vermont

Lung Cancer Screening
Rate for Eligible Vermonters
Ages 55-80

15%

Breast Cancer Screening
Rate for Eligible Vermont
Women Ages 50-74

79%

Cervical Cancer Screening
Rate for Eligible Vermont
Women Ages 21-65

84%

Colorectal Cancer Screening
Rate for Eligible Vermonters
Ages 50-74

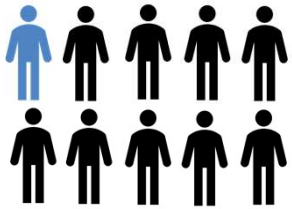
72%

**Lung cancer screening is recommended for adults who are 55-80, have a 30 pack-year smoking history, and are a current smoker or stopped smoking within the last 15 years. Additional information about lung cancer screening recommendations can be found here: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening
Data accessible at http://www.healthvermont.gov/health-statistics-vital-records/population-health-surveys-data/brfss Under "BRFSS Annual Data Summary"

Data Source: Breast, Cervical, Colorectal: BRFSS 2016;
Lung: BRFSS 2017

Disparities in Screening Eligible Population

About one in ten Vermonters ages 55-80 are eligible to receive lung cancer screening.



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19,100 Vermonters ages 55 to 80 are eligible to receive lung cancer screening.

Who is Eligible?

About one in five Vermonters ages 55-80 with a high school education level or an annual income <$25,000

About one in four Vermonters ages 55-80 with an independent living disability

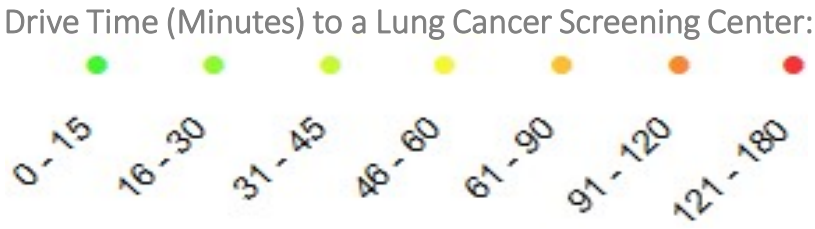
About one in three Vermonters ages 55-80 with a self-care disability

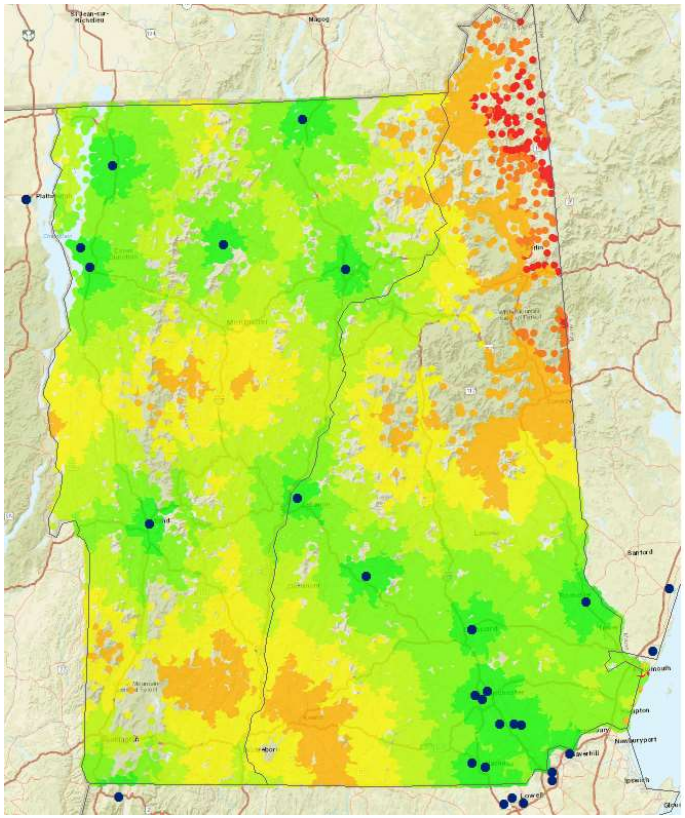
American Lung Association Lung Cancer Screening Eligibility Quiz available online at, https://www.lung.org/our-initiatives/saved-by-the-scan/quiz/

Data Source: BRFSS 2017

Drive-Time Analysis for Lung Cancer Screening in Vermont & New Hampshire Hospitals

State	Drive Time to LCSC (Minutes)	Population Aged 55-84
NH	0-15	127,553
NH	16-30	101,493
NH	31-45	44,817
NH	46-60	30,372
NH	61-90	26,076
NH	91-120	1,107
NH	120-180	337
VT	0-15	41,888
VT	16-30	47,483
VT	31-45	40,265
VT	46-60	34,362
VT	61-90	4,256



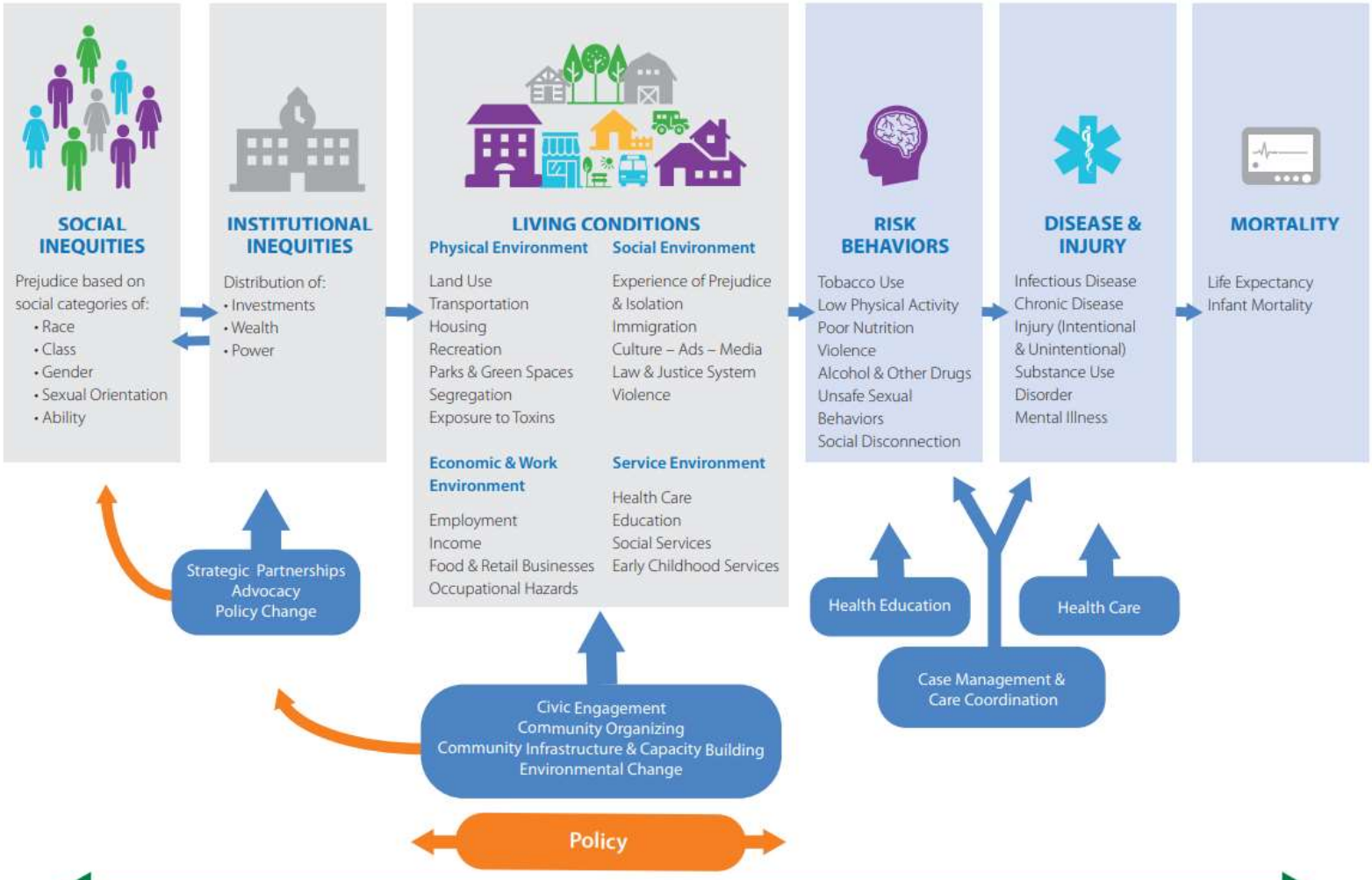


Data Source: VT & NH Drive Time Analysis Study 2018

VTAAC Lung Cancer Screening Taskforce

- Members representing six VT/NH hospitals, VTAAC, ACS, ALA, VT Department of Health
- Facilitated 2017 Survey of Vermont's lung cancer screening facilities
- Held November 2018 Lung Cancer Screening Summit
- Next Steps: Continue to support expanded access to screening and public and provider education

A Public Health Framework for Reducing Health Inequities



– Adapted from the Bay Area Regional Health Inequities Initiative

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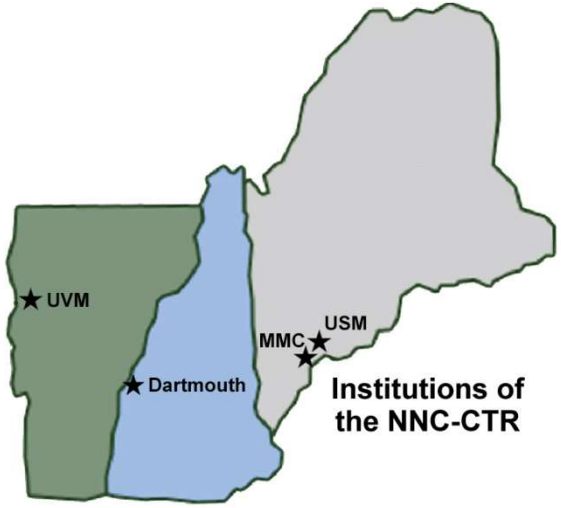

Pilot Projects Program (PPP)

Jane Lian PhD (UVM) Core Leader

Doug Sawyer MD PhD (MMC) Co-Leader

June 7 2019 EAC meeting

Maine Medical Center

The University of Vermont

UNIVERSITY OF SOUTHERN MAINE

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Mission of the NNE-CTR

Enhance rural healthcare in northern New England by fostering and coordinating clinical, translational and educational research activities.

Vision of the PPP

The Pilot Project Program goals are to encourage innovative *basic science and clinical research proposals* that meet the challenges of healthcare delivery—by leveraging NNE-CTR Core Resources to conduct collaborative clinical and translational research in the priority areas of addiction, cancer and cardiovascular disease.

NIH Expected Outcome

PPP grants are to lead to an NIH (or other extramural) proposals with collaborators in the NNE-CTR Network across multiple institutions, expanding the findings of the pilot project that can be implemented to increase better healthcare.

The PPP aims to facilitate the formation of interdisciplinary teams that conduct collaborative CTR of importance to our communities, especially those in remote areas.

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Pilot Project Core: SPECIFIC AIMS

Aim 1: Recruit investigators and facilitate the formation of interdisciplinary teams that conduct innovative collaborative CTR of importance to the rural community.

Aim 2: Assure the success of CTR Pilot Project Award investigators through maximizing use of innovative NNE-CTR Core functions.

Aim 3: Continuously assess the “value added” by the Pilot Projects to the CTR in collaboration with Tracking & Evaluation Core.

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Specific Activities of the PPP in 2018–2019

Working with applicants and funded Investigators

Prior to proposal submission

- Respond to inquiries from new investigators
- Set up contacts for collaborations between MMC and UVM
- Meet with investigator and leaders of Rural Health Research & Delivery and Clinical Research Design, Epidemiology & Biostatistics Cores to crystallize the PI's ideas into an appropriate study plan

During the funding period of each Awardee, we

- Monitor needs and may have studio sessions with PPP, Translational Research Technologies, Professional Development Core
- Document progress (Tracking & Evaluation Core)
- The PPP schedules meetings with PIs at each Institution to assure that their needs are being met particularly during the first 2-3 mo

After Grant is completed

- Drs. Sawyer (MMC) and Lian (UVM) continue to conduct ad hoc meetings with investigators to prepare abstracts for national meetings and those who are preparing extramural grants

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New Activities of the PPP 2018-2019

- **The PPP planned monthly Progress Report mini-symposium series** (started in January) in 2018 rotating n= 2 or 3 projects/month) for presentations by grantees at their 2-3 mo, 5-6 mo and 10-11 mo stages (30 min)
  - Brings the members together between MMC and UVM
  - PIs obtain valuable feedback from Core Leaders
  - We identify early if there are any hindrances

- **Consultation with Tracking & Evaluation** (conference calls, emails) to discuss PPP-prepared forms for monitoring Pilot Project progress that were complementary to the T&E annual questionnaire. *These are currently in use*.

- **Poster Session for the Annual Research Symposium Day** – at UVM this year. Invitations were extended to Investigators who submitted a proposal (and just missed getting funded) in order to stimulate collaborative grants

- **Initiated the call for Round 3 proposals** - completed the review process in a timely manner for PIs to obtain IRB approval by July 1 start dates

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Round 2 Investigators: Progress Report Mini Symposia Presentations

Held via Zoom between Maine and Vermont
Questions were asked by the audience after each 30 min presentation

Kinna Thakarar (MMC) Rural Harm Reduction Access and Regional Trends ("Rural HeART") – *Addiction Related*

Kathleen Motyl (YI - MMC) Direct and indirect mechanisms of *opioid-induced bone loss* (MMC, UVM and Dartmouth) Multisite investigators

Teresa May (MMC) An Atlas of Rural and Urban Variation in Cardiac Arrest Processes of Care and Outcomes in Northern New England: *Toward improved outcomes after rural cardiac arrest*

General Discussion: Present were 4 Core Leaders at UVM (5th was a call-in) and 5 Core Leaders at MMC

- Advice by Core Leaders was given
- PI Feedback. Awardees were asked to describe challenges of the proposal and how the PPP and other cores could help them

Post Presentation Written Report Forms (one page): Submitted by Core Leaders and by Principal Investigators

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Round 1 Investigators : Mini - symposia Progress Reports

Alexa Craig (MMC): **Leveraging Telemedicine to Reduce Disparities in Time to Initiation of Therapeutic Hypothermia in Rural Settings: a Pilot Feasibility Study.** *Used live telemedicine consults between rural hospitals and our tertiary care center to demonstrate a reduction in the time to initiate hypothermia for infants born in rural hospitals*

Janet Stein (UVM): **Discovering the Potential of tsRNA as Breast Cancer Biomarkers and Therapeutic Targets.** *Proposal determines if a recently discovered class of small molecules, tsRNAs, 1) promote aggressive characteristics of breast cancer cells and 2) are a non-invasive biomarker of breast cancer*

Jessica Heath (UVM): **Targeting Cell Adhesion in CALM-AF10 Leukemias.** *She identified that CXCR4, ITGA4 and ITGB1 are more highly expressed on the surface of CALM-AF10 + human and murine leukemia cell lines. A co-culture system was established between human mesenchymal stromal cells and leukemia cells, that can be separated for downstream analysis by CD45 expression to address interactions that contribute to this aggressive leukemia*

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Major Accomplishment: Round 3 Operational Timeline for Year 3 (July 1, 2019 to June 30, 2020)

Call for Proposals – September 2018 (a month earlier than previous year to assure IRBs would be planned and included as part of the final proposal)
Letter of Intent (LOI) – 30 RECEIVED November 2018
3 were not invited to submit full proposal (as not relevant to the NNE-CTR)
Full proposals submitted – 27 RECEIVED February 2019

- 11 addiction
- 9 cancer
- 5 cardiovascular
- 2 other
  - Early investigators
  - Multi–Institutional sites

Reviewed 23 proposals March 11, 2019

- 4 were withdrawn from full proposal
- 2 after submission, were found not eligible due to current COBRE funding

Round 3: Request for Proposals

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Outcomes

Score Ranges for 23 proposals

1.0-2.5	5 proposals + 1 (see below)
2.8 -4.5	7 proposals
5.0-8.0	8 proposals
Not Scored	(2 proposals)

Finalists

Investigator	Title
Mauriti/Mackey	Emergency Department-Initiated Buprenorphine Intervention for Opioid Use Disorder
Francis	Screening and Cardio-surveillance of Cancer Patients Undergoing Immune Checkpoint Blockade
Sammon	The development of an enhanced clinical encounter as method of improving shared decision making at the time of PSA elevation
O'Reilly	Sleep Disturbance on Bedside Electroencephalogram: A Biomarker for Severe Neonatal Abstinence Syndrome
Ahrens	Feasibility of using administrative data to follow pregnant women longitudinally over time: Maine and Vermont
Lidofsky	Harnessing the Electronic Health Record in Primary Care for Hepatocellular Carcinoma Surveillance in Cirrhosis **Note: Partial funding to replace Meisfeldt in Round 2**

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Upcoming Progress Report Oral Presentations
June 24, 2019

Michael La Mantia (YI, UVM) Feasibility and Preliminary Effectiveness of a Community Health Worker-Delivered Intervention to Slow Progression of Functional Decline among At-Risk Rural Older Adults (Co-Investigators at UVM, MMC, Dartmouth)

Timothy Plante (UVM) and Kathleen Fairfield (MMC) Leveraging Health Records to Explain Rural Cardiovascular Disease Disparities

Paul Han (MMC) and Robert Gramling (UVM) Northern New England Palliative Care Teleconsult Research Laboratory

Attendees

Pilot Project Leaders (J Lian/VT, D Sawyer/ME)
Administrative Core (C Rosen, G Stein, T Gridley, G Jensen, M Oestreicher, J Smith)
Clinical Research Design, Epidemiology & Biostatistics (S Santangelo/ME; B Cole/VT)
Rural Health Research & Delivery (J Carney/VT; N Korsen /ME)
Translational Research Technologies (F Carr/VT; B Friesel/ME)
Tracking & Evaluation (B Joly/ME; E Ziller/ME)
Professional Development (K Luebbers/VT; I Brodsky/ME)
Team members of the Awarded Grant

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Current and Future Plans

MONITORING 10 current awardees and 5 Round 3 grantees

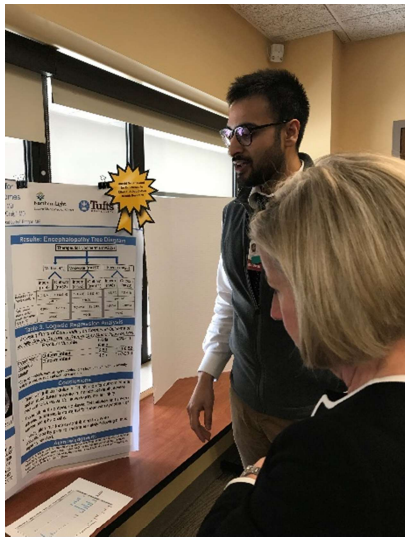
- **Meet with Round 1 and Round 2 Investigators** to follow up re submitting abstracts to national conferences and writing manuscripts.
- **If grant is not multi-Institutional**, we will facilitate collaborations with a partnering academic center for preparing and strengthening the grantees' NIH or other extramural applications.
- **Poster sessions scheduled in May at MMC and June at UVM** are fostering communication among members of the network. We extended invites to submit posters, regardless of funding status.

18 posters submitted for June session:

2 from MMC (Craig, Motyl)

11 from UVM (PP Awardees: Plante (2), Heath, LaMantia, Mackey, Stein J), Harder (Supplement), plus 4 from Non-Awardees

Core posters: 1-Prof Dev, 2-UVM Rural Health, 1-MMC Rural Health; 1-NNE-CTR



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RESEARCH NETWORK

Challenges for the PPP to Overcome

IMPROVED OUTREACH is needed to stimulate awareness of research leading to collaborations between basic and clinical researchers, practicing physicians and other facilitators of heathcare delivery in rural northern New England

GOOD GRANTS are being submitted that address rural health disparities, ~ 60%, targeted to specific situations and disorders, but only 5 can be awarded. Difficult decisions. We are encouraging more basic science grants with clinical partnerships.

A BALANCED PORTFOLIO must be maintained that includes innovative and mechanistic research leading to discoveries that meet the mission of the CTR, and expectations of NIGMS in which Pilot Projects will have generated data to move on to external funding.

TO REINFORCE A PIPELINE OF TRANSLATIONAL RESEARCH to clinical application requires multidisciplinary teams, and the PPP, along with other core leaders, are doing their best to facilitate the necessary collaborations

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Thank you

External Advisory Board

Gordon Bernard MD, Director, Vanderbilt Institute for Clinical & Translational Research
Sally Hodder MD, Director, West Virginia Clinical and Translational Science Institute
Mark Levine MD, FACP, Commissioner, Vermont Department of Health
Kenneth Pienta MD, Johns Hopkins University
Jack Westfall MD, MPH, Santa Clara Valley Medical Center

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Cliff Rosen and Gary Stein (Co-PIs)
Tom Gridley and Gordon Jensen
Meredith Oestreicher, Staff
Jennifer Smith, Staff

Rural/Urban Disparities in Cardiovascular Assessment (RUDICA)

Tim Plante, MD MHS
Assistant Professor
Larner College of Medicine

NNE-CTR Annual Retreat
June 7, 2019

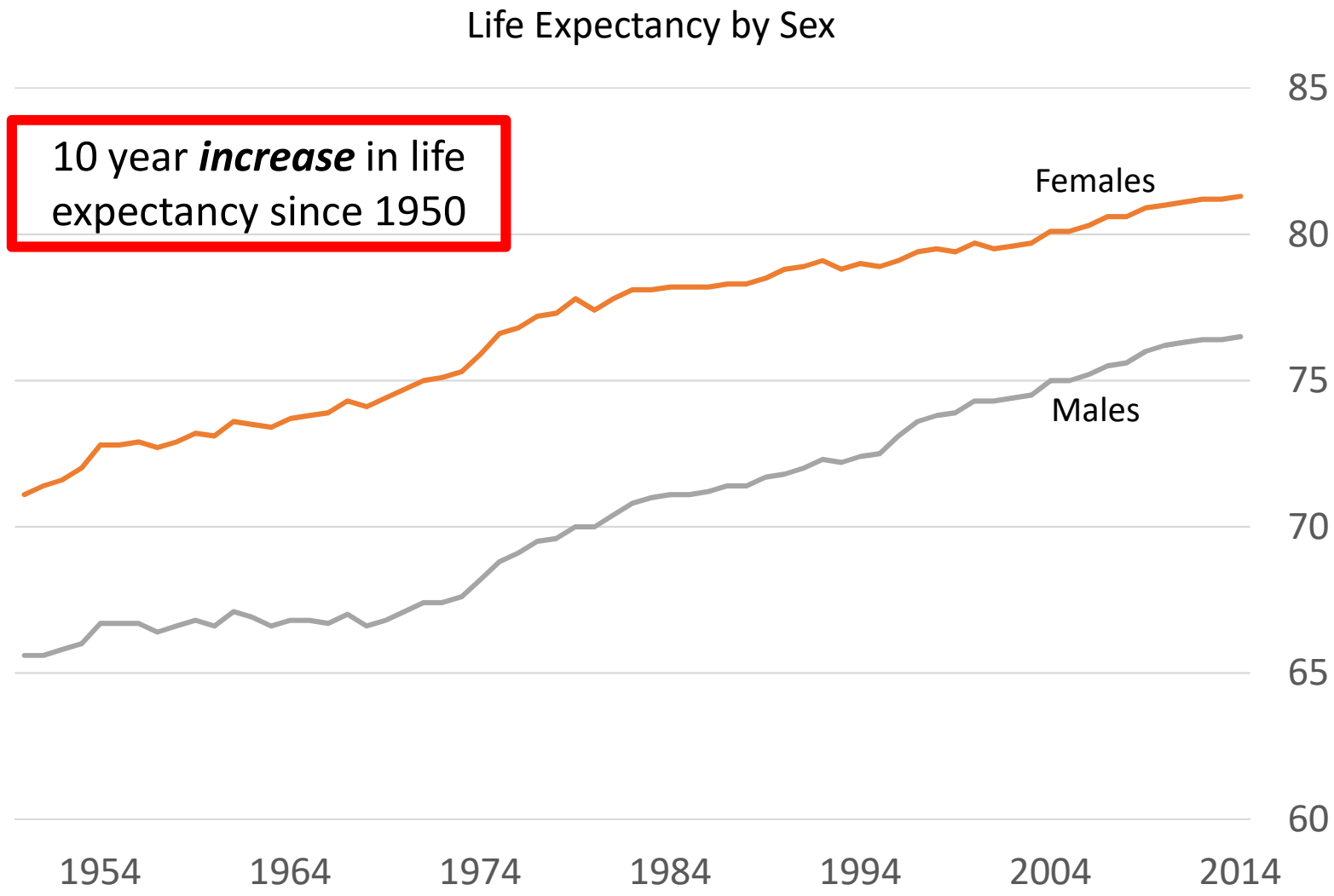
NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

RUDICA
Rural/Urban Disparities in Cardiovascular Assessment

Disclosures

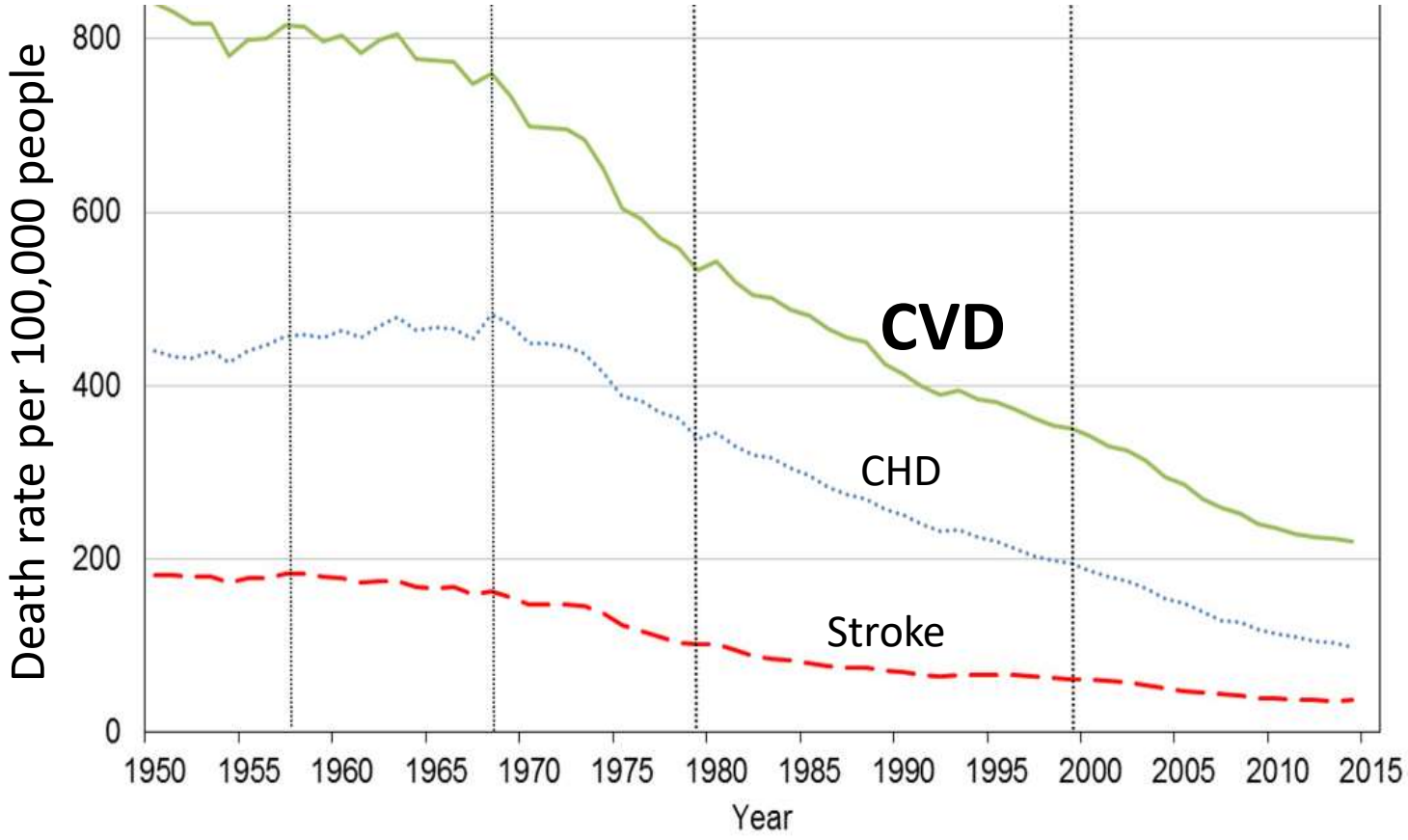
- None relevant.

We are living longer



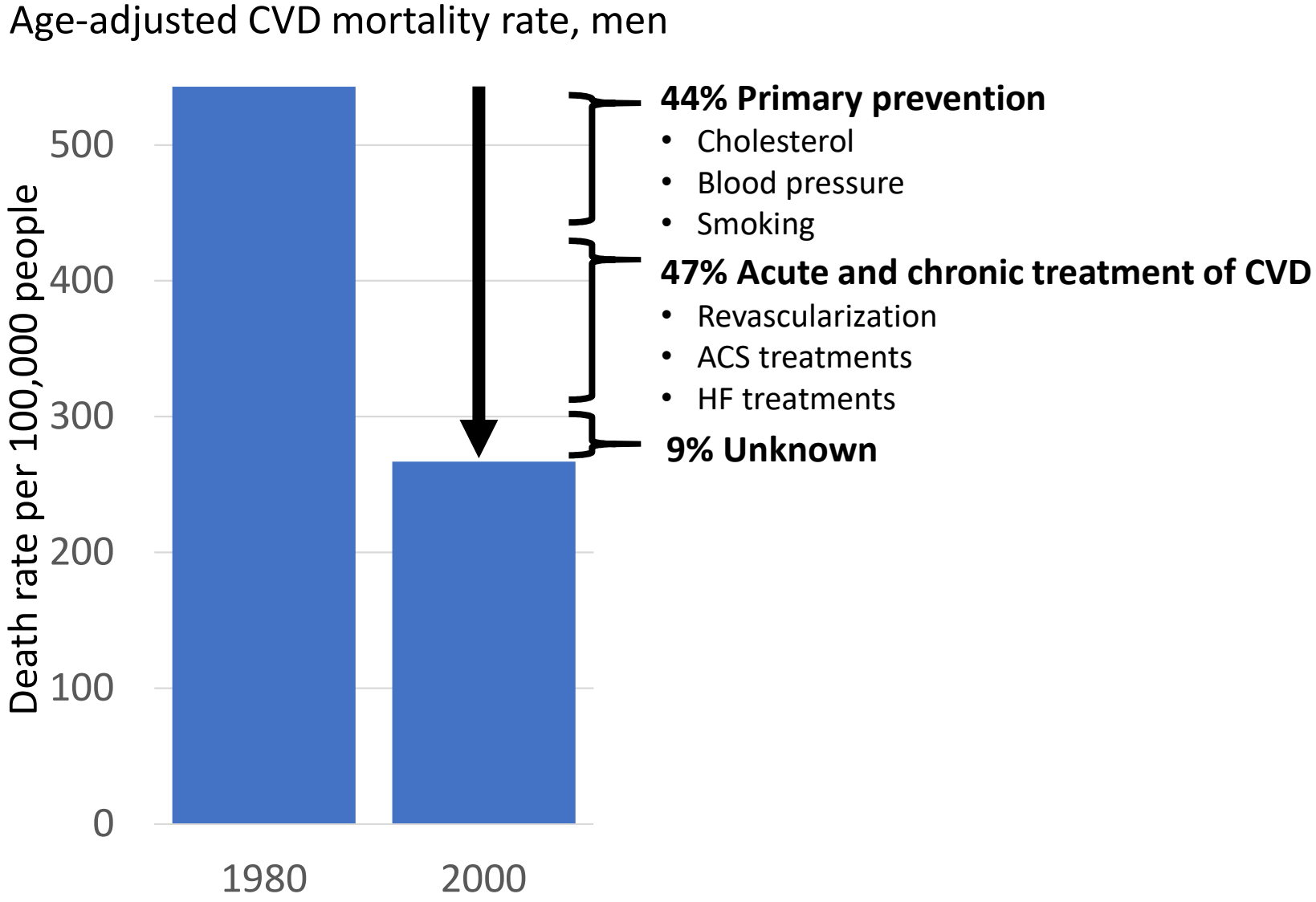
National Center for Health Statistics. https://data.cdc.gov/NCHS/NCHS-Death-rates-and-life-expectancy-at-birth/w9j2-ggv5

Cardiovascular disease is the #1 killer, incidence is declining



Mensah GA, et al. Circ Res 2017.

What has driven the reduction in CVD mortality?

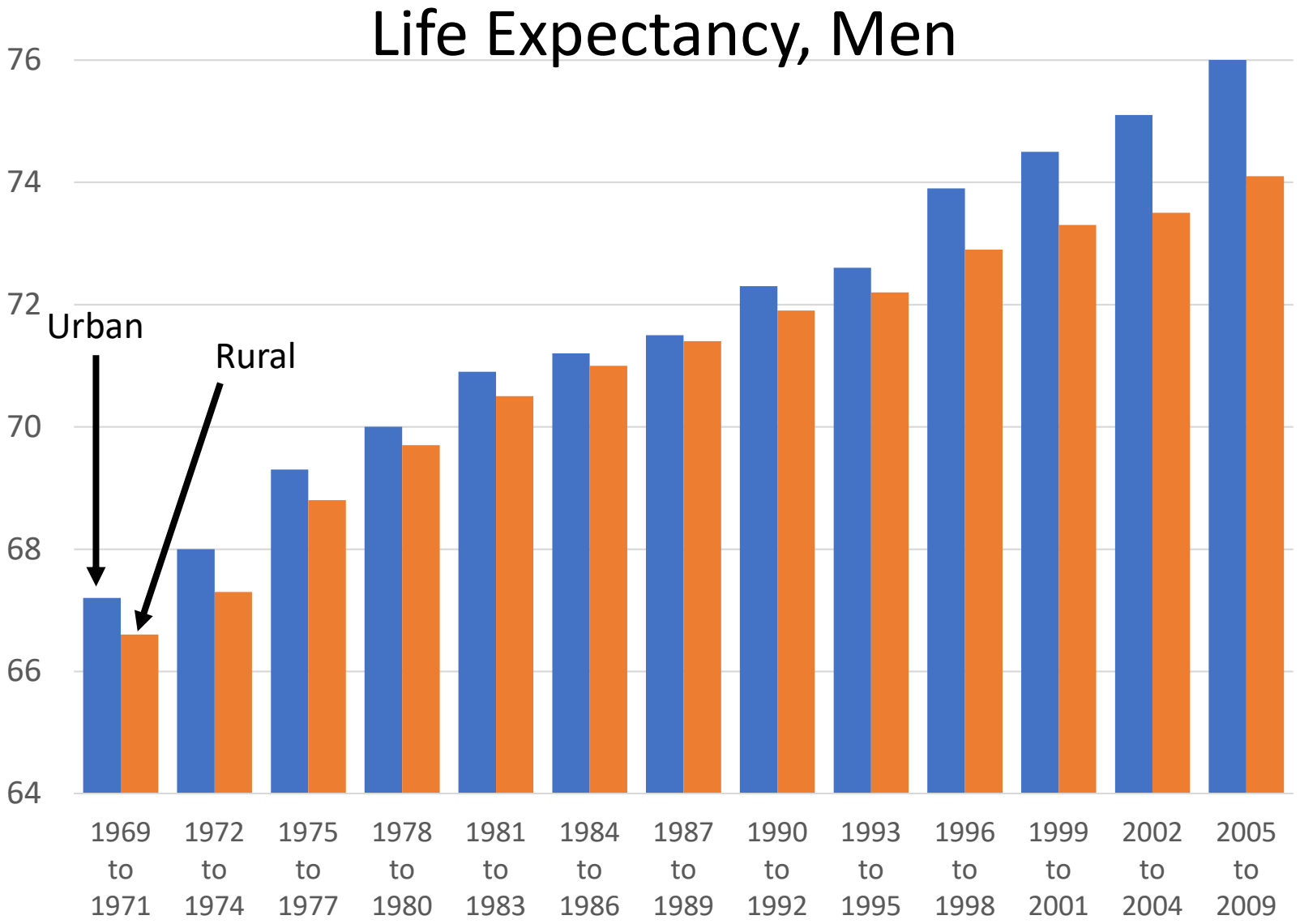


Ford ES NEJM 2007

Defining rurality

- French *ruralis: "Of the countryside*."
- Many geographical definitions
- Rural-Urban Commuting Area (RUCA) Codes
  - Defined by the USDA's Economic Research Service
  - Consider:
    - Population density
    - Urbanization
    - Daily commuting
  - Can be applied to ZIP

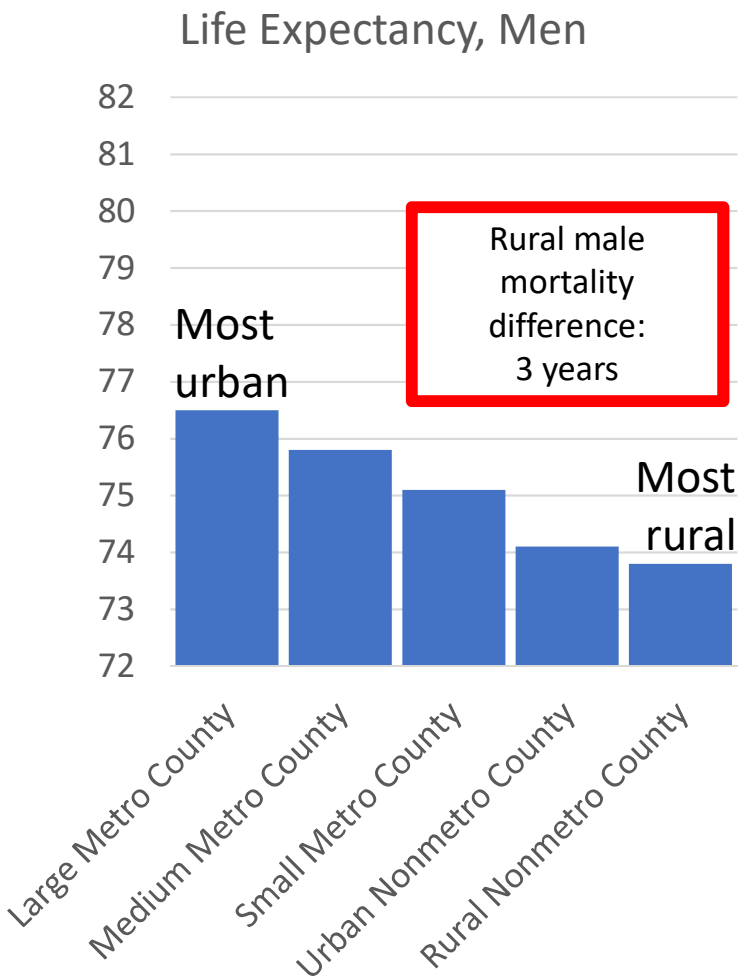
Rural adults are being left behind

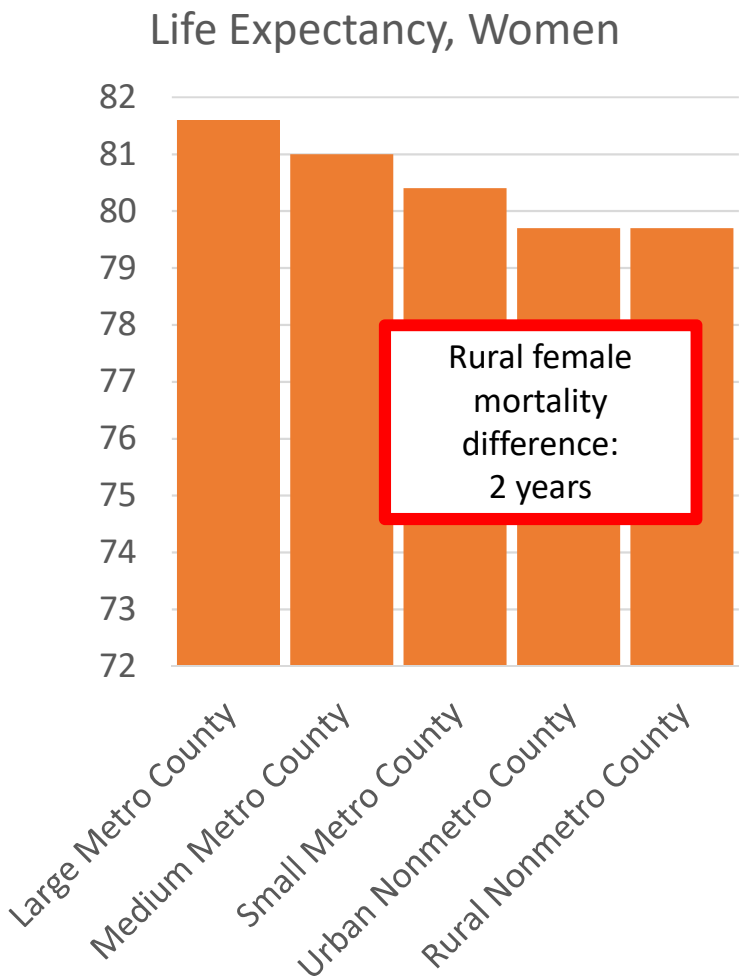


Singh and Siahpush, Am J Prev Med, 2014

Rural adults die younger

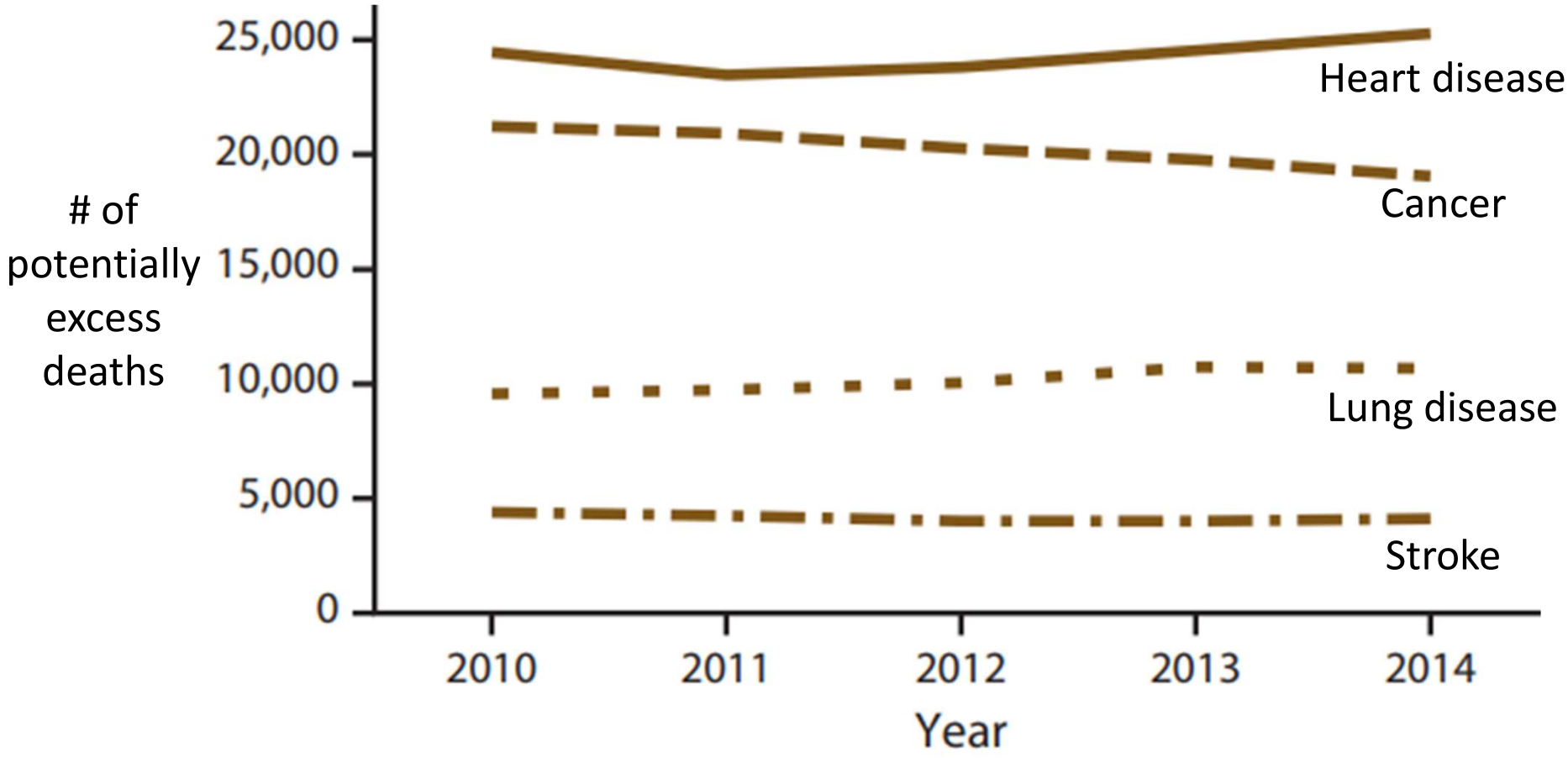
US, 2005-2009





Signh and Siahpush, Am J Prev Med, 2014

Excess deaths of rural adults by cause



Moy E, MMWR 2017. https://www.cdc.gov/mmwr/volumes/66/ss/ss6601a1.htm

Circulation

AHA PRESIDENTIAL ADVISORY

Call to Action: Urgent Challenges in Cardiovascular Disease

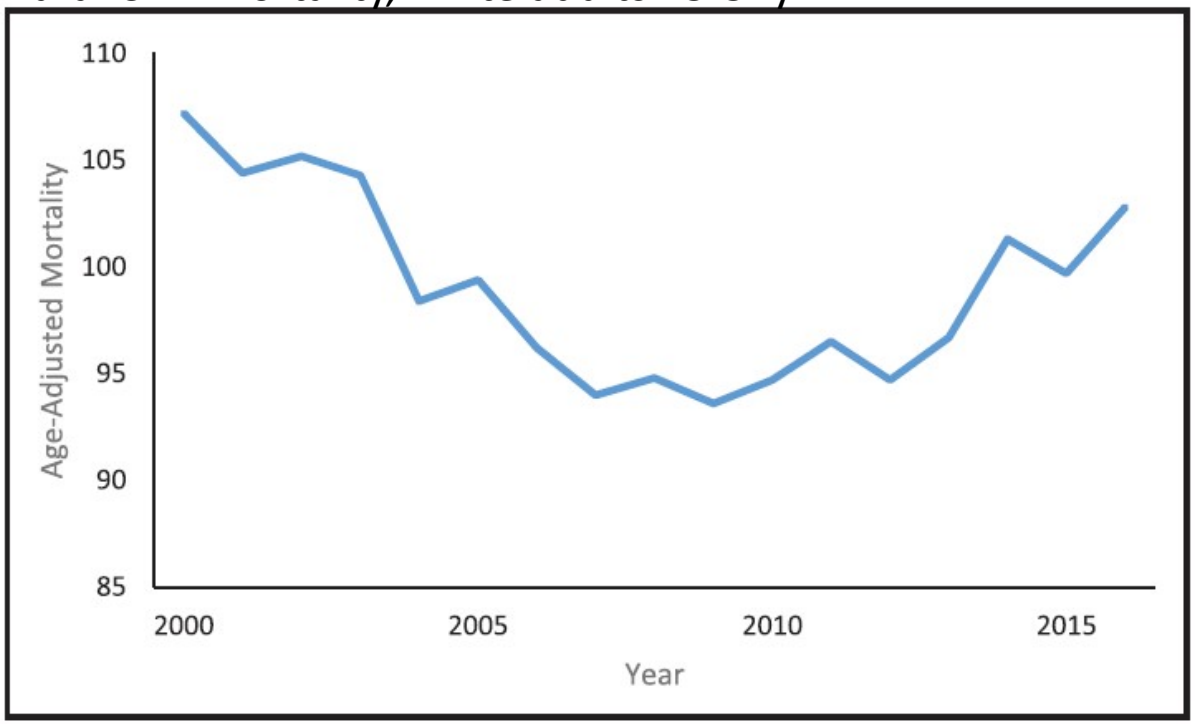
A Presidential Advisory From the American Heart Association

ABSTRACT: Although advances in care have spurred improvements in cardiovascular outcomes, cardiovascular disease remains the leading cause of death in the United States and around the world. Previous declines in cardiovascular disease mortality have slowed and even reversed for certain demographics. Further concerns exist with regard to cardiovascular drug innovation, quality of care, and healthcare costs. The Value in Healthcare

Mark McClellan, MD, PhD
Nancy Brown, BS
Robert M. Califf, MD, MACC
John J. Warner, MD, FAHA

McClellan M, et al. Circ 2019. https://www.ncbi.nlm.nih.gov/pubmed/30674212

Rural CVD mortality, white adults 45-54y

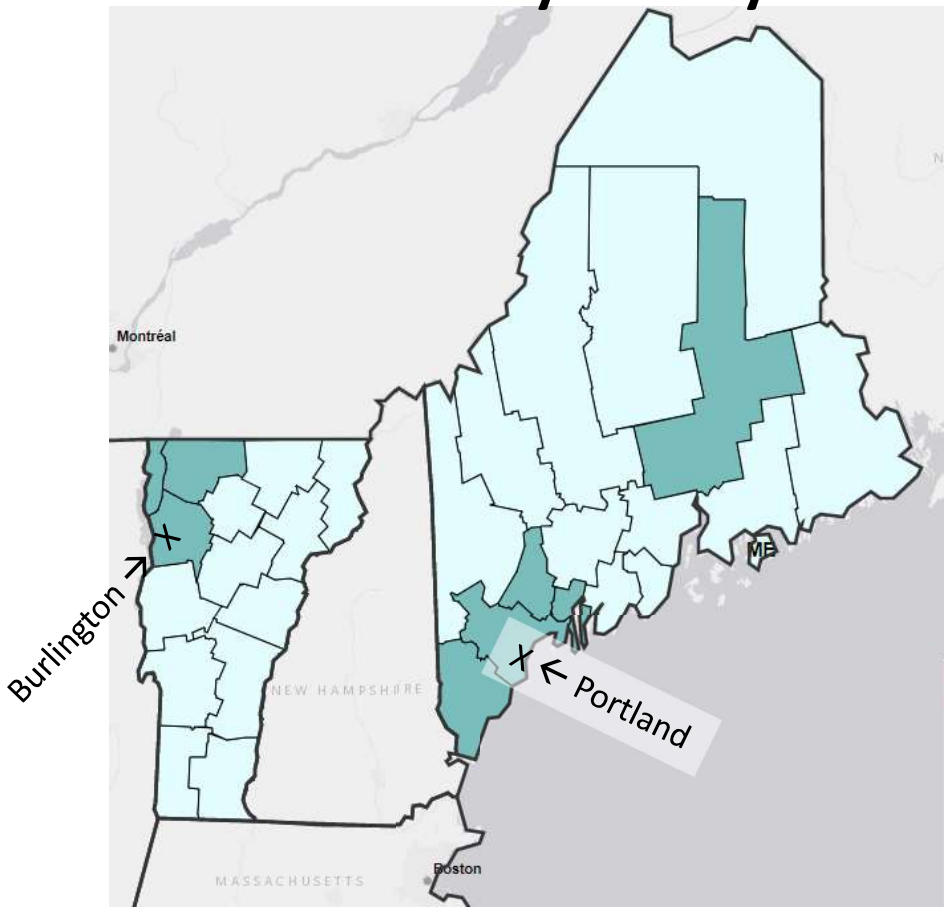


Failure to:

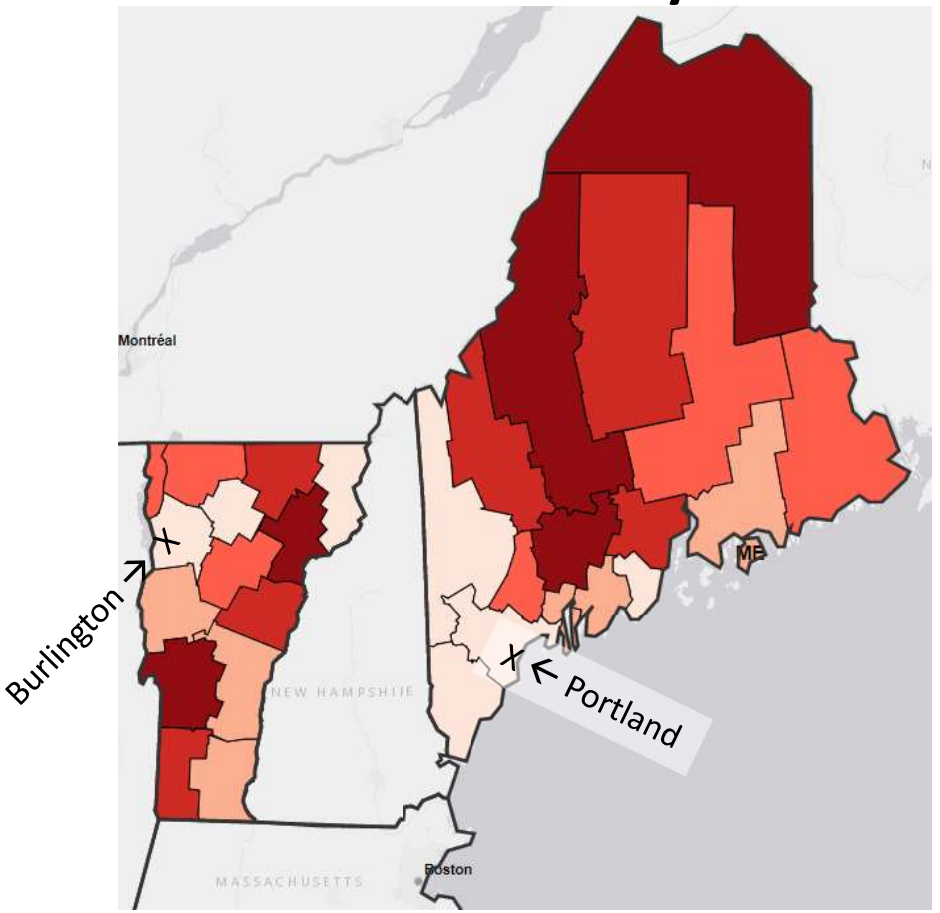
- Make risk factor modifications
- Diagnose
- Use proven first-line treatments

McClellan M, et al. Circ 2019. https://www.ncbi.nlm.nih.gov/pubmed/30674212

Counties by rurality



CVD mortality



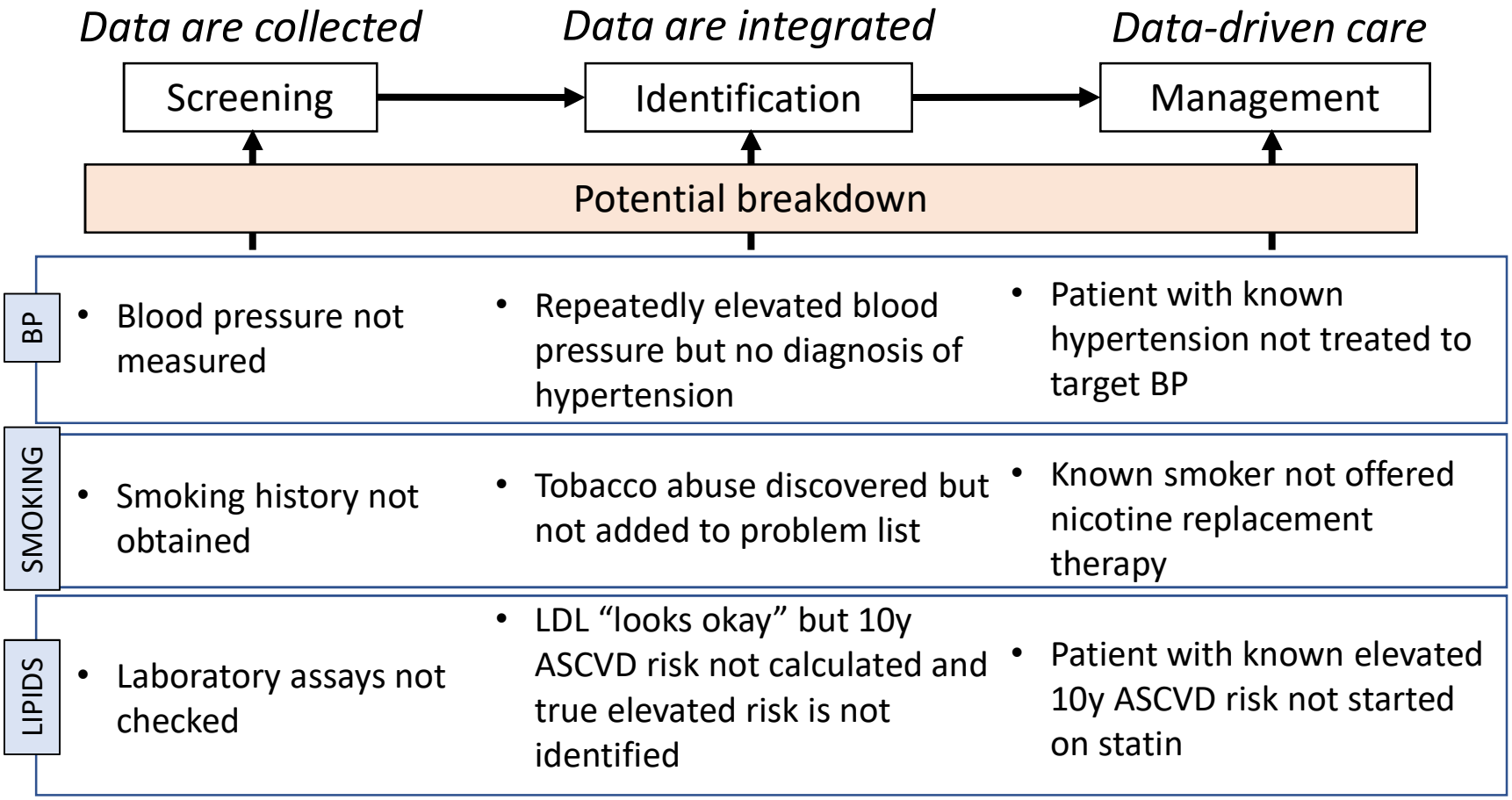
https://nccd.cdc.gov/dhdspatlas/

Contributors to rural CVD differences

- Known barriers:
  - Access to care
  - Income disparities
  - More smoking
  - More obesity
- Unknowns:
  - CVD risk factor control?

Jones CA, et al. Health Status and Health Care Access of Farm and Rural Populations. Washington, DC: USDA Economic Research Service, Economic Information Bulletin No. (EIB-57); 2009.

CVD risk factor control



RUDICA

Rural/Urban Disparities in Cardiovascular Assessment

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- **Pilot**: Identify breakdown points for CVD risk factor control among rural adults with primary care providers in Vermont and Maine.
  - UVMMC
  - Maine Medical Center (MMC; Portland, ME)
- **Future studies**: Address these breakdown points with additional interventions.
- Local research group: UVM Laboratory for Clinical Biochemistry Research
  - Colchester Research Facility

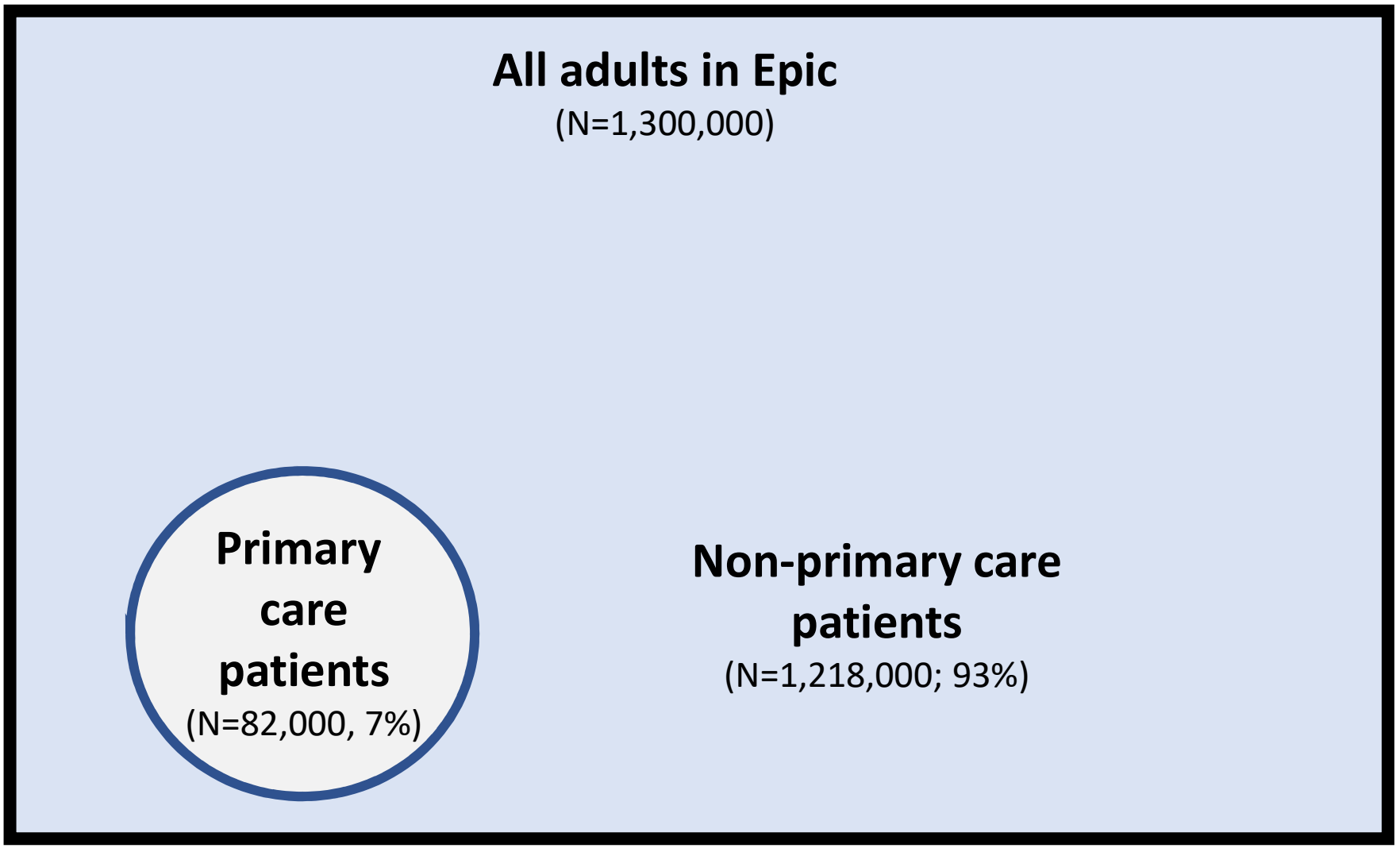
Enter the EMR

RUDICA
Rural/Urban Disparities in Cardiovascular Assessment

- UVMMC and MMC use the same EMR
  - UVMMC installation 2010
  - MMC installation 2012
- Cohort:
  - Alive and deceased adults patients with a primary care provider at UVMMC (or private practice using the EMR) or MMC
  - UVMMC: 10/1/2010 through 6/30/2018
    - Received complete data
  - MMC: 12/1/2012 through 6/30/2018
    - Actively receiving data

UVMMC patient populations

RUDICA
Rural/Urban Disparities in Cardiovascular Assessment



Why focus on primary care patients?

- Primary care patients
  - Disease prevention and management
  - Longitudinal care at UVMMC
  - Internal referrals
  - More likely to have imaging and labs at UVMMC
- Non-primary care patients
  - Disease management
  - Sporadic care at UVMMC
    - May have longitudinal care elsewhere

Primary care patients have access to care and are more likely to have continual care documented within our EMR.

RUDICA

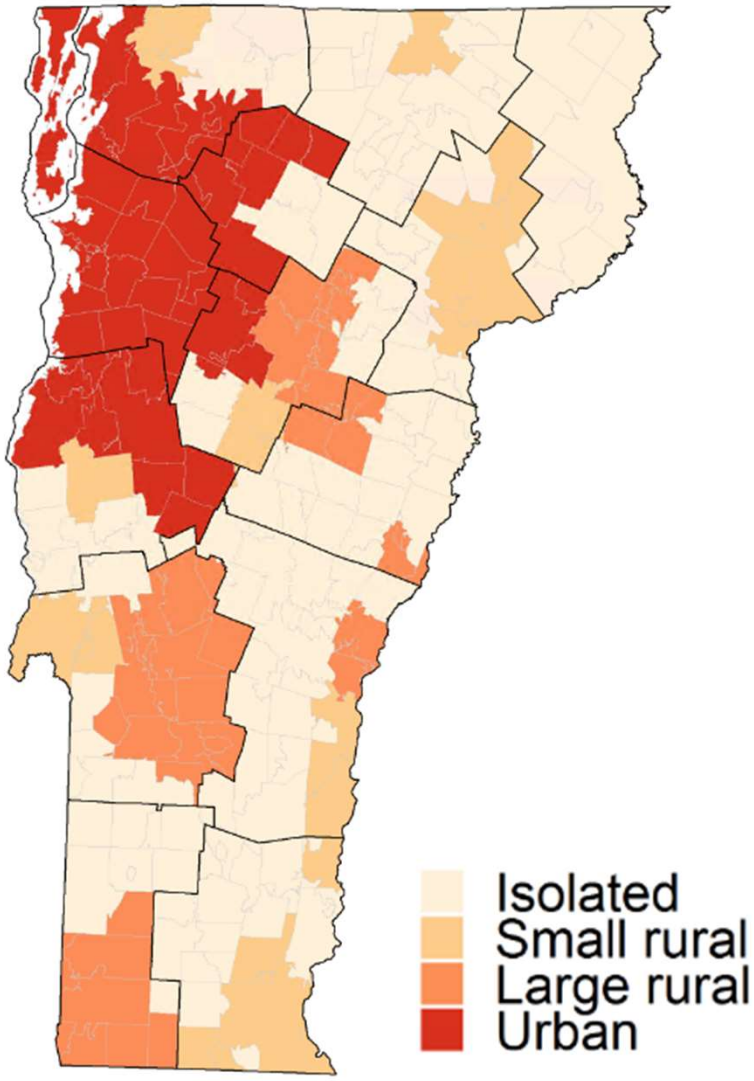
Rural/Urban Disparities in Cardiovascular Assessment

Total database:
284,000 patients

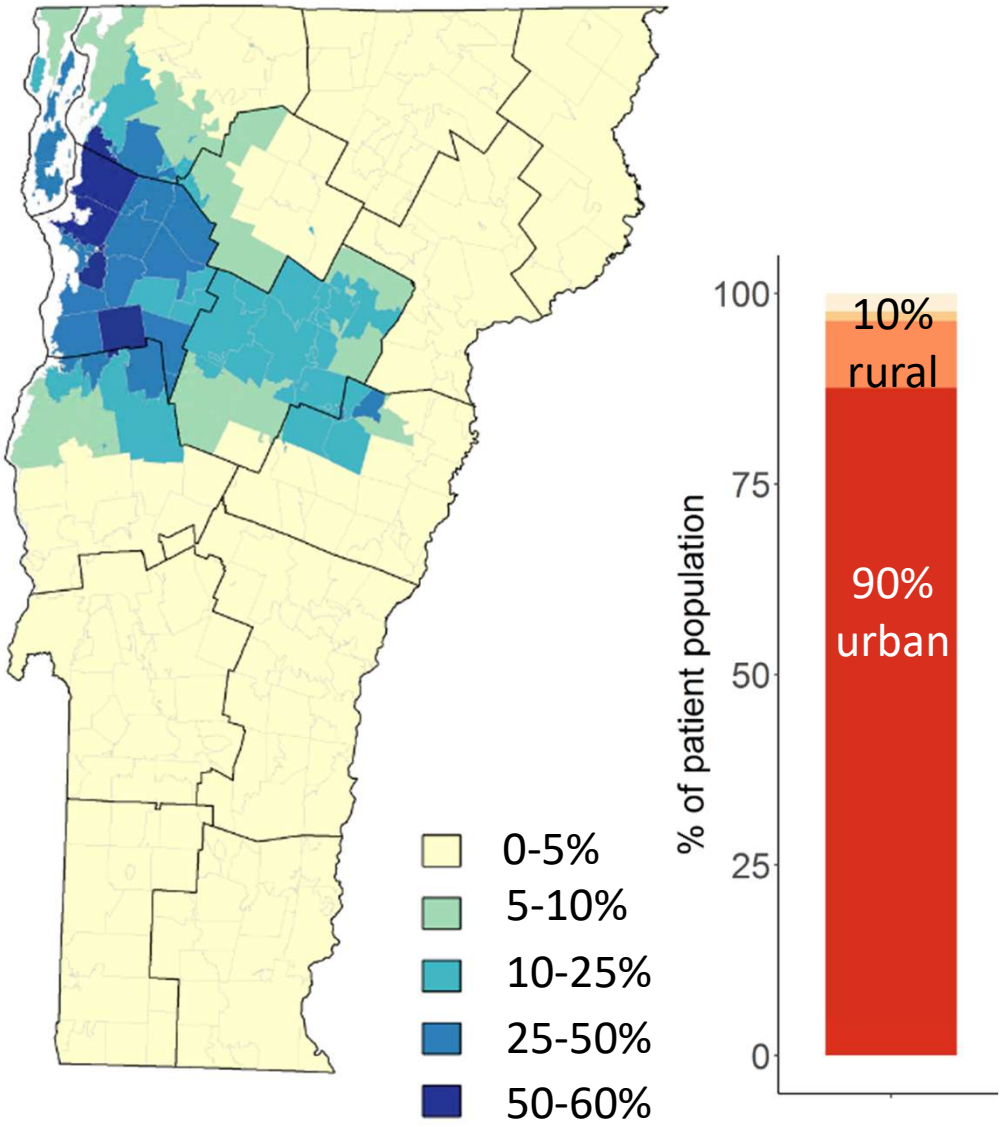
RUDICA

Rural/Urban Disparities in Cardiovascular Assessment

Urban/rural status by ZIP code



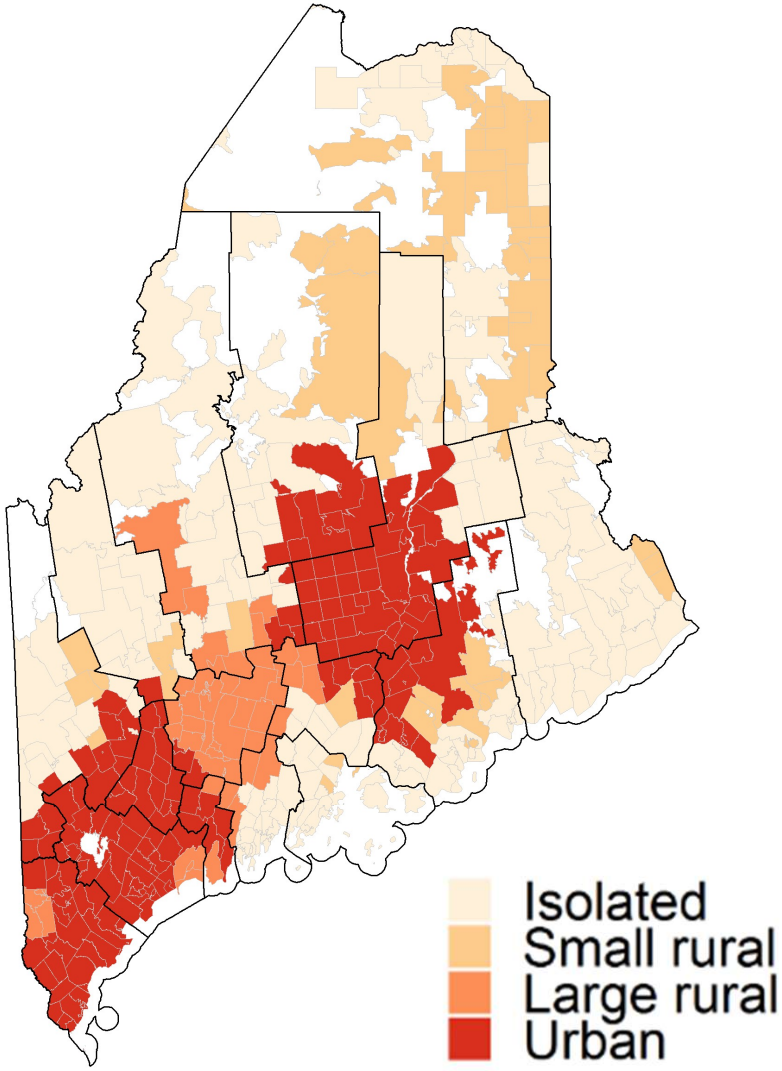
% of adults in ZIP code who are UVMMC primary care patients



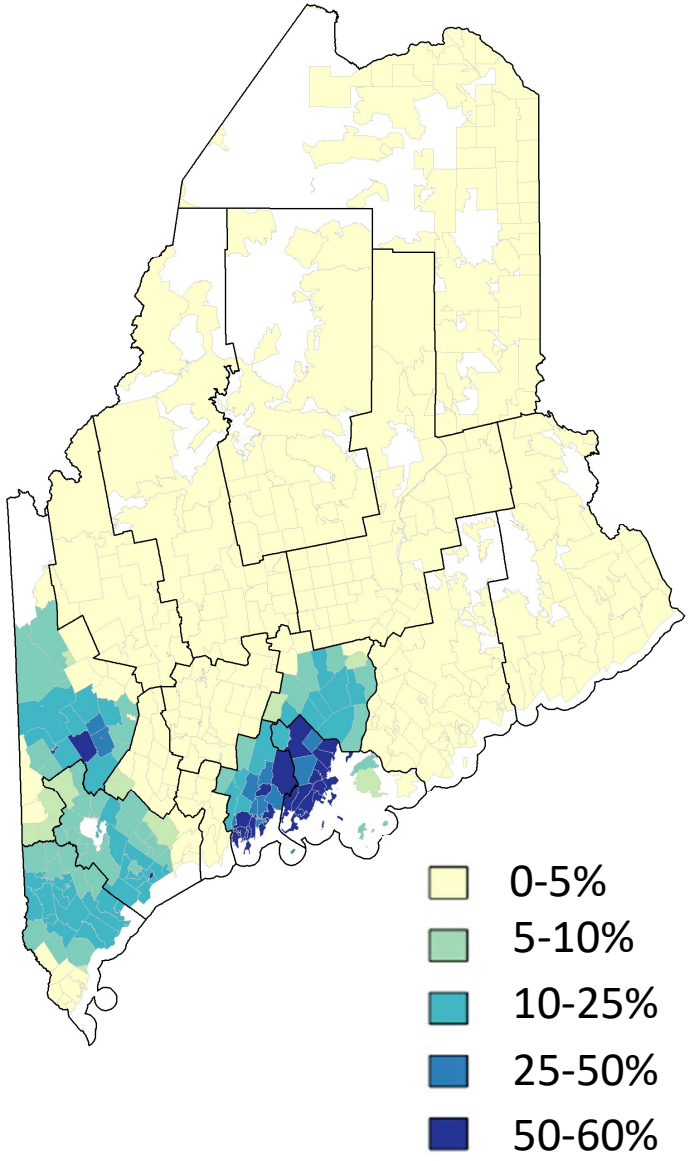
RUDICA

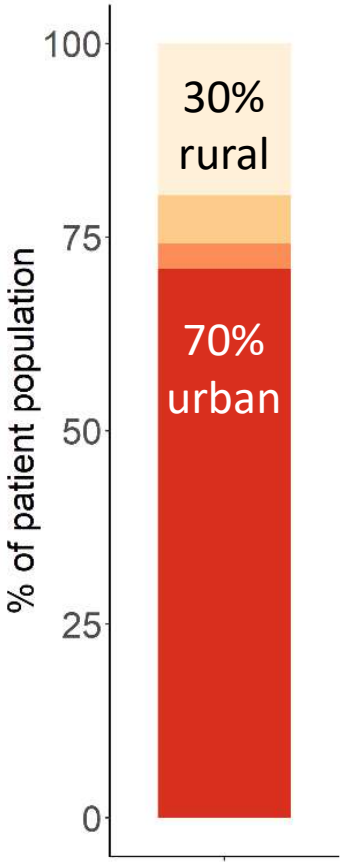
Rural/Urban Disparities in Cardiovascular Assessment

Urban/rural status by ZIP code



% of adults in ZIP code who are MMC primary care patients



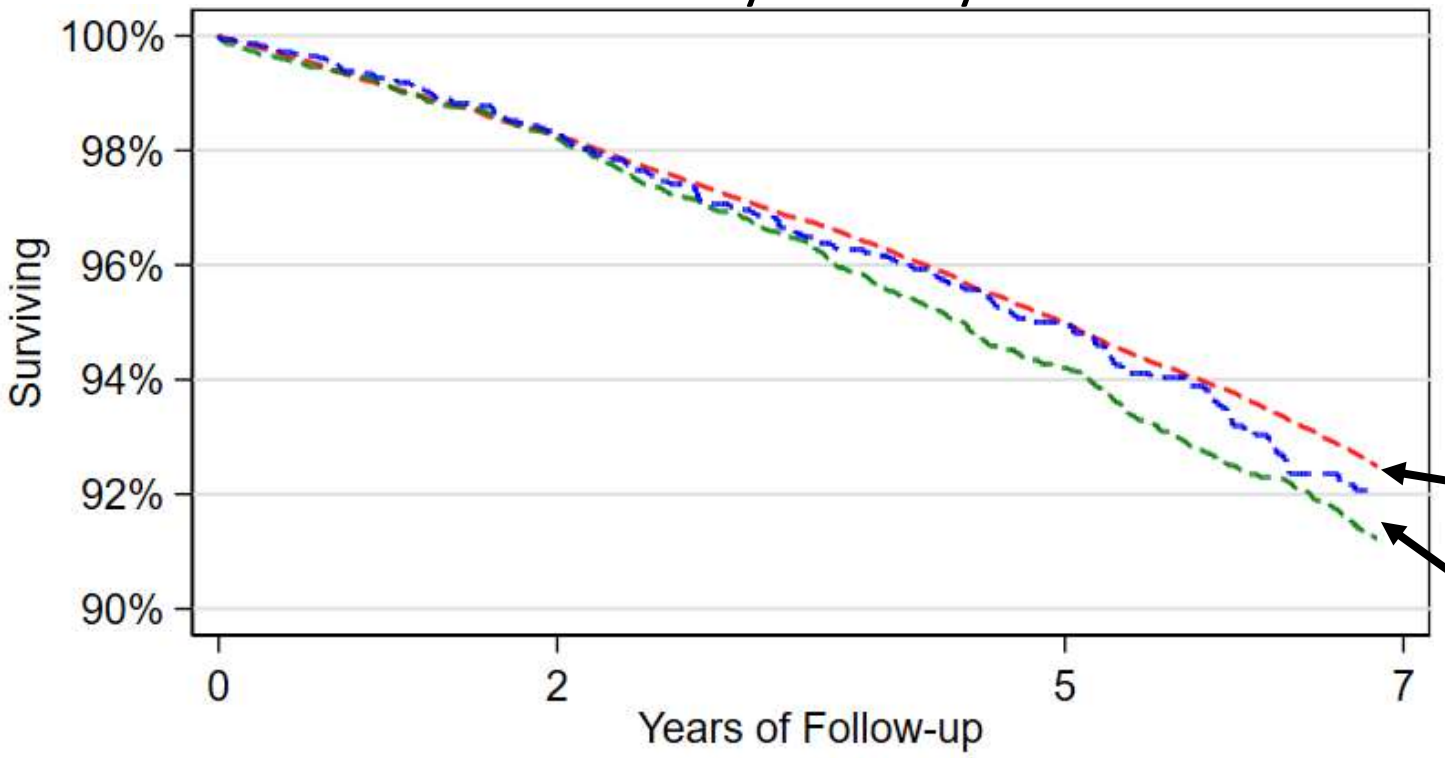


Baseline demographics, UVMMC

RUDICA
Rural/Urban Disparities in Cardiovascular Assessment

Variable	Urban	Large Rural City/Town	Small and Isolated Small Rural Town
N (% of all)	71,781 (89%)	7,549 (9%)	1,195 (1%)
Age in 2010, y (SD)*	46 (19)	47 (18)	47 (18)
Female sex, %	56%	53%	54%
Race & Ethnicity			
Black	1%	1%	1%
White	92%	94%	93%
Hispanic	1%	1%	1%
Insurance type			
Commercial	68%	62%	61%
Medicaid	5%	8%	8%
Medicare	18%	22%	24%
Uninsured	5%	5%	5%

Survival by Rurality Status



Urban

Large (green) & small/isolated (blue) rural

Number at risk

Urban	72986	58219	40344	22886
Lg Rural	7137	5769	4114	2257
Sm Rural	2960	2191	1428	713

Urban Large Rural Small Rural

Mortality outcomes, UVMMC

RUDICA
Rural/Urban Disparities in Cardiovascular Assessment

Variable	Urban	Large Rural	Small & Isolated rural
Died	6%	7%	5%
Age at death, y (SD)			
Females	**79 (14)**	**78 (16)**	**76 (14)**
Males	**75 (15)**	**73 (16)**	**70 (15)**
Follow-up time, y	6.1 (2.5-8.1)	6.3 (2.4-8.0)	4.9 (1.6-7.7)
Cause of death			
Heart disease*	**21%**	**23%**	**25%**
ASCVD**	**17%**	**19%**	**20%**
Cancer	25%	23%	27%
Dementia	10%	10%	3%
Diabetes	**3%**	**3%**	**4%**
Suicide	1%	2%	2%
Opioid-related	1%	1%	1%

*Atherosclerotic cardiovascular disease, heart failure, hypertensive heart disease, sudden cardiac death, and heart disease not otherwise specified.
**Atherosclerotic cardiovascular disease

Hazard ratio (95% CI) Age-, age^2-, sex-adjusted mortality risk by urban/rural status

Group	All-cause mortality	Heart disease mortality*	ASCVD mortality
Urban	Reference	Reference	Reference
Any rural	1.09 (1.002, 1.18)	1.21 (1.02, 1.44)	1.25 (1.03, 1.51)
Large rural	1.06 (0.97, 1.17)	1.13 (0.93, 1.38)	1.20 (0.96, 1.49)
Small and isolated rural	1.18 (1.01, 1.39)	1.48 (1.08, 2.04)	1.43 (1.00, 2.05)

*Atherosclerotic cardiovascular disease (ASCVD), heart failure, hypertensive heart disease, sudden cardiac death, and heart disease not otherwise specified.

Conclusions

- Rural primary care patients die younger, a large driver is excess cardiovascular disease.
- Identifying differences in primary prevention of cardiovascular disease can inform interventions to mitigate this risk.

Thank you!

- RUDICA
  - Kathleen Fairfield, MD DrPH, MPH (MMC)
  - Neil Zakai, MD MSc (LCBR)
  - Insu Koh, PhD (UVM)
- NNE-ROOTS pilot
  - Valerie Harder
  - Andrea Villanti
  - RUDICA group
- NNE-CTR
  - U54 GM115516
- UVMMC and MMC clinical staff
- Jeffords Institute
  - Mike Gianni
  - Allison Kaigle Holm, PhD
- MMC Quality Analytics
  - Adam Soule
  - Matt Roche
- Larner COMIS
  - Darcy Pientka
  - Jill Jemison
- UVMMC IT
  - Matt Gauthier

NORTHERN NEW ENGLAND
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Translational Research Technologies Core

Frances Carr PhD (UVM) Core Lead

Robert Friesel PhD (MMC) Co-Lead

NORTHERN NEW ENGLAND
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RESEARCH NETWORK

Goal: Provide coordinated access to state-of-the-art shared resources developed at the institutions through a combination of COBRE, INBRE, institutional and other forms of support over the last several years.

Resources crucial to the success of research by NNE-CTR investigators:

- Experimental design, selection of methodologies, analyses, presentations, education
- Infrastructure and technical expertise for genomic, epigenetic, proteomic, cell and tissue analyses and clinical and translational genomics.
- Shared instrumentation and scientific expertise

NORTHERN NEW ENGLAND
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RESEARCH NETWORK

TRANSLATIONAL RESEARCH TECHNOLOGIES CORE SPECIFIC AIMS

Aim 1: Establish a coordinated infrastructure of shared technology resources for a sustainable translational biomedical research program.

Aim 2: Provide education and training in the application and use of advanced technologies for translational research investigations.

Aim 3: Establish a robust process for evaluation of core technologies to ensure appropriate allocation of core resources, monitor core utilization, and ensure that the cores are meeting the needs of NNE-CTR investigators.

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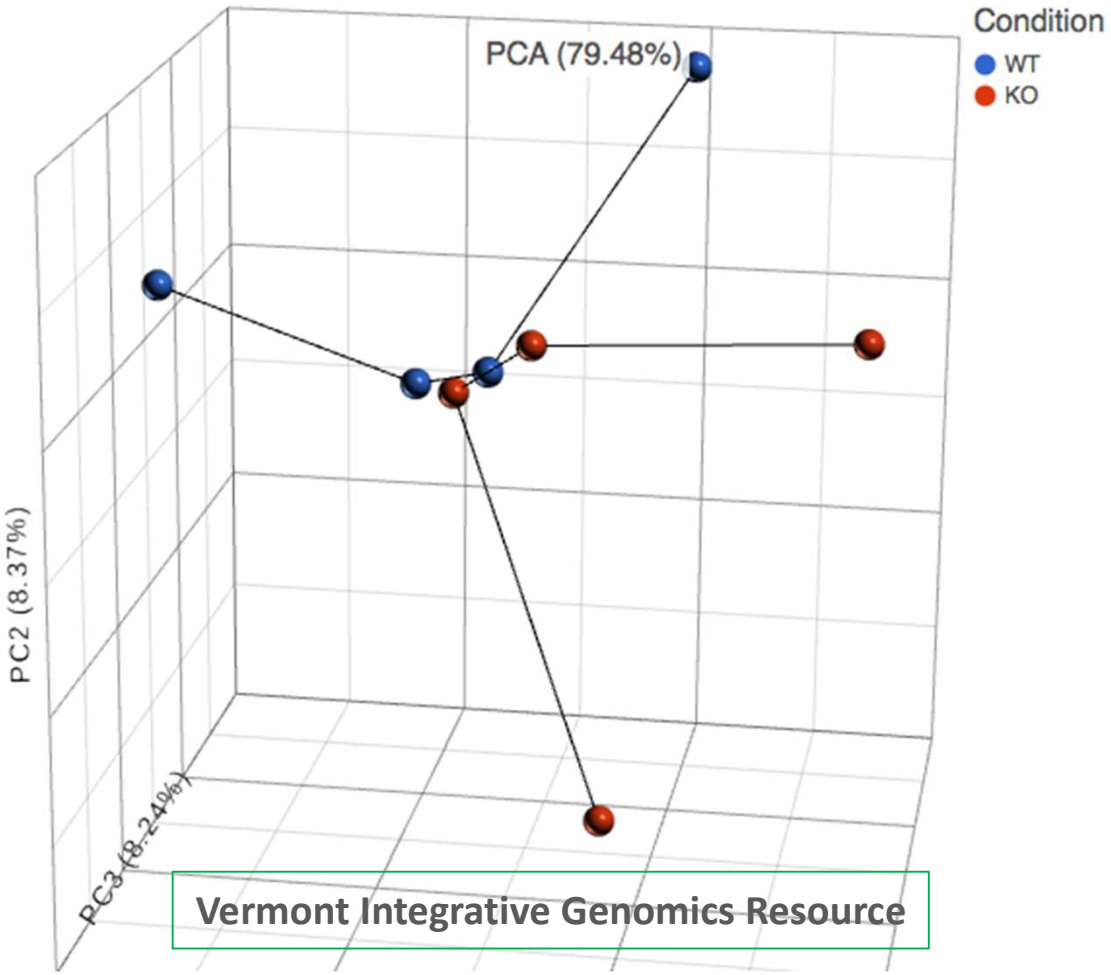
Research Highlights

What are the transcriptional changes in Spry1 knockout mice that make them more susceptible to atherosclerosis on a high fat diet? (R.Friesel, MMCRI)



Vermont Integrative Genomics Resource

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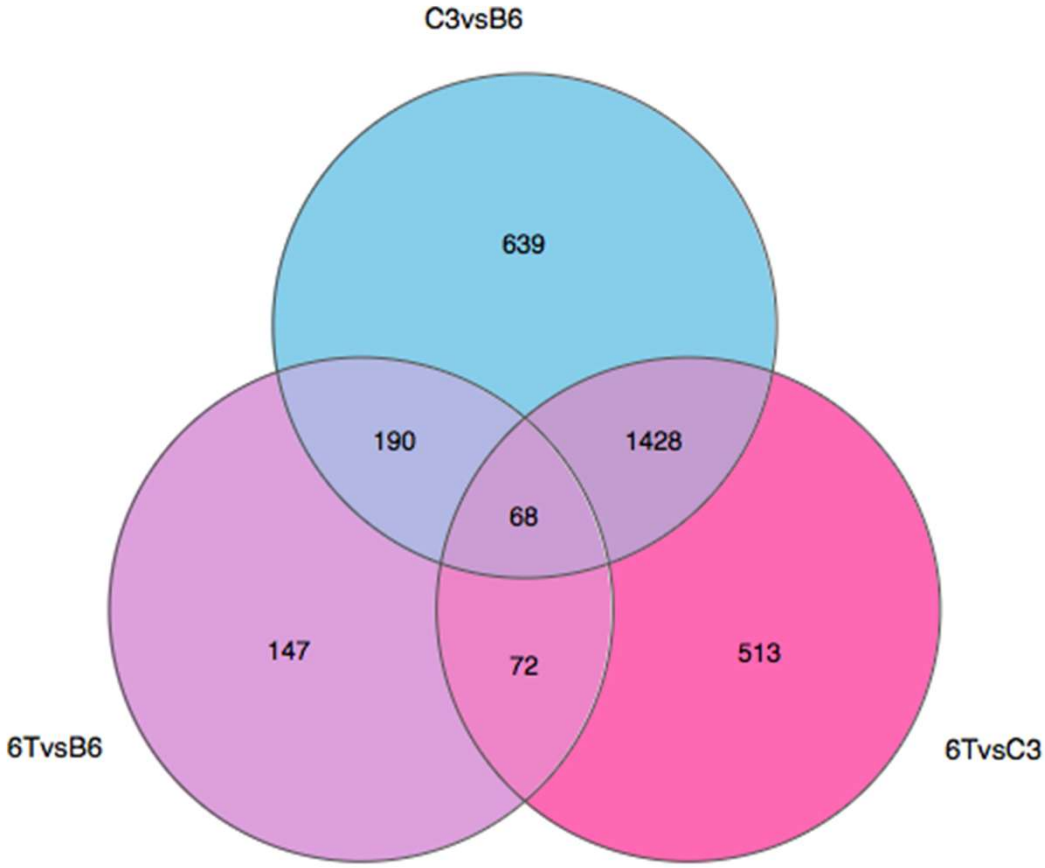
Research Highlights

What transcription changes might explain why a congenic mouse exhibits an exaggerated response to a high fat diet? (C. Rosen, MMCRI)



Vermont Integrative Genomics Resource

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Research Highlights

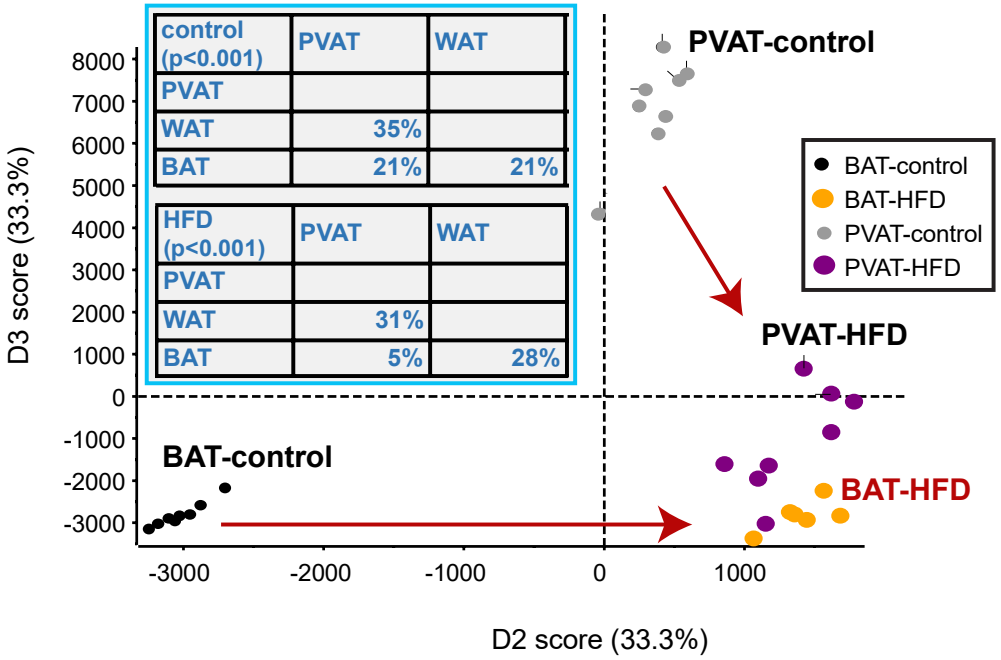
- Proteomic and lipidomic analysis of perivascular adipose tissue from mice fed a high fat diet
- SWATH (Sequential Windowed Acquisition of All Theoretical Fragment Ion Mass Spectra) proteomic analysis Notch2 knockout mice after vascular injury
- Characterization of plasma and muscle tissue lipidomic profiles of diabetic vs. non-diabetic coronary artery bypass grafting patients.
- Comparison of tissue and plasma lipidomics in diabetic patients undergoing CABG (coronary artery bypass graft) after a Mediterranean diet intervention.
- Lipidomic profiles of post-cardiac arrest patients grouped by smoking history

Proteomics and Lipidomics

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Research Highlights

SWATH analysis of mouse adipose tissue



Proteomics and Lipidomics

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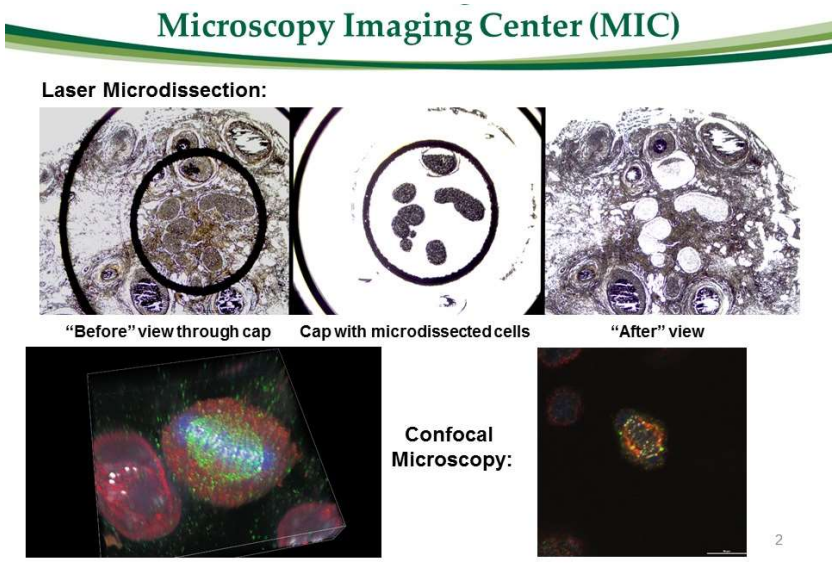
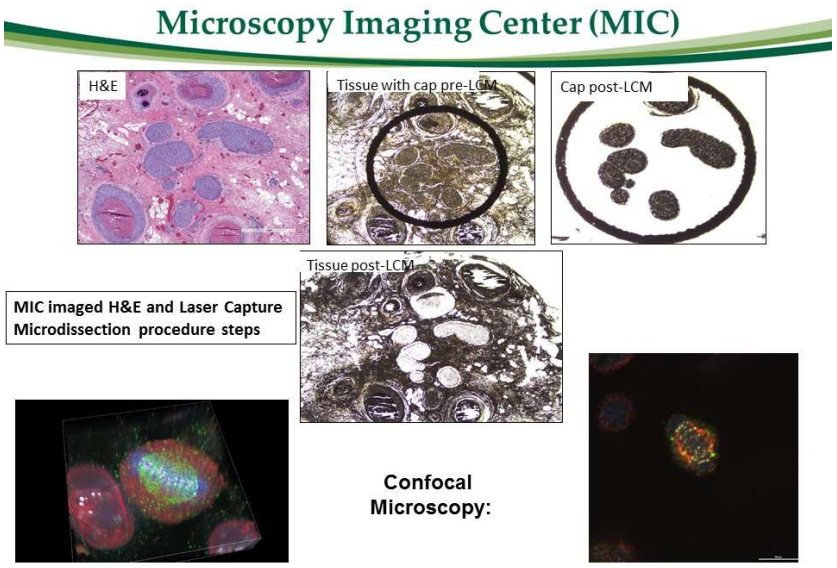
Research Highlights

The Molecular and Cellular Characterization of Screen-Detected Lesions (MCL) project is a multi-center national consortium investigating early tumors; NIH Pre-Cancer Atlas (PCA) initiative. Imaging documentation of breast ductal carcinoma *in situ* (DCIS) lesions laser capture microdissection (LCM) for next-generation sequencing (NGS) applications and correlation with multiplex immunofluorescence staining profiles of multiple biomarkers.





Microscopy Imaging Center

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Shared technology resources for a sustainable translational biomedical research program-New capabilities enhance rigor and reproducibility

Vermont Integrative Genomics Resource: 10X Genomics Chromium Single Cell Sequencer, Illumina MiSeq and epMotion Robot will support analysis of biological specimens for clinical and translational research.

Illumina MiSeq
short read sequencer

10x Chromium
Single cell sorter

epMotion 5073
liquid handler

BioRad QX200
Digital Droplet PCR

Illumina MiniSeq
short read sequencer

Oxford Nanopore
long read sequencer

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Shared technology resources for a sustainable translational biomedical research program-New capabilities enhance rigor and reproducibility

Microscopy Imaging Center: Spectral Imaging Detection for use on the Nikon A1R confocal microscope-in conjunction with multiplex IHC and autostainer allows imaging of an almost limitless number of antibodies in a tissue section.

- ***Spectral Imaging on Nikon A1R HD confocal***

  Provides enhanced methodological choices for investigators seeking to image multiple antigens on a single tissue section, cultured cell, or organoid.

- ***Leica BOND RX^{m} Autostainer***

  Automated baking, deparaffinization, cell conditioning and staining for IHC, ISH, RNAscope

  Fully automate staining protocols for enhanced reproducibility

- ***High-resolution/High-throughput microscope***

  Ability to automate fluorescence multidimensional confocal imaging of genetic and pharmaceutical effects on live samples-high resolution and speed

- ***Indica Labs HALO image analysis platform***

  Sophisticated, flexible, state-of-the-art software to simplify and automate complex analyses for high-throughput, quantitative tissue analysis in oncology

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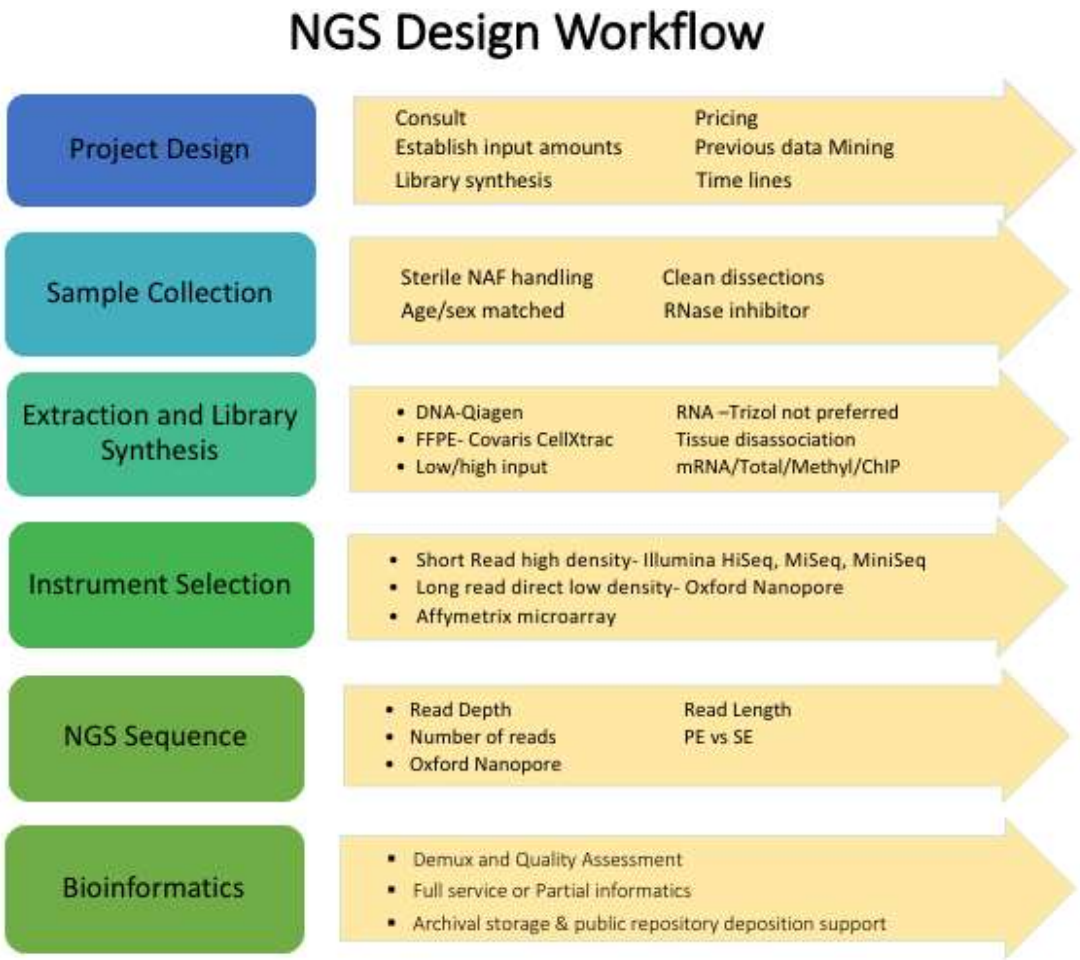
Shared technology resources for a sustainable translational biomedical research program-New capabilities enhance rigor and reproducibility

Proteomics and lipidomics: In-house nanoscale liquid chromatography column fabrication; brought on-line a new preparative HPLC platform (Agilent) with a collection of relevant columns (Phenomenex), which allows us to offer 2-dimensional proteomics and TiO_2-based phosphoproteomics. In the coming year this core will expand the use of post-translational modification analyses (Phospho-, acyl- etc.) and more top-down methods, including protein epitope mapping.

Genomic Medicine Laboratory: This resource ensures that genomic testing informs clinical trial investigation and improves the quality of care for patients in rural environments. The validated **GenePanel Solid Tumor (GPST)** has been used towards clinical trials. Currently being validated: NGS panels for Acute Myeloid Leukemia, comprehensive hematologic malignancies; an expanded gene fusion detection panel that also will include tumor agnostic *NTRK* biomarkers and pharmacogenomics testing.

Experimental design, selection of methodologies, analyses, presentations, education

Vermont Integrative Genomic Resources



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Progress

- **Aim 2:** Enhanced education and training outreach on translational research technologies
  - Seminars with partners
  - Launched collaborative technology workshops-interactive training sessions
  - Coordinated with Pilot Projects Cores to ensure that proposed and funded projects are engaged with scientific personnel in relevant cores.
- **Aim 3:** Launched evaluation tools, in collaboration with Tracking and Evaluation and Administrative Cores, to measure the use of core facilities and their effectiveness in advancing clinical and translational research in NNE-CTR as well as to determine the future infrastructure needs of NNE-CTR investigators.

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Plans

- **Aim 1: Enhance TRT integration into research planning**
  - Clinical Genomics Research Resources Seminar on Research and Collaborations
- **Aim 2: Enhance education and training outreach on TRT**
  - Coordinate with Pilot Projects Cores to ensure that proposed and funded projects are engaged with scientific personnel in relevant cores: **ongoing.**
  - Expanding TAC advisory meetings to ensure opportunities for all investigators.
- **Aim 3: Assess and expand evaluation tools, in collaboration with Tracking and Evaluation and Administrative Cores, to determine the impact of TRT**
  - Developing standardized reporting structure for technical cores.

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

New Opportunities

- **UVM Biomedical Research Shared Resource Center**
  NIH C06 Construction
  (Senior Associate Dean Gordon Jensen)

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

QUESTIONS?

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Clinical Research Design, Epidemiology & Biostatistics Core

Maine Medical Center

The University of Vermont

UNIVERSITY OF SOUTHERN MAINE

CRDEB Personnel

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Susan L Santangelo, ScD
Core lead
Maine Medical Center

Bernard (Chip) Cole, PhD
Core co-lead
University of Vermont

CRDEB Personnel

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Biostatisticians

MMC	UVM
Christine Duarte, PhD	Abby Crocker, PhD
Kim Murray, MPP	Ya Tuo, MS

Research Navigators/Catalysts

MMC	UVM
Wendy Craig, PhD	Diantha Howard, PhD
Ivette Emery, PhD	
Melissa Graham, RN CCRC	
Lee Lucas, PhD	
Ellyn Touchette, BS	
Deanna Williams, BA	

CRDEB Aim

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- Facilitate the appropriate use of computationally-intensive approaches and technologies in clinical, translational, and epidemiologic studies
  - Research navigation, study design and statistical analyses
  - Genomic analyses and data mining of publicly available genomics resources
  - Computer program and applications development for clinical bioinformatics and biomedical informatics analyses, and for mining electronic health records

Recent Hires

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

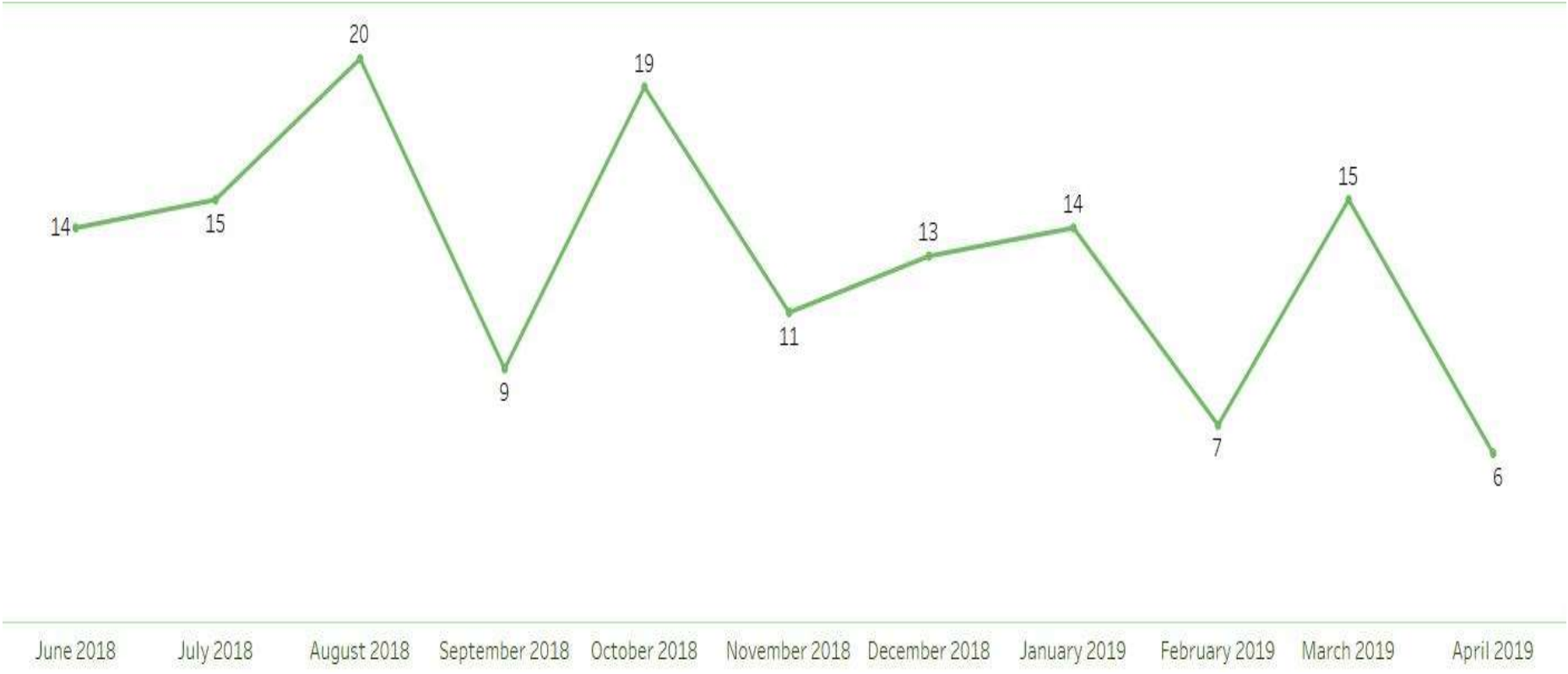
- ✓ Hired 2 new statistical analysts
  - ✓ 0.5 FTE at UVM
  - ✓ 1.0 FTE at MMC
- ✓ Hired Biomedical Informatics Engineer, David Denton
  - ✓ Started December 10, working on multiple projects
  - ✓ Is over ½ way through EPIC certification training
  - ✓ Attended national conference on uses of ‘R’ software
  - ✓ Will begin holding office hours on ‘R’ applications this month

CRDEB Core Metrics

June 1, 2018 – April 11, 2019

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

New Requests for Services



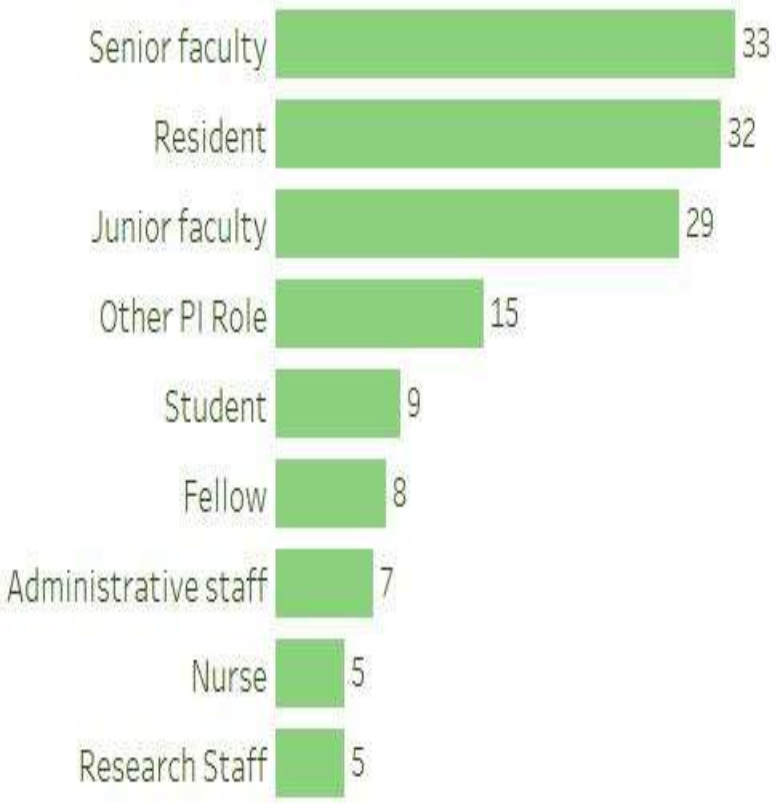
143 new requests

CRDEB Core Metrics

June 1, 2018 – April 11, 2019

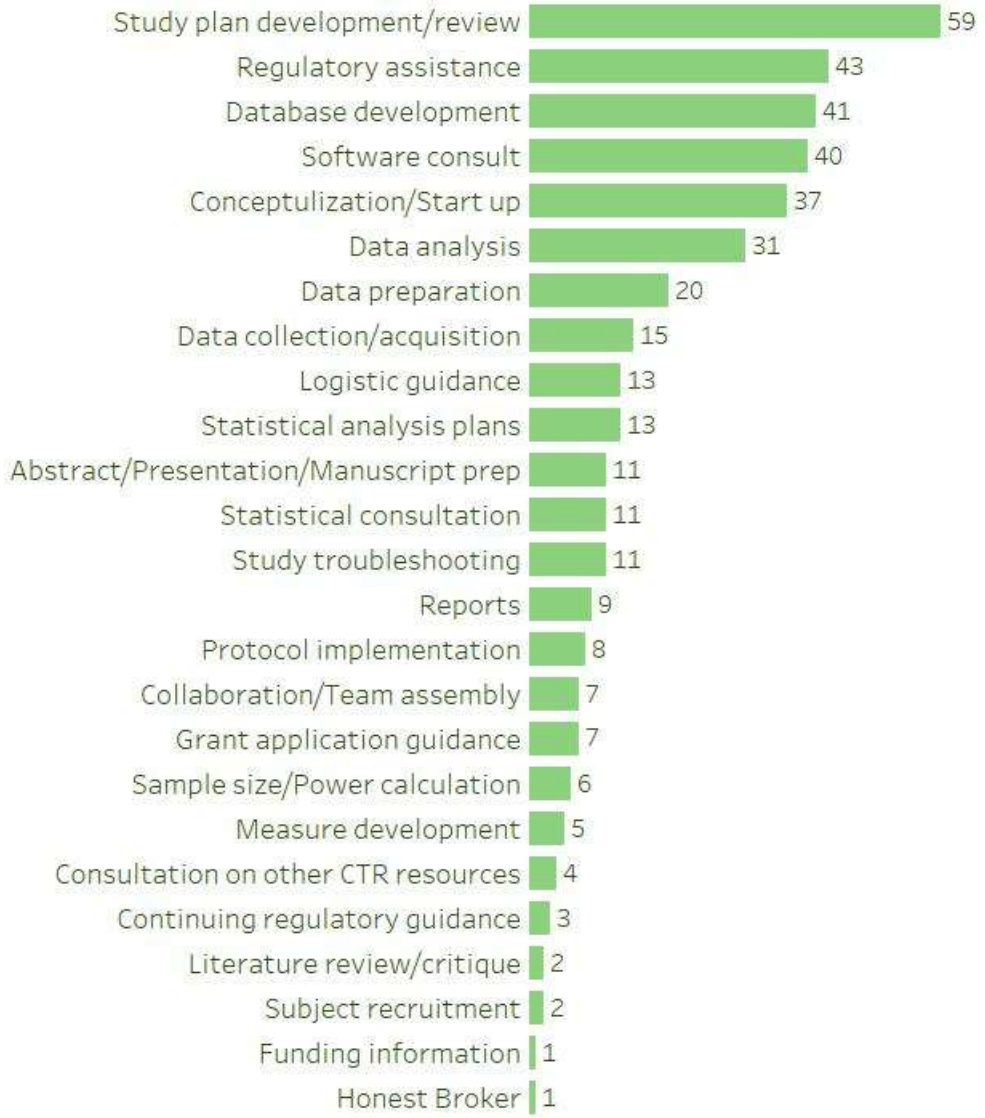
NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Roles of those requesting services



n= 129 unique users; some made multiple requests during this period.53% were students, trainees or junior faculty

Types of Services Requested



Milestones

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- ✓ Results of CRDEB Core/Research Navigation user satisfaction survey (1st sent December 2018, multiple f/up reminders)

  84 investigators responded

  - 98% of them said they would work with the Research Navigation Team again and would recommend it to a colleague.
  - 93% said they "strongly agree" or "agree" that the team was "easy to work with"
  - 96% said they "strongly agree" or "agree" that the team "responded to inquiries in a timely manner"
  - 95% said they "strongly agree" or "agree" that the team were knowledgeable
  - 95% said they "strongly agree" or "agree" that the team assisted them in working toward their goals
  - 95% reported being "highly satisfied" or "satisfied" overall with the services, resources or supports provided by the CRDEB Core and Research Navigation Team

Milestones

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- ✓ CRDEB Core leads participated in review of Pilot Project LOIs and grant applications
- ✓ Biomedical Informatics Engineer, David Denton
  - Completed Epic EHR certification training in March
    - Started in December
  - Holds weekly office hours on use of 'R' software
  - Leads R-user's support & info group, monthly
- ✓ Just received notice that grant application submitted to Tufts CTSI in December will be funded
  - $30K to help with OMOP/OHDSI build-out
  - Start date May 1, 2019

Milestones

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- ✓ A day-long Data Carpentry Workshop
  - Was held and recorded at MMC on April 2
  - With video link to UVM to accommodate participants at both locations (30 participants overall)
  - Led by an official Data Carpentry instructor
    - With local facilitation by D. Denton, and two data analysts
- ✓ 2nd (of the year) Clinical Research Course
  - Was held at MMCRI and recorded on April 4
    - Day-long, held bi-annually
  - Didactic video segments will be posted on CRDEB Core web page soon

Challenges

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- Inadequate computational infrastructure for research
  - Even with the new servers we purchased & plan to buy, infrastructure is lacking
  - Purchasing & upgrading hardware to try to keep up is not sustainable in long-run
- Ability to use cloud computing platforms for research
  - MaineHealth IT privacy & security has just agreed to allow use of cloud services for de-identified genomics data only
  - Will not allow cloud usage for patient, EHR or any PHI data
  - Will require much more education and partnership with IT
  - May require dedicated research IT team at MMC
    - MaineHealth does not have a CRIO or any dedicated IT support for research. IT focus is on supporting clinical services (99%)
    - Little recognition that research IT needs differ substantially from clinical

Next Steps

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- Continue meeting with MaineHealth IT
  - To discuss research needs & challenges and find solutions
- Largest project for Y03 will be developing clinical research data warehouse built on OMOP common data model & OHDSI tools
  - Focus of Specific Aim 3
  - To enable cohort discovery to support clinical trials and facilitate use of observational data in research
  - Grant from Tufts CTSI will enable OMOP/OHDSI build-out
    - Both Maine & Vermont hospital systems use Epic EHR
    - Initiate Epic-to-OMOP ETL at MaineHealth, followed by same work at UVM in subsequent years
- Core lead Santangelo is a founding member of the IDeA-CTR Informatics Coalition
  - Participating in monthly calls

Next Steps

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- Explore possibility of hosting our own REDCap instance at MMC/MaineHealth
  - REDCap is a secure HIPAA compliant data storage, and management platform for quality/process improvement initiatives, research, and operational processes
  - Currently we rely on Tufts CTSI for REDCap
    - MMC investigators and operations are heaviest users in number and intensity than entire Tufts community
    - MMC usage places undue burden on Tufts and there is concern they may need to restrict our use in future
  - We are currently estimating costs of hosting REDCap at MaineHealth, getting buy-in & support from IT

Project Examples

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

- Cystic Fibrosis—lung function and continuity of care
- Lung cancer location and risk of lymph node metastasis
- Sleep disturbance on bedside EEG: a biomarker for neonatal abstinence syndrome
- Community health worker-delivered intervention to slow progression of functional decline among at-risk rural older adults
- Harnessing the electronic health record in primary care for hepatocellular carcinoma surveillance in cirrhosis
- Cross-sectional study of the association between circadian phase and challenging daytime behavior in low-functioning children
- Opioid and rural-health collaborations with VDH

Current Challenges in Cancer Control

Robert T. Croyle, PhD

Director, Division of Cancer Control and Population Sciences

Acting Director, Center for Global Health

National Cancer Institute

NNE CTR Summer Retreat

June 7, 2019

NIH NATIONAL CANCER INSTITUTE

Annual Report to the Nation on the Status of Cancer, 1999–2015, Featuring Cancer in Men and Women ages 20–49

Elizabeth Ward, PhD ✉, Recinda L Sherman, PhD, MPH, CTR, S Jane Henley, MSPH, Ahmedin Jemal, DVM, PhD, David A Siegel, MD, MPH, Eric J Feuer, PhD, MS, Albert U Firth, BS, Betsy A Kohler, MPH, CTR, Susan Scott, MPH, Jiemin Ma, PhD, MHS Robert N Anderson, PhD, Vicki Benard, PhD, Kathleen Cronin, PhD, MPH

JNCI: Journal of the National Cancer Institute, djz106,
https://doi.org/10.1093/jnci/djz106
Published: 30 May 2019 **Article history** ▾

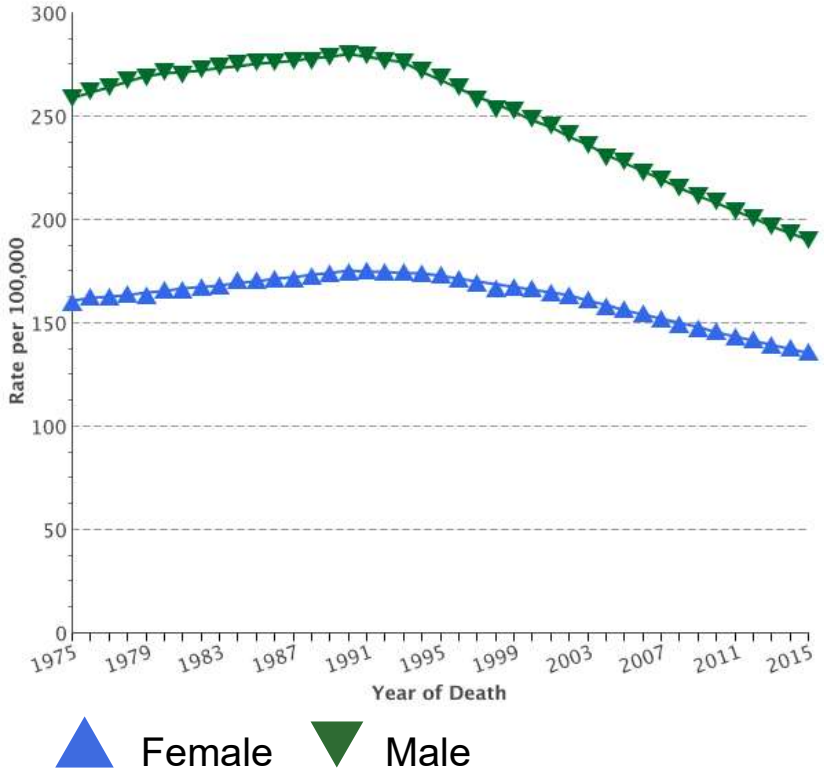
Overall Cancer Statistics

Special Topic: Cancer Among Adults Ages 20–49

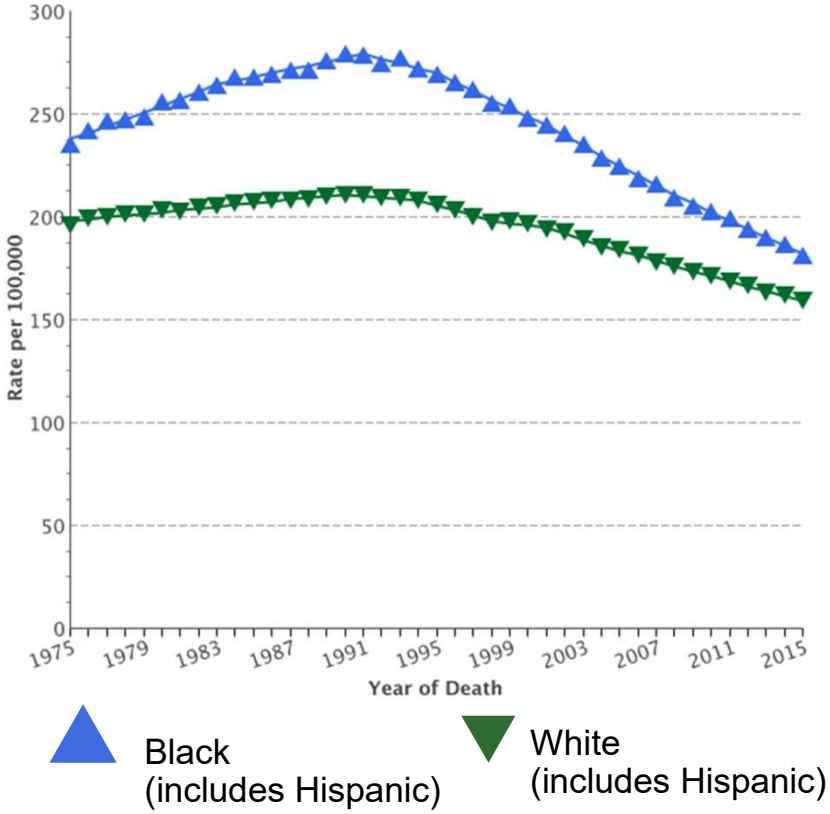
Deadliest Cancer Types for Ages 20-49, 2012 - 2016

MEN	WOMEN
1. COLORECTAL	1. BREAST
2. LUNG	2. LUNG
3. BRAIN	3. COLORECTAL

All Cancer Sites Combined
Long-Term Trends in US Mortality Rates, 1975-2015
By Sex
All Races (includes Hispanic), All Ages



All Cancer Sites Combined
Long-Term Trends in US Mortality Rates, 1975-2015
By Race/Ethnicity
Both Sexes, All Ages



Source: NCI Surveillance, Epidemiology, and End Results Program

NIH NATIONAL CANCER INSTITUTE

STATE CANCER PROFILES

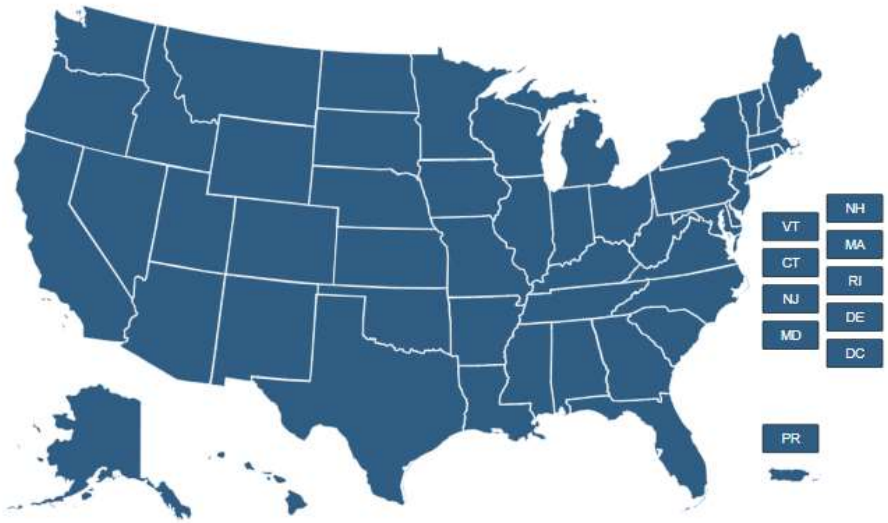
Dynamic views of cancer statistics for prioritizing cancer control efforts in the nation, states, and counties

CDC

Home | About | Help & Resources | Contact

Quick Profiles for States

Choose a state below to get a report of cancer statistics and other related topics.



--- Choose a State ---

View Quick Profile ›

Data Topics Across the Cancer Control Continuum

Cancer statistics, charts, and maps by data topic across the cancer control continuum.

- Demographics
- Screening & Risk Factors
- Cancer Knowledge
- Incidence
- Prevalence
- Mortality

NATIONAL CANCER INSTITUTE
Cancer Trends Progress Report

Dictionary | Custom Report (PDF)

Online Summary of Trends in US Cancer Control Measures

Prevention | Early Detection | Diagnosis | Treatment | Life After Cancer | End of Life | Summary Tables

The Cancer Trends Progress Report, continually updated since its first issue in 2001, summarizes our nation's advances against cancer in relation to Healthy People targets set forth by the Department of Health and Human Services. The report, intended for policy makers, researchers, and public health professionals, includes key measures of progress along the cancer control continuum and uses national trend data to illustrate where improvements have been made.

Read our Introduction and Director's Message to learn more about the report.

- About the Report
- Data Sources
- Highlights
- Trends at a Glance
- Recent Updates and Archive

Subscribe for Website Update Notifications

Prevention

Tobacco, physical activity, diet, sun, environment, HPV immunization

Early Detection

Breast, cervical, colorectal, lung, prostate cancer screening

Diagnosis

Incidence, Stage at diagnosis

Treatment

Trends in cancer treatment

Life After Cancer

Financial burden of cancer care, Cancer survivorship

End of Life

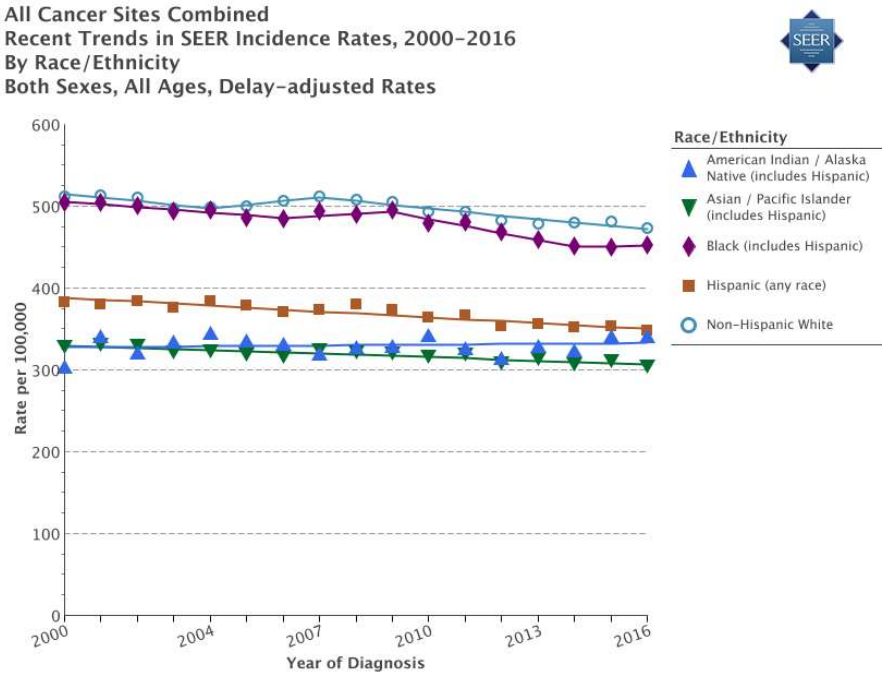
Mortality, Person-years of life lost

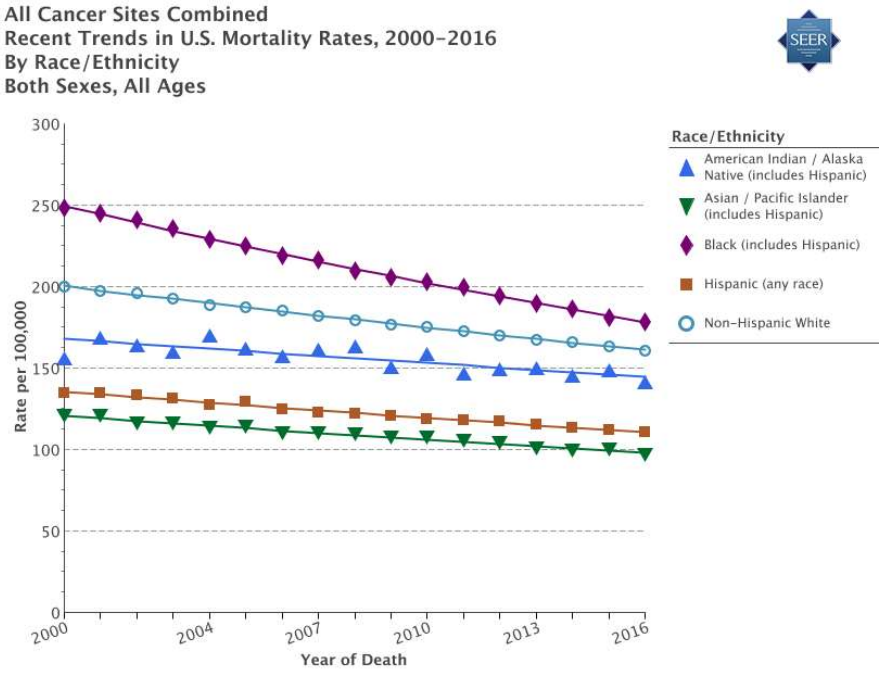
The report, available only online, can be printed in part or in its entirety. Portions of the report are updated annually, while other sections are updated as new data become available. The full report is updated every year.

Suggested Citation:

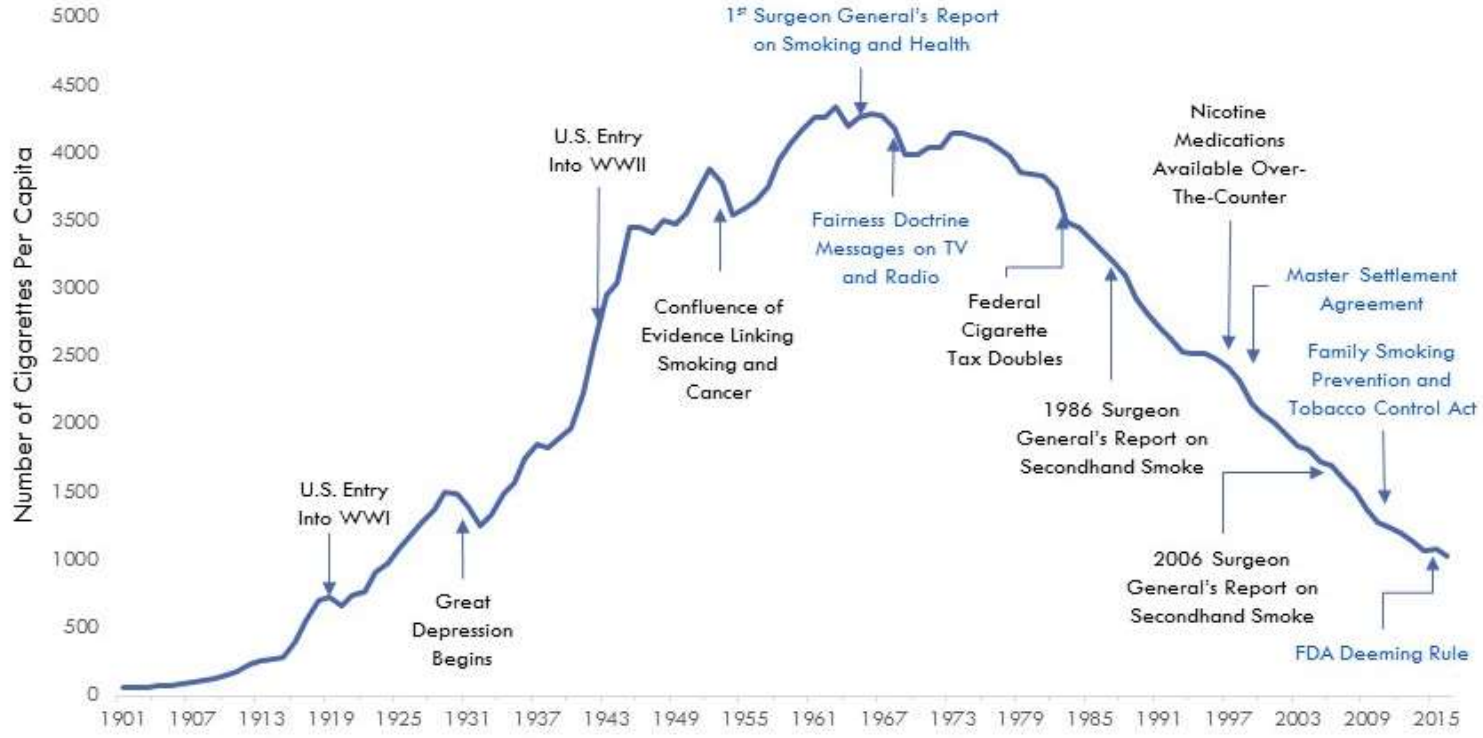
Cancer Trends Progress Report
National Cancer Institute, NIH, DHHS, Bethesda, MD, February 2018, https://progressreport.cancer.gov.

Incidence and Mortality
All Cancer Sites Combined By Race/Ethnicity





Adult per Capita Cigarette Consumption and Major Smoking-and-Health Events – US, 1900-2016

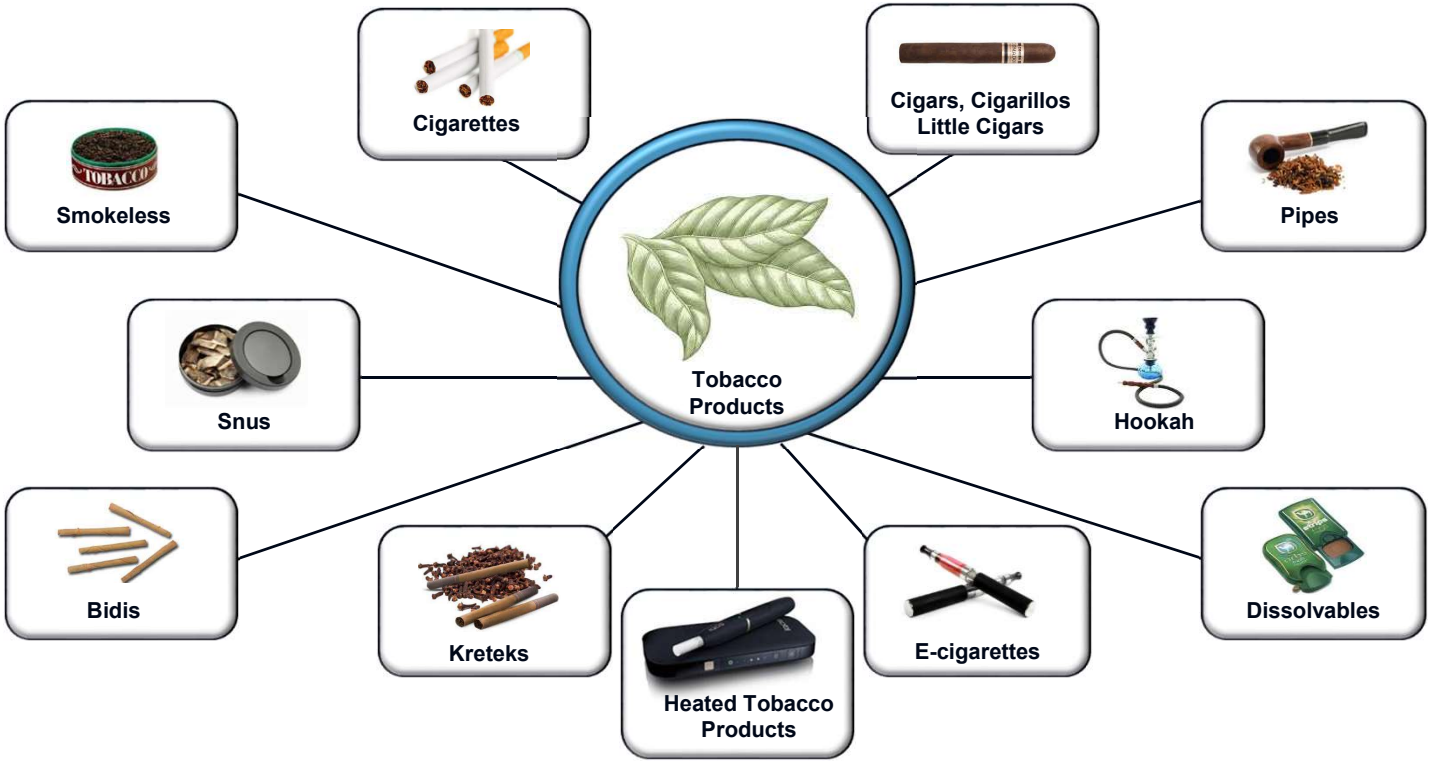


Sources: Adapted from Warner 1985 with permission from Massachusetts Medical Society, © 1985; U.S. Department of Health and Human Services 1989; Creek et al. 1994; U.S. Department of Agriculture 2000; U.S. Census Bureau 2016; U.S. Department of the Treasury 2016.

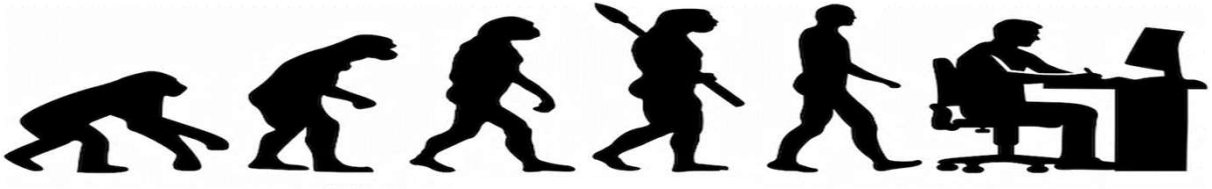
Despite remarkable progress, still a staggering toll

- US deaths per year from drug overdose: 70,000
- US deaths per year from tobacco use: 480,000

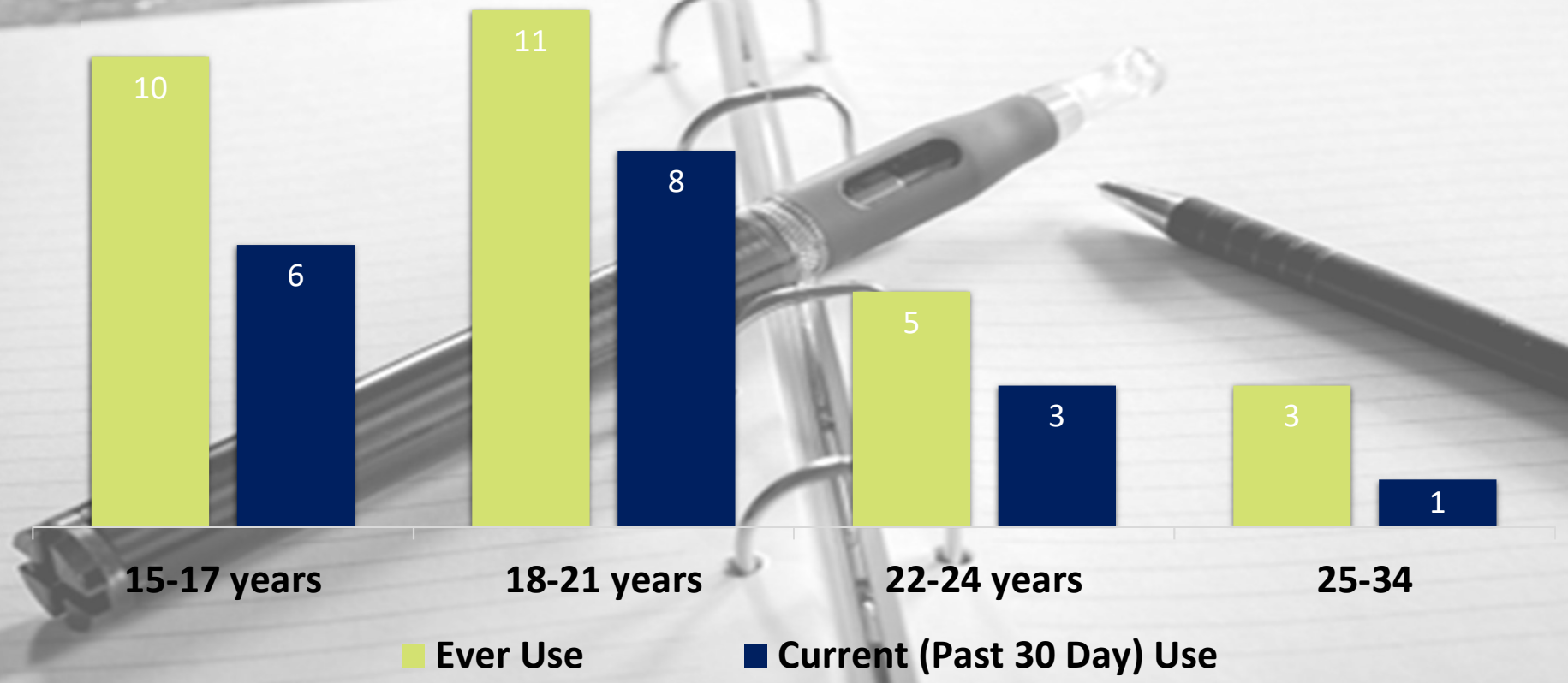
The Tobacco Product Landscape Is Evolving



The Evolution of e-cigarettes

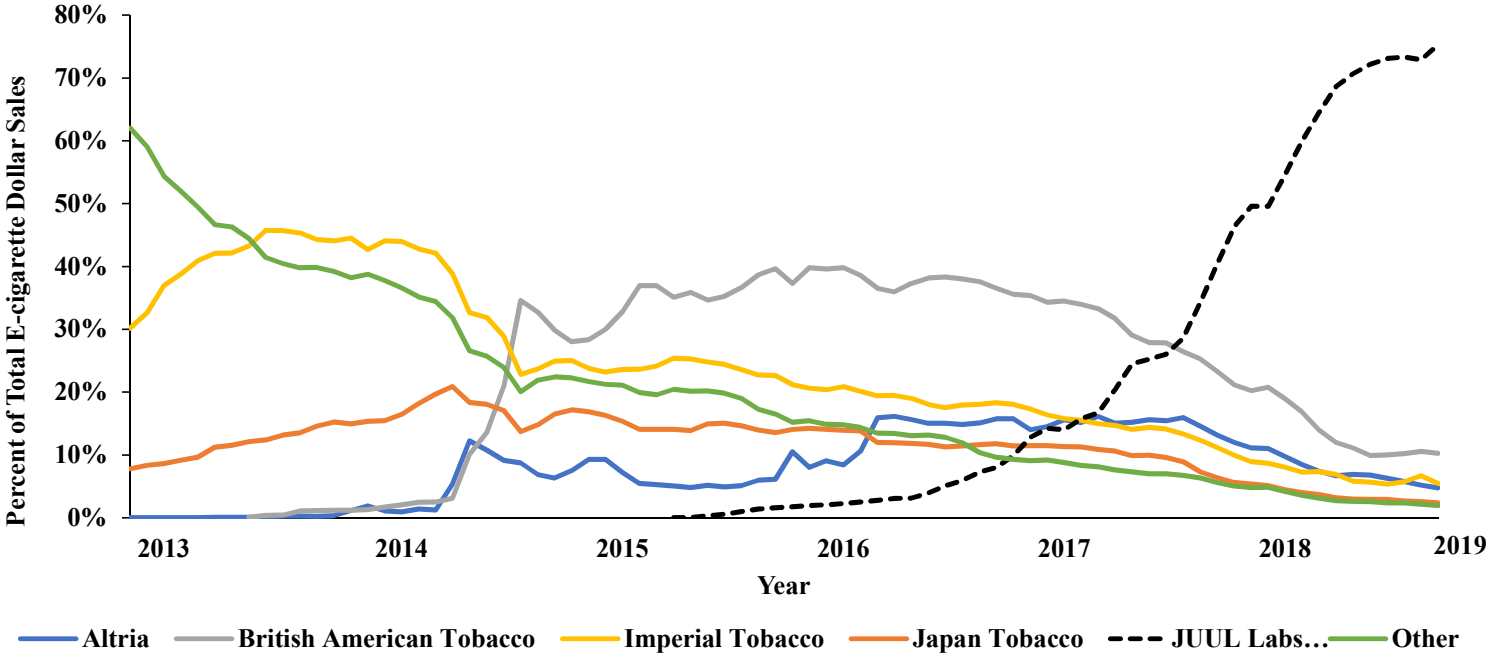


JUUL Use Among U.S. Young People (February – May, 2018)



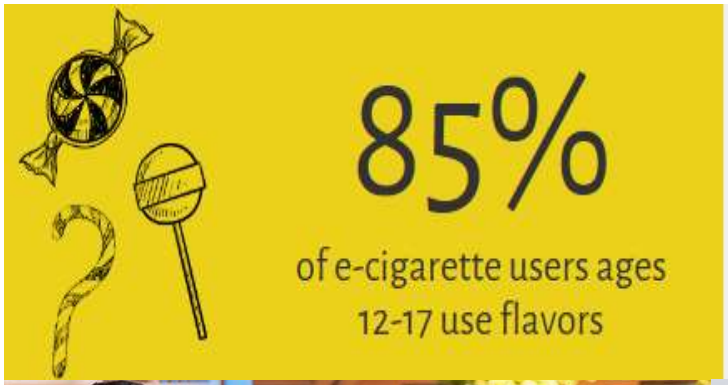
Source: Vallone DM, Bennett M, Xiao H, et al Prevalence and correlates of JUUL use among a national sample of youth and young adults Tobacco Control Published Online First: 29 October 2018.

E-Cigarette Market Share, by Dollar Sales, United States, 2013-2018



Source: King, Brian A, **The Rise of the Pod Mod:** Trends in E-Cigarette Sales in the US, 2013-2017. Paper presented at: 25th Annual Meeting of SRNT; February 2019; San Francisco, CA.

Youth Use Flavored E-cigarettes



85%

of e-cigarette users ages 12-17 use flavors

menthol
alcohol
candy

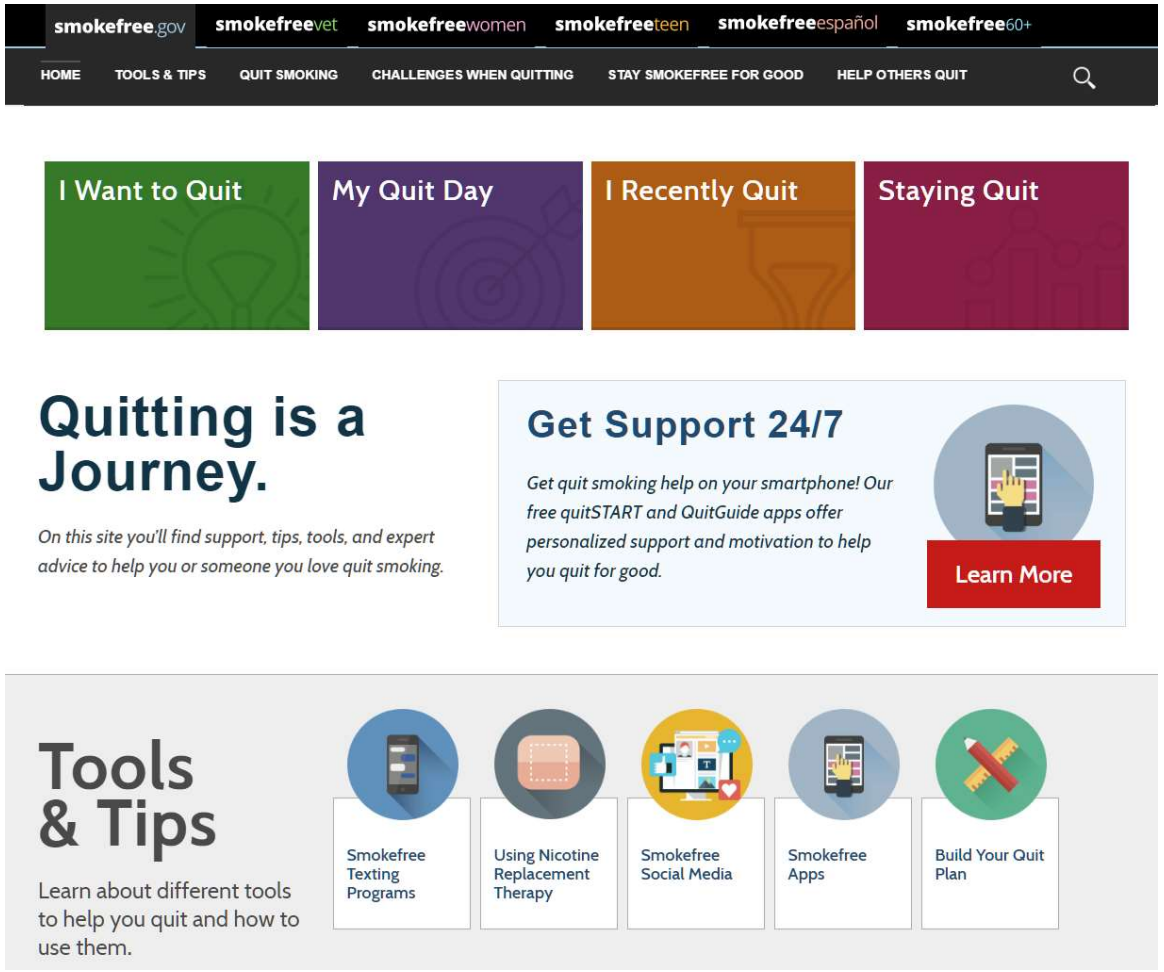
fruit
chocolate
sweets

E-cigarettes and Smoking Cessation

- Complete switching from cigarettes to e-cigarettes is required to realize potential health benefits
- Understanding the effect of e-cigarettes on cessation is complicated by
  - diversity and rapid change in product marketplace
  - wide variation in motivations for use
  - no product approved for therapeutic purpose
- Few RCTs have directly tested the efficacy of e-cigarettes for cessation – all were conducted outside the U.S.
  - IND requirement makes it impossible to conduct RCT for cessation

NIH E-cigarette Funding Opportunity Announcement

- **PAR 18-847/848: Electronic Nicotine Delivery Systems (ENDS): Population, Clinical and Applied Prevention Research** (R01/R21) - NCI, NIDA, NIDCR, NIMHD
  - Purpose: to support studies on ENDS that examine population-based, clinical and applied prevention of disease (including cancer, dental, oral, and/or craniofacial) including etiology of use, epidemiology of use, potential risks, benefits and impacts on other tobacco use behavior among different populations
  - Specific topics of interest to NCI include, but are not limited to:
    - Studies to identify risk and protective factors for ENDS use, including dual/poly-tobacco product use among youth and young adults (such as, but not limited to, perceptions of risk/benefit, parent influences, peer influences, relationship to other substance use, proximity to tobacco outlets, density of tobacco outlets and other environmental factors)
  - NCI's Scientific Contact: Rachel Grana Mayne, PhD, MPH
  - Last receipt date: June 27, 2020


smokefree.gov
smokefreevet
smokefreewomen
smokefreeteen
smokefreeespañol
smokefree60+
HOME
TOOLS & TIPS
QUIT SMOKING
CHALLENGES WHEN QUITTING
STAY SMOKEFREE FOR GOOD
HELP OTHERS QUIT
I Want to Quit
My Quit Day
I Recently Quit
Staying Quit
Quitting is a Journey.
On this site you'll find support, tips, tools, and expert advice to help you or someone you love quit smoking.
Get Support 24/7
Get quit smoking help on your smartphone! Our free quitSTART and QuitGuide apps offer personalized support and motivation to help you quit for good.
Learn More
Tools & Tips
Learn about different tools to help you quit and how to use them.
Smokefree Texting Programs
Using Nicotine Replacement Therapy
Smokefree Social Media
Smokefree Apps
Build Your Quit Plan

FDA Approves New Lung Cancer Treatment and First Next-Gen Companion Diagnostic

Posted on June 29, 2017 by Karen Honey, PhD

Recent decisions by the U.S. Food and Drug Administration (FDA) are significantly advancing the field of precision medicine.

Hot on the heels of the FDA's landmark approval of an anticancer immunotherapeutic for use based on whether a patient has a tumor with certain

HEALTH

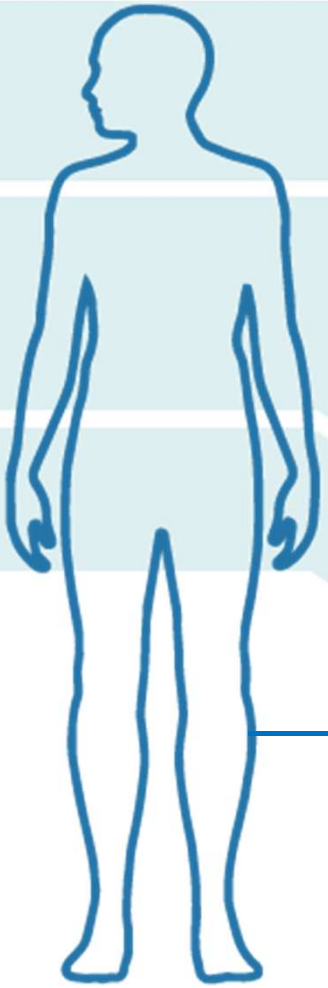
Cancer-fighting immunotherapy recommended for FDA approval

Concerns about drug's long-term safety remain

By MICHAEL NEDELMAN , CNN

Posted: 7:26 PM, July 12, 2017
Updated: 5:20 PM, July 13, 2017

Cancer Drug Approvals in 2018



Cutaneous squamous cell cancer
- Cemiplimab-rwlc

Merkel cell cancer
- Pembrolizumab

Melanoma
- Encorafenib + binimetinib
- Dabrafenib + trametinib

Thyroid cancer
- Dadrafenib + trametinib

TSC-associated seizures
- Everolimus

Adrenal gland (PPGL)
- Iobenguane I-131

Breast Cancer
- Talazoparib
- Ribociclib
- Abemaciclib
- Olaparib
- Trastuzumab-pkrb

Colorectal cancer
- Ipilimumab + nivolumab

GEP-NET
- Lutetium Lu-177 dotatate

Hepatocellular cancer
- Pembrolizumab
- Lenvatinib

Lung cancer
- Dacomitinib
- Lorlatinib
- Pembrolizumab
- Nivolumab
- Osimertinib
- Durvalumab
- Afatinib
- Atezolizumab

Renal cancer
- Ipilimumab + nivolumab

***NTRK* fusion-positive cancers (histology agnostic)**
- Larotrectinib

Cervical cancer
- Pembrolizumab

Ovarian cancer
- Bevacizumab
- Rucaparib
- Olaparib

Prostate cancer
- Enzalutamide
- Apalutamide
- Abiraterone acetate

Urothelial cancer
- Pembrolizumab
- Atezolizumab

Leukaemia
- Gilteritinib
- Duvelisib
- Moxetumomab pasudotox-tdfk
- Ivosidenib
- Venetoclax
- Blinatumomab
- Nilotinib
- Calaspargase pegol-mknl
- Glasdegib

Lymphoma
- Tisagenlecleucel
- Brentuximab vedotin
- Duvelisib
- Rituximab-abbs
- Pembrolizumab

MF/SS
- Mogamulizumab-kpkc

BPDCN
- Tagraxofusp-erzs

HLH
- Emapalumab

Supportive care
- Pegfilgrastim-jmdb
- Epoetin alfa-epbx

From Blumenthal and Pazdur, Nat Rev Clin Oncol, 2019

Trends in Five-year Relative Survival Rates (%), 1975-2012

Site	1975-1977	1987-1989	2006-2012
All sites	49	55	69
Breast (female)	75	84	91
Colorectum	50	60	66
Leukemia	34	43	63
Lung & bronchus	12	13	19
Melanoma of the skin	82	88	93
Non-Hodgkin lymphoma	47	51	73
Ovary	36	38	46
Pancreas	3	4	9
Prostate	68	83	99
Urinary bladder	72	79	79

5-year relative survival rates based on patients diagnosed in the 9 oldest SEER registries from 1975-1977, 1987-1989, and 2006-2012, all followed through 2013.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2016.

With Scientific and Public Health Progress Comes New Challenges

President's Cancer Panel Report, 2018

- Most new cancer drugs are priced higher than $100,000 per patient per year
- "Financial Toxicity" can lead to
  - Skipped medication doses
  - Shortened survival
  - Debt, depleted savings, and bankruptcy

US Healthcare Spending and Return

JJ Prochaska, A Sanders-Jackson

JAMA Internal Med
176(1):41-42 (2016)

- Health care spending (2013)
  - $2.9 trillion total
  - $9,255 per capita
  - 42% higher than the next highest per-capita spender
- Return: life expectancy rank
  - 50th among 221 nations
  - 27th among 34 industrialized Organization for Economic Co-operation & Development (OECD) countries

The Growing Number of Ex-Smokers:

What Do We Have to Offer?

NLST Results

- Nearly 55,000 subjects randomized
- Compliance with LDCT very high (~ 95%)
- LDCT screen positivity rates: ~27% at year 0,1; 16% at year 2
- LDCT positive predictive value: 3-4%
- Mortality benefit: reduction of 16-20% in lung cancer mortality (statistically significant)
- Number needed to screen: ~ 320
- Statistically significant 6.7% reduction in all-cause mortality also observed

Current LDCT Lung Cancer – Screening Recommendations

- US Preventive Services Task Force: age 55-80, 30+ pack years, current smoker or quit within 15 years (NLST criteria, age expanded to 80) – Grade B recommendation
- American Cancer Society: NLST criteria
- American College of Chest Physicians, American Society of Clinical Oncology: NLST criteria (exclude those with severe comorbidities)
- National Comprehensive Cancer Network: NLST criteria or age 50+, ≥ 20 pack years, 1 additional risk factor (e.g., COPD, occupational exposure)

USPSTF Clinical Considerations

- **Smoking cessation is the most important intervention to prevent NSCLC.**
- Advising smokers to stop smoking … is the most effective way to decrease the morbidity and mortality associated with lung cancer.
- Current smokers should be informed of their continuing risk for lung cancer and offered cessation treatments.
- Screening with LDCT should be viewed as an adjunct to tobacco cessation interventions.

Smoking Cessation at Lung Examination (SCALE) Collaboration

Purpose

- Determine key components and characteristics of a successful cessation program at low-dose computed tomography (LDCT) screening
- Focus on innovative interventions or implementation methods
- Share data and methods using common measures for cross-project research

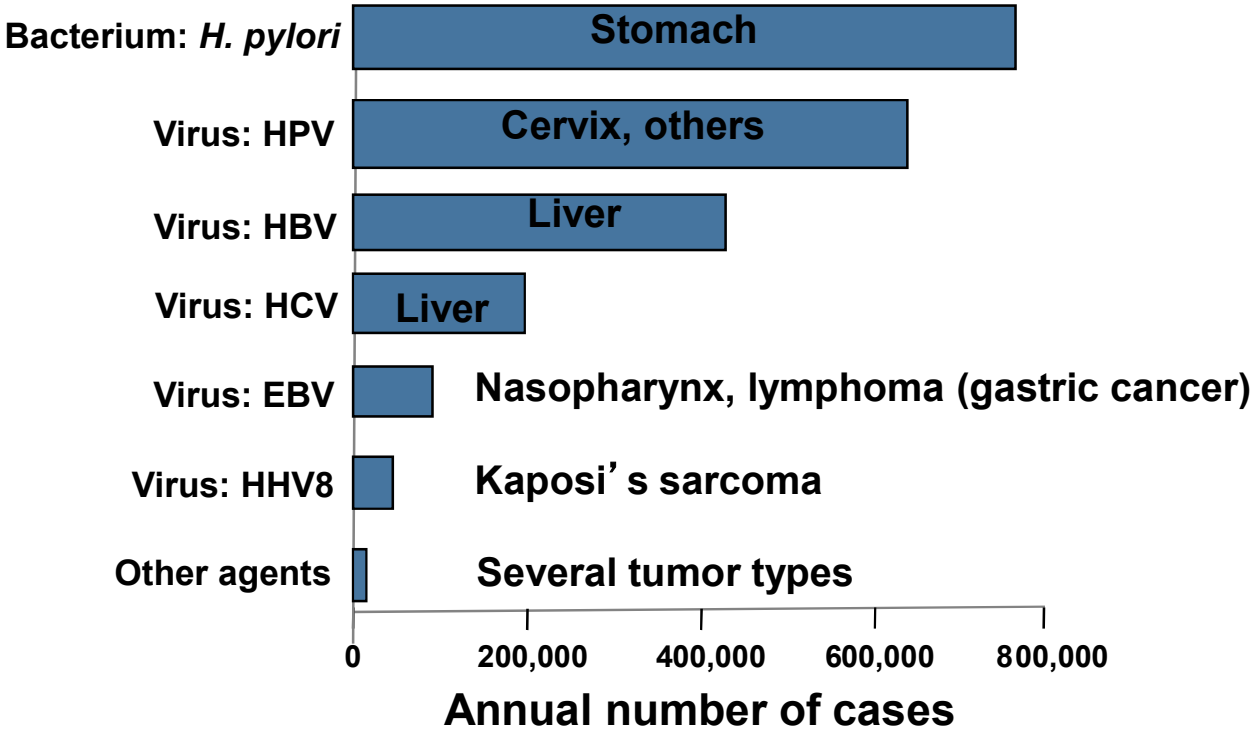
Collaborators: 5 R01s funded under RFA CA-15-011 plus 3 related projects

- Cinciripini (MD Anderson)
- Foley/Chiles (Wake Forest)
- Ostroff/Shelley (Memorial Sloan Kettering)
- Taylor (Georgetown)
- Toll (MUSC)
- Joseph (U Minnesota)
- Zeliadt (Fred Hutchinson)
- Park/Rigotti/Haas (Partners HealthCare)

Another Challenge and Opportunity

The Underappreciated Role of Infections in Cancer Etiology and Prevention

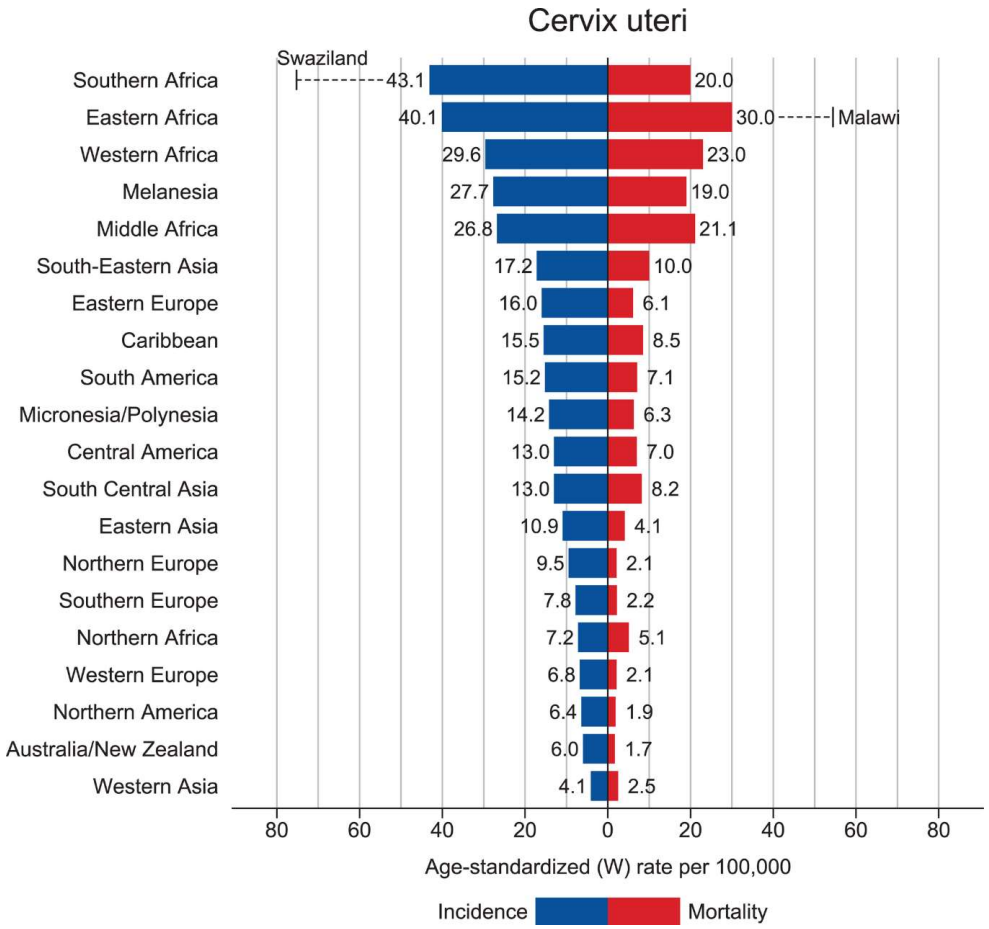
Infectious Agents Cause 15-18% of Cancer Worldwide: Rates Are Higher in LMIC's Than in HIC's

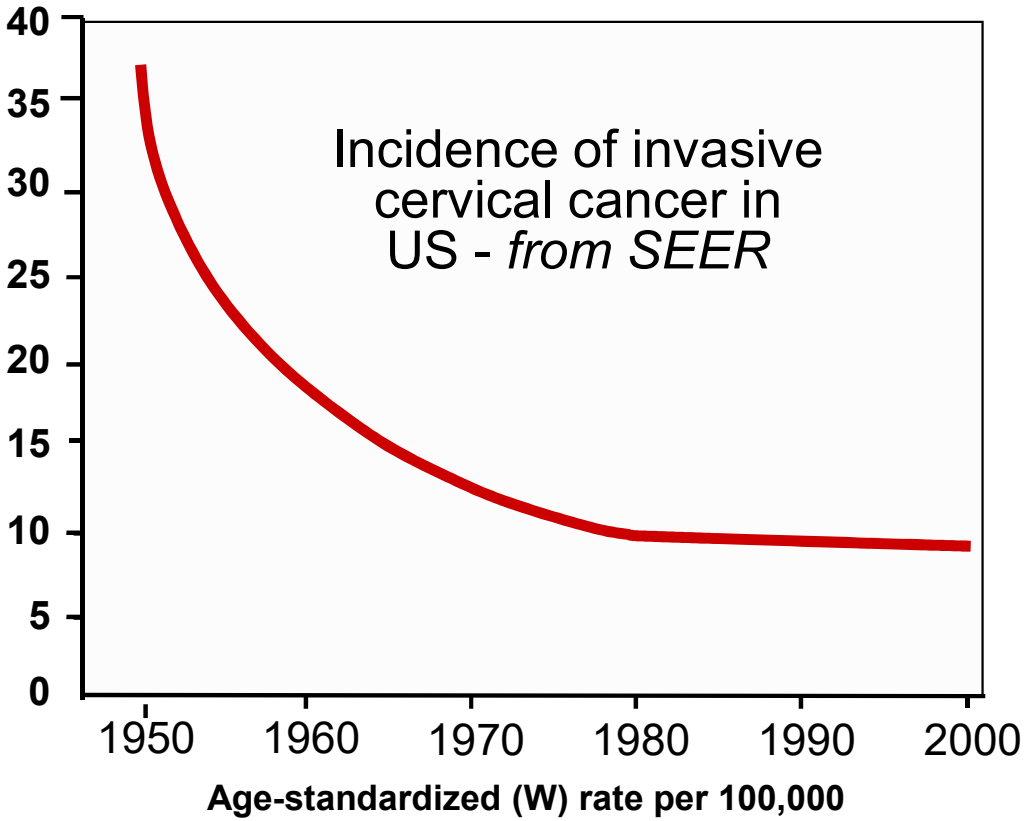


- EBV-associated gastric cancer appears to be a distinct clinico-pathological entity: high promoter methylation & PI3'K mutation: TCGA Research Network. Nature 513: 202-9, 2014

Adapted from Plummer et al, Lancet Glob Health 4: 609-16, 2016

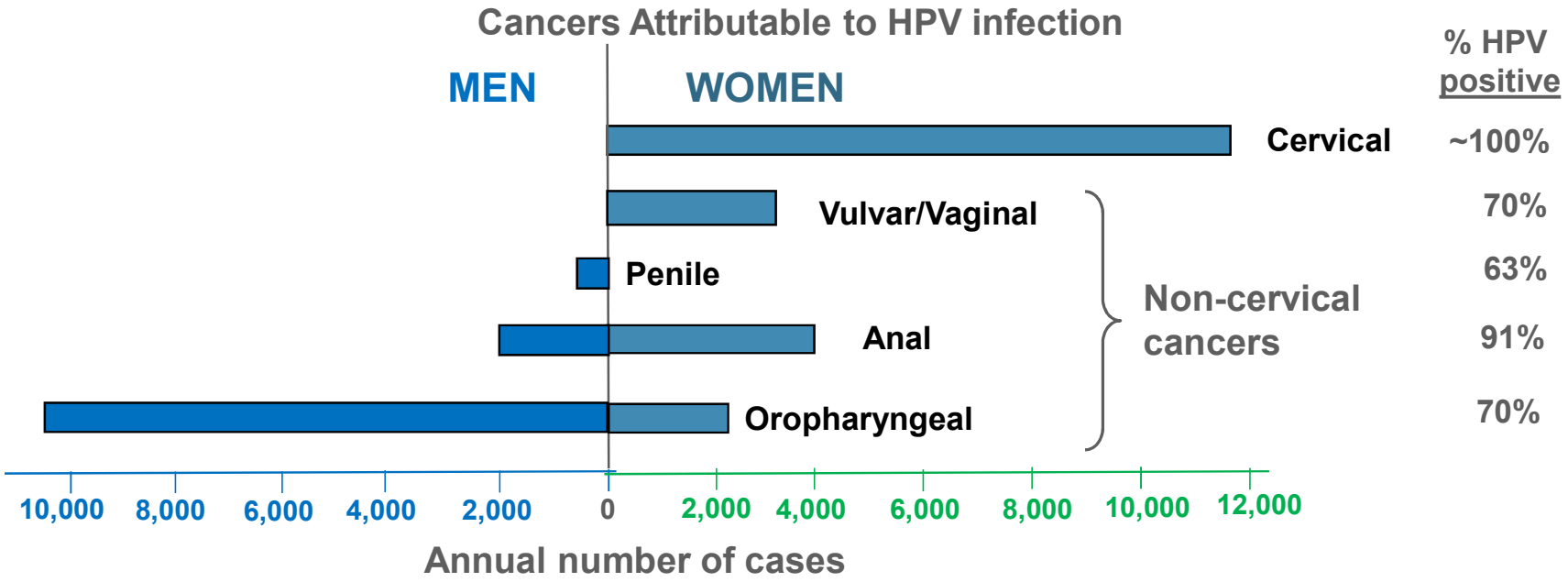
Cervical Cancer: A Largely Preventable Cancer with Wide Global Disparities; 90% of Cervical Cancer Deaths Occur in Low- and Middle-Income Countries





From Bray et al, Global cancer statistics 2018, Cancer 2018

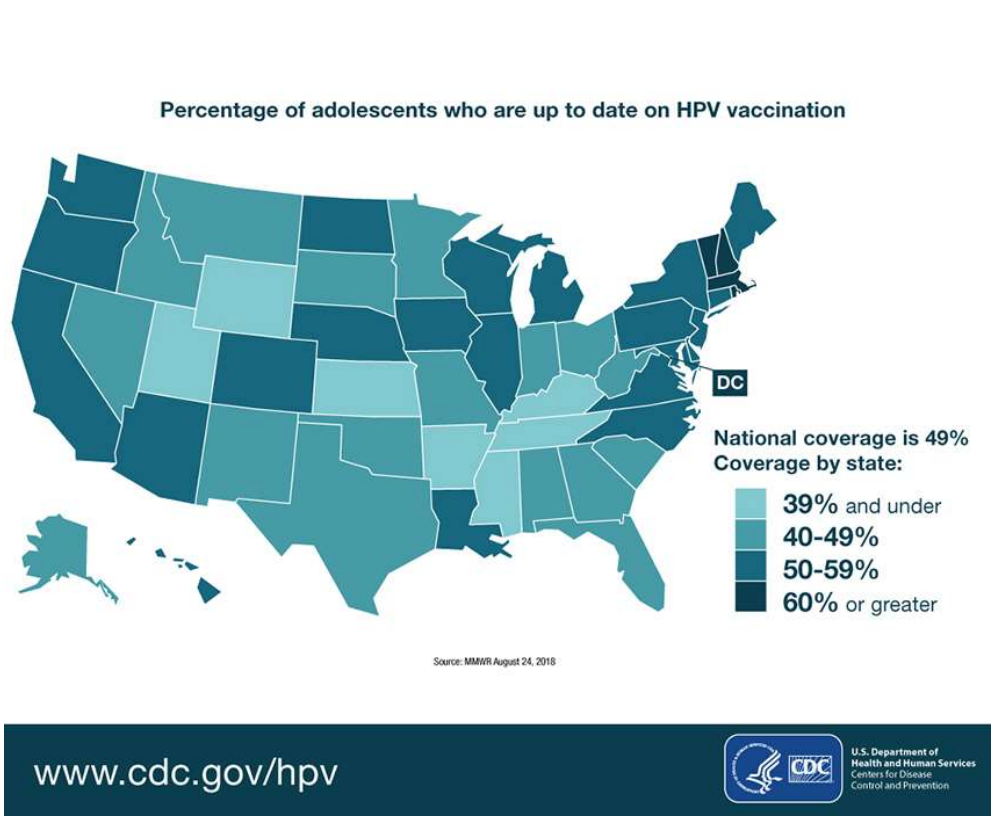
US: HPV-Associated Cancers Affect Both Sexes

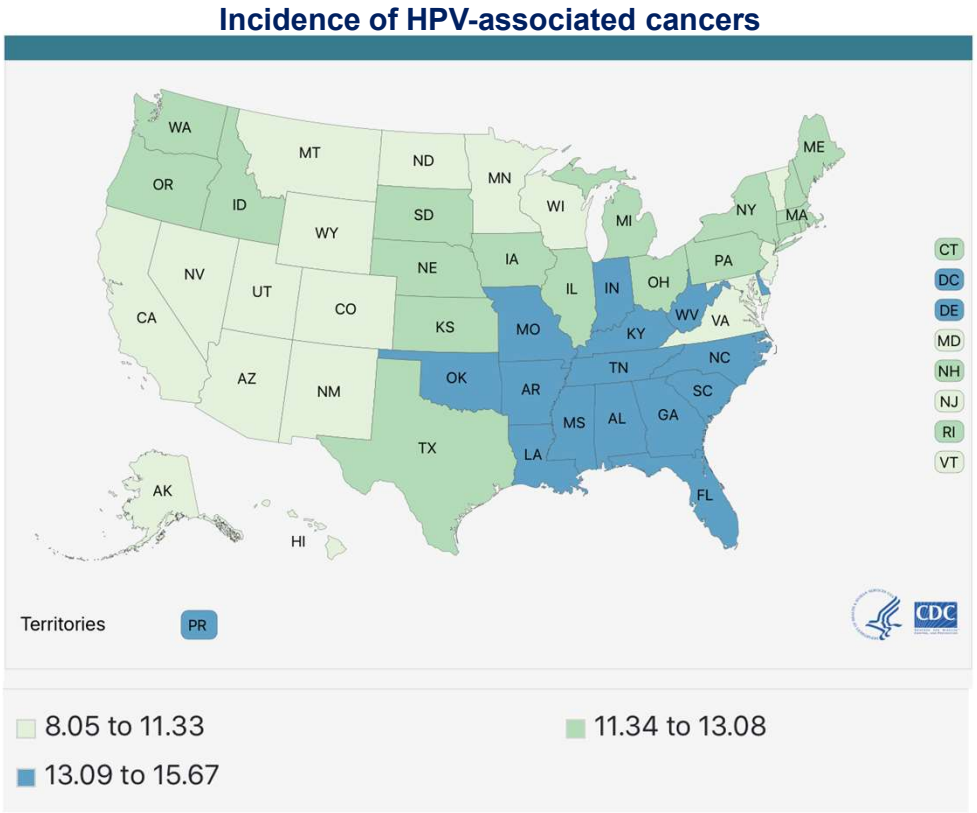


- Total number of HPV-positive cancers = ~33,000. 60% women; 40% men
- HPV16/18: Accounts for ~70% of cervical cancers, ~90% of non-cervical cancers
- Incidence of HPV-positive oropharynx cancer 1988-2004 increased >3-fold
- Vaccination reduces oral HPV16/18 prevalence by ~90%

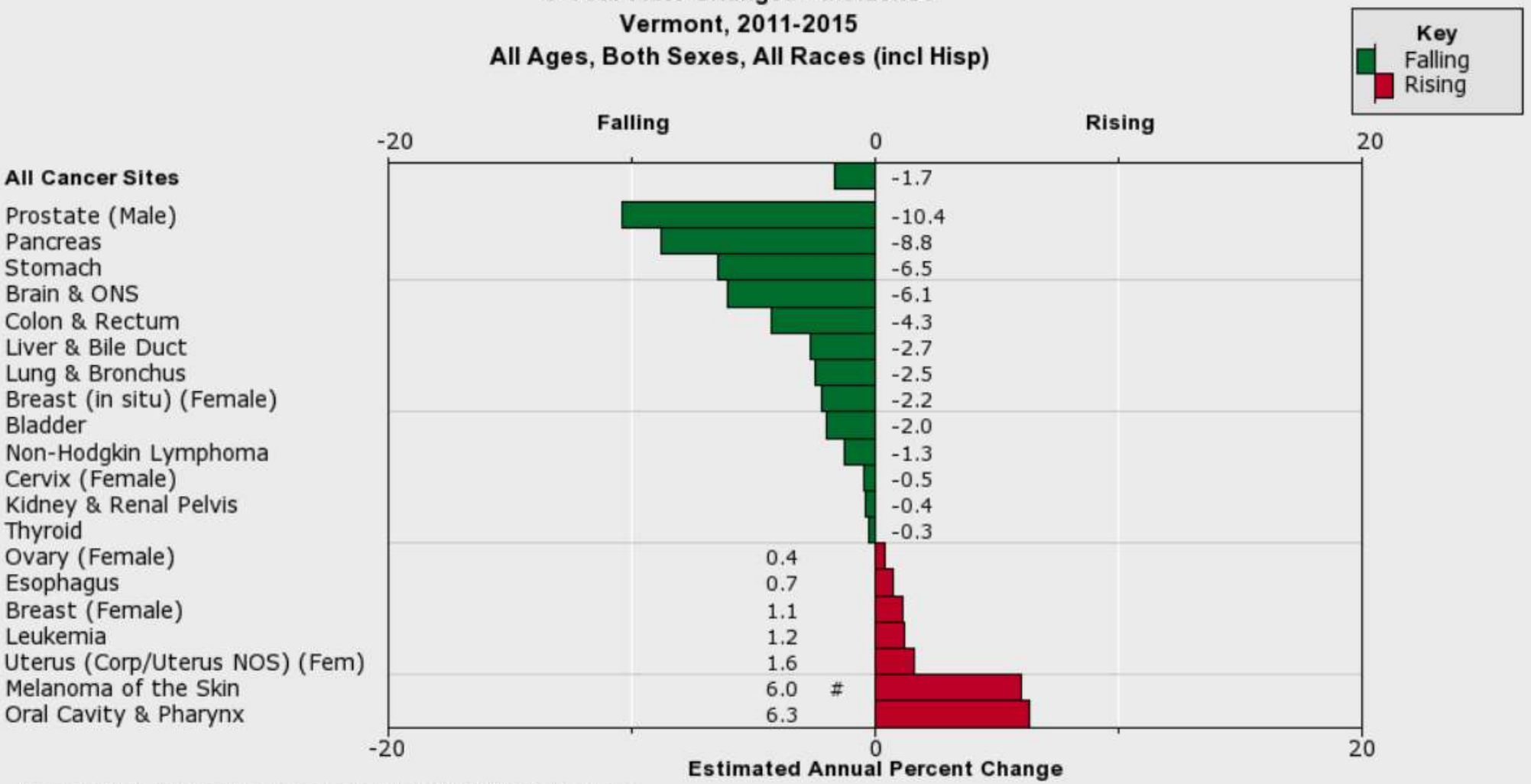
Adapted from Van Dyne, et al., MMWR, 2018;

Higher HPV Vaccine Uptake in States with Lower Incidence of HPV-Associated Cancer



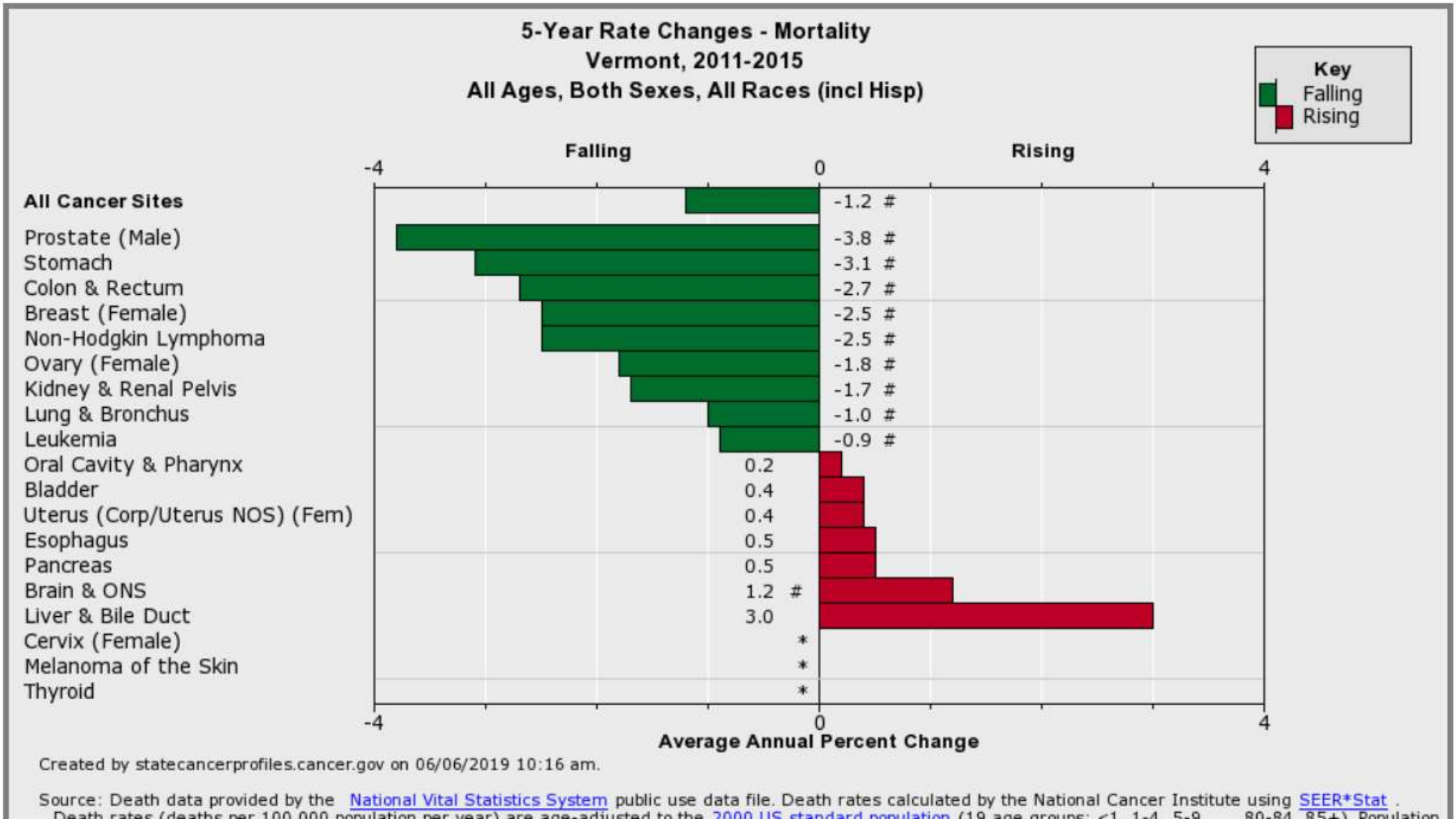


5-Year Rate Changes - Incidence
Vermont, 2011-2015
All Ages, Both Sexes, All Races (incl Hisp)



Created by statecancerprofiles.cancer.gov on 06/06/2019 10:15 am.

Source: Incidence data provided by the National Program of Cancer Registries (NPCR). EAPCs calculated by the National Cancer Institute using SEER*Stat. Rates are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84,85+). Rates are for invasive cancer only (except for bladder cancer which is



Created by statecancerprofiles.cancer.gov on 06/06/2019 10:16 am.

Source: Death data provided by the National Vital Statistics System public use data file. Death rates calculated by the National Cancer Institute using SEER*Stat . Death rates (deaths per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ..., 80-84, 85+). Population

hints

History: In 1998, Experts Recommend National Communication Surveillance Program

Cancer Risk Communication: What We Know and What We Need to Learn

JNCI Monograph, No. 25, 1999.

- Monitor changes in health information environment
- Document media use across channels and sources
- Examine associations between media use and knowledge, attitudes, behaviors
- Provide evidence base for planners, administrators, communicators, practitioners, and policy makers

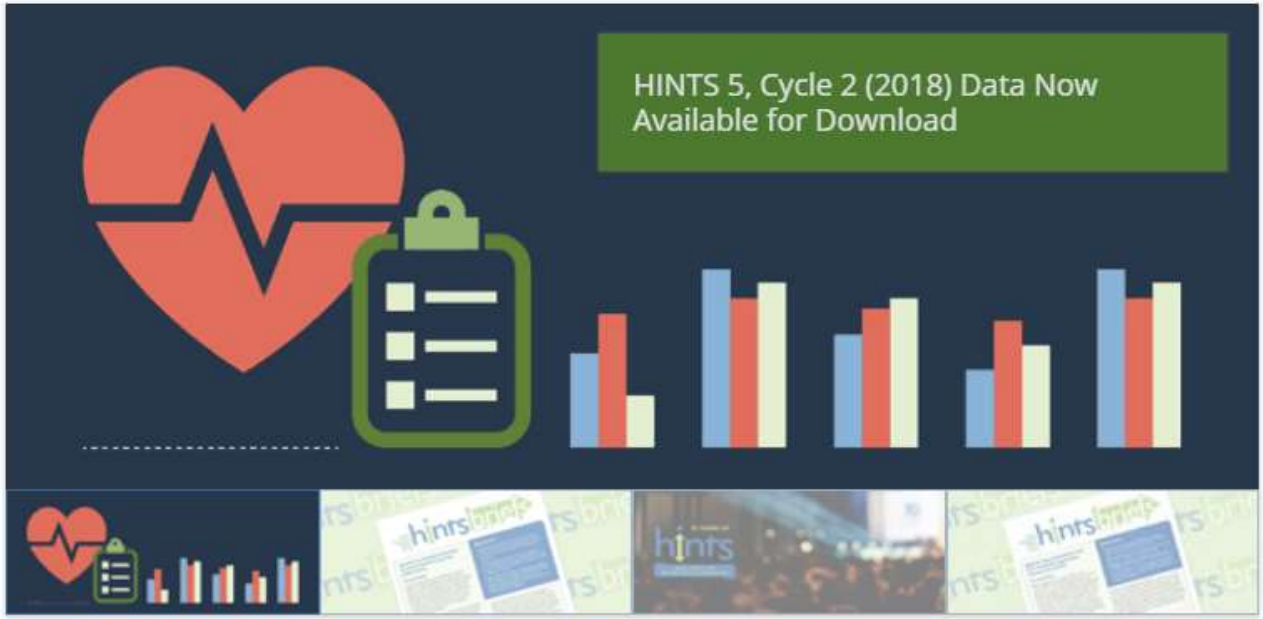
Health Information National Trends Survey

Part of NCI's Division of Cancer Control and Population Sciences

Advanced Search

Search Questions | enter keyword...

About HINTS | Data | View Questions/Topics | Publications/Reports | Meetings/Trainings



What is HINTS?

HINTS collects data about the use of cancer-related information by the American public. These data provide opportunities to understand and improve health communication. **Read More >**

Get and Use HINTS Data

Download publically available, nationally representative HINTS data for your

Our Latest Tweets

#DIY you can sign up to get updates on the latest HINTS data releases, website features, and publications? Subscribe today!
https://buff.ly/2VAjYCE

Social Media

New HINTS Publication?

Submit Here

What's New

HINTS Data Users Conference Rescheduled for May 22-23, 2019

HINTS 5, Cycle 2 (2018) public use data available for download

New Videos on How to Merge HINTS Data Now Available

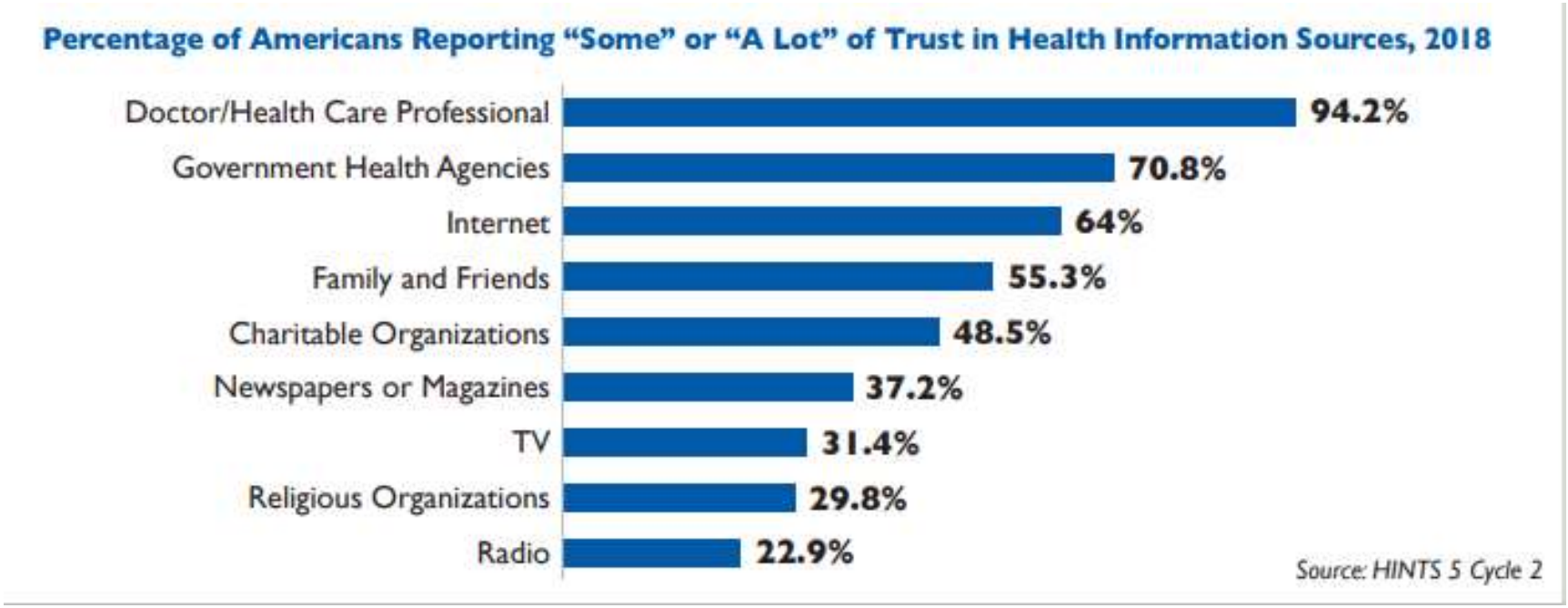
Current HINTS Briefs

HINTS Brief 38: Growth in Patient-Provider Internet Communication (2003–

Health Information National Trends Survey

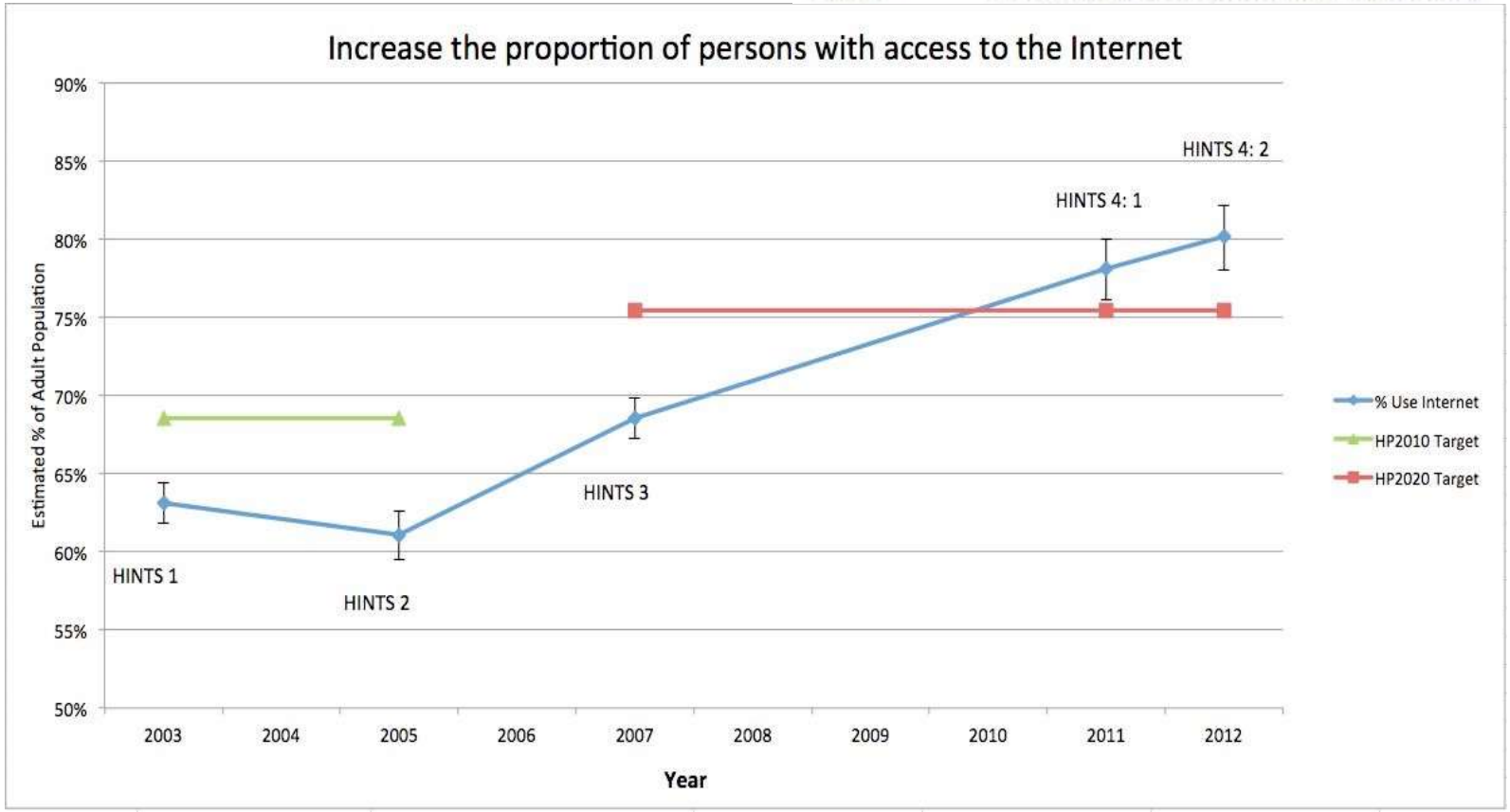
hints briefs

NUMBER 39

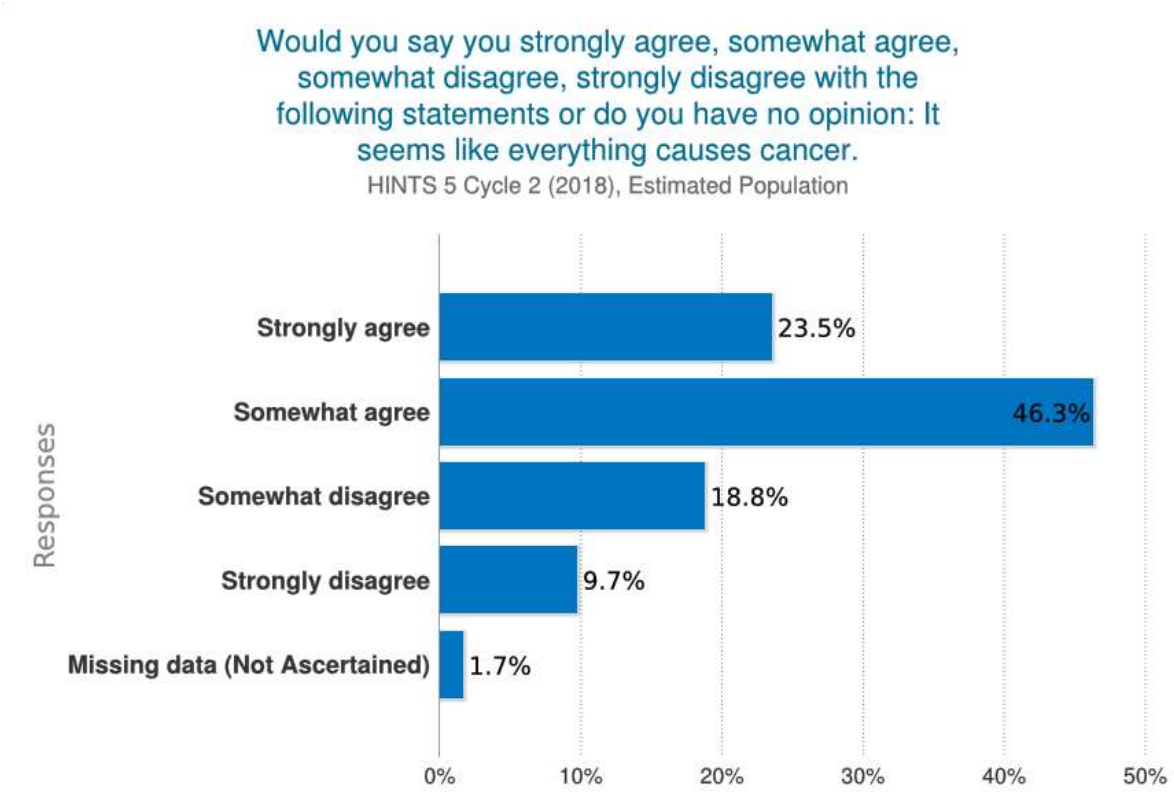


Tracking HP 2020 Objectives

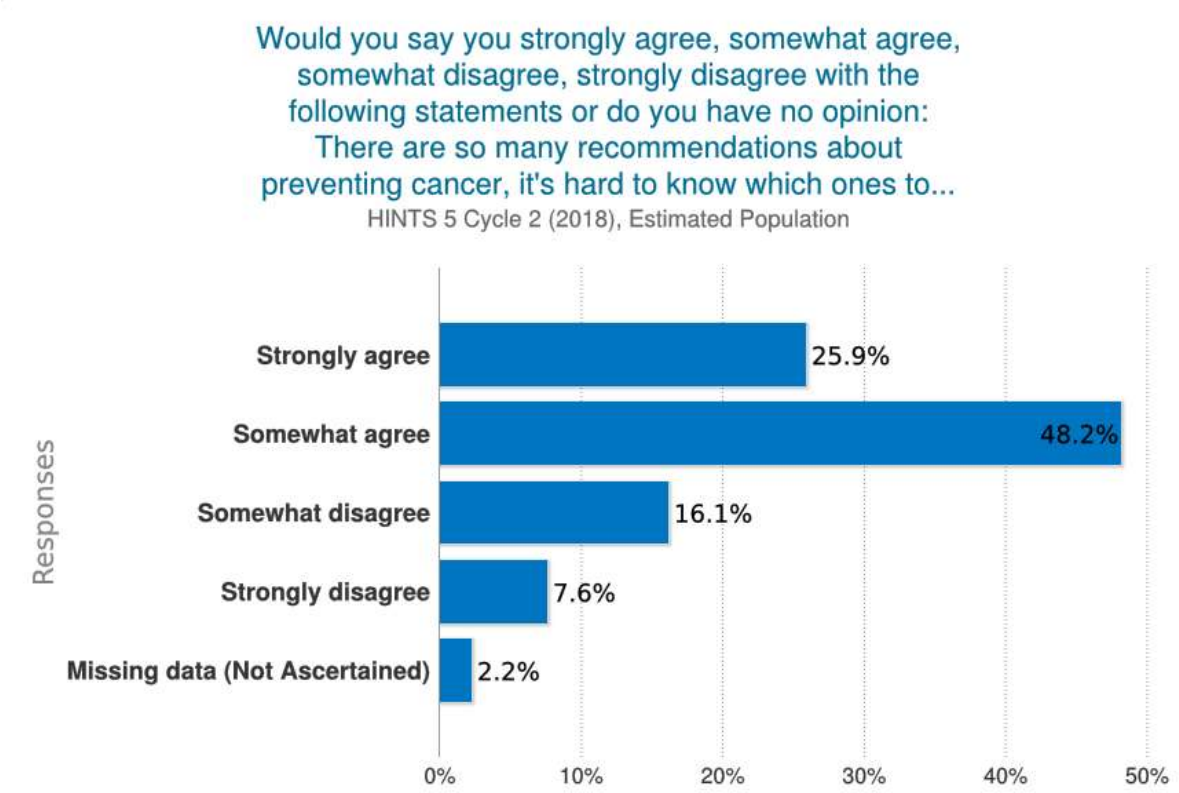
Number	Objective Short Title
11-1	Households with Internet access



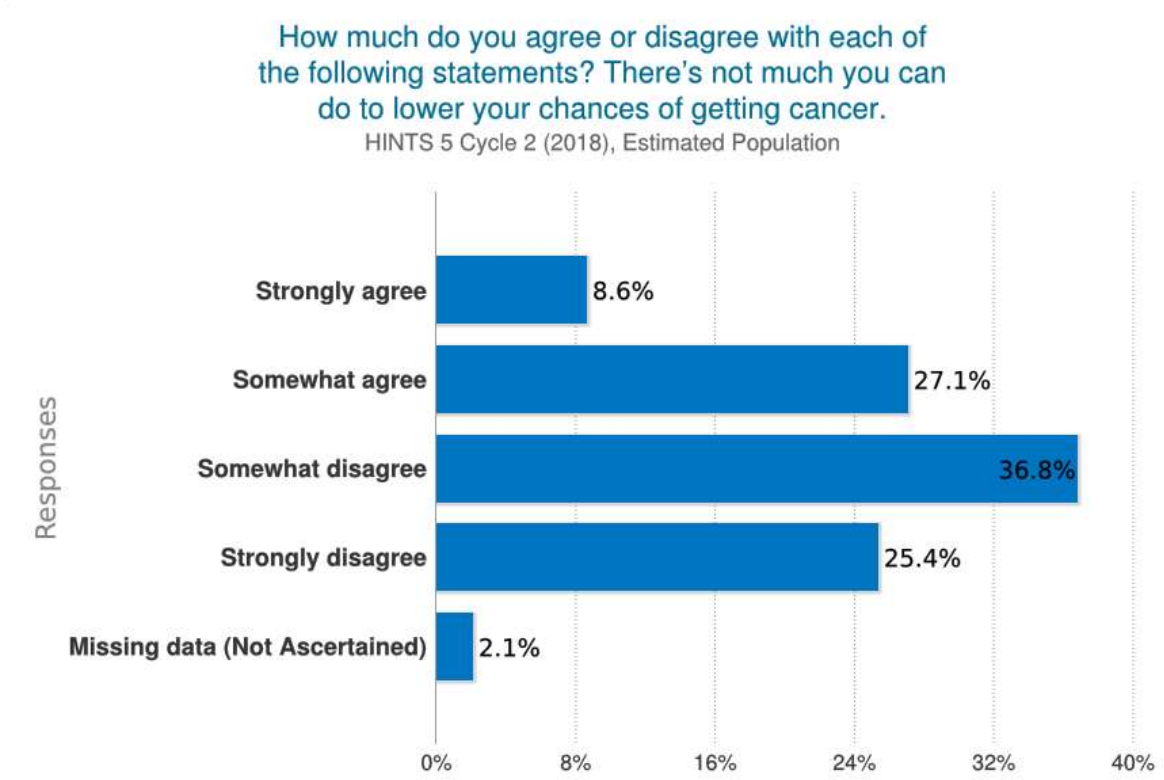
Seems like everything causes cancer…



So many recommendations about preventing cancer, it's hard to know which ones to follow…



Not much you can do to lower your chances of getting cancer…



JAMA
The Journal of the American Medical Association

December 18, 2018

Addressing Health-Related Misinformation on Social Media

Wen-Ying Sylvia Chou, PhD, MPH[1]; April Oh, PhD[1]; William M. P. Klein, PhD[2]

» Author Affiliations | Article Information

JAMA. 2018;320(23):2417-2418. doi:10.1001/jama.2018.16865

A Pragmatic Research Agenda

Focus on Consequences

- Does misinformation exposure matter to behavior change/health outcomes?
- What's the threshold of exposure?

Improve Surveillance Efforts

- Information poverty/communities most at risk?
- Bubbles and information silos?
- Longitudinal and spatial distributions of misinformation
- Implied vs. explicit forms of misinformation

Raise Awareness and Education

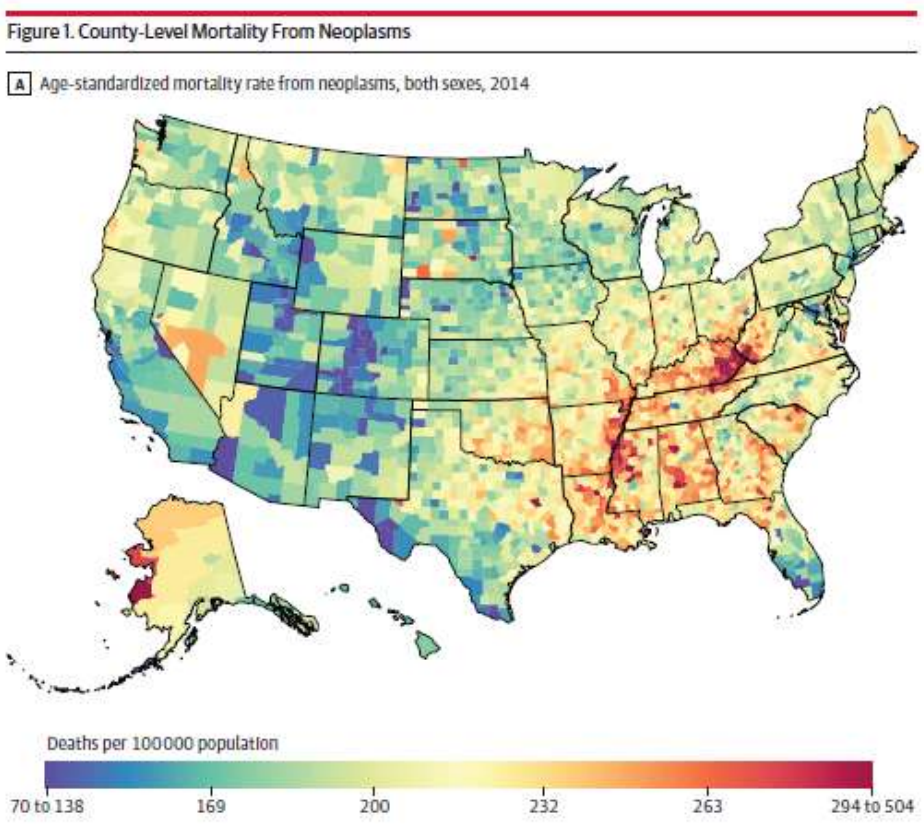
- How to create and sustain trust?
- How to leverage trusted influencers?
- How to foster science literacy in general?

Intervention Development

- Interventions to address/mitigate misinformation
- Correction interventions – backfire effect?
- Role of identity, values, and emotions

Chou, Oh, Klein. Addressing health-related misinformation on social media. *JAMA*. 2018;320(23):2417-8.

Cancer Mortality Rates



Mokdad, AH, et al. Trends and Patterns of Disparities in Cancer Mortality among US Counties, 1980-2014. JAMA 2017;317(4):388-406.

Published OnlineFirst June 9, 2017; DOI: 10.1158/1055-9965.EPI-17-0092

Commentary

Cancer Epidemiology, Biomarkers & Prevention

Making the Case for Investment in Rural Cancer Control: An Analysis of Rural Cancer Incidence, Mortality, and Funding Trends

Kelly D. Blake, Jennifer L. Moss, Anna Gaysynsky, Shobha Srinivasan, and Robert T. Croyle

Abstract

Estimates of those living in rural counties vary from 46.2 to 59 million, or 14% to 19% of the U.S. population. Rural communities face disadvantages compared with urban areas, including higher poverty, lower educational attainment, and lack of access to health services. We aimed to demonstrate rural–urban disparities in cancer and to examine NCI-funded cancer control grants focused on rural populations. Estimates of 5-year cancer incidence and mortality from 2009 to 2013 were generated for counties at each level of the rural–urban continuum and for metropolitan versus nonmetropolitan counties, for all cancers combined and several individual cancer types. We also examined the number and foci of rural cancer control grants funded by NCI from 2011 to 2016. Cancer incidence was 447 cases per 100,000 in metropolitan counties and 460 per 100,000 in nonmetropolitan counties ($P < 0.001$). Cancer mortality rates were 166 per 100,000 in metropolitan counties and 182 per 100,000 in nonmetropolitan counties ($P < 0.001$). Higher incidence and mortality in rural areas were observed for cervical, colorectal, kidney, lung, melanoma, and oropharyngeal cancers. There were 48 R- and 3 P-mechanism rural-focused grants funded from 2011 to 2016 (3% of 1,655). Further investment is needed to disentangle the effects of individual-level SES and area-level factors to understand observed effects of rurality on cancer. *Cancer Epidemiol Biomarkers Prev; 1–6. ©2017 AACR.*

Introduction

Estimates of the total population living in nonmetropolitan (rural) counties in the United States vary from 46.2 (1) to 59 million (2) people, compared with more than 250 million people living in urban areas. This represents 14% to 19% of the U.S. population (1, 2). Rural communities face notable disadvantages compared with urban areas, including higher poverty rates, lower educational attainment, a higher proportion of elderly individuals, lack of access to health services, and a lack of resources needed to support the public health infrastructure (3). As a result of these and other factors, rural communities face elevated rates of morbidity and mortality, as well as greater percentages of potentially excess deaths from the five leading causes of death, including cancer (4). Individuals in rural counties not only have an 8% higher overall cancer mortality than those in urban areas, but a rural–urban disparity in mortality has also been observed for lung, colorectal, prostate, and cervical cancers, although, in several cases, adjusting for socioeconomic status attenuates or completely explains the relationship between rurality and higher cancer mortality (5).

Additional rural–urban disparities across the cancer control continuum have been documented, although the existing literature is nascent and methodologically inconsistent compared with other research identifying race-, economic-, and age-based disparities in diagnosis, treatment, and survival of cancer (6). At least two studies have demonstrated that cervical cancer incidence is higher in rural areas (7, 8). There is also some evidence that rural residents are less likely to get screened for cancer (6): for example, an analysis of 2008 Behavioral Risk Factor Surveillance System data showed that rural women were less likely to meet recommendations for mammography than urban women, that the proportion of women reporting appropriate cervical cancer screening decreased as rurality increased, and that individuals from rural areas were less likely to report colorectal cancer screening than individuals from urban areas (9). Furthermore, rural individuals may be less likely to receive follow-up testing after receiving abnormal screening results (10), and although findings are not consistent with regard to rural–urban differences in stage at diagnosis, some research suggests that women from rural areas are more likely to be diagnosed with more advanced breast cancer compared with their urban counterparts (11).

Evidence also suggests that there are rural–urban differences in cancer treatment. For example, rural women are more likely to receive mastectomies than breast-conserving surgery, and rural patients with either endometrial cancer or prostate cancer are less

Invasive Cancer Incidence, 2004–2013, and Deaths, 2006–2015, in Nonmetropolitan and Metropolitan Counties — United States

Surveillance Summaries / July 7, 2017 / 66(14);1–13

S. Jane Henley, MSPH[1]; Robert N. Anderson, PhD[2]; Cheryll C. Thomas, MSPH[1]; Greta M. Massetti, PhD[1]; Brandy Peaker, MD[1]; Lisa C. Richardson, MD[1] (View author affiliations)

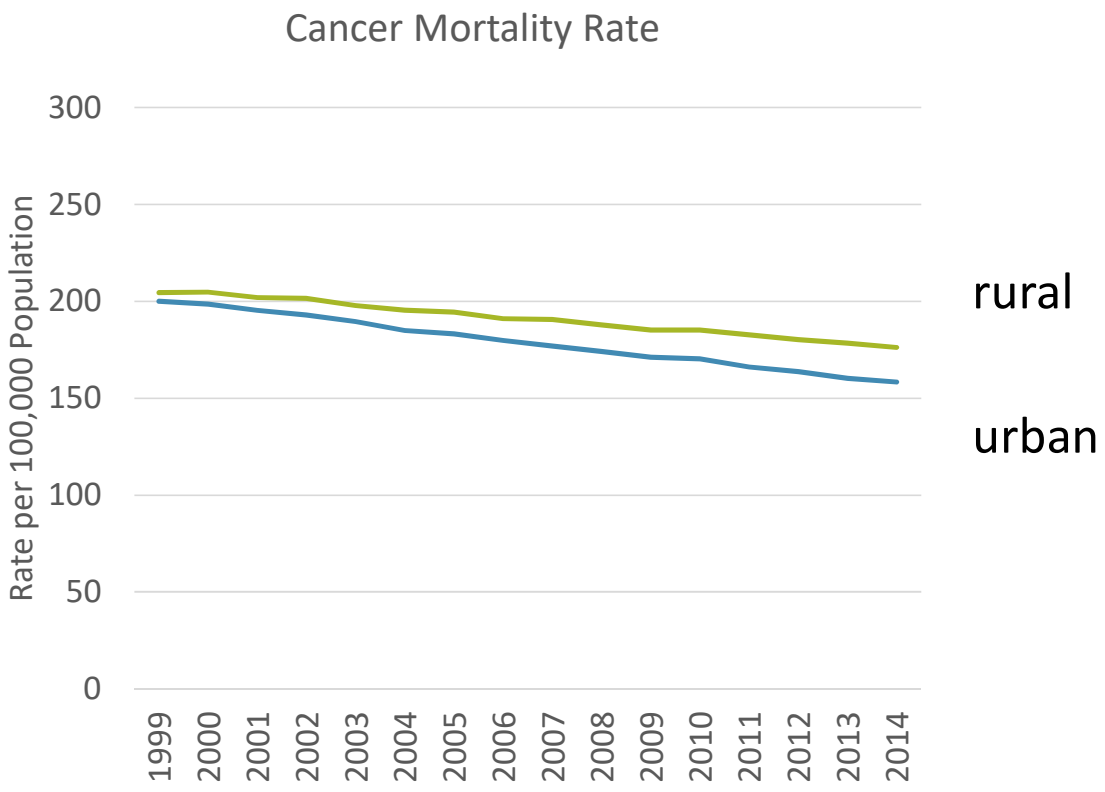
View suggested citation and related materials

Abstract

Problem/Condition: Previous reports have shown that persons living in nonmetropolitan (rural or urban) areas in the United States have higher death rates from all cancers combined than persons living in metropolitan areas. Disparities might vary by cancer type and between occurrence and death from the disease. This report provides a comprehensive assessment of cancer incidence and deaths by cancer type in nonmetropolitan and metropolitan counties.

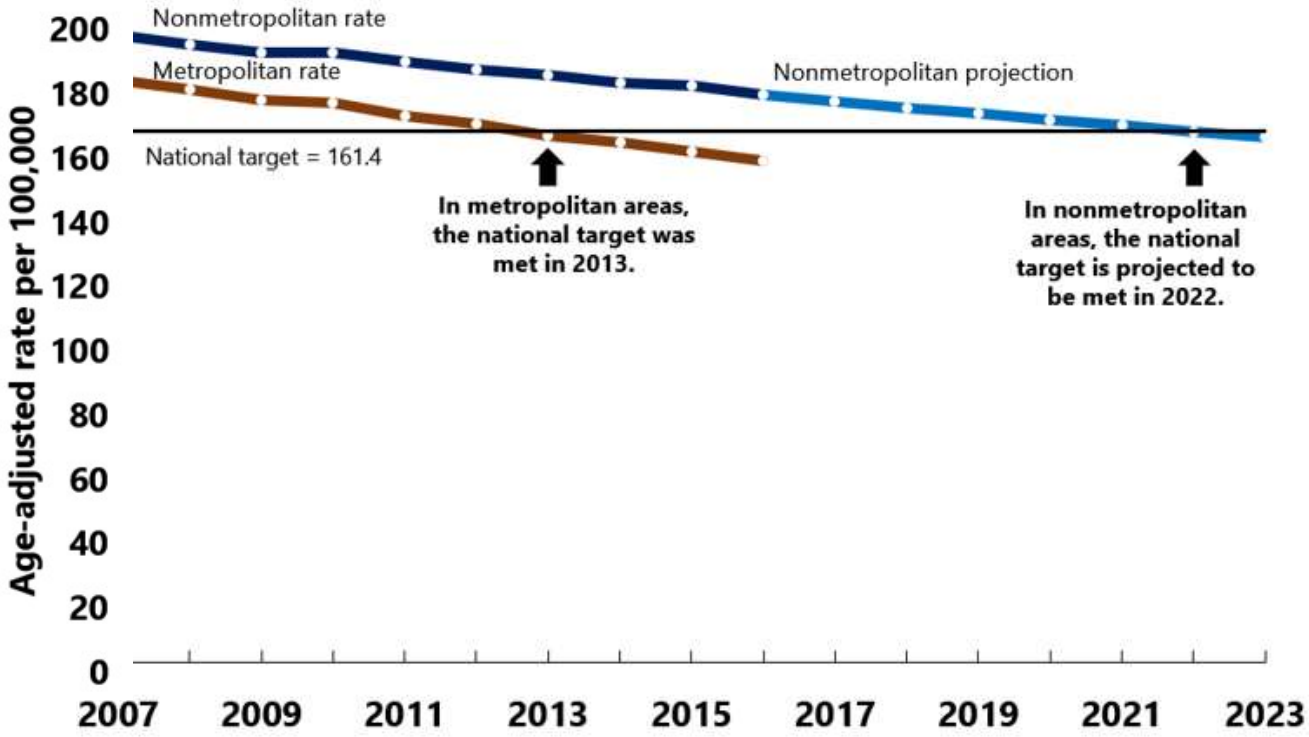
Reporting Period: 2004–2015.

As Mortality from Cancer Has Fallen, Rural-Urban Disparities Have Grown Larger



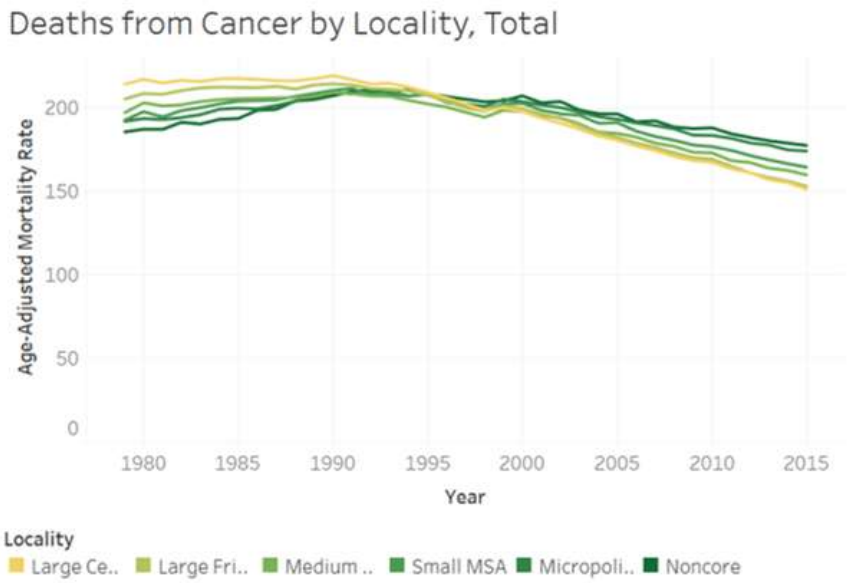
PRELIMINARY RESULTS

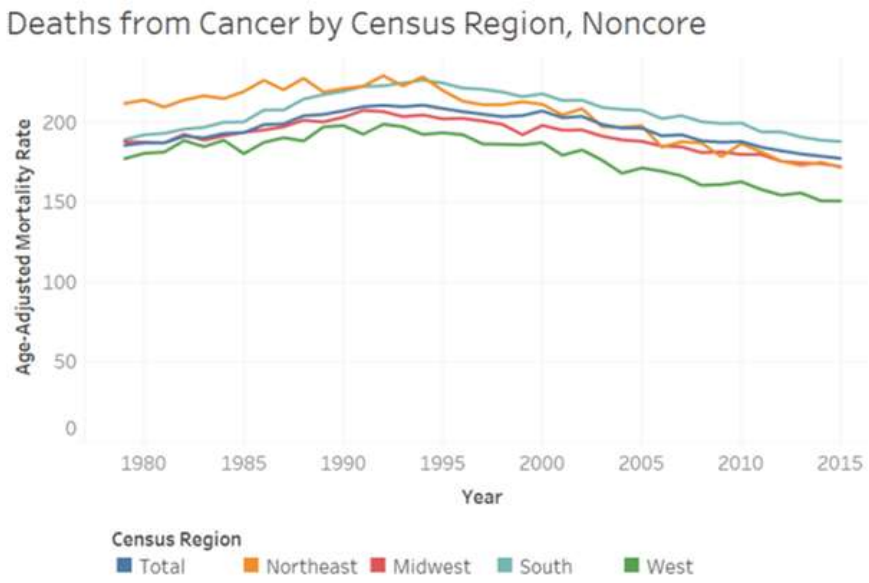
Healthy People 2020 objective C-1: Overall cancer deaths among persons of all ages — National Vital Statistics System, United States, 2007–2016



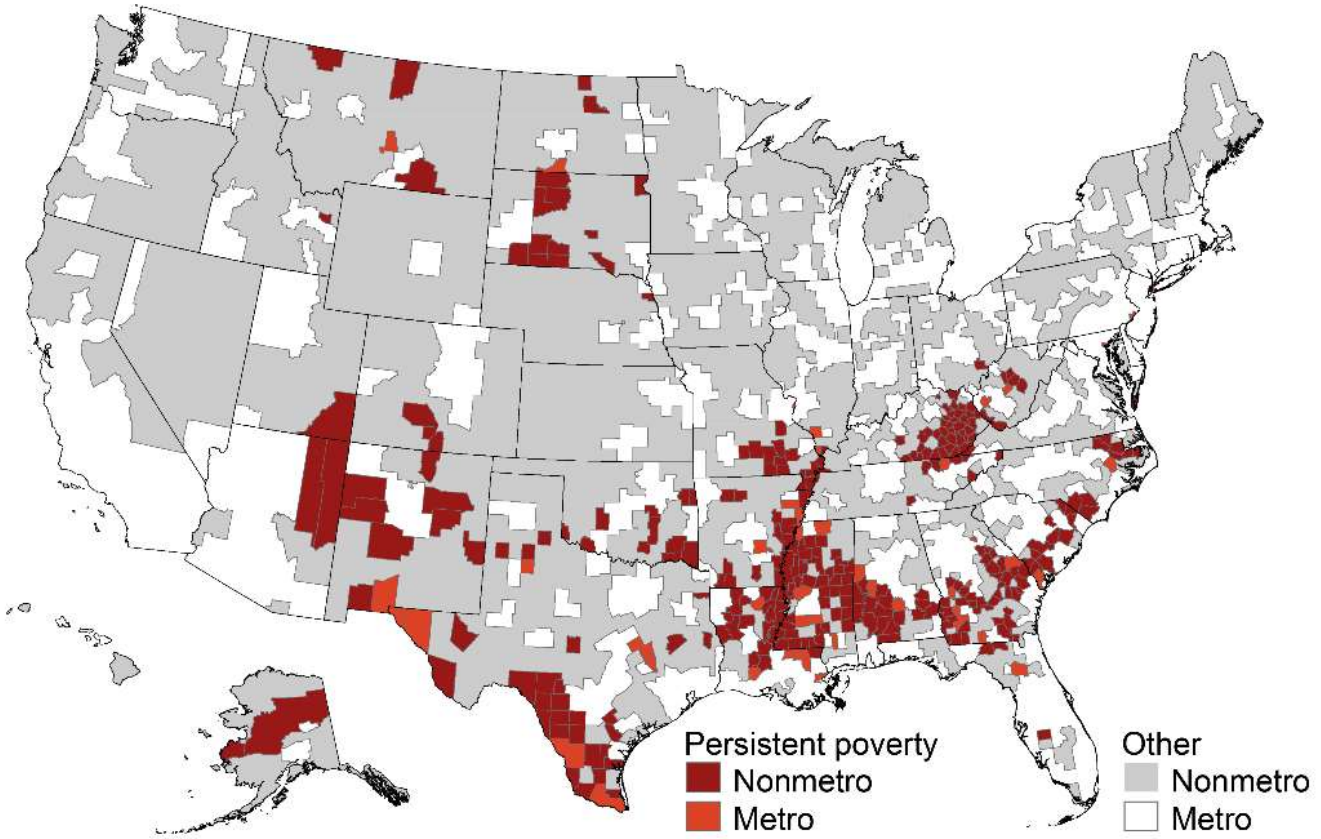
METHODS: The average annual percent change (AAPC) was calculated based on 2007–2016 mortality rates using the National Cancer Institute Joinpoint software. The nonmetropolitan trend was extended from the 2016 mortality rate until it crossed the target, assuming a constant AAPC.

Trends in Cancer Mortality by Locality and Within Rural Region ("Noncore")



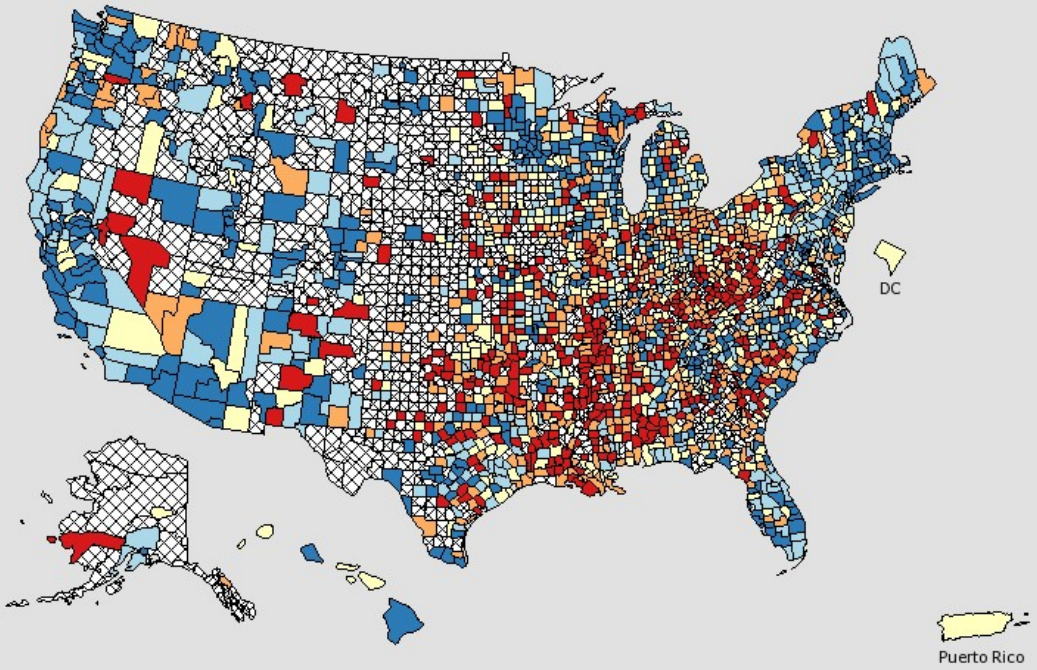


Persistent poverty counties, 2015 edition



Persistent poverty counties are those where 20 percent or more of county residents were poor, measured by the 1980, 1990, 2000 censuses, and the 2007-11 American Community Survey.
Note that county boundaries are drawn for the persistent poverty counties only.
Source: USDA, Economic Research Service using data from U.S. Census Bureau.

Death Rates for United States by County
Colon & Rectum, 2011 - 2015
All Races (includes Hispanic), Both Sexes, All Ages



Age-Adjusted
Annual Death Rate
(Deaths per 100,000)

Quantile Interval

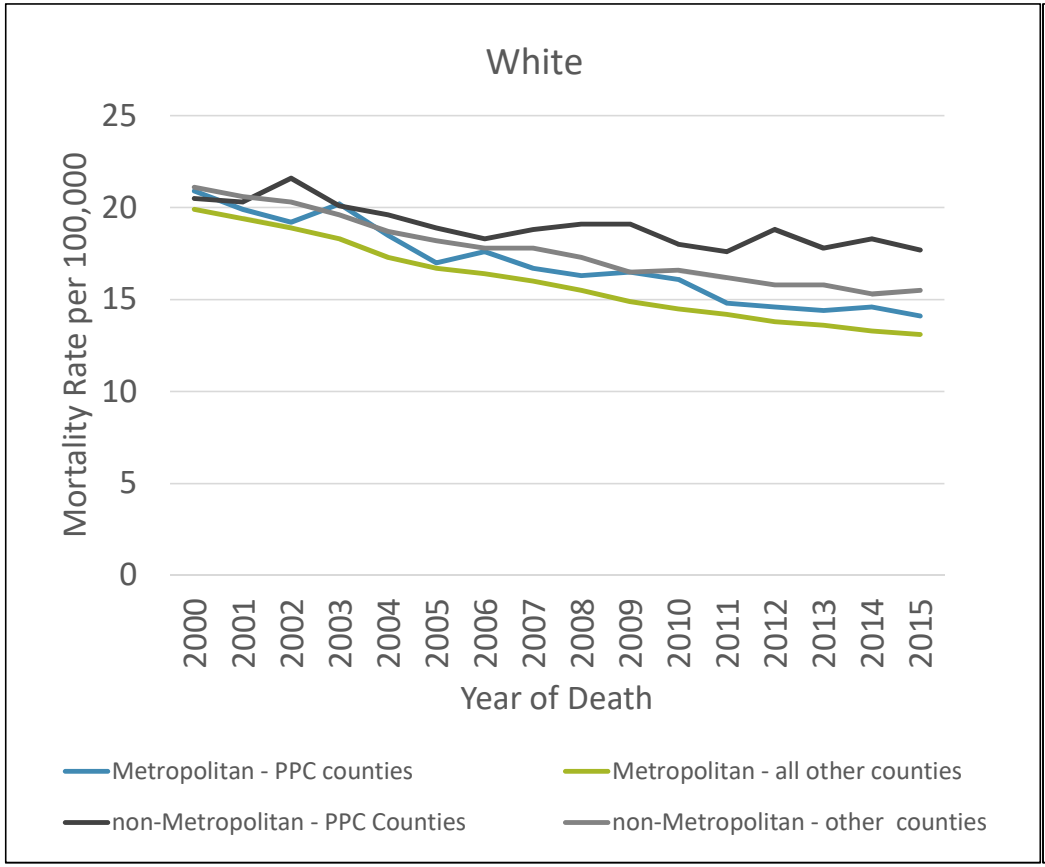
- 6.1 to 13.0
- > 13.0 to 15.0
- > 15.0 to 16.9
- > 16.9 to 19.6
- > 19.6 to 47.5
- Suppressed *

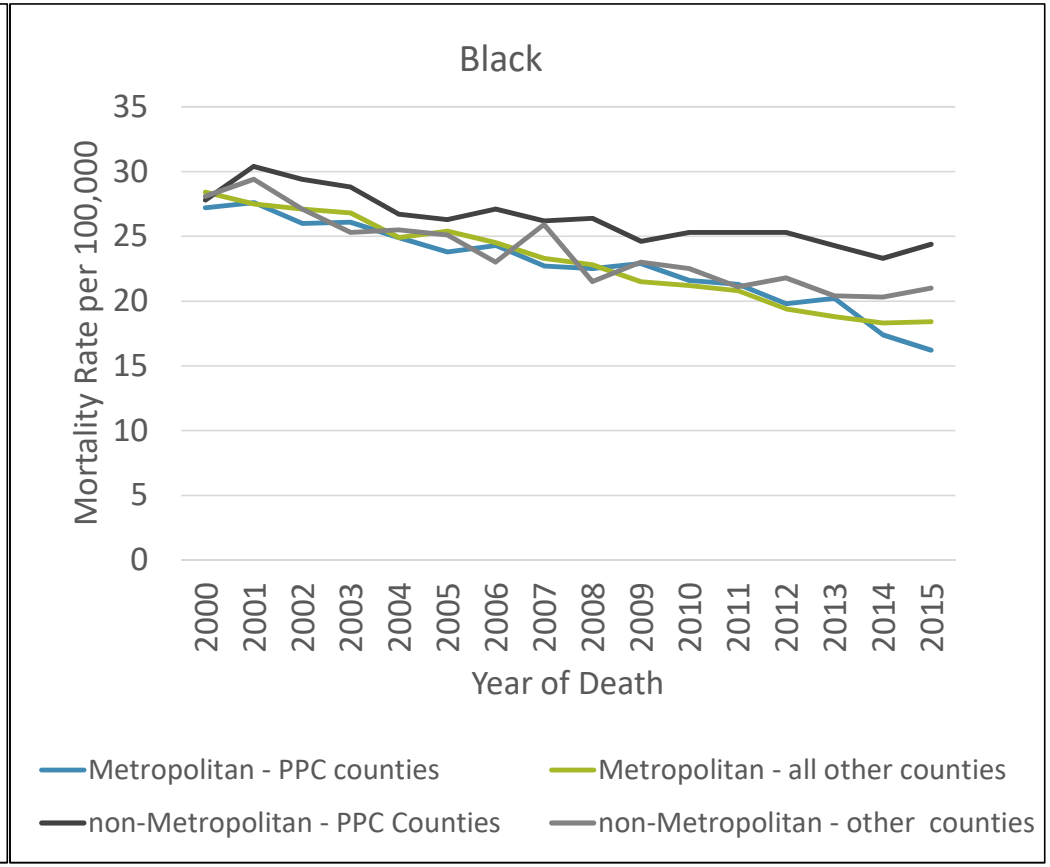
United States
Rate (95% C.I.)
14.5 (14.4 - 14.5)

Healthy People 2020
Goal C-5
14.5

Notes:
Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
State Cancer Registries may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).

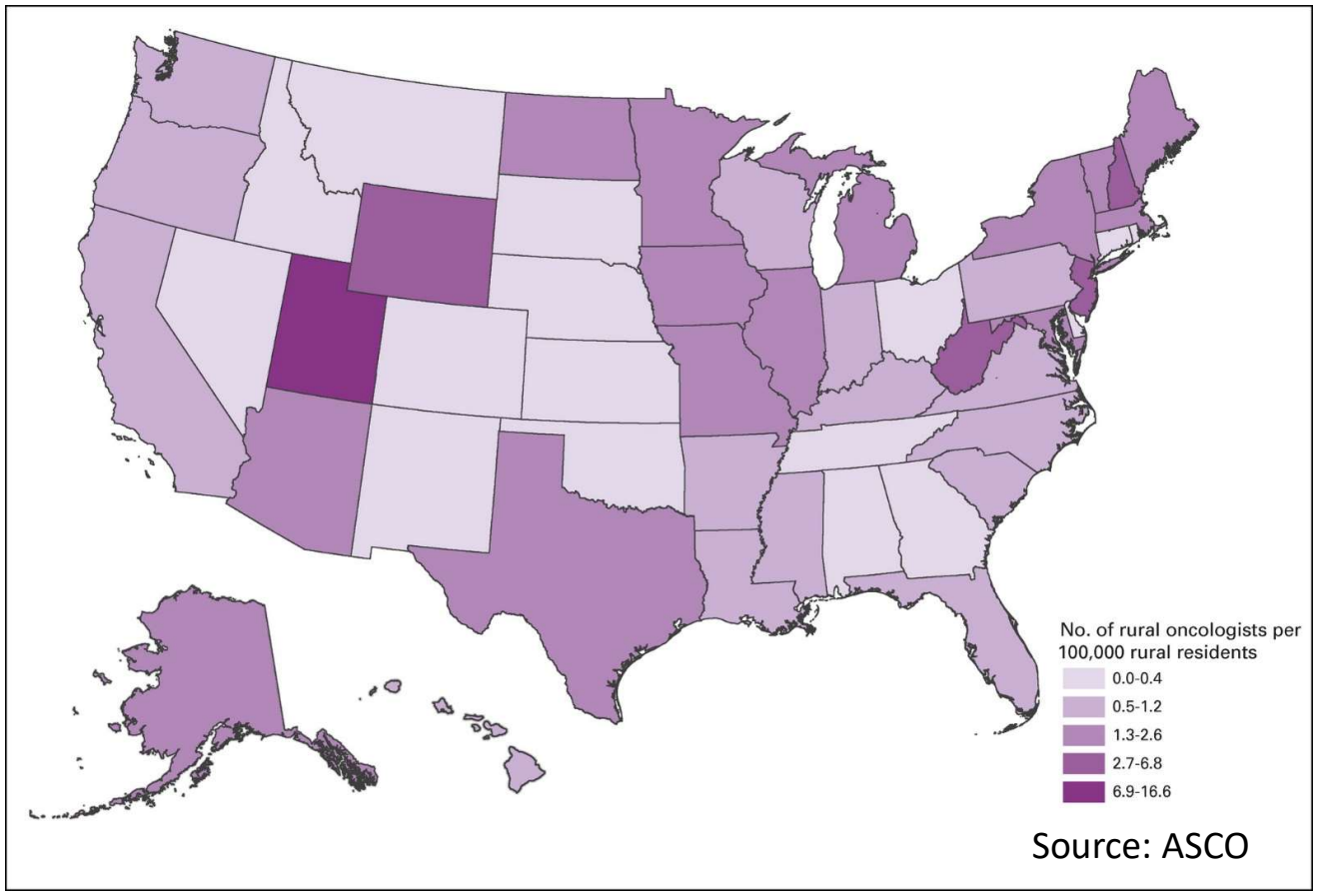
Colorectal Cancer Mortality
By Persistent Poverty Counties and Rural-Urban Continuum





Mortality data from NCHS- US population
Metropolitan, non-Metropolitan county classification based on 2013 Rural-Urban Continuum Code
PPC= Persistent Poverty Counties

Number of Rural Oncologists Per 100,000 Rural Residents



Source: ASCO

Scientific Challenges

Heterogeneity of "Rural"

- Example: rural Alaska vs. rural Mississippi
- "Grain size" of counties (and, therefore, data sources):
    - 3,142 total; Iowa has 99; Arizona has 15

Structural Factors that Affect both Research and Practice

- Access to care
- Limited access to clinical trials
- Lower physician density
- Distance to facilities – transportation
- Poor telecommunication infrastructure for telemedicine/telehealth
- SES and other area-level correlates and confounders

Cultural Factors

- Trust in institutions, medical providers, and government-sponsored programs
- Non-traditional comorbidities such as opiate drug use
- Cancer-related fatalism

NCI's Role as a Research Agency

- Leverage extensive research infrastructure (e.g. cancer registries), grant portfolio and scientific community
- Encourage more grant applications focused on rural populations
- Extend reach of clinical trials programs
- Engage NCI-funded cancer centers (n=70) in rural cancer control research (new community outreach and engagement requirement)
- Support partnerships and training in implementation science

NCTN Infrastructure

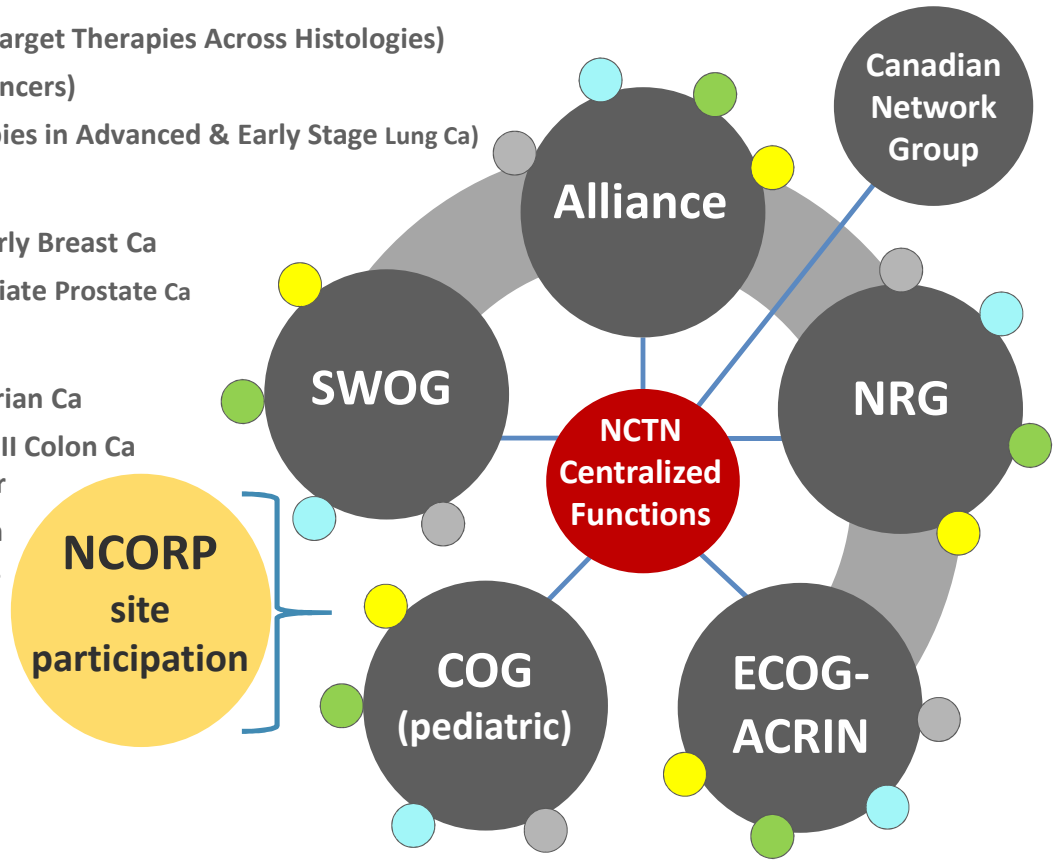
Selected Major NCTN Trials – Diverse Mix of Trials

≈ 19,000 enrolling patients/year
≈ 2,200 potential enrolling sites across North America (plus international sites)

- **Large Umbrella Trials with Screening & Assignment to Multiple Interventions Requiring a National Patient Catchment Area**
  - ADULT MATCH & PEDIATRIC MATCH (Target Therapies Across Histologies)
  - DART (Dual Immunotherapy in Rare Cancers)
  - LUNG MAP, ALCHEMIST (Target Therapies in Advanced & Early Stage Lung Ca)
- **Multimodality & Non-Drug Trials**
  - Role of Weight Loss in Treatment of Early Breast Ca
  - Dose-Escalated RT +/- ADT in Intermediate Prostate Ca
- **Combination Therapy Trials**
  - Cediranib & Olaparib in Recurrent Ovarian Ca
  - Chemo + Immunotx in Resected Stage III Colon Ca and Deficient DNA Mismatch Repair
  - Brentuximab Vedotin or Crizotinib with Chemotx for Newly Diagnosed ALCL

New Initiatives

- NCTN/NCORP Data Archives
- Navigator Biospecimen Access



LEGEND:

- **Central Functions:**
  - CIRB
  - IROC
  - ITSCs
  - CTSU
  - Common Data System & Hosting
  - Network Accrual Team (ACT)
- **Lead Academic Participating Sites (LAPS)**
- Operations Centers
- Statistics/Data Ctrs
- Tumor Banks
- Member Sites

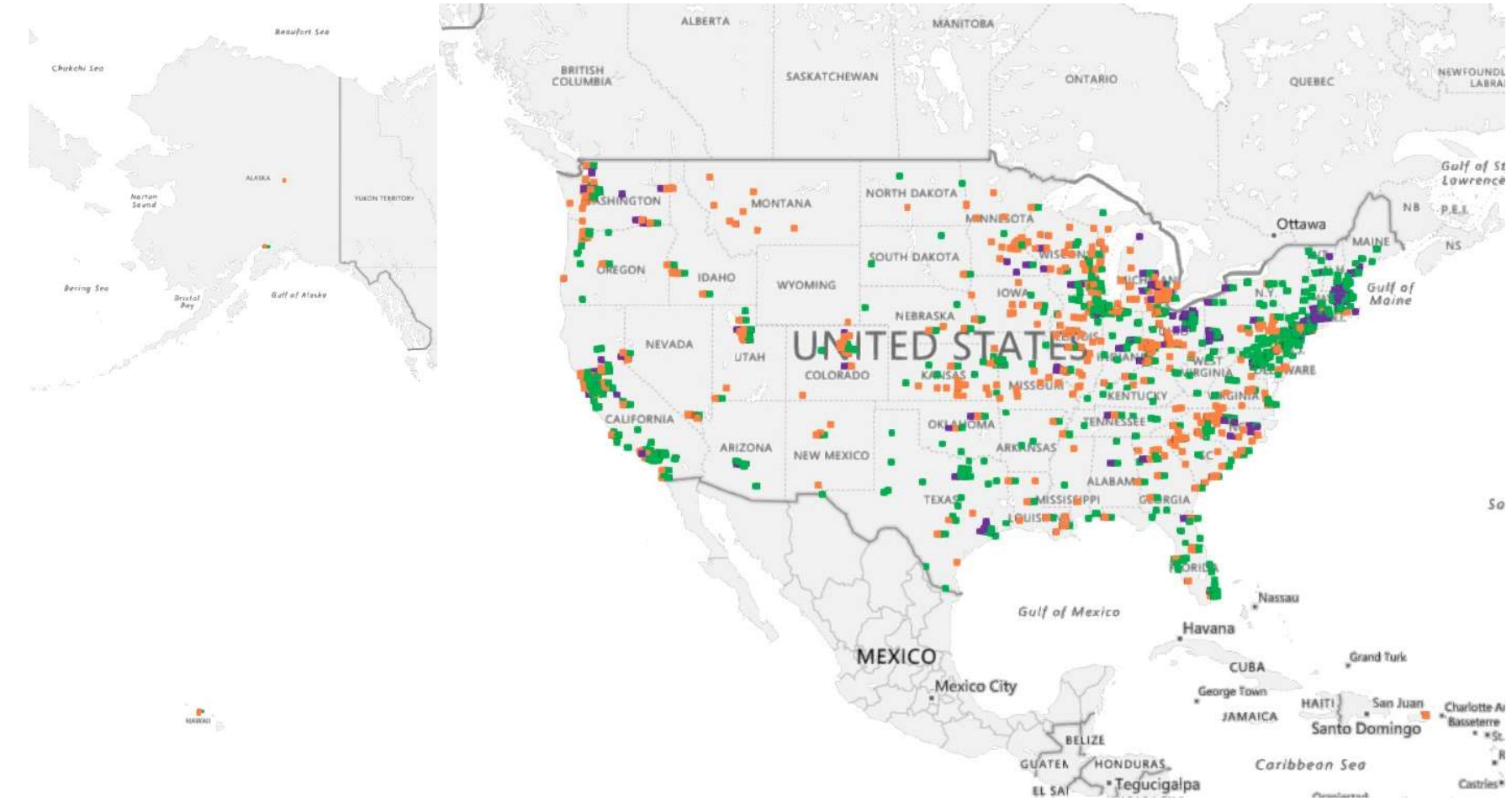
Sites with at Least 1 Enrollment to NCTN studies - Mar 1, 2014 to Feb 28, 2018

(First 4 Years of the NCTN Program)

NCTN LAPS sites

NCORP sites

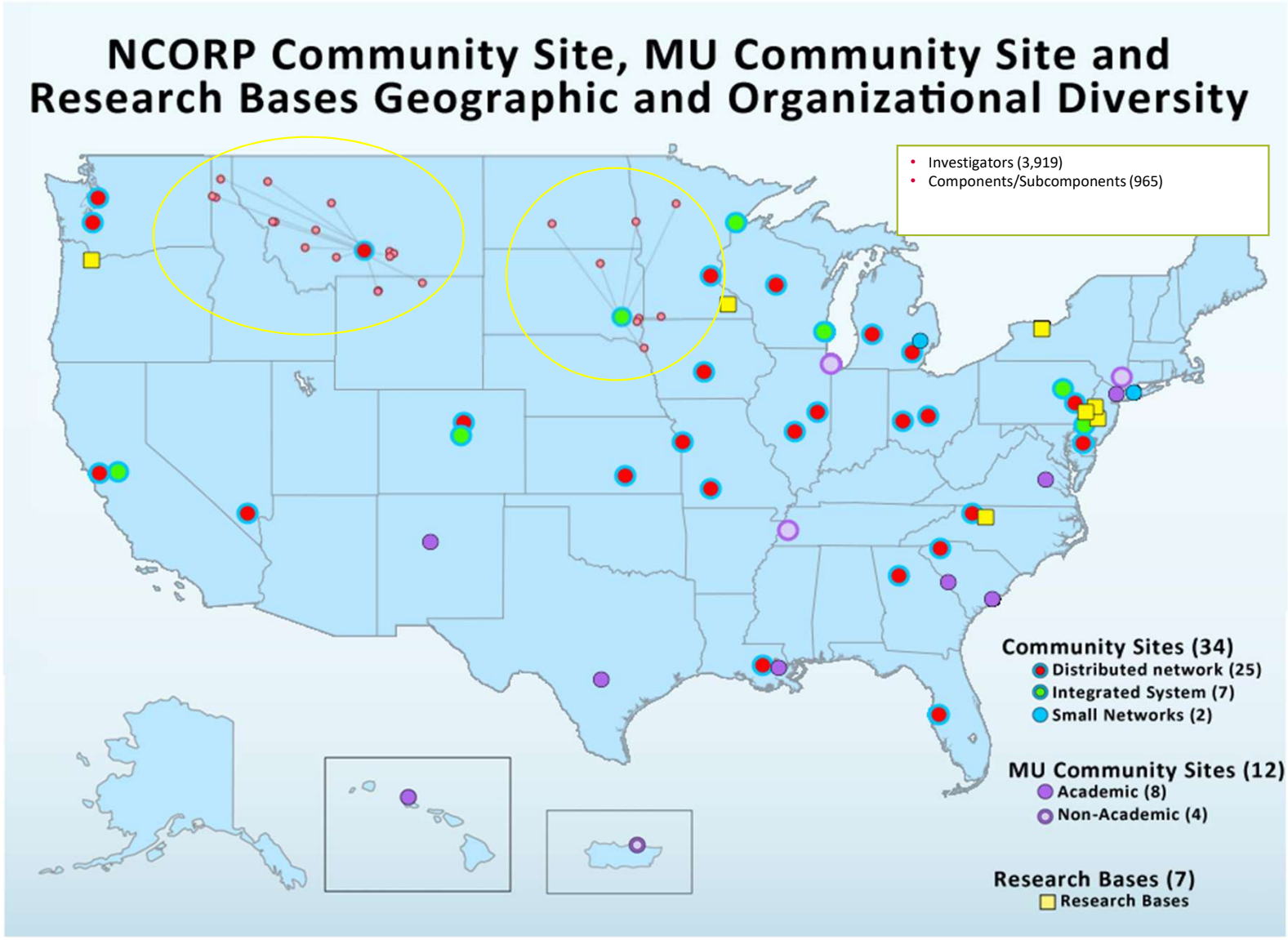
NCTN US Member



National Community Oncology Research Program (NCORP) Overview

- A national NCI-supported network that brings cancer prevention clinical trials and cancer care delivery research (CCDR) studies to local communities
  - designs and conducts cancer prevention, control, screening, and post-treatment surveillance clinical trials;
  - designs and conducts cancer care delivery research (CCDR) studies;
  - participates in treatment and imaging clinical trials conducted by the NCI National Clinical Trials Network (NCTN); and
  - integrates health disparity questions into its research priorities.

NCORP Community Site, MU Community Site and Research Bases Geographic and Organizational Diversity



RURAL CANCER CONTROL RESEARCH

Rural Cancer Control

Improving the Reach and Quality of Cancer Care in Rural Populations (R01 Clinical Trial Required)
RFA-CA-18-026

- To support observational/analytic research and pilot testing of interventions to identify, understand, and address predictors of low quality of cancer care in rural low-income and/or underserved populations
- To support cancer control intervention research to address known predictors of low quality of care (e.g., low reach due to distance) in rural low-income and/or underserved populations
- All studies will be required to employ the USDA's Rural Urban Continuum Code (RUCC) to define nonmetropolitan geographic target areas of study
- To be awarded in FY19 (summer 2019)

Connected Health: Improving Patients' Engagement and Activation for Cancer-Related Health Outcomes

President's Cancer Panel
2014-2015 Series

The power and utility of connected health technologies are growing. Many forces are catalyzing a national U.S. effort to engage and activate individuals to be more proactive about their health and healthcare and to translate this engagement to enhanced activation among patients. These forces have important implications for the prevention and treatment of cancer and for optimal survivorship. They include but are not limited to:

- **"Meaningful Use"** incentives to healthcare providers focus on requirements to demonstrate "patient engagement" through health information technology (Phases 2 & 3).
- **The "Quantified Self"** movement is creating new tools to encourage and reinforce a variety of healthy behaviors relevant to cancer control.
- **The Internet** has made vast amounts of health information available, and social media platforms have

A patient with a complex chronic condition receives a prescription for an app that is downloaded to a mobile device. Using information the patient enters, the app delivers automated clinical coaching and sends reports to the physician, recommending evidence-based protocols for adjusting the patient's treatment regimen, if needed. Equipped with a tool that offers personal, relevant

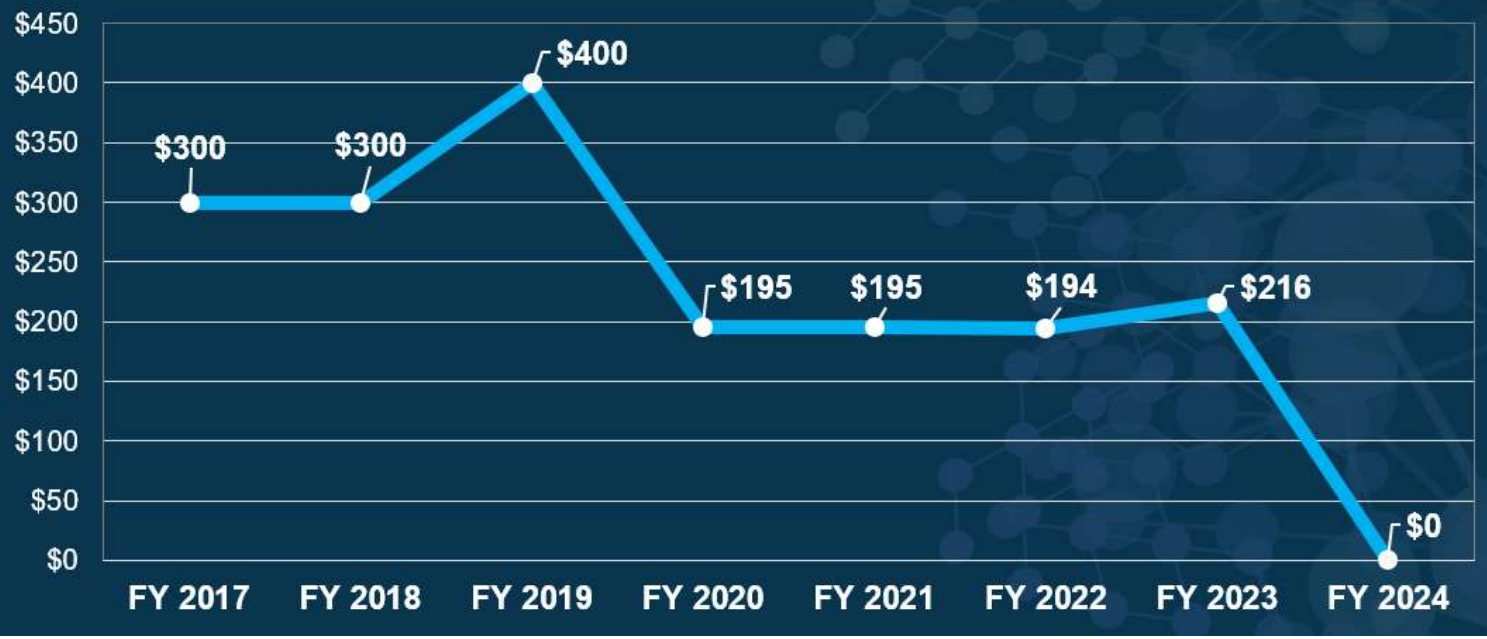
Linking and Amplifying User-Centered Networks through Connected Health (L.A.U.N.C.H.)

- NCI has partnered with the Federal Communications Commission to address the broadband health connectivity gap in rural areas of the U.S.
- The long-term goal of this partnership is to improve cancer outcomes by better connecting rural patients to their cancer care teams.
  - Pilot Demonstration Project: University of California at San Diego, the University of Kentucky, and the biopharmaceutical company Amgen to redesign access to care using biosensors, smartphones, patient-reported outcomes

NCI Appropriations
FY 2013 – 2020 (in millions)

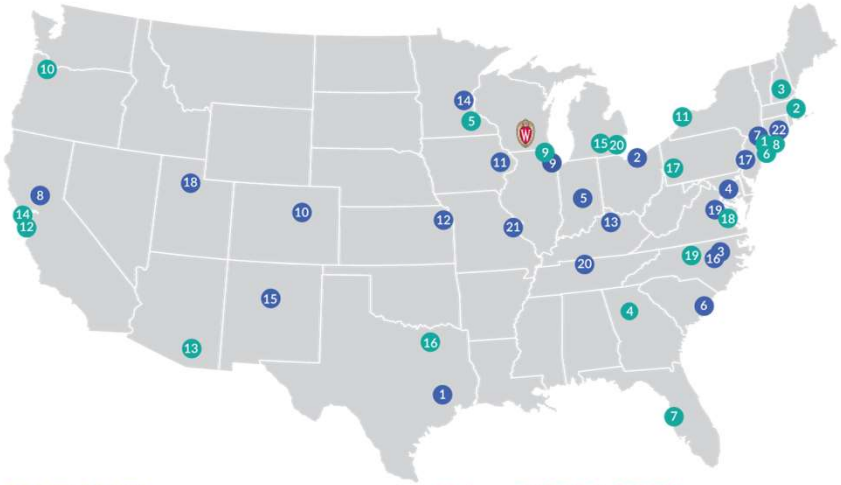
21st Century Cures Act – orange
Childhood Cancer Initiative - green

Cancer Moonshot Funding Authorized Under the 21st Century Cures Act (dollars in millions)



Cancer Center Cessation Initiative (C3I)

"Administrative supplements to develop tobacco cessation treatment capacity and infrastructure for cancer patients that should lead to the implementation and dissemination of a sustainable tobacco cessation treatment program within the cancer center."



Cohort 1 (2017-2019)

1. Baylor College of Medicine
2. Case Western Reserve University
3. Duke University
4. Georgetown University
5. Indiana University
6. Medical University of South Carolina
7. New York University
8. University of California Davis
9. University of Chicago
10. University of Colorado
11. University of Iowa
12. University of Kansas
13. University of Kentucky
14. University of Minnesota
15. University of New Mexico
16. University of North Carolina at Chapel Hill
17. University of Pennsylvania
18. University of Utah
19. University of Virginia
20. Vanderbilt University
21. Washington University
22. Yale University

Cohort 2 (2018-2020)

1. Columbia University
2. Dana-Farber/Harvard Cancer Center
3. Dartmouth College
4. Emory University
5. Mayo Clinic
6. Memorial Sloan Kettering
7. Moffitt
8. Mount Sinai
9. Northwestern University
10. Oregon Health and Sciences University
11. Roswell Park
12. Stanford University
13. University of Arizona
14. University of California San Francisco
15. University of Michigan
16. University of Texas Southwestern
17. UPMC Hillman
18. Virginia Commonwealth University
19. Wake Forest University
20. Wayne State University

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C3I Coordinating Center
Carbone Cancer Center
UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE AND PUBLIC HEALTH

- NCI Lead: **Stephanie Land**
- Natural laboratory for understanding implementation of tobacco cessation within cancer center care delivery
- Capturing data on Implementation strategies used to integrate cessation services

Coordinating Center: University of Wisconsin Madison (Lead: Michael Fiore)

DCCPS Cancer Moonshot Initiatives – with a focus on rural health

- Accelerating Colorectal Cancer Screening and follow-up through Implementation Science (ACCSIS) –
  - to generate effective implementation strategies that substantially improve CRC screening and follow-up rates in populations where baseline rates remain low
  - Funded 3 research grants and 1 coordinating center in FY18 (see next slide for details)
  - Plans to fund more research centers in FY19.

- Improving CRC Screening for American Indian populations –
  - FY18 funding to allow three cancer centers to build partnerships, procure tribal support; get tribal and Indian Health Service IRB approvals; and pilot test CRC implementation processes in each state
  - Funding planned for FY19 and 3 additional years.
  - University of New Mexico Cancer Center, University of Arizona Cancer Center, Stephenson Cancer Center at University of Oklahoma

ACCSIS Projects

- ***ACCSIS-Chicago (*1 UG3 CA233220); Karen Kim, Blase Polite, U Chicago**

Investigators propose to study the effectiveness of a multilevel intervention to improve CRC incidence and mortality **among at-risk populations in safety-net clinics** in Cook County, Chicago, Illinois. Multi-level intervention includes provider education; community outreach; provider reminder, assessment, & feedback system; patient navigation.

- ***ACCSIS in Appalachia (*1 UG3 CA233282); Mark Dignan, U Ky; Electra Paskett, OSU**

Investigators propose to examine the impact of a multilevel intervention on improving CRC outcomes among **Appalachian populations** in Kentucky and Ohio. The intervention will consist of academic detailing, patient activation to include distribution of fecal immunochemical tests kits, and social support via a patient navigator.

- ***Scaling Colorectal Cancer Screening Through Outreach, Referral, and Engagement (SCORE): A State-Level Program to Reduce Colorectal Cancer Burden in Vulnerable Populations (*1 UG3 CA233251); Daniel Reuland, UNC-Chapel Hill**

Investigators propose to assess the effectiveness of a multilevel intervention to improve CRC outcomes among **low-income and racial and ethnic minority populations in North Carolina**. The intervention will consist of a centralized colorectal cancer screening registry, distribution of fecal immunochemical test kits, patient navigation, an in-clinic patient decision aid, and establishing a colonoscopy access network.

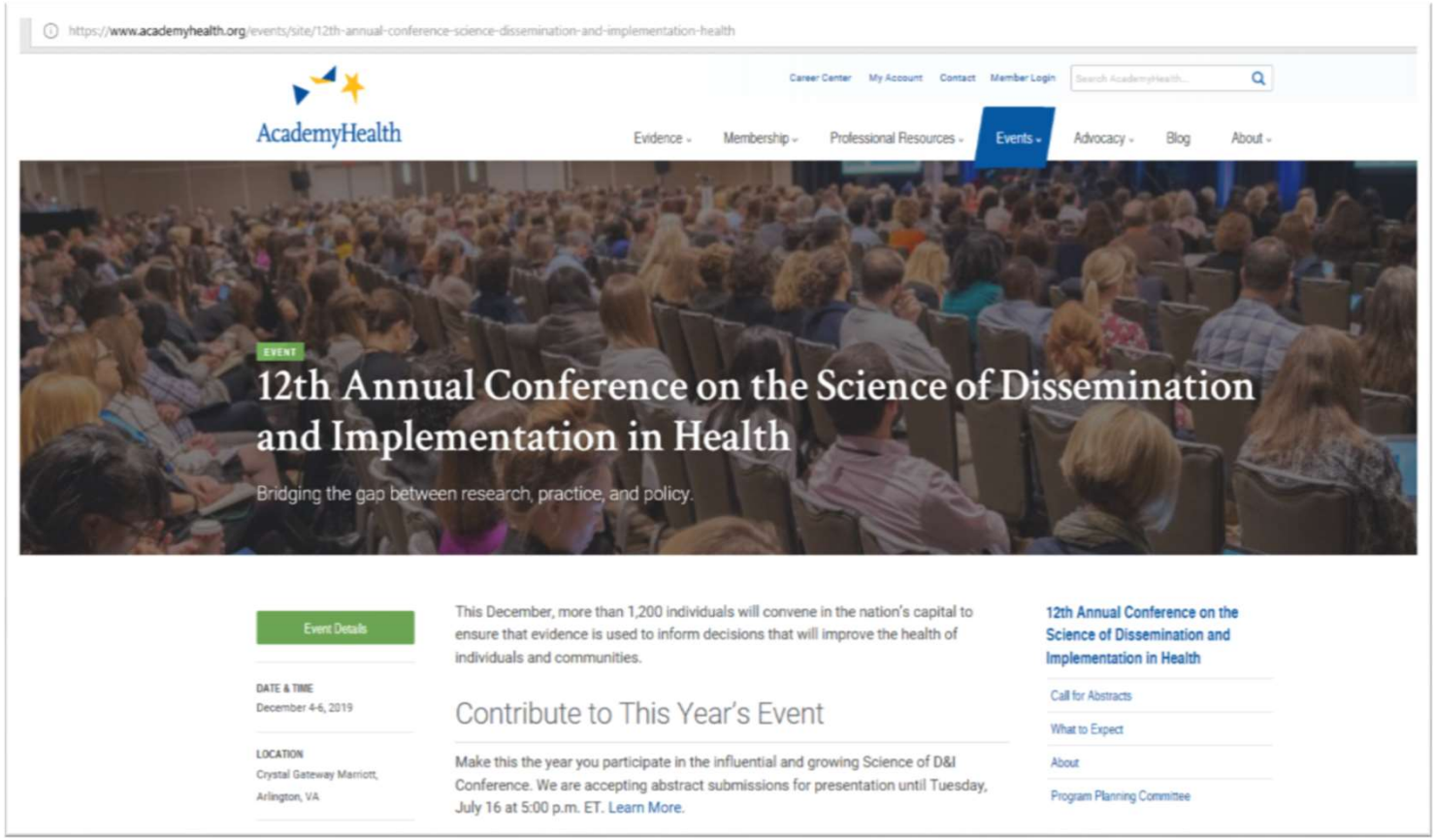
Implementation Science Centers for Cancer Control

- **NCI Leads: Cynthia Vinson and April Oh**
- **RFAs-CA-19-005/6 (P50): Currently in Scientific Review**
  - "Scaling Up Implementation Science in Cancer"
  - Advanced Ctrs in established areas (Cancer Prevention, Screening, Symptom Mgmt)
  - Developing Ctrs in newer areas (precision medicine, de-implementation)
  - Centers will include:
    - Implementation "Laboratories"
    - Methods and Measure Development
    - Rapid and Iterative Pilot Implementation Studies
    - Common Data Repositories
  - Added Goal: Build a Field-wide IS Consortium (Moonshot and beyond)

Upcoming: Pilot of IS Consortium Meeting (@NCI, July 2019)

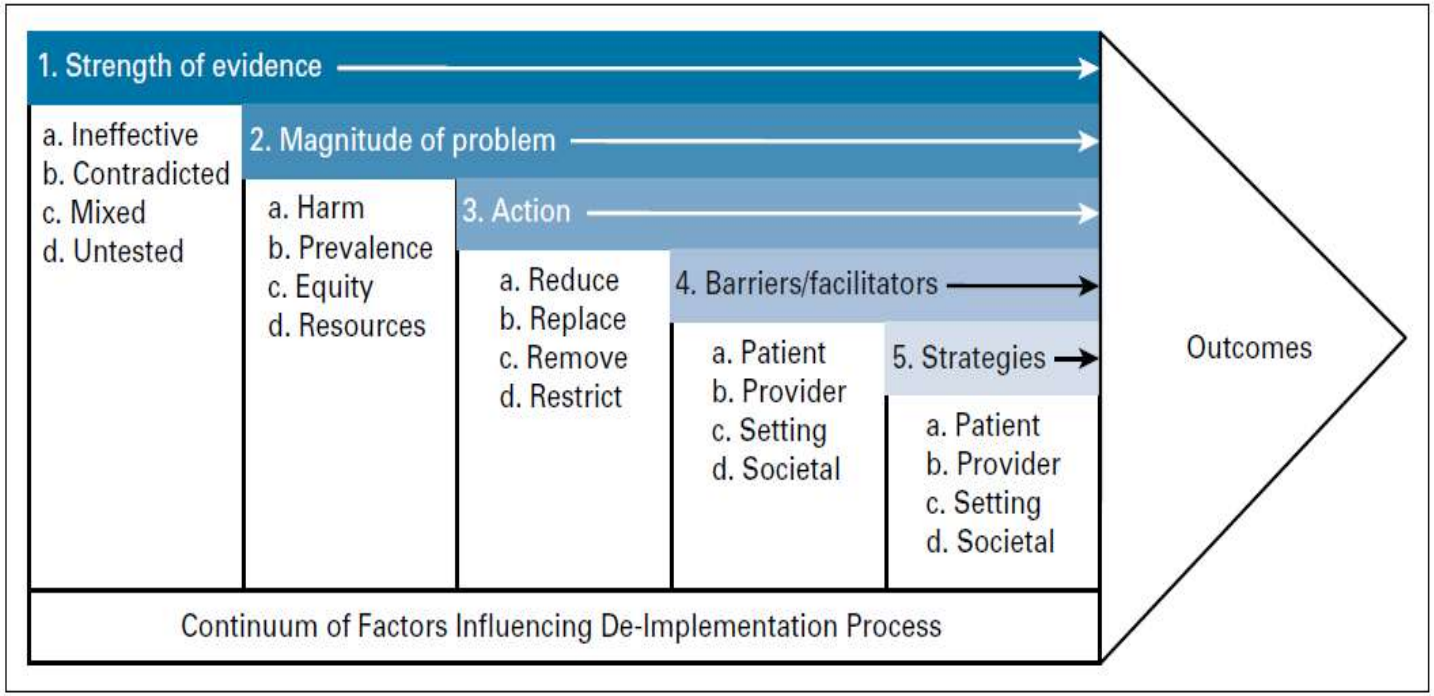
Dissemination and Implementation Research in Health Funding Announcements

PAR-19-274 (R01, Clinical Trials Optional)	**PAR-19-275** (R21, Clinical Trials Optional)	**PAR-19-276** (R03, Clinical Trials Not Allowed)
NCI, NCCIH, NHGRI, NHLBI, NIA, NIAAA, NIAID, NIAMS, NICHD, NIDA, NIDCD, NIDCR, NIEHS, NIMH, NIMHD, NINDS, NINR, ODP*, OBSSR*, ORWH*	NCI, NCCIH, NHGRI, NIA, NIAAA, NIAID, **NIAMS**, NIDA, NIDCD, NIEHS, NIMH, NINDS, NINR, Fogarty (FIC), ODP*, OBSSR*, ORWH*	NCI, NHGRI, NIA, NIAAA, NICHD, NIDA, NIDCR, NIEHS, NIMH, NINDS, FIC, ODP*, OBSSR*, ORWH*



Call for Abstracts Live!

Advancing De-Implementation



Norton, Chambers, & Kramer, 2018

IMPACT:

Improving the Management of Symptoms During and Following Cancer Treatment (UM1, U24)

RFA-CA-17-042
RFA-CA-17-043

Ashley Wilder Smith, PhD, MPH
On behalf of the IMPACT Team

September 12, 2018

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Cancer Moonshot^{SM} Initiative

RECOMMENDATION F:
Minimize cancer treatment's debilitating side effects
Accelerate the clinical adoption of integrated systems to monitor patient-reported symptoms and provide decision support using implementation science approaches and evidence-based symptom management guidelines

https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative

Goals of the Companion RFAs

Create a Research Consortium to:

- Develop scalable, transferable, and sustainable symptom management systems to monitor and address common cancer symptoms
- Rigorously examine impact on symptom control, functioning, treatment delivery, and healthcare utilization
- Using consortium-wide data, evaluate effects across:
  - Symptoms
  - Cancer continuum
  - Minority and medically underserved populations
- Produce findings and materials for wider implementation

NCI Cohort Consortium

Summary paper on the Cohort Consortium

Published OnlineFirst July 17, 2018; DOI: 10.1158/1055-9965.EPI-18-0182

Minireview

Cancer Epidemiology, Biomarkers & Prevention

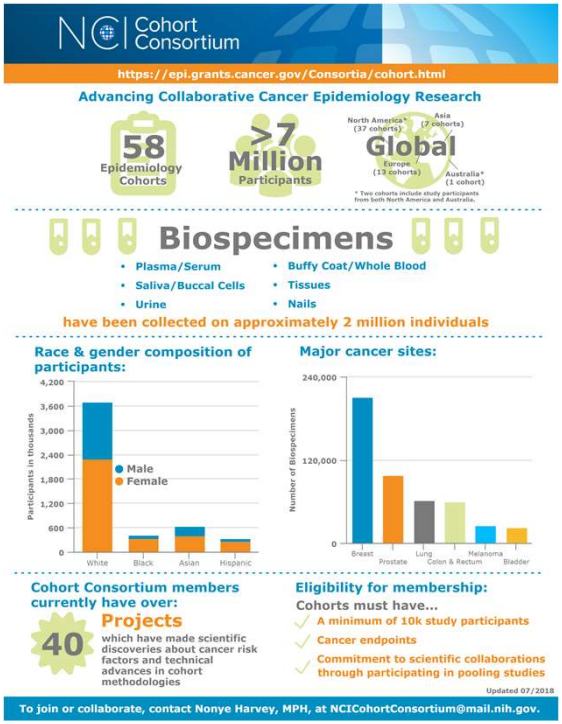
The National Cancer Institute Cohort Consortium: An International Pooling Collaboration of 58 Cohorts from 20 Countries

Anthony J. Swerdlow[1,2], Chinonye E. Harvey[3], Roger L. Milne[4,5], Camille A. Pottinger[3], Celine M. Vachon[6,7], Lynne R. Wilkens[8], Susan M. Gapstur[9], Mattias Johansson[10], Elisabete Weiderpass[11,12,13,14], and Deborah M. Winn[3]

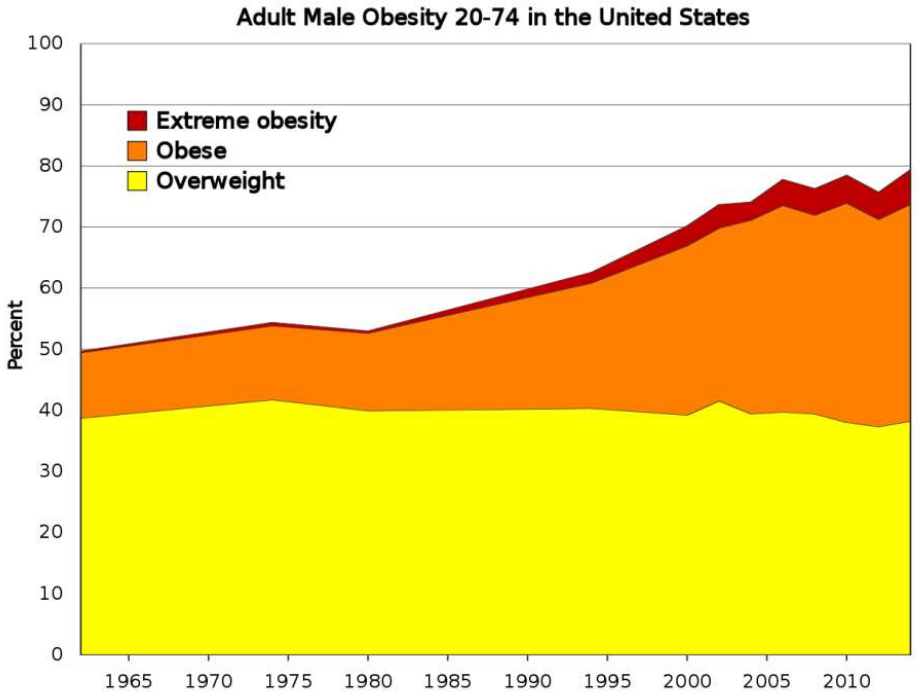
Abstract

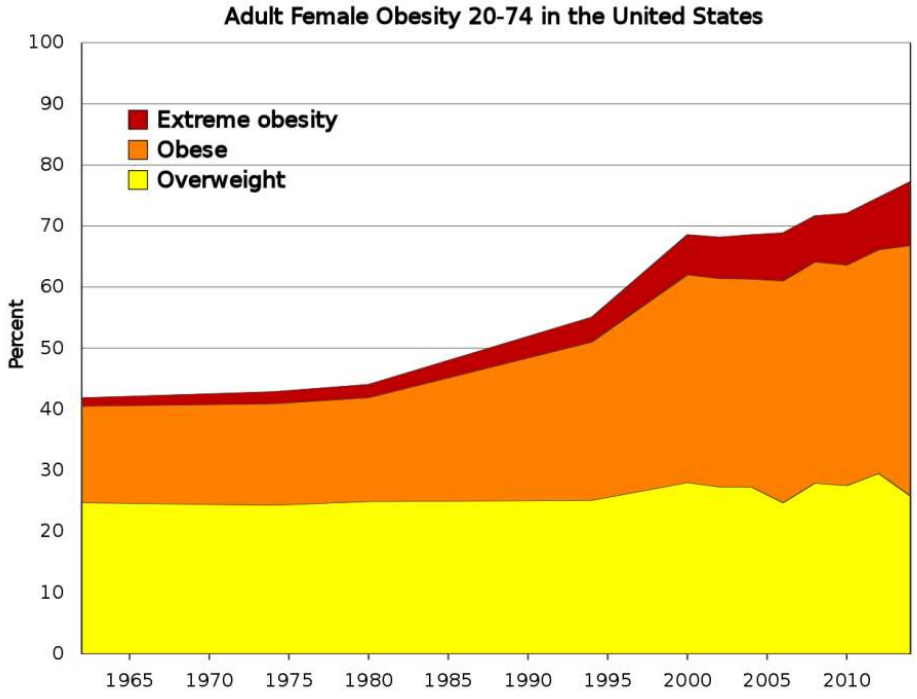
Cohort studies have been central to the establishment of the known causes of cancer. To dissect cancer etiology in more detail—for instance, for personalized risk prediction and prevention, assessment of risks of subtypes of cancer, and assessment of small elevations in risk—there is a need for analyses of far larger cohort datasets than available in individual existing studies. To address these challenges, the NCI Cohort Consortium was founded in 2001. It brings together 58 cancer epidemiology cohorts from 20 countries to undertake large-scale pooling research. The cohorts in aggregate include over nine million study participants, with biospecimens available for about two million of these. Research in the Consortium is undertaken by >40 working groups focused on specific cancer sites, exposures, or other research areas. More than 180 publications have resulted from the Consortium, mainly on genetic and other cancer epidemiology, with high citation rates. This article describes the foundation of the Consortium; its structure, governance, and methods of working; the participating cohorts; publications; and opportunities. The Consortium welcomes new members with cancer-oriented cohorts of 10,000 or more participants and an interest in collaborative research.

Cancer Epidemiol Biomarkers Prev; 27(11); 1–13. ©2018 AACR.



Trends (Male and Female) in US Adult Obesity





Courtesy of Michael Leitzman, based on on Fryar et al., NCHS Health E-Stats 2016.

Relations of physical activity and obesity to cancer

Courtesy of Michael Leitzman from Giovannucci, J Natl Cancer Inst. 2018;110(9):935-941.

Esophageal adeno	0.58 (0.37-0.89)	1.48 (1.35-1.62)
Liver	0.73 (0.55-0.98)	1.30 (1.16-1.46)
Kidney	0.77 (0.70-0.85)	1.30 (1.25-1.35)
Gastric cardia	0.78 (0.64-0.95)	1.23 (1.07-1.40)
Endometrial	0.79 (0.68-0.92)	1.50 (1.42-1.59)
Myeloid leukemia	0.80 (0.70-0.92)	1.26 (1.09-1.46)
Myeloma	0.83 (0.72-0.95)	1.10 (1.06-1.14)
Colon	0.84 (0.77-0.91)	1.07 (1.05-1.09)
Rectal	0.87 (0.80-0.95)	1.02 (1.01-1.04)
Breast	0.90 (0.87-0.93)	1.12 (1.09-1.15)
Lung	0.74 (0.71-0.77)	0.78 (0.74-0.83)
Head and neck	0.85 (0.78-0.93)	0.94 (0.90.0.98)
Bladder	0.87 (0.82-0.92)	1.04 (1.00-1.09)

Alcohol and Cancer

- Period of renewed focus on alcohol as a target for cancer prevention and control
- Key research challenges include
  - Knowledge and awareness
  - Patient-provider communications
  - Effects of alcohol consumption on treatment and recurrence
  - Evaluation of natural experiments in alcohol policy
- Creation of further resources and opportunities
  - Promoting existing funding opportunities
- Expanding this research community

Population-attributable risk of lifestyle factors for cancer mortality

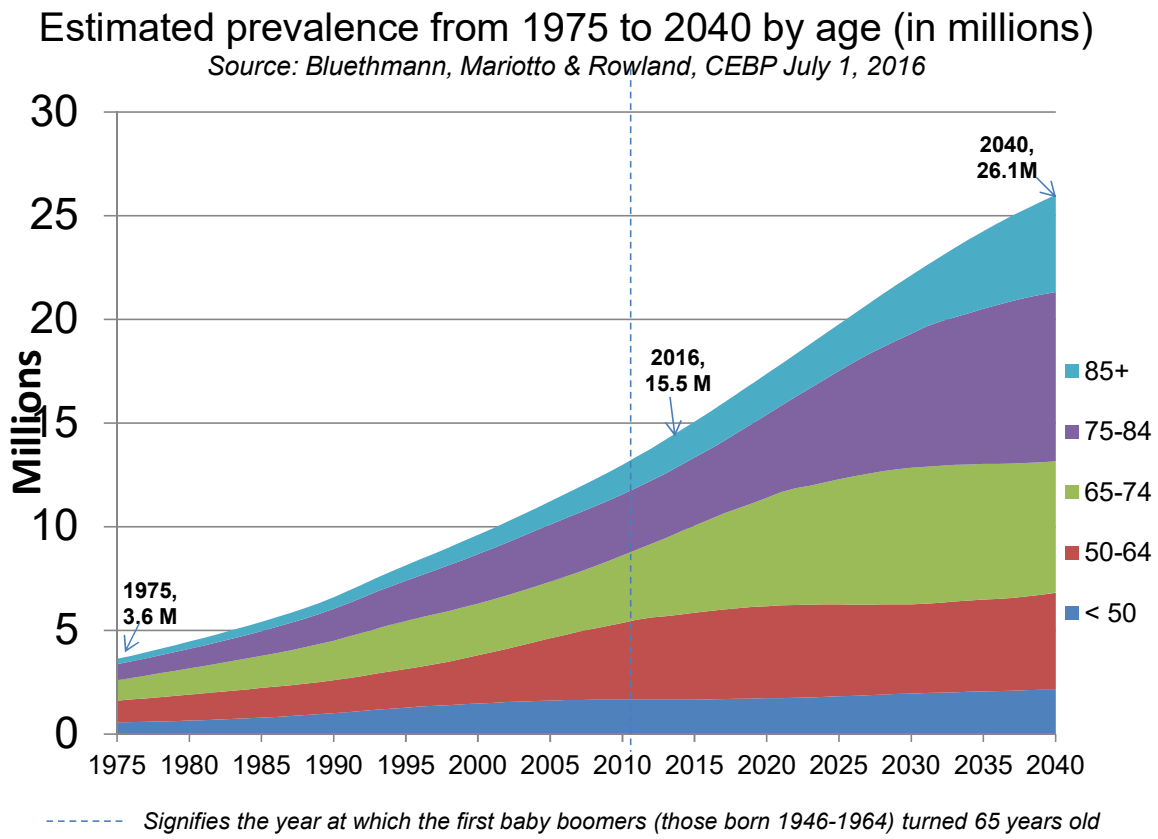
Song & Giovannucci

(JAMA Oncology, 2016)

- "Healthy lifestyle":
  - non-smoking, normal BMI, low alcohol, physically active

- Women: 48%
- Men: 44%

Challenge and Opportunity: Rapidly Increasing Numbers of Cancer Survivors



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Rural Health Research and Delivery Core: Progress and Challenges

Jan K. Carney, MD, MPH
Professor of Medicine; Associate Dean for Public Health
Rural Health Research and Delivery Core Leader
Neil Korsen, MD, MS
Core Co-Leader, Maine Medical Center
June 7, 2019

Maine Medical Center
MaineHealth

The University of Vermont
LARNER COLLEGE OF MEDICINE

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Rural Health Research and Delivery Core: Progress

- Assisting healthcare practitioners in rural areas to connect with research resources and launch projects
- Assessing the landscape of research engagement at rural healthcare practices in Vermont and Maine with 2 qualitative research studies
- Linking rural practices to the NNE-CTR network Pilot Project Program, Professional Development Core, and Clinical Research Design Core
- Connecting healthcare professionals in rural Vermont and Maine with potential collaborators and mentors in medical centers and in other NNE states
- Development of Addiction and Cancer Working Groups
- Accessing professional development opportunities including meetings, professional organizations, training sessions, and progress evaluation activities

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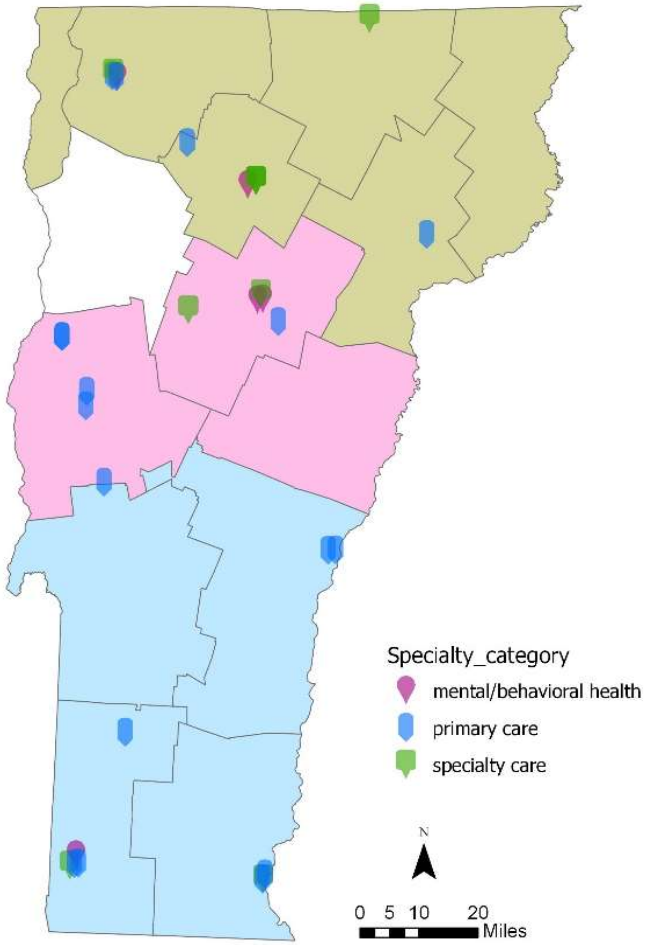
Identification of Barriers and Facilitators to Engagement in Health Research in Rural Vermont

- Created a comprehensive list (directory) of Vermont healthcare practices
- Developed and implemented a qualitative study (IRB Exempt)
- 31 structured interviews as of May 24, 2019 (see map)
- Continuing recruitment efforts for rural healthcare practices including mailed letters, phone calls, and emails
- Fifteen of 31 practices visited are interested in discussing potential research engagement; one has initiated a project (study design/discussion phase)



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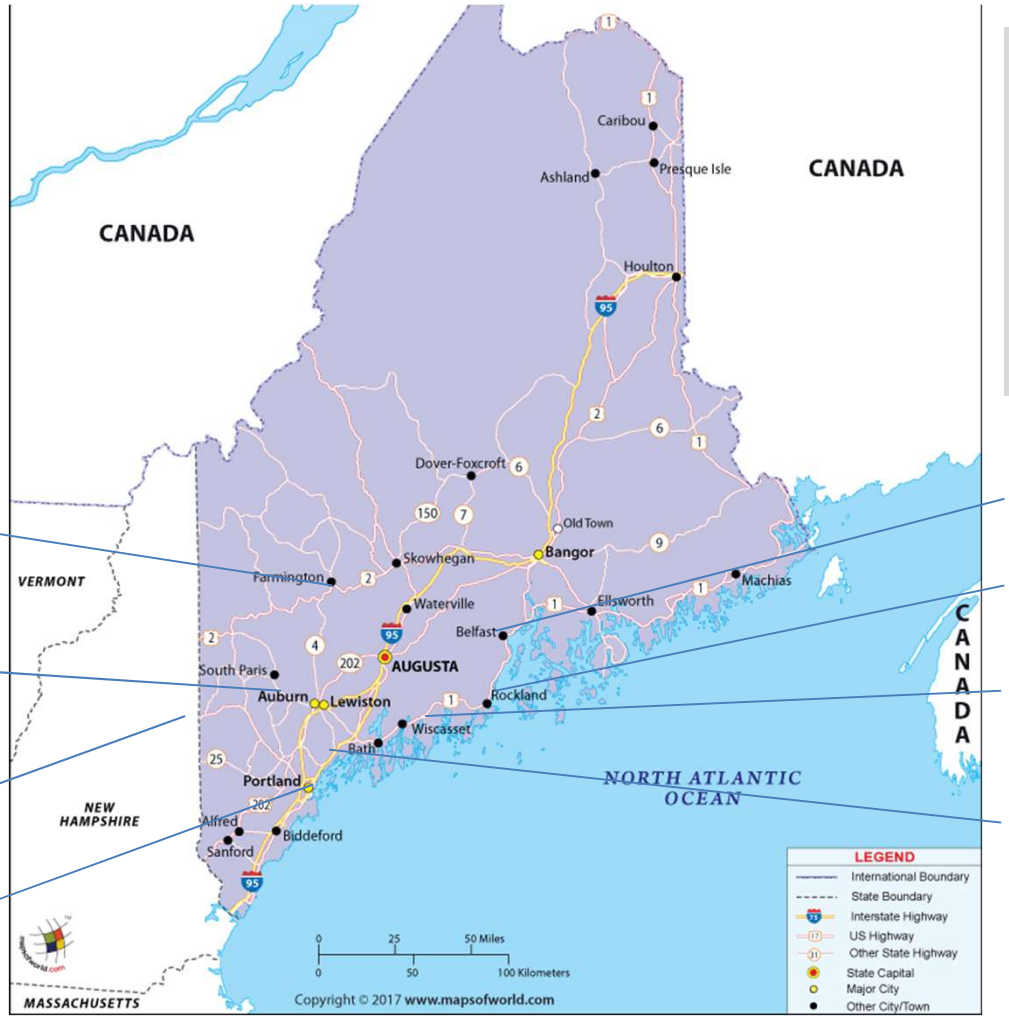
A qualitative study to identify Barriers and Facilitators to Engagement in Health Research in Maine



21 interviews with clinicians, administrators and health system leaders across Maine

Farmington, N=2

Norway, N=4

No Conway, NH, N=1

Portland, N=1

Belfast, N=4

Rockport, N=2

Damariscotta, N=4

Brunswick, N=3

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Vermont Community & Healthcare Practice Engagement

- Study design is in process with Kathryn Saccocci, PT, DPT of Southwestern Vermont Health Care, Outpatient Rehabilitation to evaluate outcomes of adding a novel exercise component to CDC diabetes prevention program focused on lifestyle change.
- Assisting co-investigator, Ryan Clouser, MD (UVM MC) with project originating in rural Maine on patient transfers from critical access hospitals to academic medical centers
- Jan Carney, MD and Charles MacLean, MD are co-investigators on the Steven Lidofsky, MD PhD (UVM MC) pilot project application titled, *Harnessing the Electronic Health Record in Primary Care for Hepatocellular Carcinoma Surveillance in Cirrhosis,* submitted to the NNE-CTR Pilot Project Program

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Vermont Community & Healthcare Practice Engagement

- UVM Larner College of Medicine has a robust and long-term community-academic partnership with many area non-profit organizations
- Community engagement: planned single focus group with non-profit partner organizations
- Goal: Identify benefits of long-term community-academic engagement and how this might relate to healthcare practices and promoting rural research
- Sample Topics: Benefits of sustained engagement; strategies for healthcare practice linkages; topic areas for research collaboration; needs for education related to research and linkages to other NNE-CTR Cores

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Vermont Community & Healthcare Practice Engagement

The Doula Project

- The Doula Project is a program of Washington County Mental Health Services (WCMHS) that is partially supported by Central Vermont Medical Center (CVMC)
- It provides prenatal, intrapartum, and postnatal support to WCMHS clients, and has been running for about 4 years

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Vermont Community & Healthcare Practice Engagement

The Doula Project

- Project is at the IRB stage
- The NNE-CTR is assisting in development of a retrospective study to describe and evaluate the existing program
- Based on the process and results, the network will help WCMHS/CVMC design a prospective study of outcomes and opportunities for potential Pilot Project development

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Additional Vermont Partnerships

- Vermonter's Taking Action Against Cancer (VTAAC)
  - Responsible for putting the Vermont Cancer Plan into action
  - Synergy with NNE-CTR Cancer Working Group
- Larner College of Medicine, Medical Student Education and Research: Public Health Projects
  - 17 community-driven projects per year, presented at annual January poster session
- Participation and leadership in Dartmouth COOP Research Network
- Coordination of NNE-CTR Addiction and Cancer Working Groups
- Vermont Department of Health
  - Research partnerships in areas of opioid addiction and chronic conditions
  - Cancer survivorship
  - HPV Initiatives
  - Rural health and healthcare disparities
- Collaborative relationships with Massachusetts, New Hampshire CTSA's

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Maine Rural Site #1: Norway

Community Engaged Research:

- Meeting held with community members and Western Maine Health clinicians on March 26, 2019.
- Topic of Adverse Childhood Experiences (ACEs) were discussed, including how to work on research that will complement and enhance current community/clinical activities.
- The research question has been narrowed to two potential areas:
  - What community assets exist and how can they be used in clinical care for referrals? What impact will they have on health outcomes?
  - What are baseline attitudes of teachers and other school staff about ACE's and how are those modified by training in trauma-informed approaches?
- An additional teleconference will be held in July to choose a research question and to begin to develop a research proposal.

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Maine Rural Site #1: Norway

Clinical research supported by Rural Research Navigator:

- Integrated Medication Assisted Therapy: measuring the impact on utilization of the local emergency department
- A Pilot Study of NOHA as a monitoring biomarker in triple negative breast cancer (PI: MMCRI)
- A Pilot Study of NOHA levels in BRCA positive Breast Cancer (PI: MMCRI)
- Screening for Adverse Childhood Experiences in adult internal medicine (PI: Dartmouth COOP)

Continued partnership with community organization:

- Ongoing discussions with Healthy Oxford Hills about the feasibility of a community asset mapping program, which could serve as a future resource for research about linking patients with social needs to appropriate community resources.
- Continued learning about community asset mapping and referral platforms in conjunction with community and statewide partners.

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Maine Rural Site #2: Rockport

Next step for unfunded pilot project proposals:

The Maine Rural Core is exploring next steps for two pilot project proposals which were not selected for funding:

- Effectiveness of Primary Care Intervention in a Hospitalized Cohort
- An occupational-specific investigation into the prevention and treatment of opioid use disorder in the Knox county fishing industry

Clinical research supported by Rural Research Navigator:

- A Pilot Study of NOHA as a monitoring biomarker in triple negative breast cancer (PI: MMCRI)
- A Pilot Study of NOHA levels in BRCA positive Breast Cancer (PI: MMCRI)
- Screening for Adverse Childhood Experiences in adult internal medicine (PI: Dartmouth)
- PCORI funded- MORE: Moms in Recovery (PI: Dartmouth)
- Effectiveness of a Hepatitis C Screening Protocol for Psychiatric Inpatients

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Upcoming training activities in Maine

- Community engagement tracking and outcome measurement workshop facilitated by the Institute for Community Health was held **May 22-23** in Portland, Maine, and included members from the Tracking & Evaluation and Rural Cores.

- Boot Camp Translation (BCT) is an evidence-based approach to translating guidelines and recommendations into language meaningful to patients and community members, to facilitate their involvement in research.
  - 3-day BCT Facilitator training **June 12-14** in South Portland, Maine.
  - Participants: community partners (Norway and Rockport); Dartmouth COOP Research Network, staff from the Maine Health community health improvement department; Vermont NNE-CTR Rural Core.

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Plans for Next 6 to 12 Months

1. Maximize effective community engagement
2. Complete the Identification of Barriers and Facilitators to Engagement in Health Research in Rural Vermont and Maine research studies
3. Continue to develop projects in Vermont and Maine, linking rural practices to the NNE-CTR Pilot Project Program and other relevant funding sources
4. Multilayer Rural Engagement Strategy
   - Continue ad hoc identification and practice visits
   - Participate in network Addiction and Cancer Working Groups
   - Engage with new and existing community groups to develop research ideas and priorities
   - Utilize relationships with Dartmouth COOP PBRN
5. Compile information on potential additional research funding sources, (eg. Foundations and other government agencies)
6. Developing NNE-Center for Rural Health & Cancer – will coordinate and catalyze efforts in Vermont, New Hampshire, and Maine
7. Ongoing consultation and collaboration with other NNE-CTR cores

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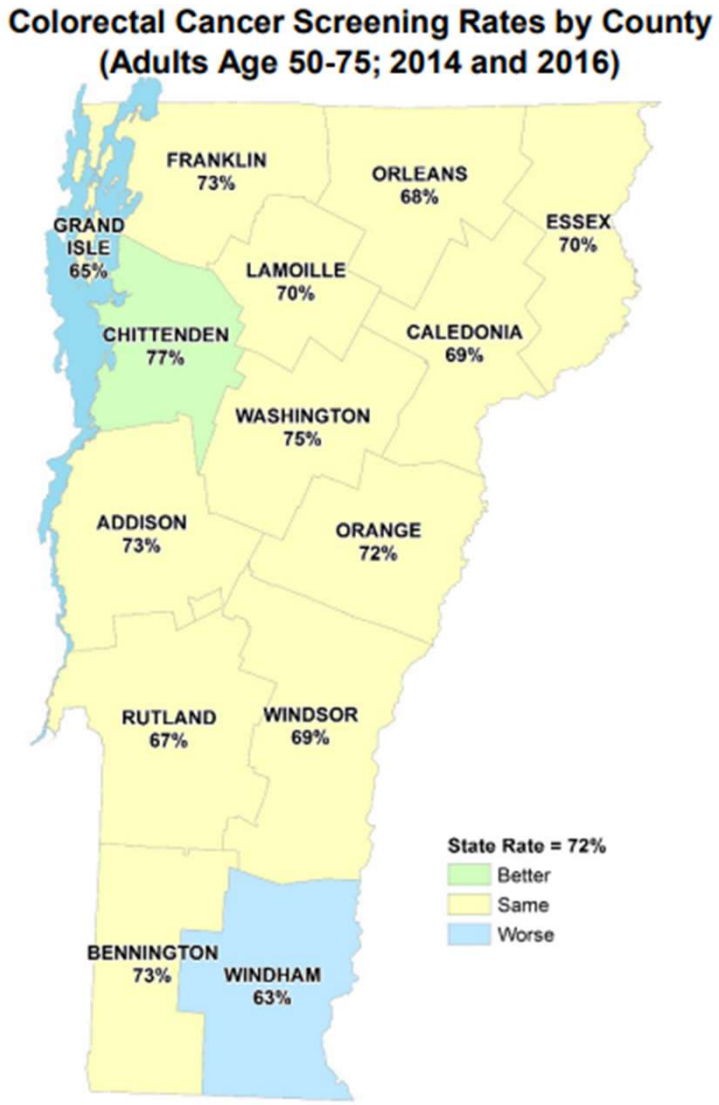
Rural Health Disparities & Challenges



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Cancer Related Risk Factors & Behaviors

Cancer County Fact Sheets

Cancer Related Risk Factors and Preventive Behaviors

Chittenden County rates for adult smoking, adult obesity (ages 20+), and youth sunburn (grades 9-12) are better than Vermont overall. The percentages of males and females ages 13-17 who are up-to-date on HPV vaccination recommendations are also better in Chittenden County than Vermont overall.

	Percent		
	Chittenden	Vermont	Goal Type[G]
Smoke Cigarettes, Currently (Adults)*	13	18	HV, SCP
Obesity (Ages 20+)*[D]	20	28	HV, SCP
Sunburn, Past 12 Months (Youth, Grades 9-12)	63	65	SCP
Adolescent Females who are up-to-date for HPV Vaccination (Ages 13-17) ◆ [D]	67	60	SCP
Adolescent Males who are up-to-date for HPV Vaccination (Ages 13-17) ◆ [D]	60	51	SCP

Data Sources: Smoking, Obesity: BRFSS; County: 2015-2016, State: 2016. Youth Tanning: YRBS, 2015. HPV vaccination: IMR, 2016.

Technical Notes

Indicates statistically worse[D] than Vermont.	
Indicates statistically better[D] than Vermont.	

*Age adjusted to U.S. 2000 population.

† Due to a difference in how the cervical cancer questions were asked in 2016††, comparisons over time cannot be made.

†† Usually women who have had a hysterectomy are excluded from cervical cancer screening calculations. In 2016, women 45-65 were not asked whether they've had a hysterectomy, and as such the proportion meeting Pap test screening recommendations is underestimated.

‡ Rates based on 5 or fewer cases are not individually calculated.

◆ *New or changed Vermont State Cancer Plan Goal*

Data Sources:

BRFSS: Behavioral Risk Factor Surveillance System
VCR: Vermont Cancer Registry
YRBS: Youth Risk Behavior Survey
IMR: Immunization Registry
Vital Statistics: Vermont Vital Statistics

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Rural Health Research and Delivery Core: Challenges

- Engaging rural healthcare practices to prioritize research as part of their mission
- Supporting rural clinicians who are interested in research to have time and funding
- Educating rural healthcare practices about NNE-CTR resources to facilitate research opportunities in their own practices and local communities
- Measurement challenges of some goals, e.g. decrease in barriers to research in rural settings

Professional Development Core

June 2019

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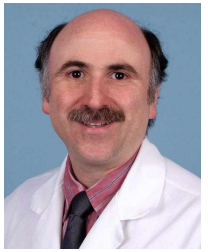
RESEARCH NETWORK

Kimberly Luebbers, MSHS, R.N., BSN – Core Lead UVM

Irwin Brodsky, M.D. – Core Co-Lead, MMC

(Don St. Germain, M.D. – former Core Lead, MMC)


Ivette F. Emery, Ph.D. – Associate Core Lead, MMC

Emily Tarleton, RD, Ph.D. – Associate Core Lead, UVM


<u>Core Liaisons:</u>

Erica Ziller, Ph.D., MS – University of Southern Maine

Ardis Olsen, M.D. – Dartmouth College

Karen Freund, M.D., MPH – Tufts University

Professional Development Core

June 2019

NORTHERN NEW ENGLAND
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RESEARCH NETWORK

OUTLINE

1. Summary of Core Aims
2. Accomplishments
3. Challenges
4. Year 3 Plans

Professional Development Core
CORE AIMS

NORTHERN NEW ENGLAND
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RESEARCH NETWORK

Aim 1: To promote multidisciplinary translational research projects.

Aim 2: To develop educational programs to enhance research competency.

Aim 3: To develop mosaic mentorship teams to support mentees.

Aim 4: To develop a unique catalyst certificate program.

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Aim 1: To promote multidisciplinary translational research projects.

Supported the formation of four new multi-disciplinary teams at MMC.

1) Study Title: Cardio-surveillance of Cancer Patients Undergoing Immune Checkpoint Blockade
Team PIs: Cardiologist, S. Francis, and Oncologist, S. Remick
Status: Preparing submission to IRB

2) Study Title: Anti-Diabetic Potential of Patient-Derived Brown Adipocytes
Team PIs: Bariatric surgeon, K. Sahagian, and basic scientist, A. Brown
Status: IRB-approved and preparing to enroll first patient

3) Study Title: Effect of Mediterranean diet vs std cardiac diet in lipid profile of CABG patients
Team PIs: Cardiologist, D. Sawyer, and basic scientist, I. Pinz
Status: IRB-approved and enrolling patients

4) Study Title: Perivascular fat and human cardiometabolics
Team PIs: Cardiac surgeon, M. Robich, and basic scientist, L. Liaw
Status: IRB-approved and enrolling patients

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Aim 1: To promote multidisciplinary translational research projects.

Supported CTR related teams in the development, submission, conduct of their research .

1) Study Title: Rural Implementation of a Modern Approach to Prostate Cancer Screening (RI-MAPS)
Team PIs: H. James Wallace, M.D. & A. Landry, M.D. (UVM), W. Sturrock, M.D. & B. Sorondo, M.D., MBA (EMMC)
Status: Submitted Pilot Project Proposal for Round 2, Spring 2018, scored/not funded, initial pilot data under analysis, possible resubmission for funding

2) Study Title: Sleep Disturbance on Bedside Electroencephalogram: A Biomarker for Severe Neonatal Abstinence Syndrome
Team PIs: Deidre O'Reilly, M.D. (UVM), Alexa Craig, M.D. (MMC) and Tyler Hartman, M.D. (DHMC)
Status: Submitted Pilot Project Proposal for Round 3, approved for funding, UVM IRB approval pending clarifications

3) Study Title: Harnessing the Electronic Health Record in Primary Care for Hepatocellular Carcinoma Surveillance in Cirrhosis
Team PIs: Steve Lidofsky, M.D. (UVM)
Status: Submitted Pilot Project Proposal for Round 2&3, approved for funding Round 3, UVM IRB submission being prepared

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Aim 2: To develop educational programs to enhance research competency.

- Developed UVM/UVM Medical Center Research Professionals Network
- Partnered with BU/BMC to deliver the Research Professionals Network Workshop Series at UVM. Academic Year 18-19 workshops include:

2018-2019 RPN Workshop Series with Boston University

Date	Topic	Presenter	Level
September 18, 2018	Why Do We Need IRB review?	Melanie Locher, BS, CIP (UVM)	Fundamental
October 16, 2018	Single IRB and Reliance Agreements	Kim Luebbers, MSHS, RN, BSN, OCN (UVM), Matthew Ogrodnik, MS, CIP (BU), and Donna Silver, CIP (UVM)	Fundamental
November 27, 2018	Research Design and Data Analysis	Abby Crocker, MS, PhD (UVM), Sarah Qin, MBA (BMC), and Nellie Shippen (BMC)	Fundamental
December 17, 2018	Developing Effective Data Collection Tools	Alana Ewen, MPH (BMC)	Fundamental
January 24, 2019	Having Difficult Conversations/Words Matter	Alix Rubio (BMC), Nellie Shippen (BMC), and Emily Tarleton, PhD, RD (UVM)	Advanced
February 4, 2019	UVM Only – Common Rule Changes and Click Tips & Tricks	Melanie Locher, BS, CIP and Kim Luebbers, MSHS, RN, BSN, OCN (UVM)	Fundamental
February 20, 2019	ClinicalTrials.gov	Karla Damus, MSPH, MN, BSN, RN, FAAN (BU)	Advanced
March 19, 2019	Protocol Compliance	Michelle St. Paul, MA (BU)	Fundamental
April 24, 2019	SOP Development	Jessica Howard, MPH, MA (BU) and Kimberly Parker, MS (BMC)	Advanced
May 23, 2019	Preparing for an FDA Audit/Audit Preparedness	Thomas Cheng, MS (BU) and Eric Stratton, MPH (BU)	Fundamental
June 18, 2019	Developing Effective Corrective and Preventative Action Plans (CPAs)	Mary-Tara Roth, RN, MSN, MPH (BU)	Advanced
July 18, 2019	Drugs/Devices (IND/IDE)	Ross Colgate, Ph.D., MPH (UVM)	Advanced

- Partnered with Vanderbilt University for their "G*etting Started in Sponsored Research*" webinar series.

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Aim 2: To develop educational programs to enhance research competency.

Other educational offerings:

- Department of Biochemistry, NNE-CTR & Cancer Research and Technology Seminars
- Research Tapas & Career Matters (LCOM Faculty Affairs Office)

2018-2019 Department of Biochemistry, NNE-CTR & Cancer Research and Technology Seminars

Date	Topic	Presenter
February 22, 2019	The Cancer Genome Atlas: Mining public data can inform your research (and you can do it yourself!)	Julie Dragon Ph.D., Director VIGR UVM
March 8, 2019	The Cancer Genome Atlas: Practical Tools for Clinical Data Exploration & Hypothesis Development	Joe Boyd M.S., Biochemistry UVM
March 22, 2019	Targeting Cell Adhesion in CALM-AF10 Transformed Leukemia	Jessica Heath M.D., Ped-Hem/Onc & Biochemistry UVM
April 12, 2019	CRISPR/Cas Strategies for Making Novel Genetically Modified Mouse Models	Lucy Liaw, PhD, Director, Mouse Transgenic Core Facility Main Medical Center Research Institute
April 26, 2019	In situ Vaccination and Other Perspectives on Tumor Immunotherapy	Steve N Fiering, PhD, Microbiology and Immunology, Geisel School of Medicine at Dartmouth
May 10, 2019	Choosing a sequencing platform: MiSeq, HiSeq	Scott Tighe, Chair ABRF Metagenomics Research Group

Programs livestreamed to MMC:

- "*Canines, Cancer, and Comparative Genomics*", Elaine Ostrander, Ph.D., National Institute of Health Distinguished Investigator - October 30, 2018
- "*A Physicist's Approach to the Lung*", Larner College of Medicine Research Laureate Lecture - Jason Bates, Ph.D.

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Aim 2: To develop educational programs to enhance research competency.

- ***Delivered two seminars from Grant Writer's Seminars and Workshops (GWSW) at MMC and UVM.***

  1. Write a Winning Grant Proposal (geared towards writing R01)
     Attendance: 25 senior faculty, junior faculty, postdocs and students at MMC and 15 at UVM
  2. Write a Winning Career Development Grant (geared towards K-F awards)
     Attendance: 12 senior faculty, junior faculty, postdocs and students at MMC and 10 at UVM

  "excellent presenter who is clearly knowledgeable, very clear, articulate and energetic. I wish we could do this quarterly. The materials alone are priceless."

- ***Partnered with Tufts to add more research education videos to our website's inventory.***

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
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RESEARCH NETWORK

Aim 3: To develop mosaic mentorship teams to support mentees.

- ***Assembled mentoring team for three new clinical-investigators.***
  Vascular surgeon, K. Malka
  Pediatric neurologist, A. Craig
  Pharmacologist, S. Mohan (UNE)

- ***Mentored two pilot project investigators in their IRB resubmissions.***
  Neurologist, H. Henninger
  Cardiologist, S. Francis

- ***Assembled "supermentors" for group-to-group mentoring sessions.***
  Bone biologist, C. Rosen
  Cardiologist, D. Sawyer
  Critical care physician, D. Seder
  Nephrologist, E. Taylor
  Endocrinologist, I. Brodsky

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Aim 3: To develop mosaic mentorship teams to support mentees.

- ***Continue to develop and implement UVM Resident Research Mentoring program.***

  UVM Department of Medicine collaboration to develop individualized mentoring plans with assessments to evaluate outcomes mentorship goals.

- ***CTR Pilot Project Mentors***

  Study Title: Sleep Disturbance on Bedside Electroencephalogram: A Biomarker for Severe Neonatal Abstinence Syndrome
  Team PIs: Deidre O'Reilly, M.D. (UVM), Alexa Craig, M.D. (MMC) and Tyler Hartman, M.D. (DHMC)
  Mentors: Deborah Hirtz, M.D. (UVM) & Gregory L. Holmes, M.D. (UVM)
  Status: Submitted Pilot Project Proposal for Round 3, approved for funding, UVM IRB approval pending clarifications

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Aim 4: To develop a unique catalyst certificate program.

Translational Research Catalyst Certificate Program

PROGRAM SCHEDULE

	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	
Pre-existing				NIH Course: Intro to Principles & Practice of Clin Res									I
	Core Course: Study Design/Epidemiology						Core Course: Applied Biostatistics						II
	Elective course (fill knowledge base gaps)						Elective course (T1/T2 or T2/T3/T4 path)						III
In development	Translational Team Science Seminar Series and Journal Club												IV
	Medical rotation												V
	Regulatory/Compliance rotation						Finan Project Mgt rotation			Clin Trials Office rotation			VI
	Internship/Practicum as Catalyst → Level of independence												VII

Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
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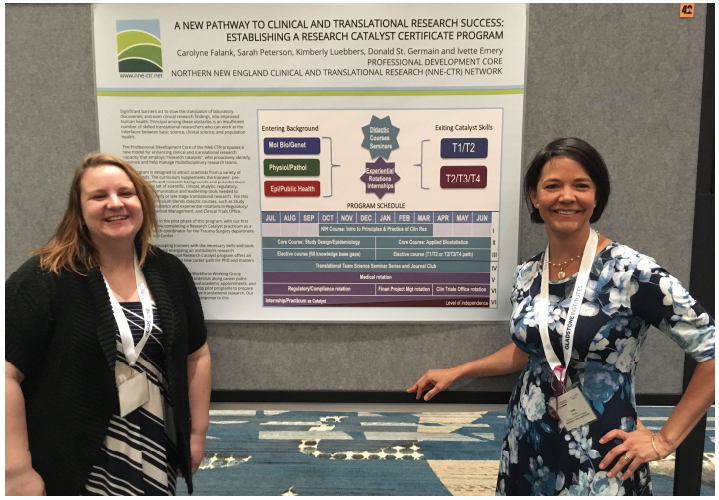
RESEARCH NETWORK

Aim 4: To develop a unique catalyst certificate program.

First pilot student near completion of second semester.
Post-doctoral fellow, C. Falank, now in the 2nd semester, serving as trauma catalyst and pilot student for refinement of curriculum.

Presented poster about program.
I. Emery and C. Falank presented at
National Postdoc Association Annual Meeting.
Orlando, Florida - April 12-14, 2019



Professional Development Core
YR 2 PROGRESS per CORE AIM

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

Professional Development Core Milestones and Timeline

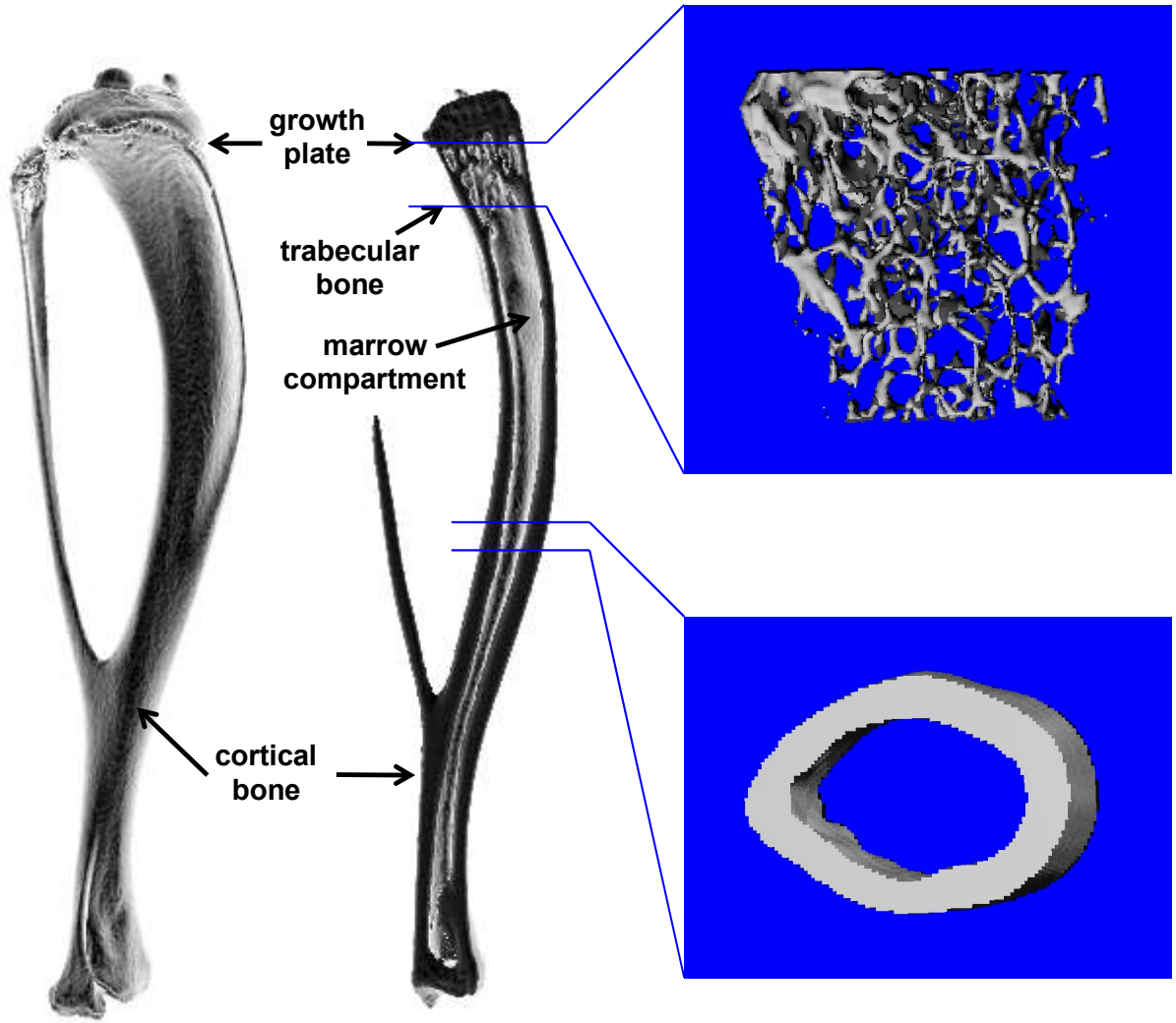
Common Milestones	Y1	Y2	Y3	Y4	Y5
Organize PDCCC and prioritize tasks	√				
Establish communication channels across institutions and cores	√				
Develop/maintain inventories of faculty, trainees, and educational offerings	√	√	√	√	√
Develop/maintain relational, searchable database	√	√	√	√	√
Develop algorithms to assist in organizing research & mentoring teams	√				
Perform initial and periodic needs assessments of educational offerings	√	√	√	√	√
Develop standard curriculum for commonly encountered educational needs	√				
Aim 1 Milestone					
Support development of multi-disciplinary T1 translational research teams	√	√	√	√	√
Aim 2 Milestone					
Identify and support engagement of clinicians in research activities	√	√	√	√	√
Aim 3 Milestone					
Identify mentees and support development of team-based mentoring model	√	√	√	√	√
Aim 4 Milestones					
Refine curriculum tracks for training T1 and T2/T3/T4 research catalysts	√				
Develop needed unique course offerings for certificate program	√	√	√		
Publicize availability of the program and recruit students		√	√	√	√

Completed or nearing completion Underway Not yet started

Direct and indirect mechanisms of opioid-induced bone loss

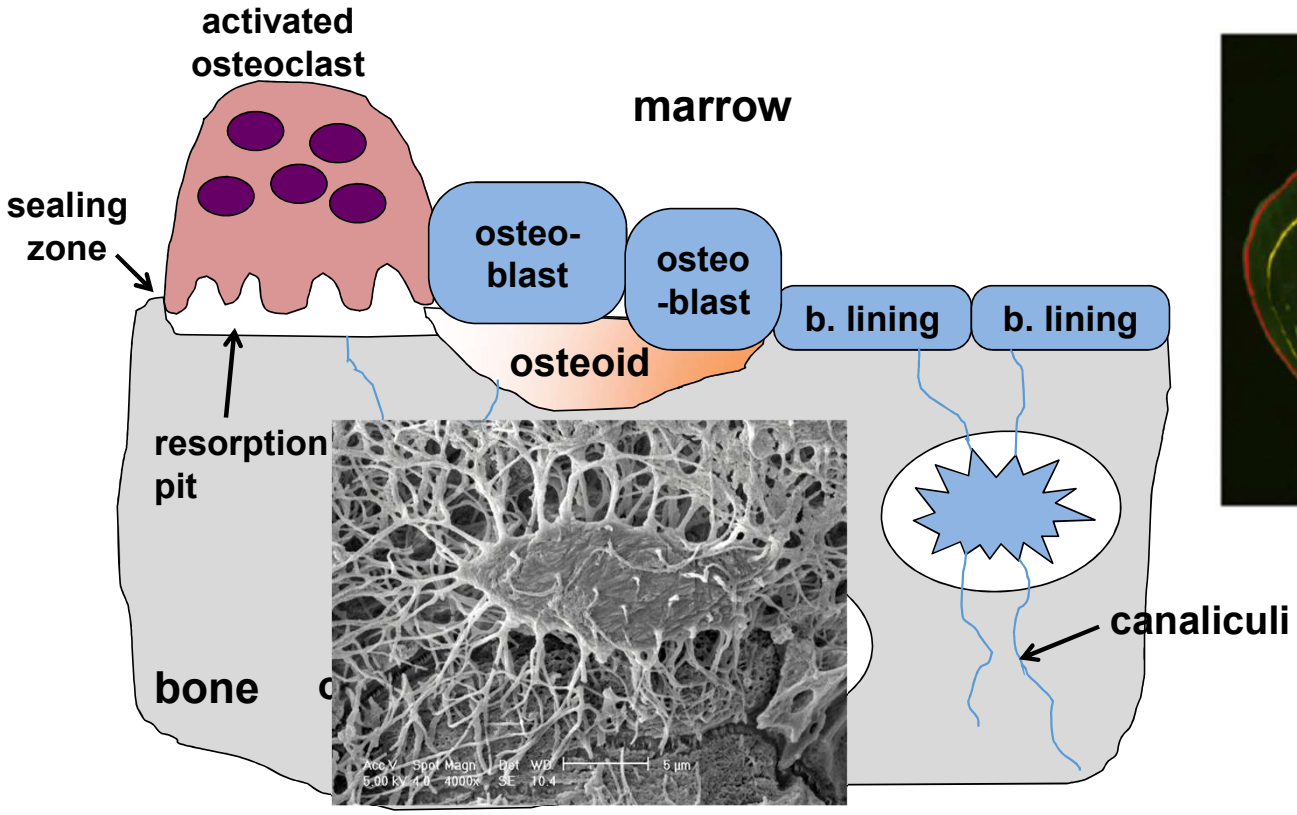
Katherine Motyl

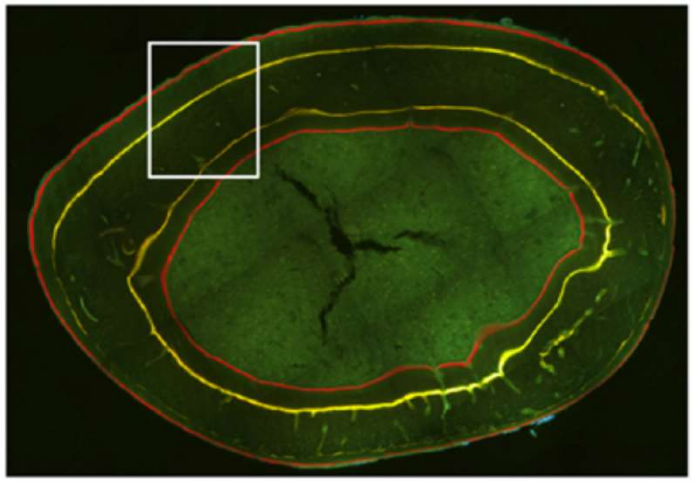
CTR Retreat 6-3-19



Photos: Motyl KJ, McCabe LR and Rosen CJ, unpublished

Bone Cells Actively Model and Remodel Bone

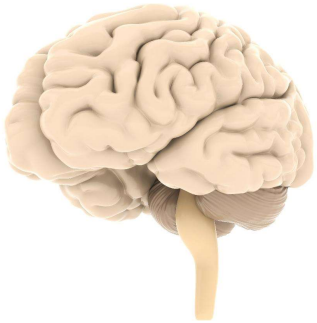




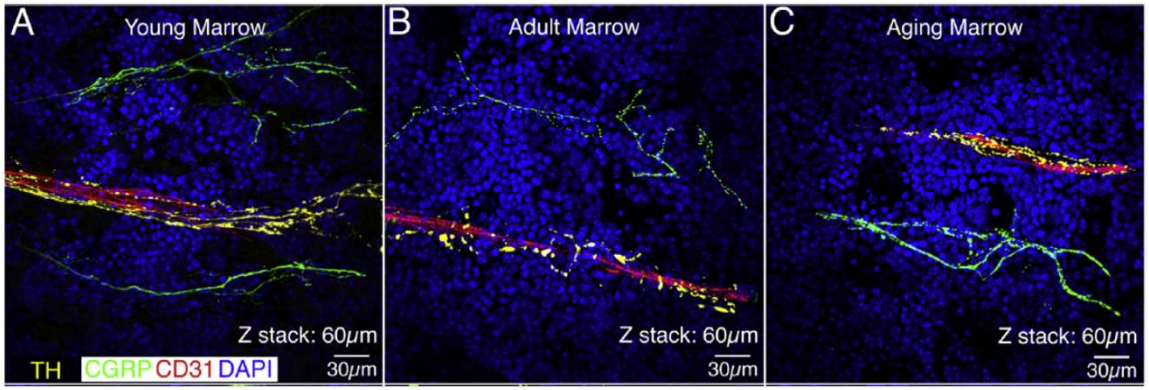
IBMS BoneKEy (2009) 6, 63–70 (2009)

Witcher PC et al. *JCI Insight*. 2018; 3(11)e98673

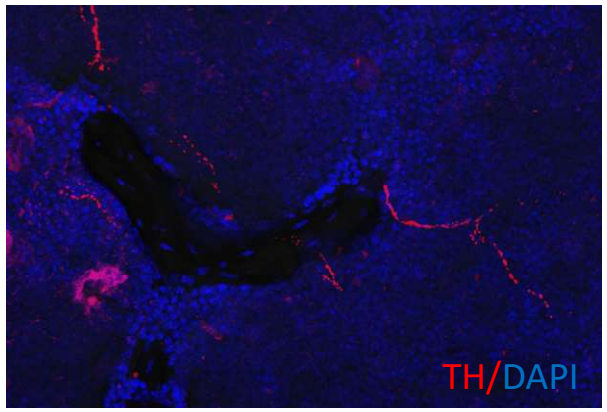
Bone density is also regulated by the central and peripheral nervous systems



Appendicular Skeleton
(Femur Medulla)



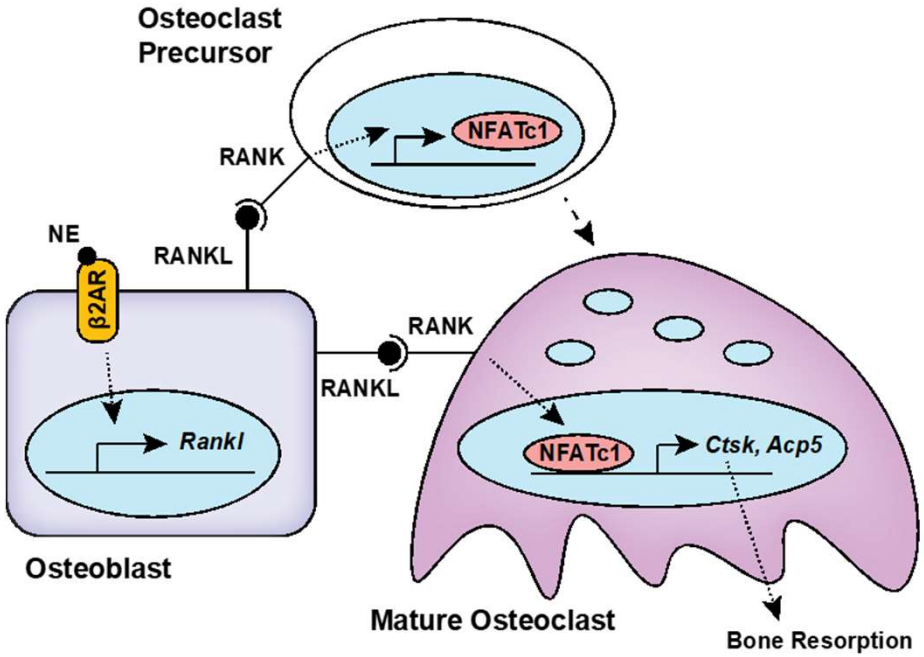
Axial Skeleton
(Vertebral Body)

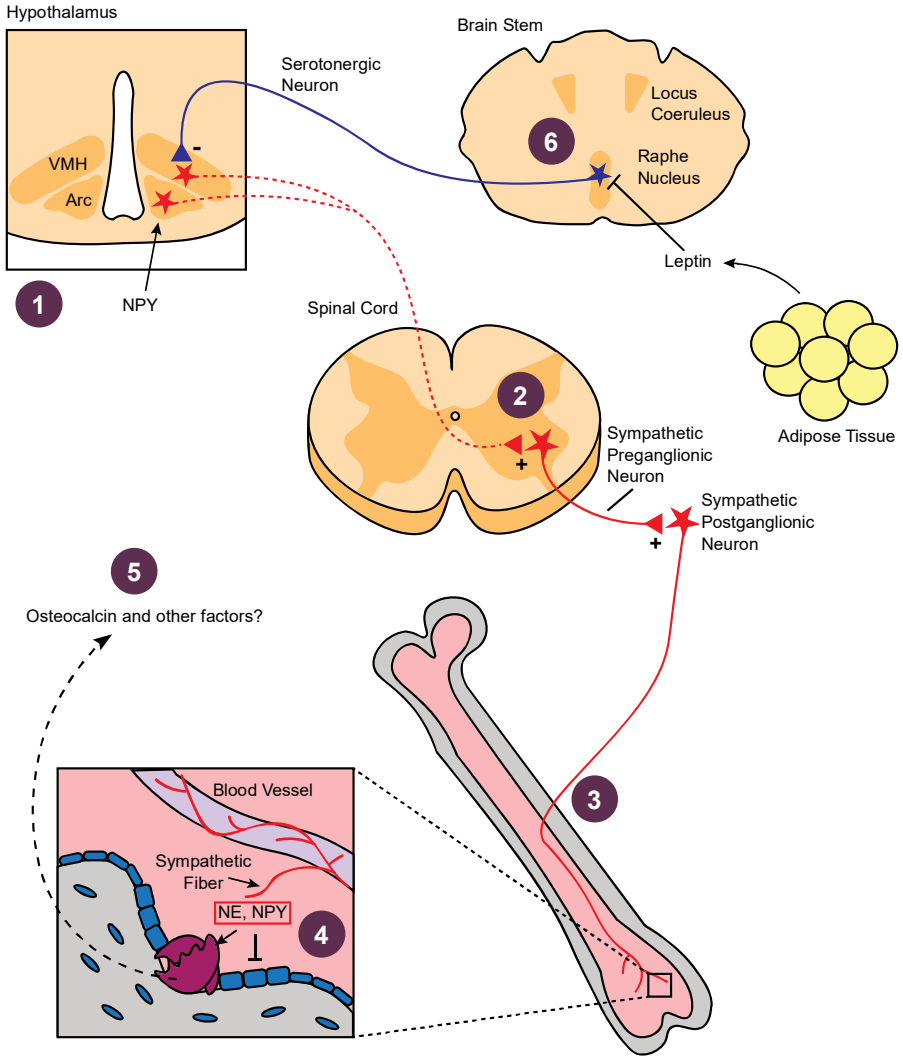


Motyl Lab, unpublished

S. R. Chartier et al. / Neuroscience 387 (2018) 178–190

SNS output to bone

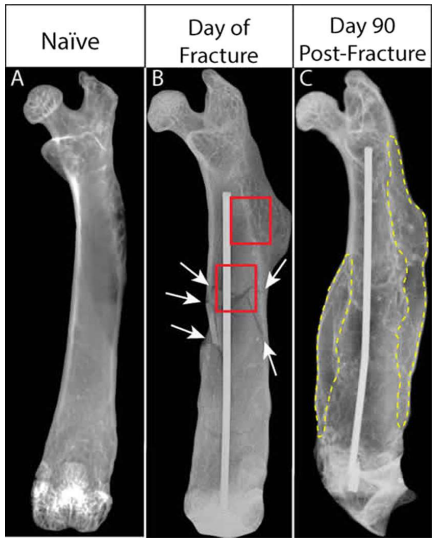


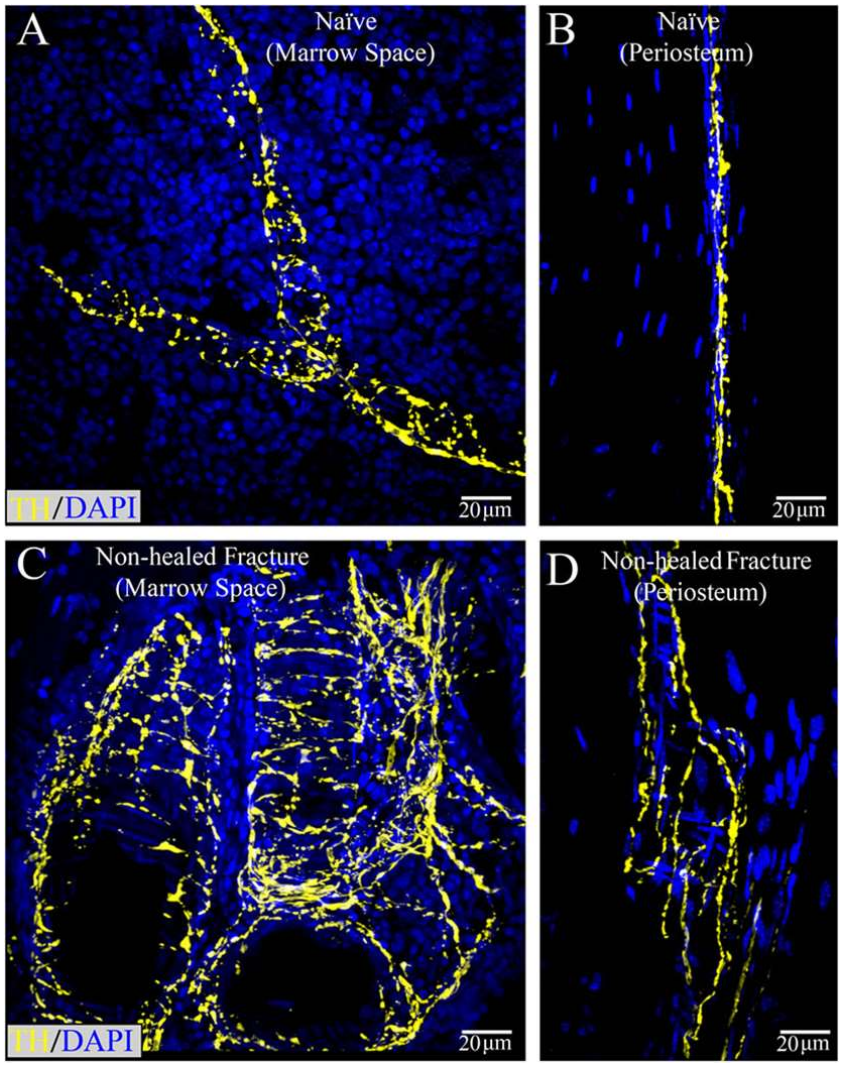


Motyl KJ and Barbe MF. Brain and Bone. Basic and Applied Bone Biology, 2nd Ed. Elsevier Academic Press.

Fracture

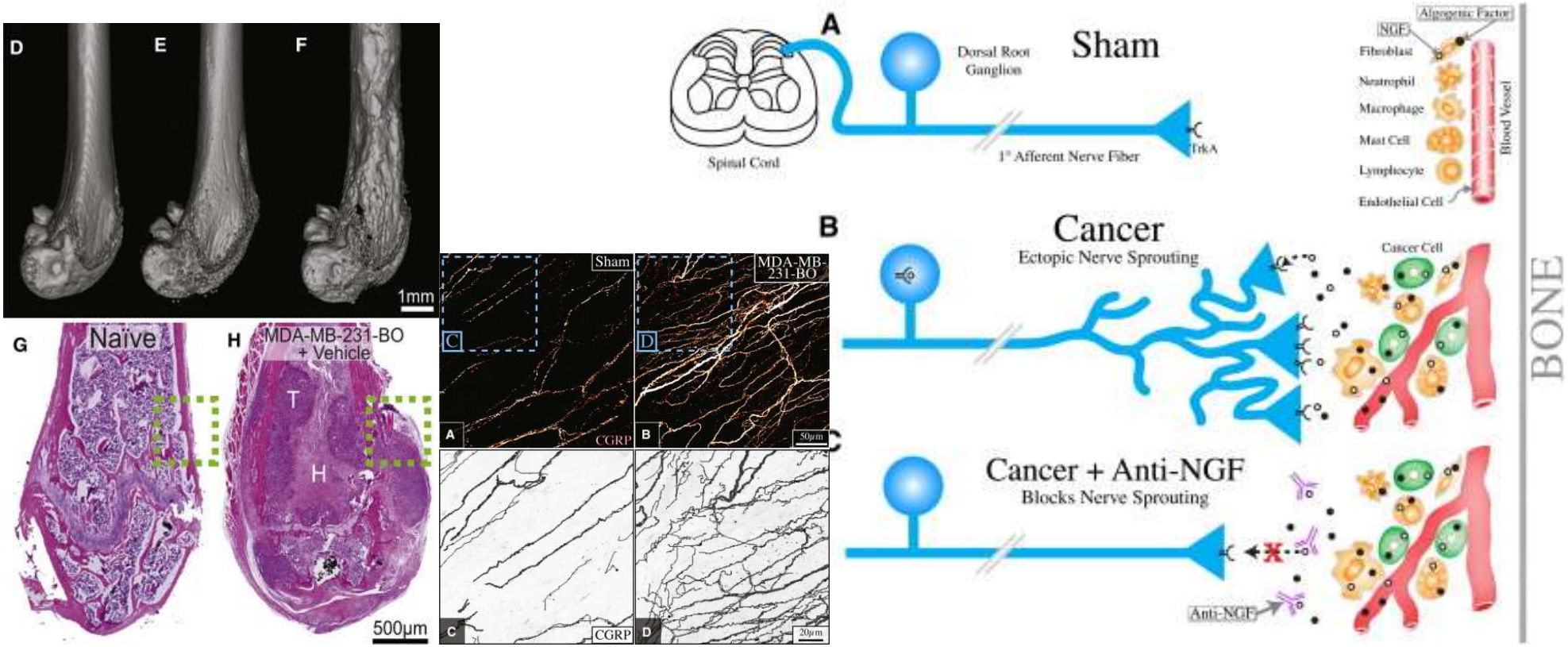
- Nonhealed fracture associated with sprouting of sensory and sympathetic nerves
- Anti-NGF therapy can reduce fracture pain





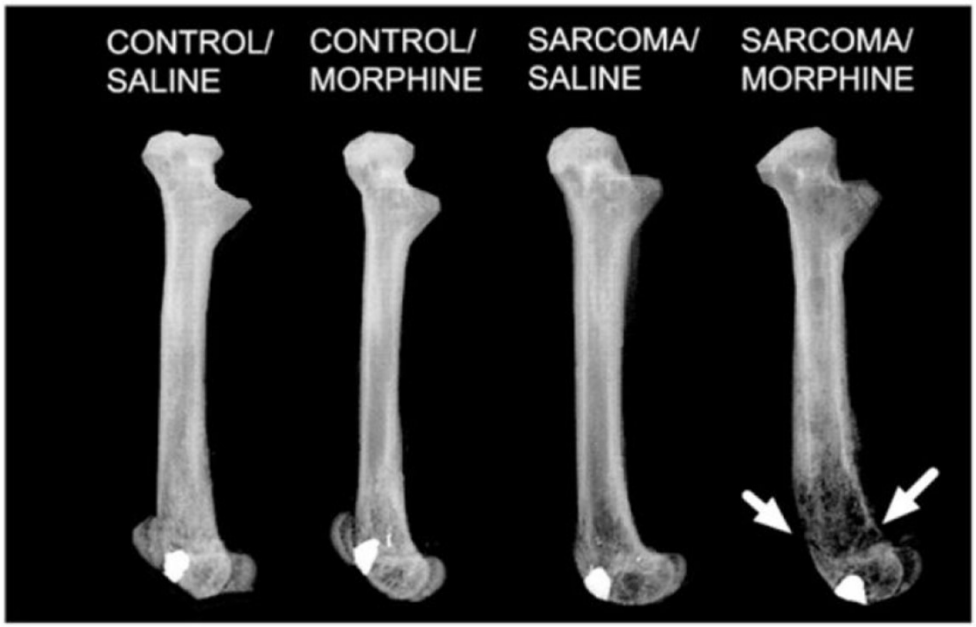
Pain. 2014 Nov;155(11):2323-36.

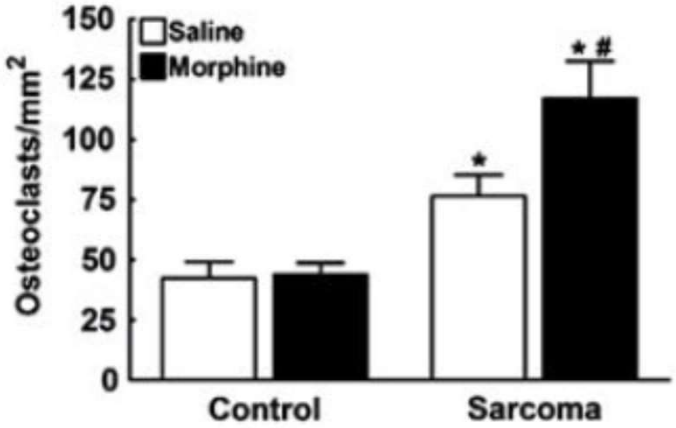
Breast Cancer Metastases Cause Nerve Sprouting



Bloom, et al. 2011. Journal of Pain. 12(6).

Cancer-induced bone loss exacerbated by morphine





Pain. 2007 November ; 132(1-2): 154–168.

WHAT ARE OPIOIDS?

Opioids is a term used for the entire family of opiate drugs, including natural, synthetic and semi-synthetic.

These drugs are chemically related and interact with opioid receptors on nerve cells in the body and brain.

OPIOID DRUGS INCLUDE:

- **Heroin**
- **Buprenorphine**
- **Codeine**
- **Fentanyl**
- **Hydrocodone**
- **Hydromorphone**
- **Meperidine**
- **Methadone**
- **Morphine**
- **Oxycodone**

https://www.cdc.gov/drugoverdose/opioids

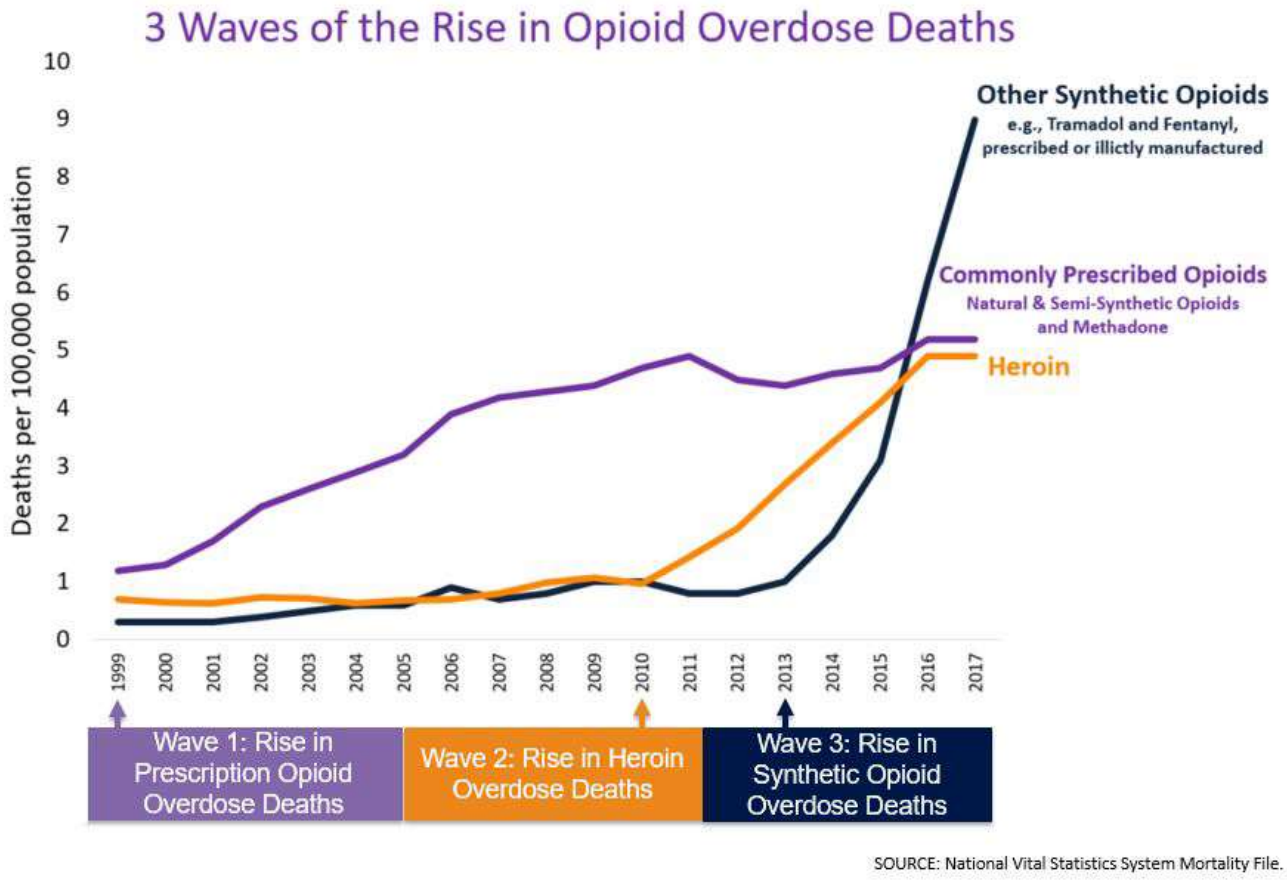
Morphine

- Morphine is derived from opium and was first isolated between 1805 and 1816 by a pharmacist's assistant Friedrich Wilhelm Serturner, who named it after the Greek God of dreams, Morpheus.
- Began being used clinically in the mid-1850s for pain and to treat opium addiction, but itself is addicting.
- In the 1980s, WHO guideline officially included morphine administration for cancer pain treatment.
- Current clinical uses: MI, bone and joint pain from sickle cell crisis, pain relief before, during and after surgery.

Opium poppy plant
Papaver somniferum

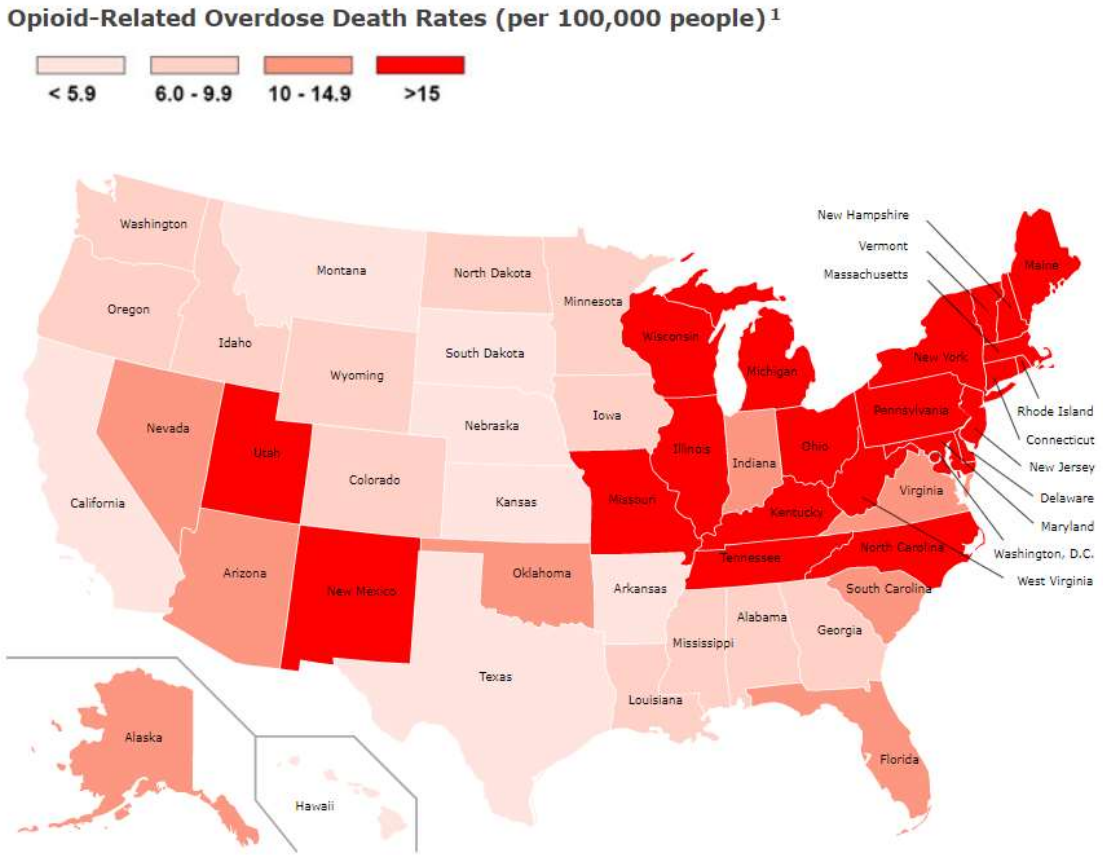
(Winter et al., Cochrane Database of Systematic Reviews, 2017; https://www.cdc.gov/drugoverdose/opioids)

Recent rise in opioid-related deaths due to synthetic opioids, but commonly prescribed opioids are still significant contributors



https://www.cdc.gov/drugoverdose/opioids

Rate of opioid-related overdoses are among the highest in Maine



(https://www.cdc.gov/drugoverdose/opioids ; https://www.drugabuse.gov/drugs-abuse/opioids)

In addition to overdoses, people taking opioids have endocrine side effects

Effects of opioid use on:	
Hypothalamic-pituitary-gonadal (HPG) axis	**Inhibitory effect:** **↓ testosterone or estradiol**
Hypothalamic-pituitary-adrenal (HPA) axis	Inhibitory effect: ↓ cortisol
Hypothalamic-pituitary-thyroid axis	TSH levels (controversial)
Somatotropic axis	growth hormone (GH) secretion
Prolactin	Stimulatory effect ↑
Skeleton	↑ Fracture risk ↓Bone Mineral Density (BMD)

(Fountas et al., European Journal of Endocrinology, 2018)

Potential mechanisms of opioid-induced fracture and bone loss

- Higher Risk of Falls (dizziness)
- Hypogonadism, however, postmenopausal women in use of opioid treatment for pain still have ↑ fracture risk.
- Other mechanisms?
  1. Direct effects on osteoblasts and osteoclasts.
  2. Modulation of autonomic control of bone (low PSNS associated with impaired gastric motility)
  3. Modulation of sensory neuropeptides release.

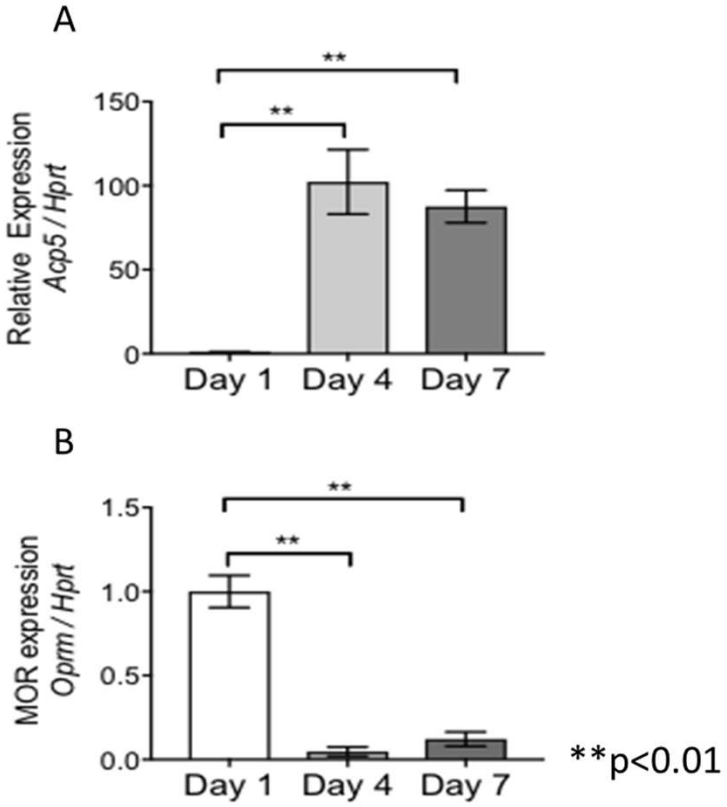
(Perez-Castrillon, Neuroendocrinology, 2000; Vestergaard et al., Journal of Internal Medicine, 2006; Fountas et al., European Journal of Endocrinology, 2018)

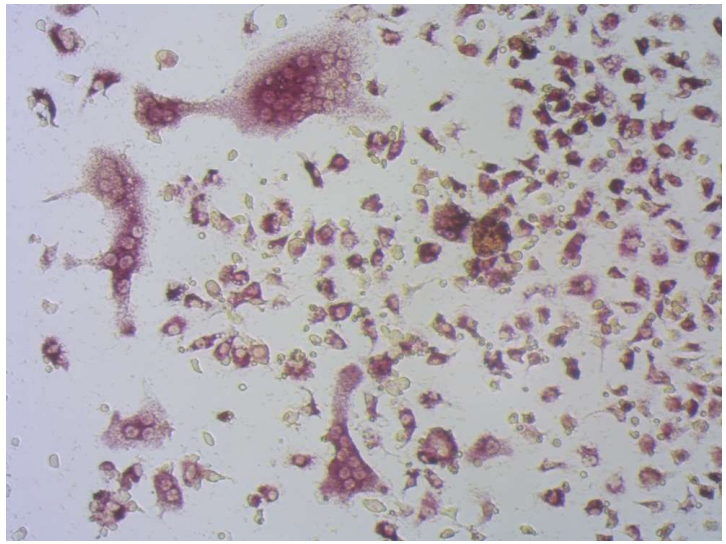
Opioid receptors mediate analgesic effects

- **Mu (μ) opioid receptor (MOR)**
  - **analgesia**
  - sedation
  - respiratory depression
  - bradycardia
  - nausea and vomiting (reduction in gastric motility)
- Delta (δ) opioid receptor (DOR)
- Kappa (κ) opioid receptor (KOR)

(Pathan and Williams, British Journal of Pain, 2012)

Primary osteoclasts express MOR, but osteoblasts did not express it in our hands

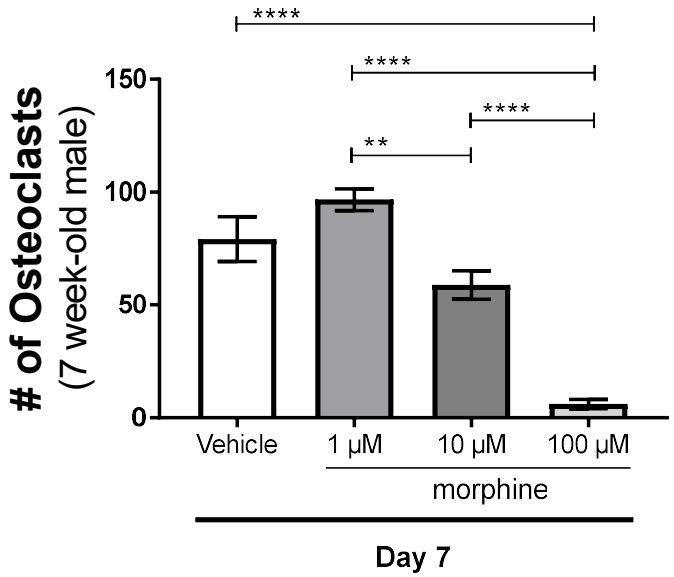


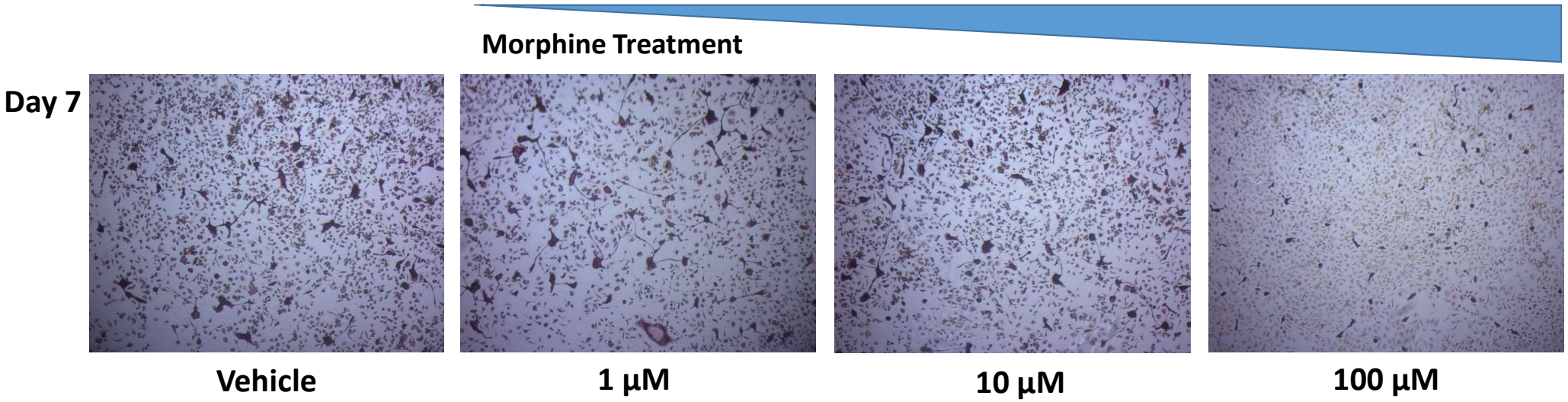


High dose morphine suppresses osteoclast differentiation, but lower doses may increase osteoclast numbers

- Similar results with DAMGO

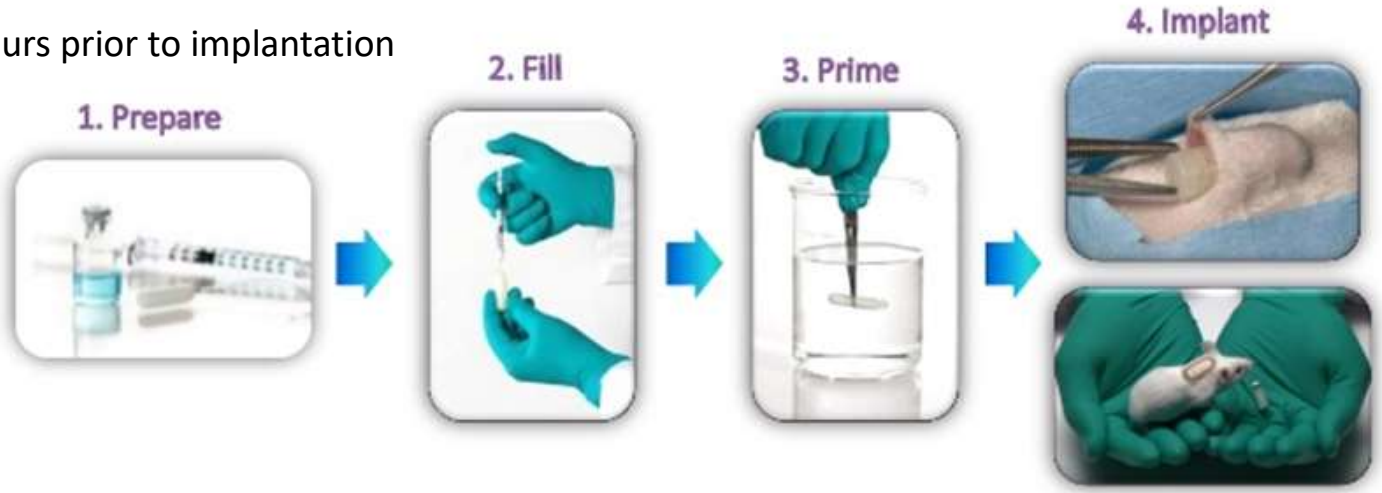
([D-Ala^2, N-Me-Phe^4, Gly^5-ol]-Enkephalin acetate salt)



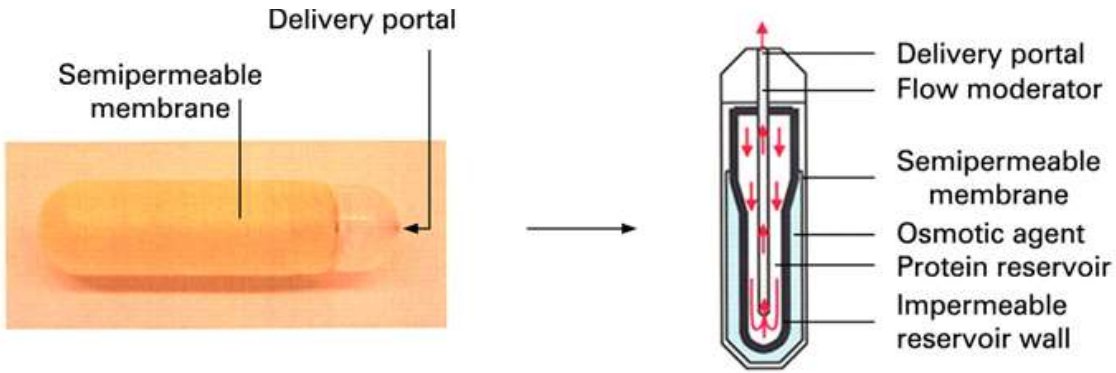


Model of opioid-induced bone loss

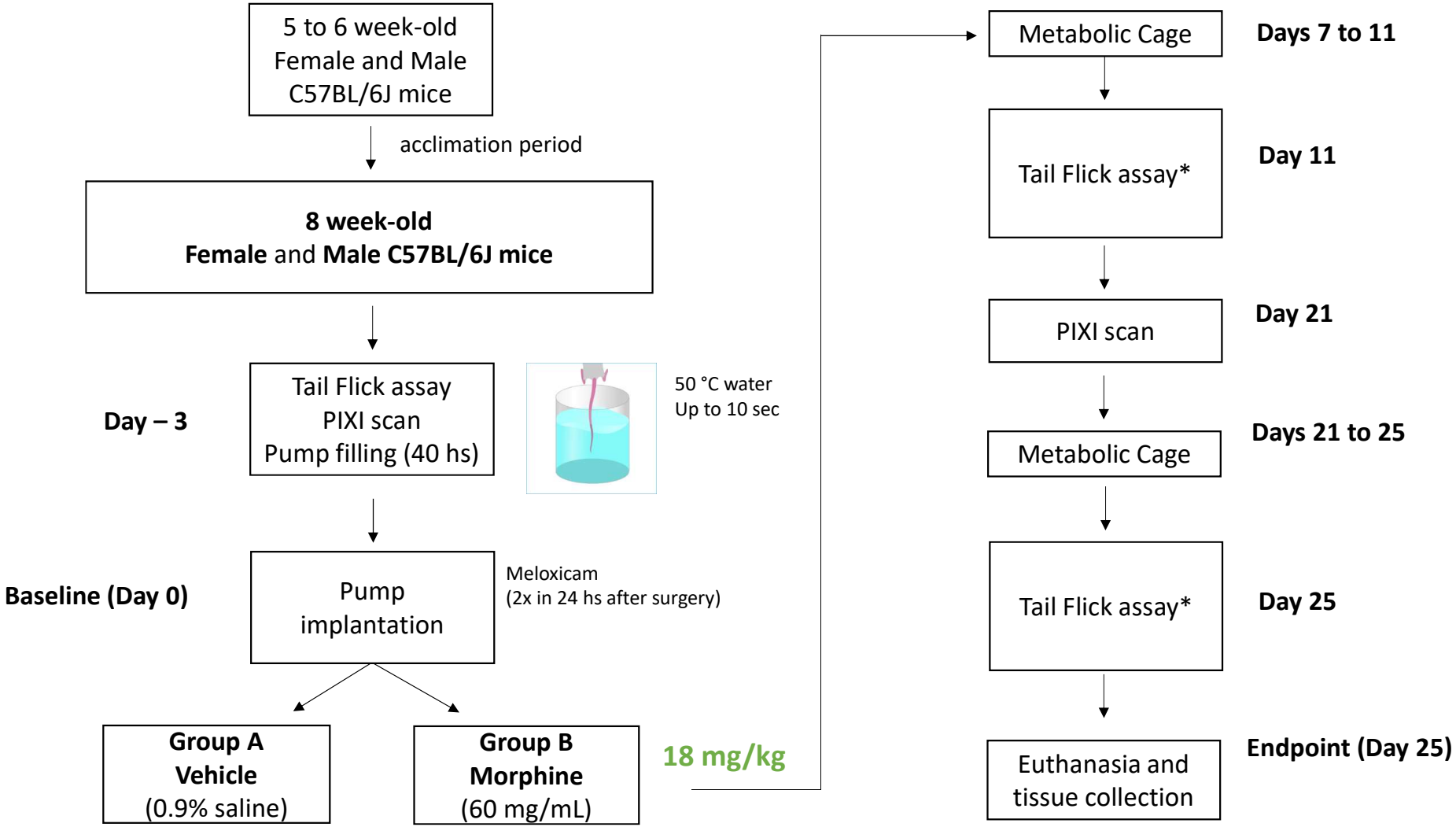
40 hours prior to implantation



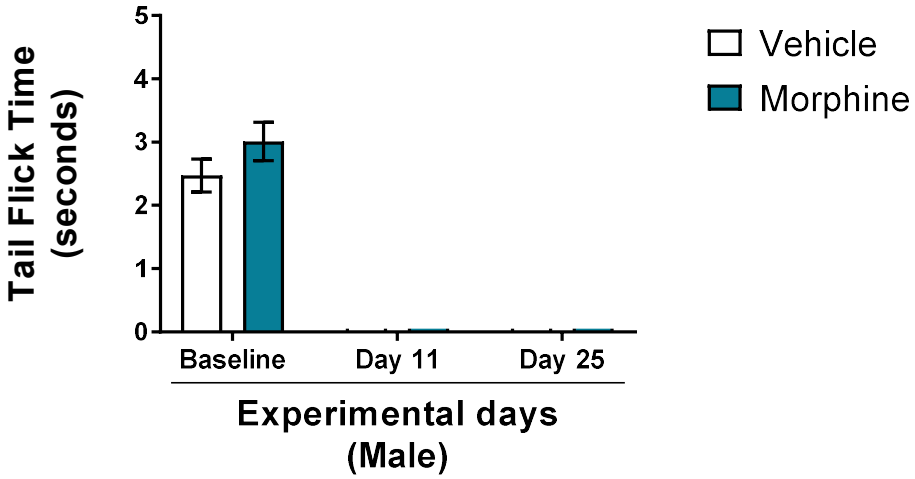
Delivery rate: 0.25 µl/hr
Capacity: 220 µl
Final dose: 18 mg/kg/day

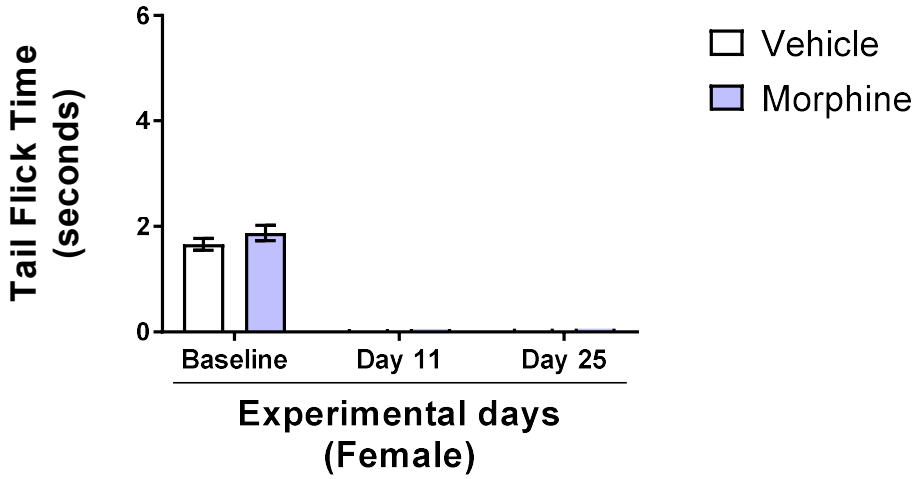


Experiment #1 – Establish a model of morphine-induced bone loss.

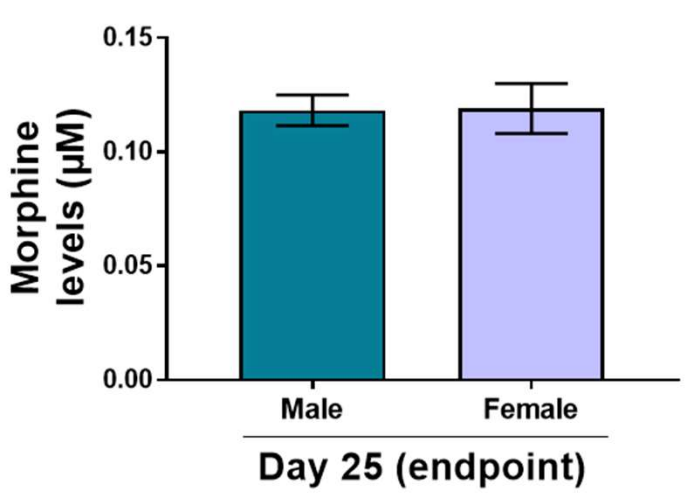


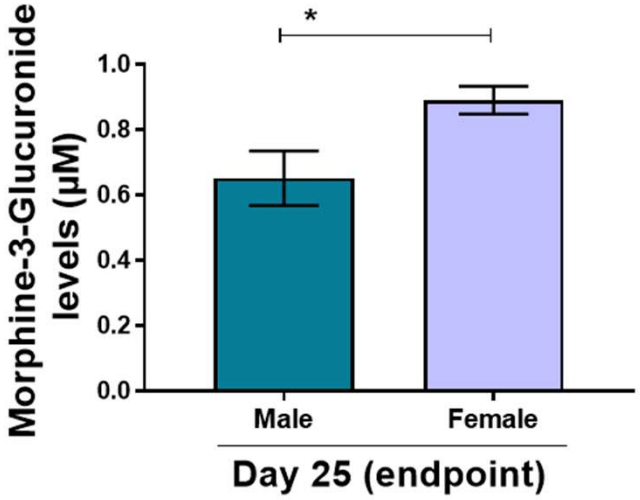
Tail flick assay indicates morphine-induced analgesia may be reduced by endpoint



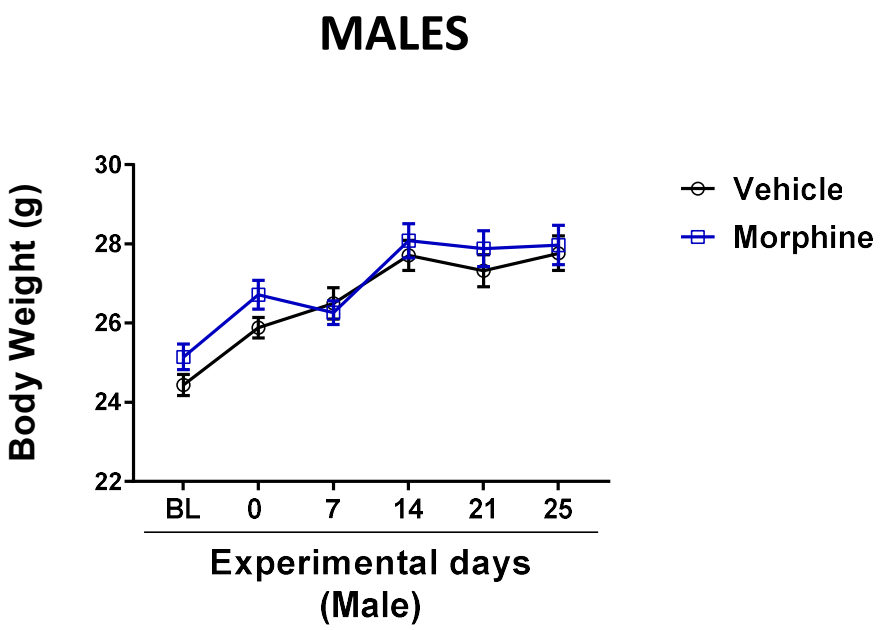


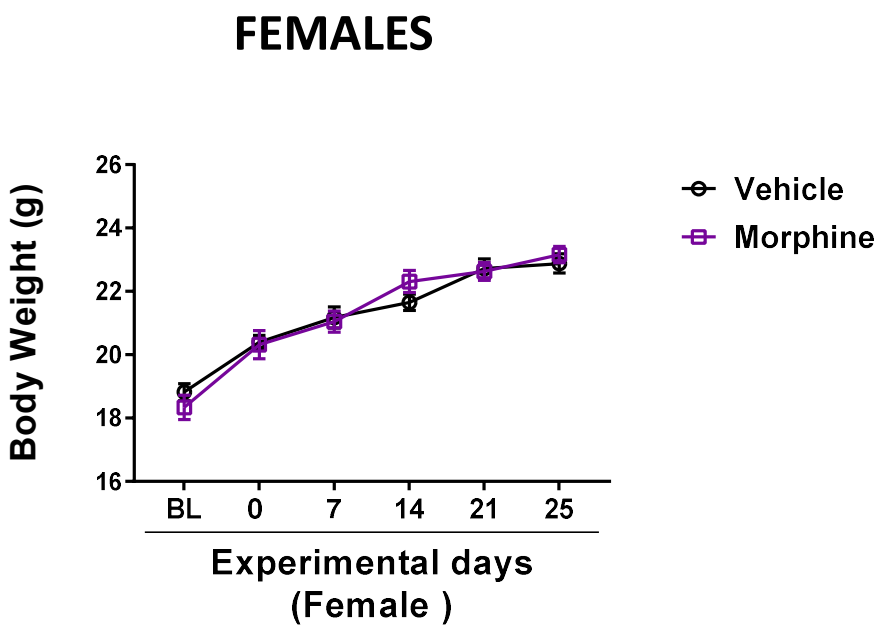
Morphine and metabolite still detectable in serum at the end of the study



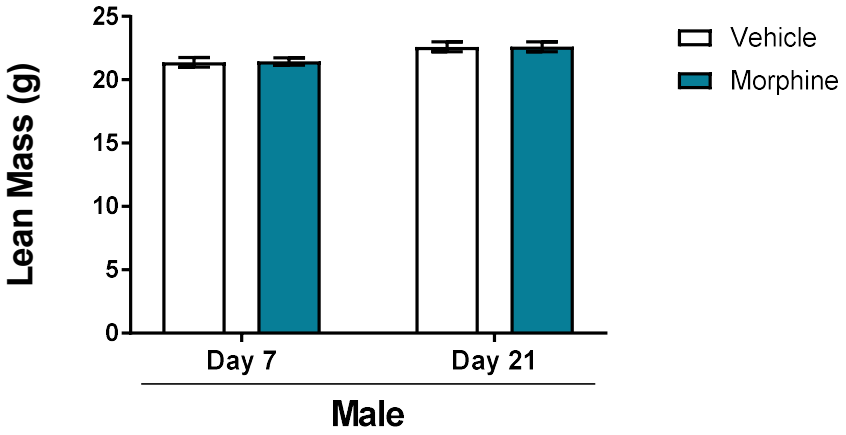


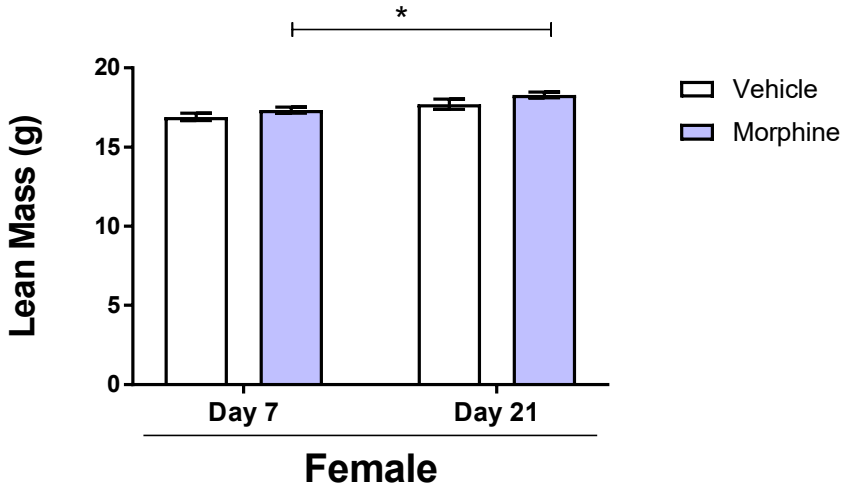
Body weight was not affected by morphine treatment

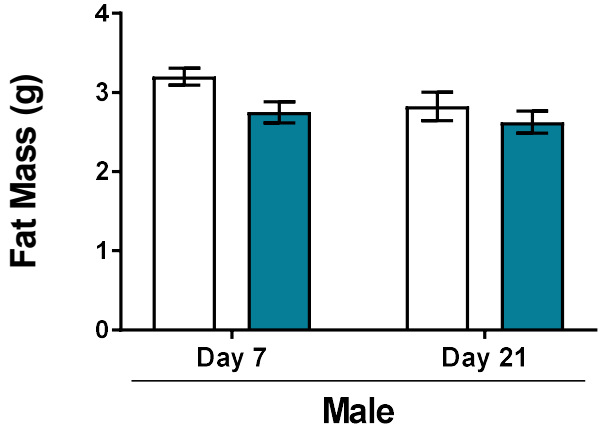


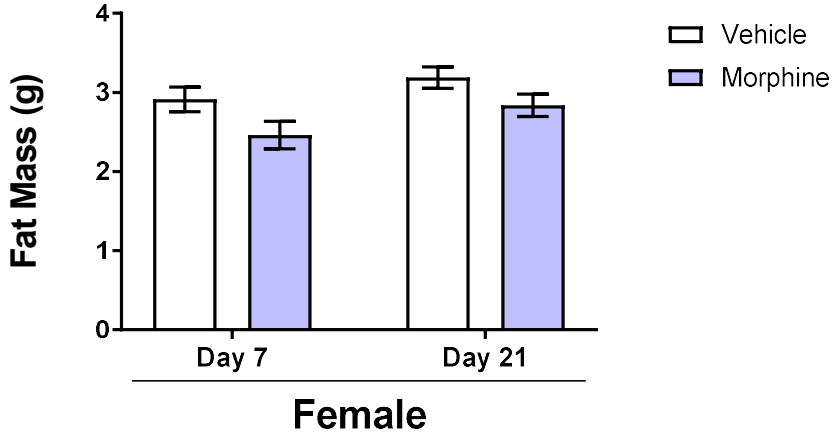


Subtle changes in body composition during the study

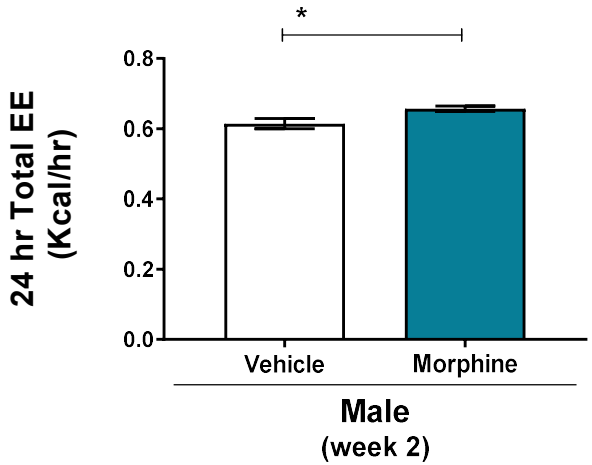






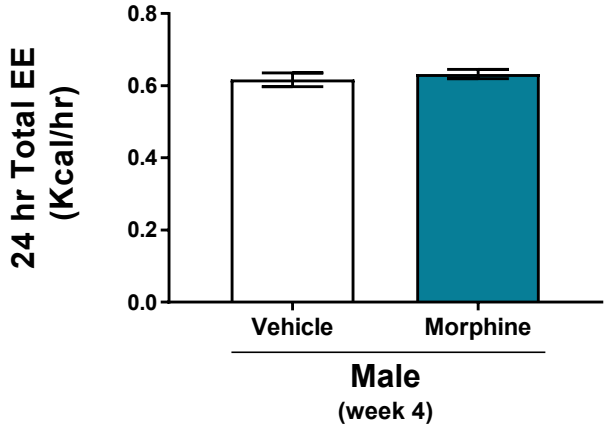


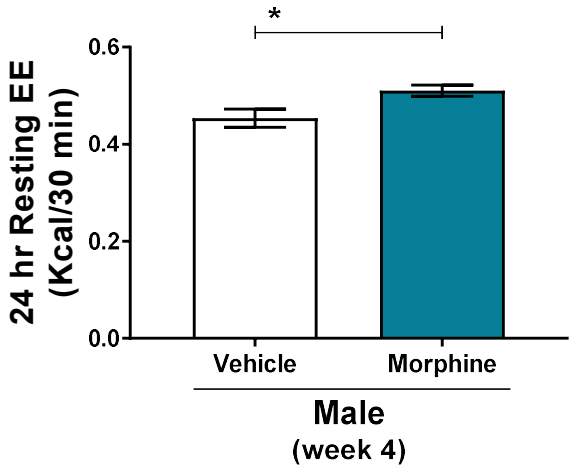
Morphine induced increase in Energy Expenditure (EE)



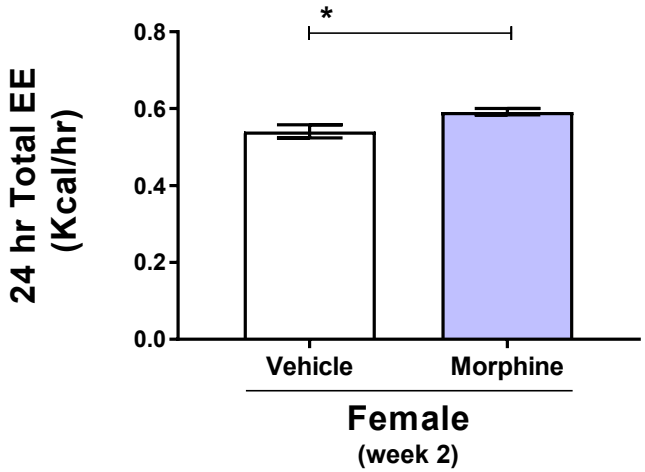
Morphine-treated Males:

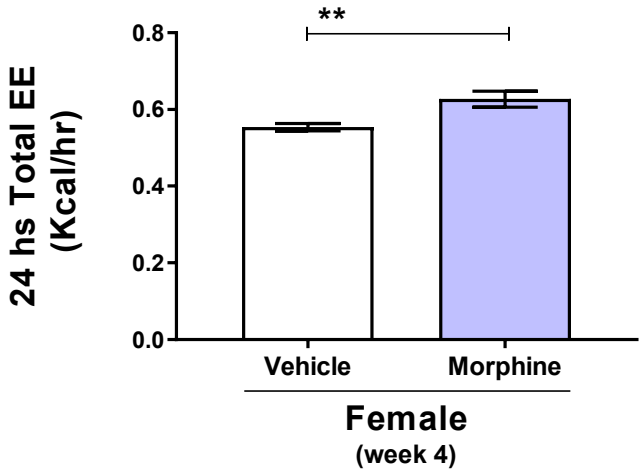
↑ **Resting EE** throughout the study





Morphine induced increase in Energy Expenditure (EE)

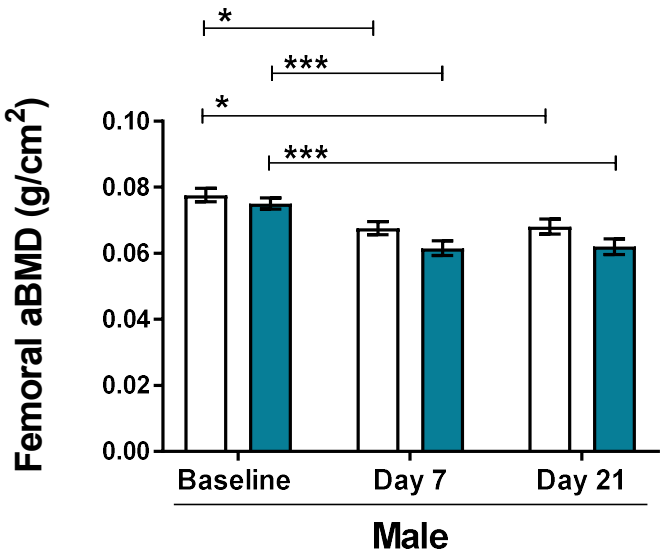


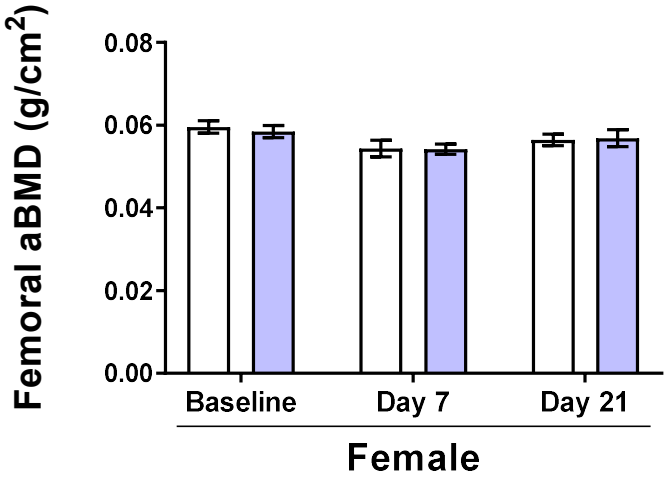


Morphine-treated Females:

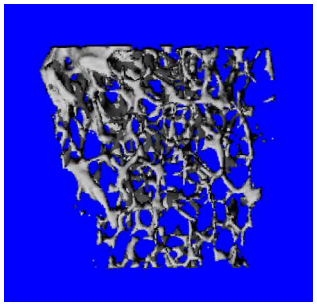
↑ **Total EE** throughout the study

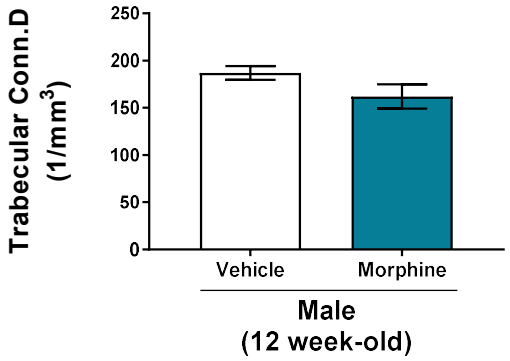
DXA results suggest bone loss in males but not females

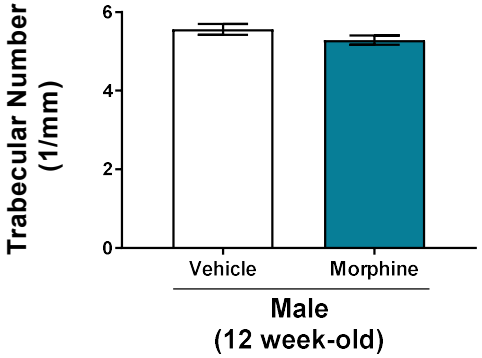


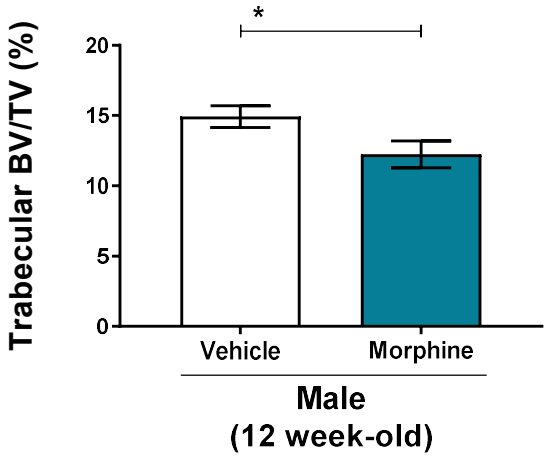


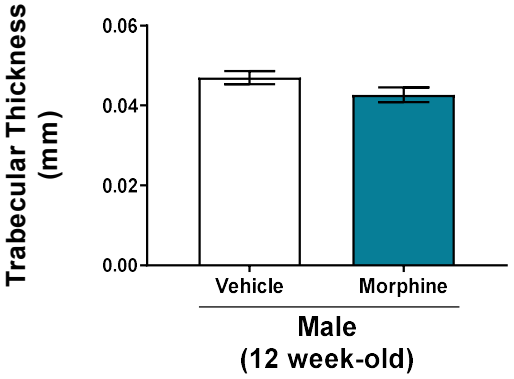
Trabecular bone volume was reduced in Male morphine-treated mice (µCT), but not females

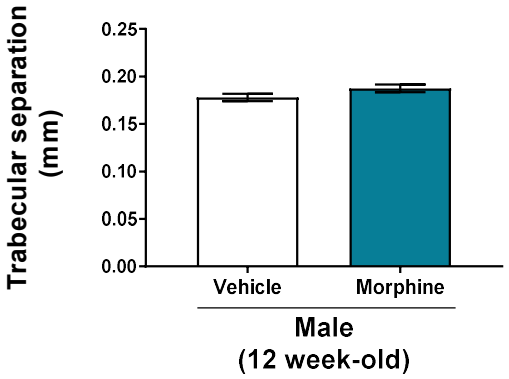




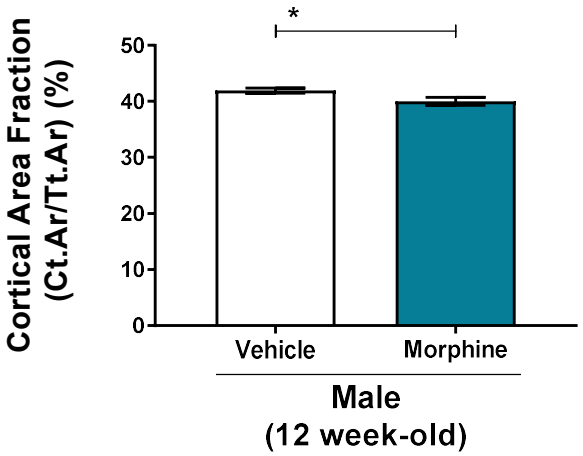


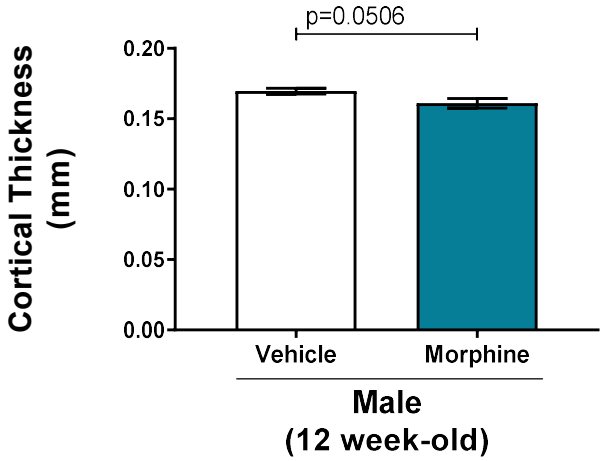


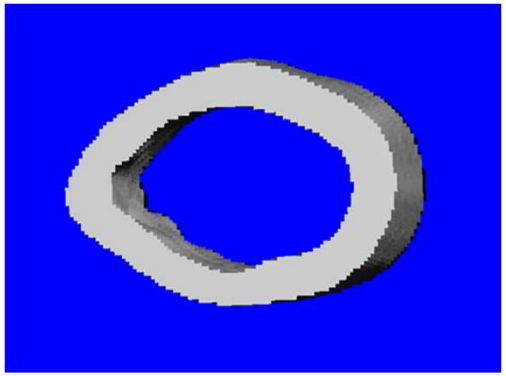


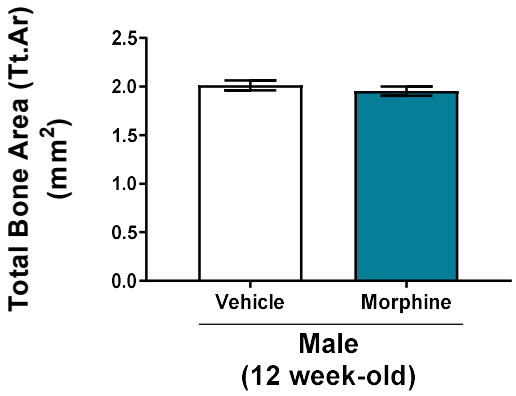


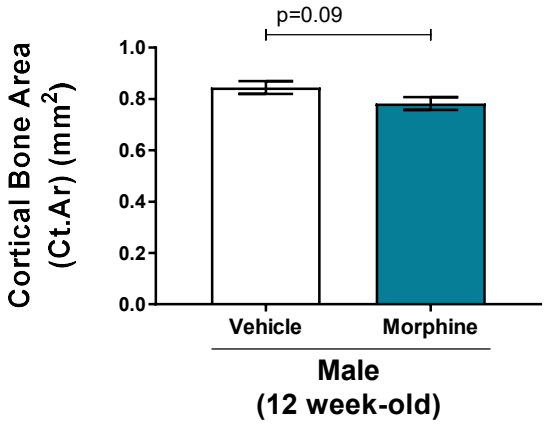
Male, but not female morphine-treated mice exhibited impaired cortical expansion

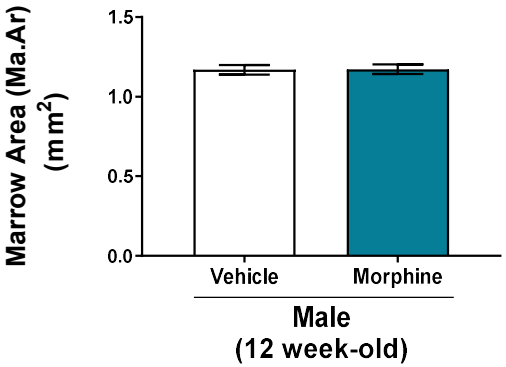










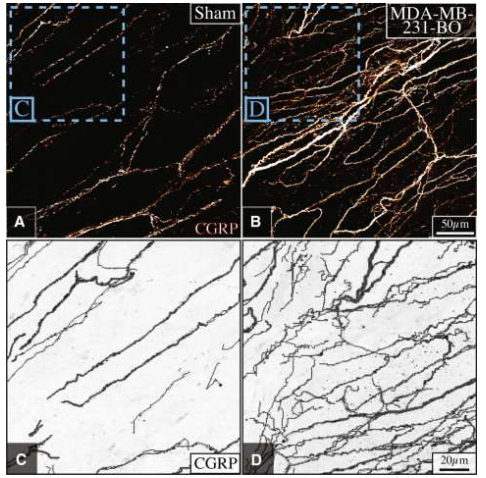


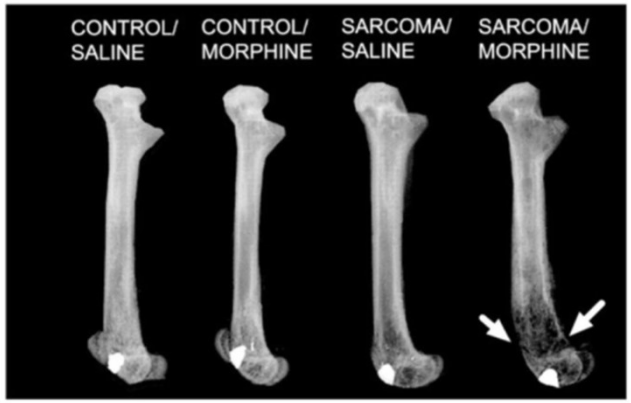
Summary

- Morphine reduced osteoclast differentiation *in vitro*.
- Morphine did not significantly alter body composition *in vivo*.
- Male, but not female, mice exhibit trabecular and cortical bone loss from 25-day morphine treatment, despite equivalent drug exposure.
- Either indirect effects, or direct effects on osteoblasts are responsible for morphine-induced bone loss.

Future directions

- Test whether there is a direct effect of morphine on osteoblasts.
- Test the cellular mechanism of morphine-induced bone loss *in vivo*.
- Perform limited omic studies to identify novel mediators of morphine-induced bone loss (miRNA).
- Test whether OVX females would lose bone with morphine.
- Test whether β-blocker would limit morphine-induced bone loss.
- Test how sensory neuropeptide release is modulated by morphine.





Acknowledgements

Co-PI:
Anyonya Guntur

Adriana Carvalho
Audrey Bergeron
Audrie Langlais
Kathy Nevola
Nick Banks
Roni Kunst
Annika Treyball
Hina Hashmi

Funding Sources:
U54GM115516
P20GM12130
K01AR067858
MMCRI Institutional Funds

NNE-CTR:
Pilot Projects Program
Clinical Research Design, Epidemiology and Biostatistics Core
Professional Development Core
Translational Research Technologies Core
Rural Health Research and Delivery Core

MMCRI Core facilities:
Animal Facility
Molecular Phenotyping Core
Physiology Core
Histology and Histomorphometry Core
Small Animal Imaging Core

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Rebecca Emery, Dartmouth Institute
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Tracking and Evaluation Core (TEC)

Brenda Joly PhD, (USM) Core Lead
Erika Ziller PhD, (USM) Co-Lead

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Overview

NORTHERN NEW ENGLAND
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Our Data

- Registration
- Needs assessment
- Service utilization
- Billing data
- Interviews
- Surveys
- Administrative records
- Core-specific data

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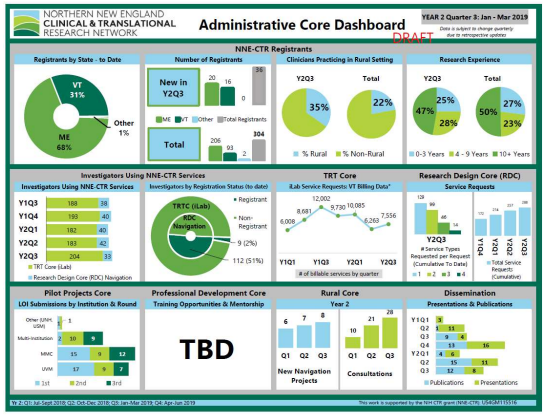
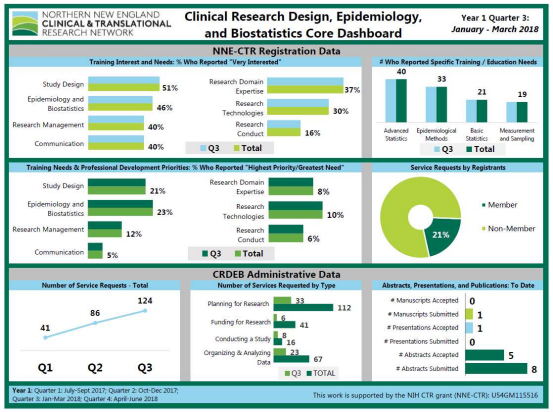
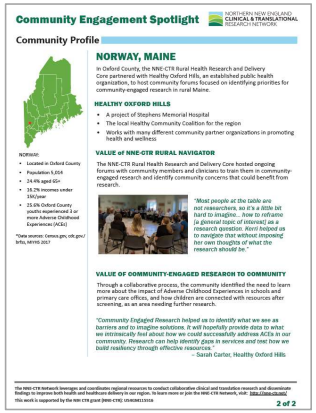
How Do We Share the Data?





Research skills and experience	Research specialty	NIH investigator status	Priority training & professional development needs						
			Study design	Epidemiology and biostatistics	Research conduct	Research technologies	Research management	Research domain expertise	Commun-ication
Expert	Public Health	New Investigator			X		X		
Expert	Basic biomedical research					X			
Beginner	Public Health	New Investigator	X	X			X		X
Intermediate	Behavioral	Early Stage Investigator	X	X	X	X	X	X	X
Beginner	Behavioral	New Investigator	X	X	X	X	X	X	X



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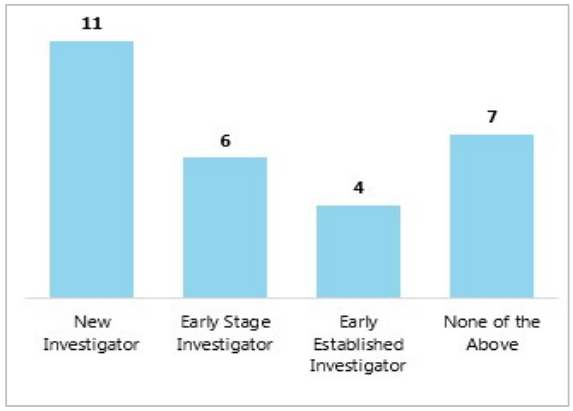
Reflections

A Few Successes

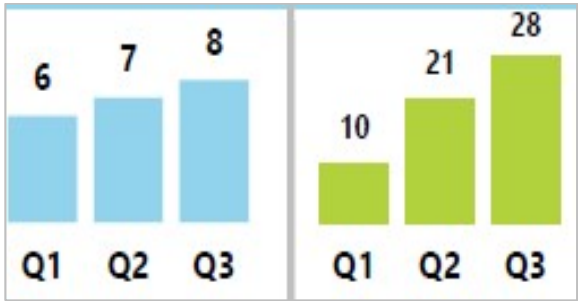
- **Pilot Projects**
  - Describe applicants
  - Follow group
  - Link to registration

- **Rural Health Core**
  - Describe service recipients
  - Describe assistance
  - Measure reach and spread

Researcher Status: Round 3 (n=28)



Rural Core Navigation Services



New Navigation Projects

Consultations

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Reflections

Registration and Needs Assessment

- **Our only mechanism to describe investigators and training needs**
- **Challenges and opportunities:**
  - Limited communication and outreach
  - Benchmarks are unclear
  - The process is voluntary (except for pilot applicants)
- **Moving forward:**
  - Is this processed valued?
  - Do we want to boost registration?
  - Ho do we incentivize registration?
  - Are there additional information needs?
  - Should we keep the needs assessment?

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Reflections

Utilization of Core Services

- **We use a flexible approach to assess utilization**
- **Challenges and opportunities:**
  - Differences across sites in data collection processes
  - Capturing NNE-CTR “users”
  - Collecting the right data
- **Moving forward:**
  - Do we feel comfortable with our progress?
  - Will we have what we need for the reapplication?
  - What else can we do to showcase utilization rates?

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Reflections

Investigator Satisfaction with Services

- **We use survey data and interviews to assess satisfaction**
- **Challenges and opportunities:**
  - Standardized items exist
  - Without clear NNE-CTR “user” database, efforts are core-specific
  - Progress is slow
- **Moving forward:**
  - Is this a priority for year three?
  - Do we want to assess satisfaction with everyone?

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Reflections

Other Metrics

- **Our efforts to assess other key metrics are underway including:**
  - Collaboration
  - Research capacity and productivity
  - Grants, presentations, and publications
  - Community engagement
- **Challenges and opportunities:**
  - Adding additional burden to each core
- **Moving forward:**
  - What the best approach for decision-making?

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Reflections

Next Steps

- **Talk -** remaining evaluation needs, goals and benchmarks
- **Decide -** priorities, opportunities and potential areas holding us back
- **Plan -** data collection efforts
- **Collect -** commit to standardization
- **Report -** share findings
- **Review -** reflect on our efforts

Northern New England Palliative Care TeleConsult Research Laboratory

(MPI: Paul Han & Bob Gramling)

Northern New England CTR Annual Meeting
University of Vermont
June 7, 2019

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Bob Gramling, M.D., D.Sc.
Holly & Bob Miller Chair of Palliative Medicine
Professor, Department of Family Medicine
University of Vermont

I have no conflicts of interest to disclose.

PALLIATIVE CARE

“patient and family centered care that improves quality of life by anticipating, preventing and treating suffering…”

National Consensus Definition

PALLIATIVE CARE

"patient and family centered care that improves quality of life by anticipating, preventing and treating suffering…"

Triple Aim in Serious Illness

Kavalieratos et al, *JAMA* 2016 (43 RCT, 12,731 people)

Hoerger et al, *Ann Behav Med* 2019 (9 outpatient RCT, 2,029 people)

May et al, *JAMA Internal Med*, 2018 (6 Cohort, 133,118 people)

Context

PALLIATIVE CARE

"patient and family centered care that improves quality of life by anticipating, preventing and treating suffering…"

Triple Aim in Serious Illness

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Demand >> Access

Schenker Y & Arnold R, *JAMA Oncology* 2017

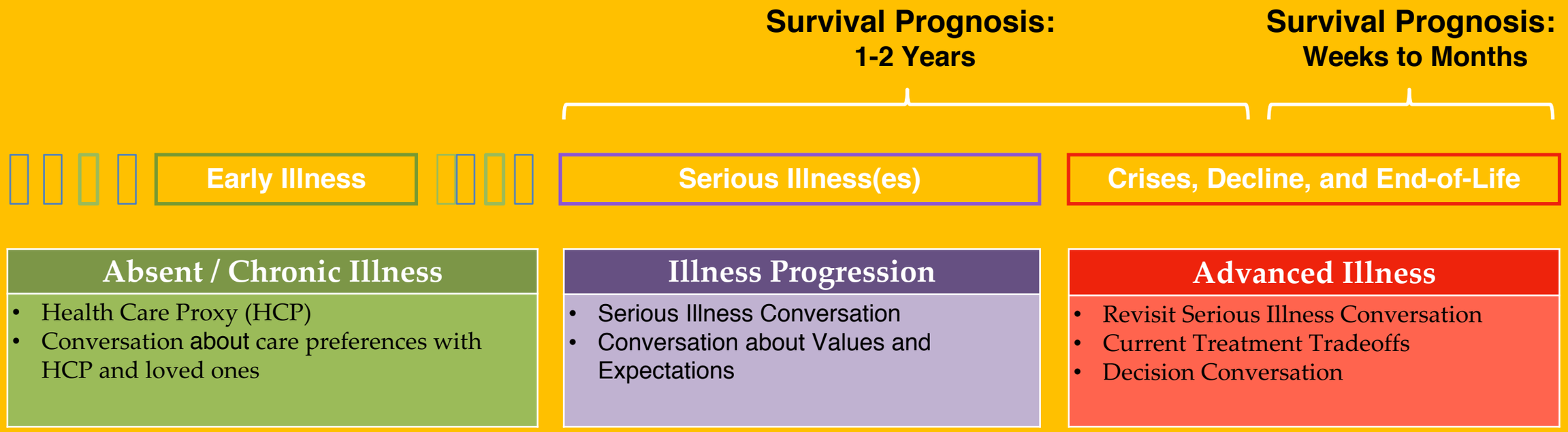
Kamal AH et al, *Am Journal Medicine* 2017

Lupu D et al, *J Pain Symptom Management* 2018

Abernethy & Quill, *NEJM* 2013

Context

Scientific Context: Conversations



Advance Care Planning = Planning in Advance of Serious Illness

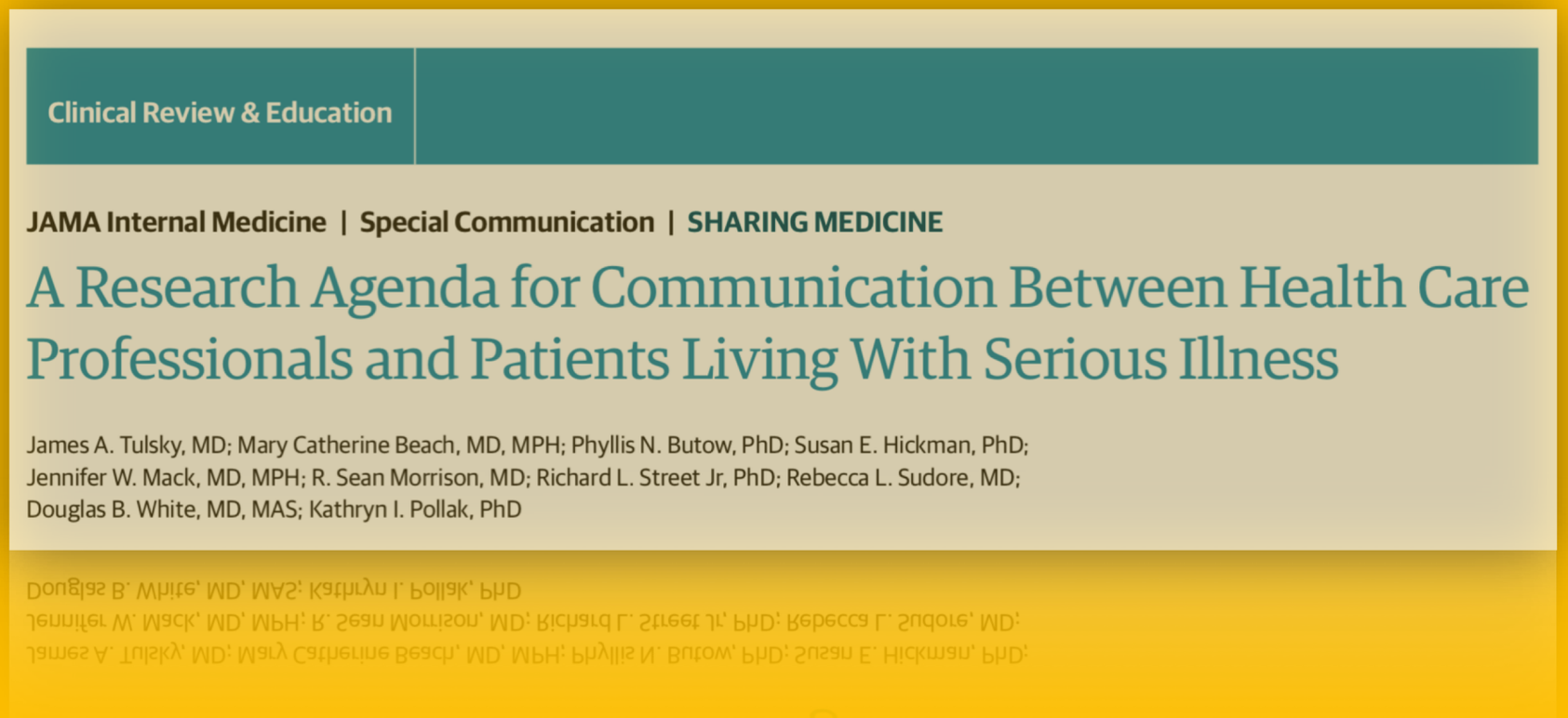
Serious Illness Conversation(s) = Planning in the context of progression of serious illness, may or may not include clinical decisions, revisit when needed

Decisions Conversation(s) = Revisit serious illness conversation and make treatment decisions in context of clinical progression / crisis / poor prognosis

borrowed with permission from S. Block, Ariadne Labs,
Harvard School of Public Health

Scientific Context: Measurement

"...dependence on human manual coding makes them slow and cumbersome and not easily disseminated. For such methods to provide feedback to clinicians or reviewers on a mass scale, high-quality **automated coding will be required**."



AIM ONE

To assess the feasibility and acceptability of NNE Palliative Care TeleConsult Research Laboratory among seriously ill people of rural Vermont (advanced cancer) and Maine (Stage D heart failure)

AIM TWO

To develop our capacity for automating measurement of conceptually-important conversation features for the TeleConsult medium

AIMS

ELIGIBILITY

Adults being cared for by non-hospice home health nursing and are diagnosed with either Stage 3 or 4 solid tumor (Vermont, n=10) or Stage D heart failure (Maine, n=10)

INTERVENTION

-TeleConsultation with specialty palliative care physician or APRN

-Facilitated in home by home health nurse

OUTCOMES

Reach: Potential eligible / approached / enrolled / completed

Barriers: Re-scheduling / “no shows” / technical malfunctions

Acceptability: Satisfaction with TeleHealth (*TeSS*)

Patient / Loved One /Clinician Experience: PCCRI *Heard & Understood*

Qualitative Interviews: Unstructured

AIM ONE Feasibility & Acceptability

“Clinicians engaging in conversations about serious illness have 3 primary tasks—establishing connection; eliciting values, goals, and preferences; and delivering information.”

(Tulsky et al, *JAMA Internal Medicine* 2017)

AIM TWO Feature Recognition

“Clinicians engaging in conversations about serious illness have 3 primary tasks—establishing connection; eliciting values, goals, and preferences; and delivering information.”

Tulsky et al, *JAMA Internal Medicine* 2017

AIM TWO Feature Recognition

Words (transcripts)

Sounds (acoustic signal)

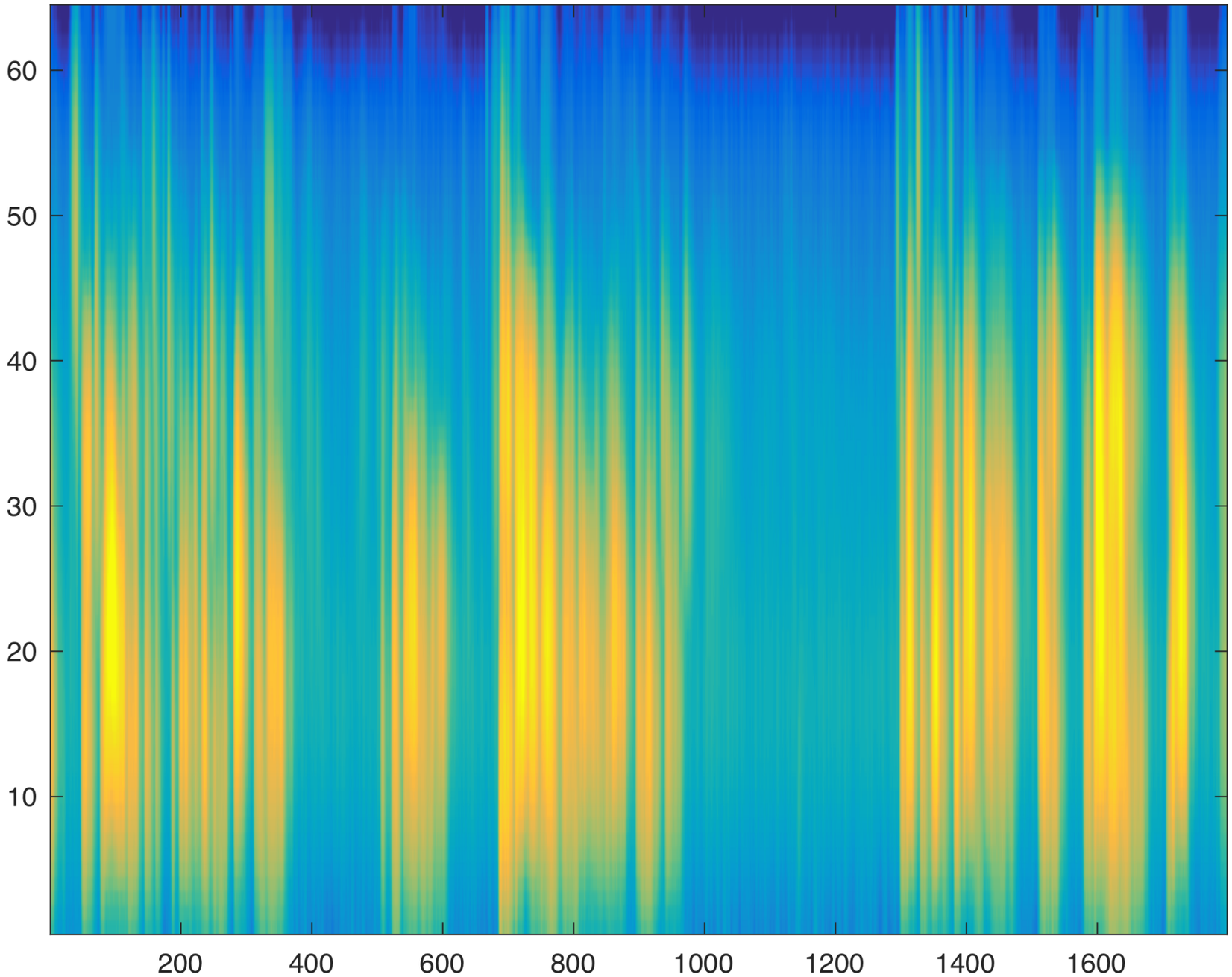
Images (video signal)

AIM TWO Independent Data

Connectional Silence

Emotional Synchrony

AIM TWO Dependent Data

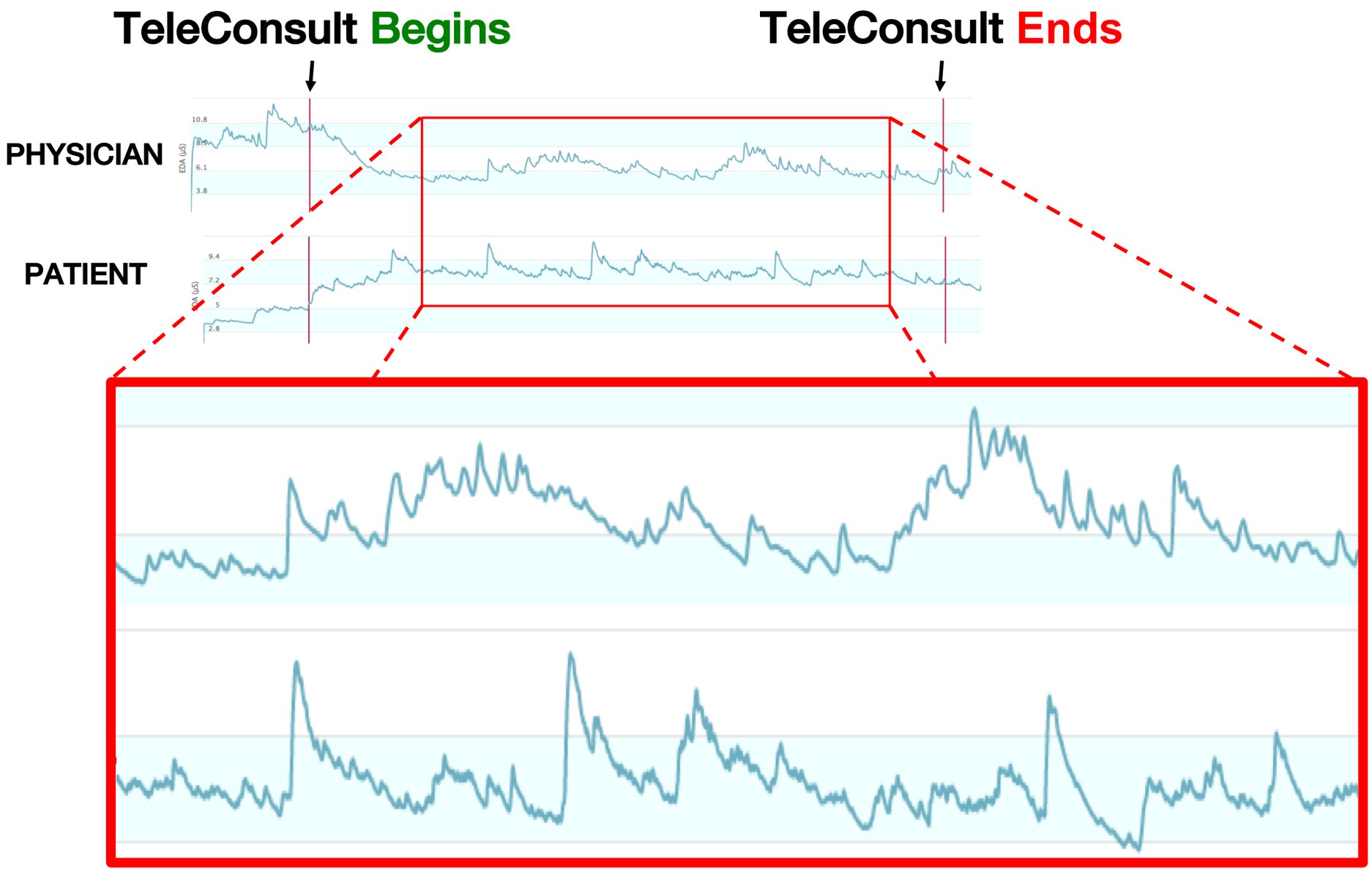


Manukyan et al, *Journal of Palliative Medicine*, 2018

Durieux et al, *Journal of Palliative Medicine*, 2018

Conversational Pauses

Electrodermal Activity (μS)



Emotional Synchrony

This [telehealth] is so important…

Patient

Palliative Care via telemedicine is a really beneficial resource, especially for a patient with chronic illnesses who needs PC support and feels lost in the system. The biggest issue with our population is that people have difficulty leaving their homes and so this is valuable.

Home Health Nurse

Having the nurse present for the visit was very helpful. I did feel there was less room for 'small talk' in the early stage of the conversation…. The sign-off process felt awkward.

Palliative Care Specialist Physician

Participant Comments

My sincere gratitude to

the **patients, families, and palliative care clinicians** who make this work both meaningful and possible

my **amazing teammates** who make us all better

the **NNE CTRN** for funding this work

NNE PCTC Laboratory Team
Eric Anderson | Ava Daruvala | Maggie Eppstein
Liz Gajary-Coots | Bob Gramling | Paul Han
Rebecca Hutchinson | Liam John | Donna Rizzo
Kathy Walsh | John Wax

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(UU54 GM115516; MPI: Gary Stein PhD & Cliff Rosen MD)

with GRATITUDE

The University of Vermont
LARNER COLLEGE OF MEDICINE

Maine Medical Center
MaineHealth

Hospital Utilization for Opioid Overdose:

A Community Engaged Multidisciplinary Approach to Measure the Impact of Policy Change & Inform Interventions

Lead Investigator:

Valerie Harder,
PhD, MHS

Co-Investigators:

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DrPH, MD, MPH
Maine Medical Ctr

Timothy Plante,
MD, MHS

Andrea Villanti,
PhD, MPH

June 7, 2019

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Opioid Prescribing Policies

July 1, 2017: Prescribing restrictions # of pills / dose

- Moderate pain: up to 120 MME total
- Severe pain: up to 160 MME total
- Extreme pain (documented): up to 350 MME total

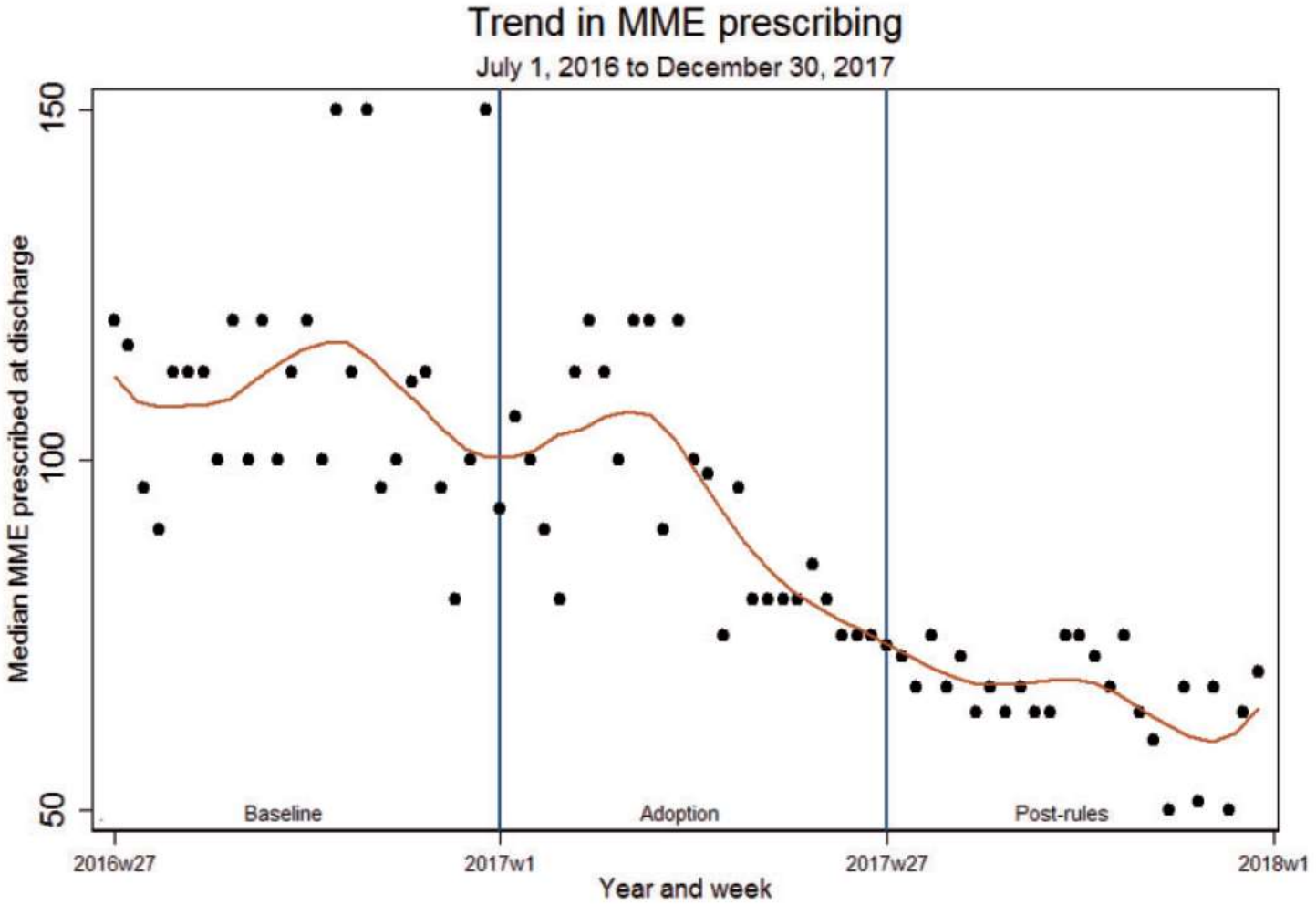
Prescription Monitoring Program check required

July 29, 2016: 100 morphine milligram equivalent (MME) prescribing restriction

January 1, 2017: Prescription Monitoring Program check required

July 1, 2017: All prescriptions must be electronic

Impact of Policy Interventions at UVMMC on Postoperative Opioid Prescribing



Source: MacLean, Fujii, et al. 2018. Pain Medicine

➢**30+ meetings with community partners across Maine and Vermont**

Objective

Quantify the impact of opioid prescribing policies on opioid overdoses and related events to inform treatment interventions.

Specific Aims

1. Measure the impact of opioid prescribing policies on hospital utilization (Emergency Dept. and Inpatient) due to opioid overdose, adverse effects, & medical events

2. Identify patient-level clinical predictors of hospital utilization for opioid overdose and related medical events in relation to opioid prescribing policies

Original Hypotheses

Specific Aim 1: *Measure the impact of opioid prescribing policies on hospital utilization (ED and inpatient) due to opioid overdose, adverse effects, & medical events*

- Hypothesis 1a: Opioid-related hospital utilization rates will decrease after the implementation of prescribing policies.

- Hypothesis 1b: Changes in opioid-related hospital utilization rates will be moderated by type of opioid or opiate, age category, and geographic area.

Measure Specification

Measure Title:

Opioid Related Emergency Department & Hospitalization Visit Rate

Measure Description:

The rate (person-time) of visits to the emergency department (ED) or inpatient hospital with diagnoses for opioid overdose/poisoning, opioid-related adverse effects, or opioid-related medical events during the measurement period.

Population:

Patients 15 years and older

Overdose Rate =

Numerator: # of ED visits and hospitalizations for opioid overdose

Denominator: Person - Time

Opioid Overdose / Poisoning

OPIOID OVERDOSE/POISONING, ANY REASON	ICD-10-CM			
ANY OPIUM OVERDOSE	T40.0X1	T40.0X2	T40.0X3	T40.0X4
ANY HEROIN OVERDOSE	T40.1X1	T40.1X2	T40.1X3	T40.1X4
ANY OTHER OPIOID OVERDOSE	T40.2X1	T40.2X2	T40.2X3	T40.2X4
ANY METHADONE OVERDOSE	T40.3X1	T40.3X2	T40.3X3	T40.3X4
ANY SYNTHETIC NARCOTIC OVERDOSE	T40.4X1	T40.4X2	T40.4X3	T40.4X4
→ ANY UNSPECIFIED NARCOTIC OVERDOSE	T40.601	T40.602	T40.603	T40.604
ANY OTHER NARCOTICS OVERDOSE	T40.691	T40.692	T40.693	T40.694

LESSONS LEARNED:

- ED physicians often choose Any Unspecified Narcotic Overdose
  Therefore, it is difficult to separate heroin from opioid pills

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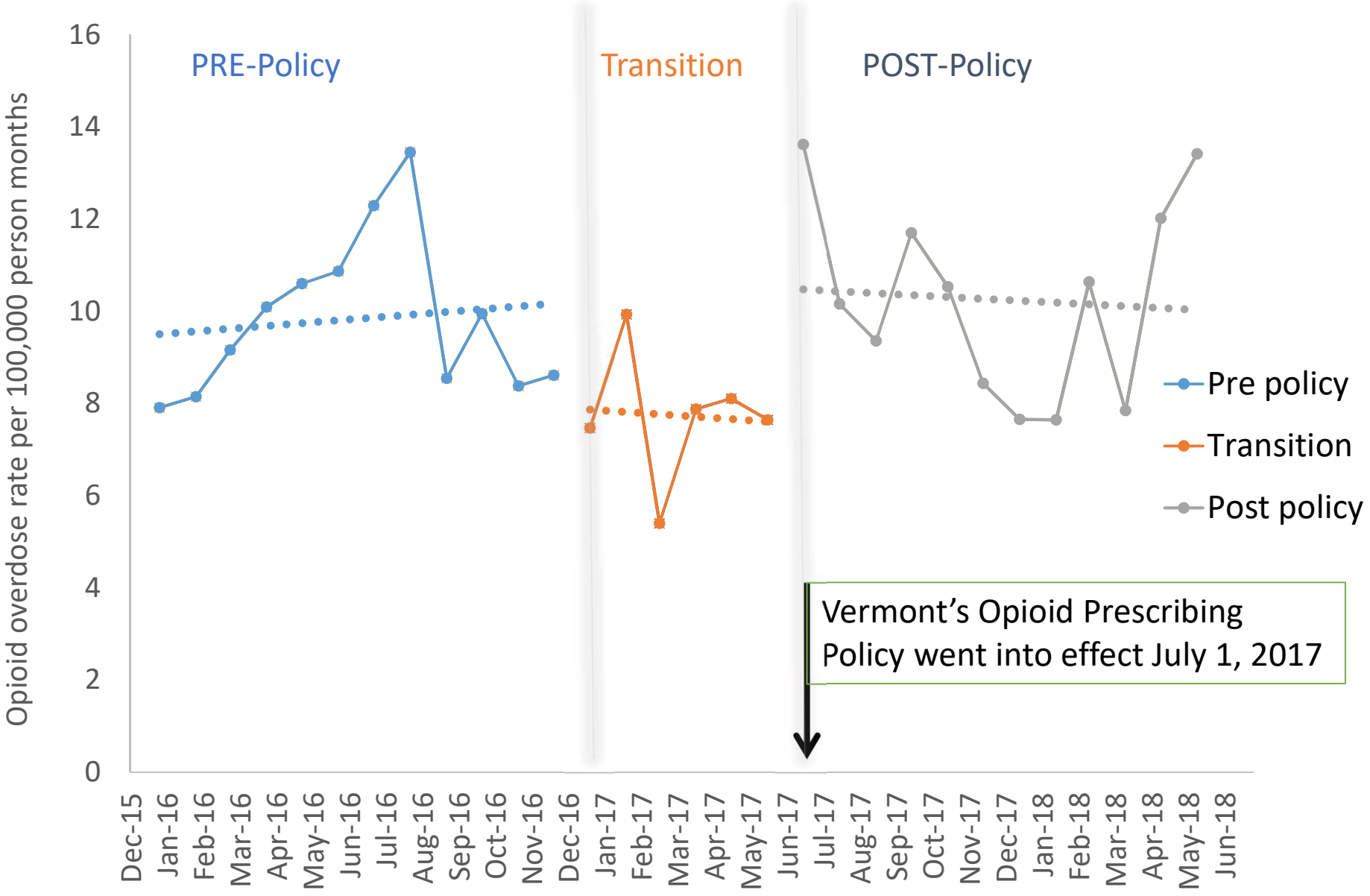
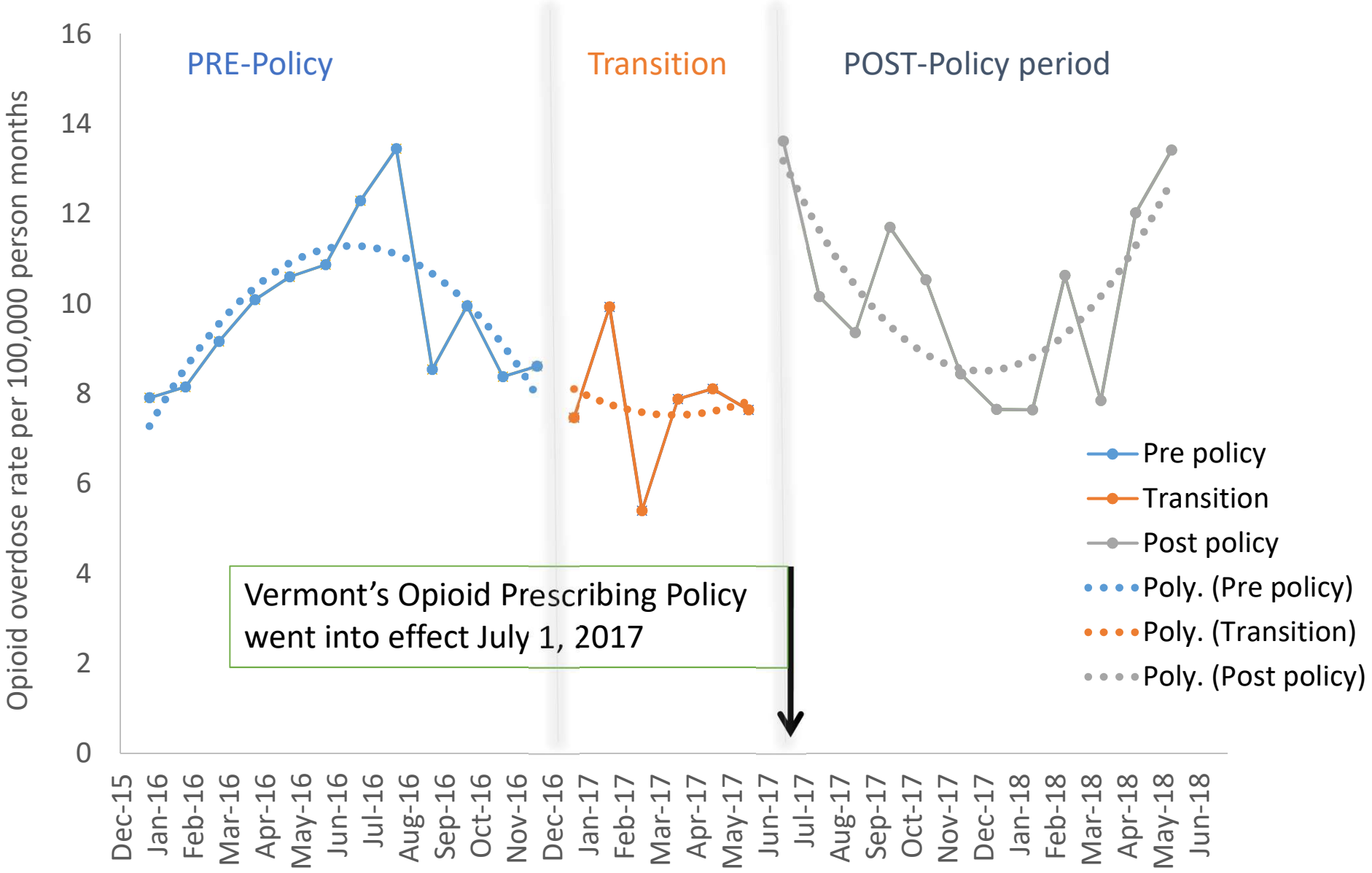
Opioid Overdose Rates



Opioid Overdose Rates



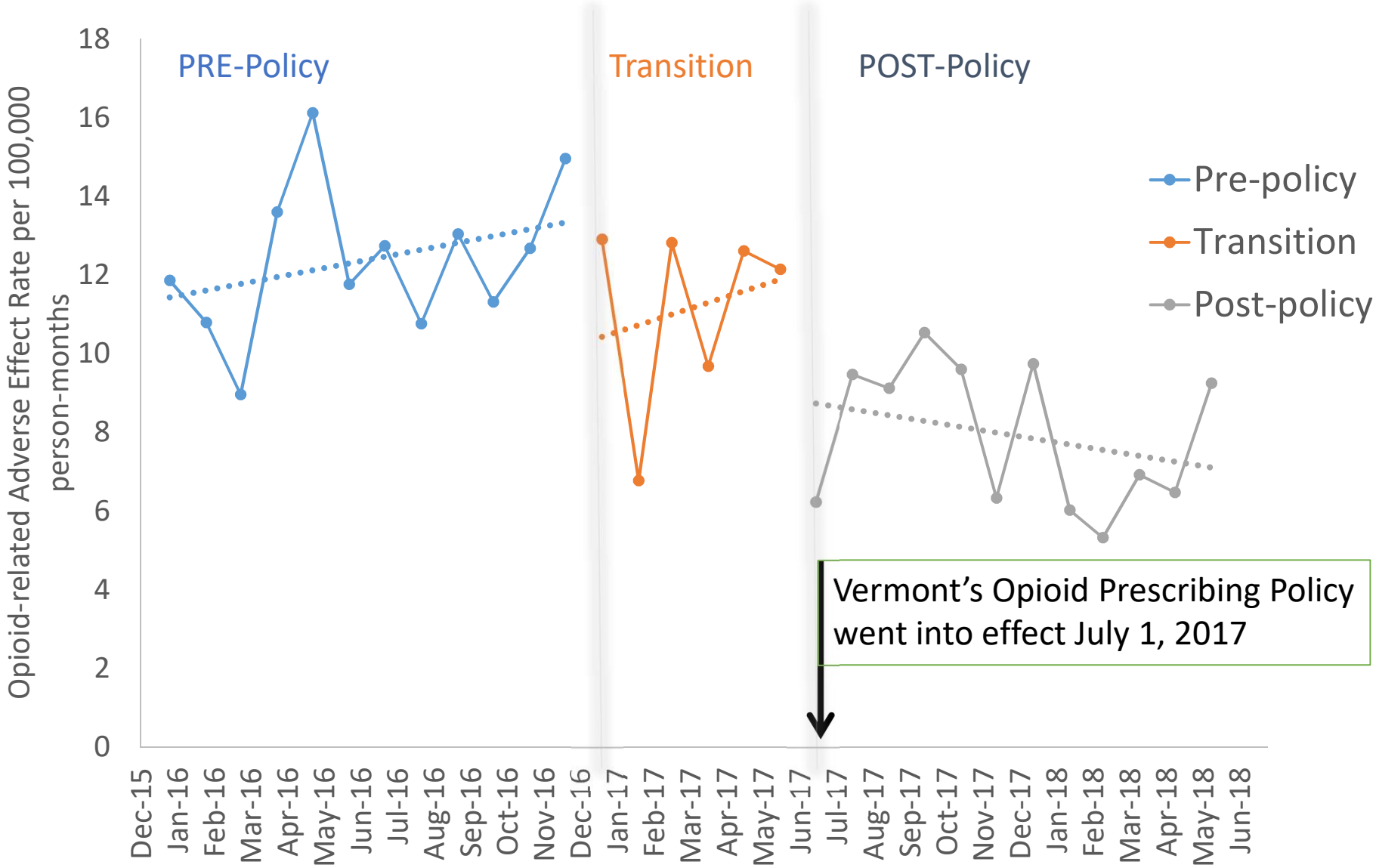
Opioid-Related Adverse Effects

ANY OPIOID ADVERSE EFFECT	ICD-10-CM
OPIUM ADVERSE EFFECT	T40.0X5
OTHER OPIOID ADVERSE EFFECT	T40.2X5
METHADONE ADVERSE EFFECT	T40.3X5
SYNTHETIC NARCORTICS ADVERSE EFFECT	T40.4X5
UNSPECIFIED NARCOTICS ADVERSE EFFECT	T40.605
OTHER NARCOTICS ADVERSE EFFECT	T40.695

Specific medical problems that are a result of opioid misuse

- Sedation, slow respiration, loss of consciousness, cardiac arrhythmia, altered mental status

Opioid-Related Adverse Effects

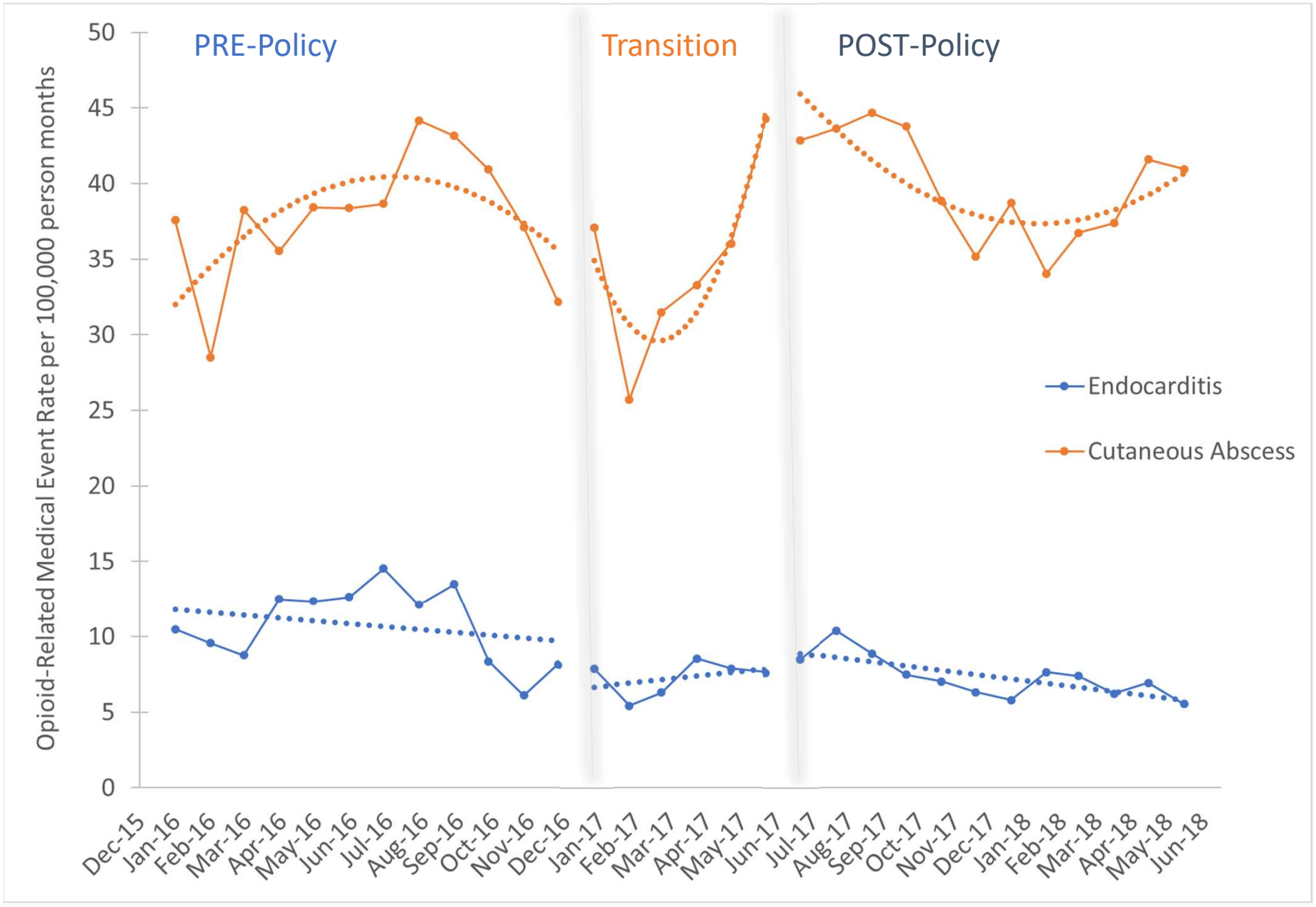


Opioid-Related Medical Events

Specific medical events that may be related to opioid misuse

ANY OTHER OPIOID-RELATED MEDICAL EVENTS
BACTERIAL INFECTION
GANGRENE
SEPTIC ARTHRITIS, ANY LOCATION
CELLULITIS OR LYMPHANGITIS, ANY LOCATIONS
ACUTE OR SUBACUTE OSTEOMYELITIS, ANY LOCATION
ENDOCARDITIS
EPIDURAL ABSCESS
ENDOPHTHALMITIS
CUTANEOUS ABSCESS
OTHER ABSCESS
HIV
HEPATITIS B
HEPATITIS C
LUNG DISEASES DUE TO EXTERNAL AGENTS
RESPIRATORY FAILURE

Medical Event Rates: Opioid related



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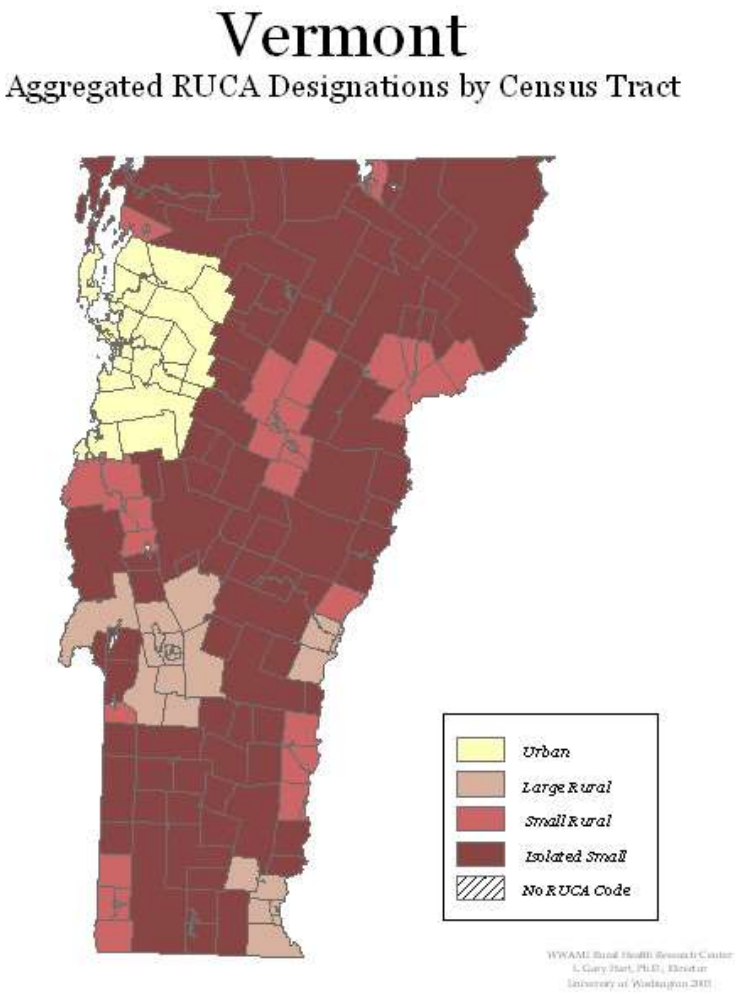
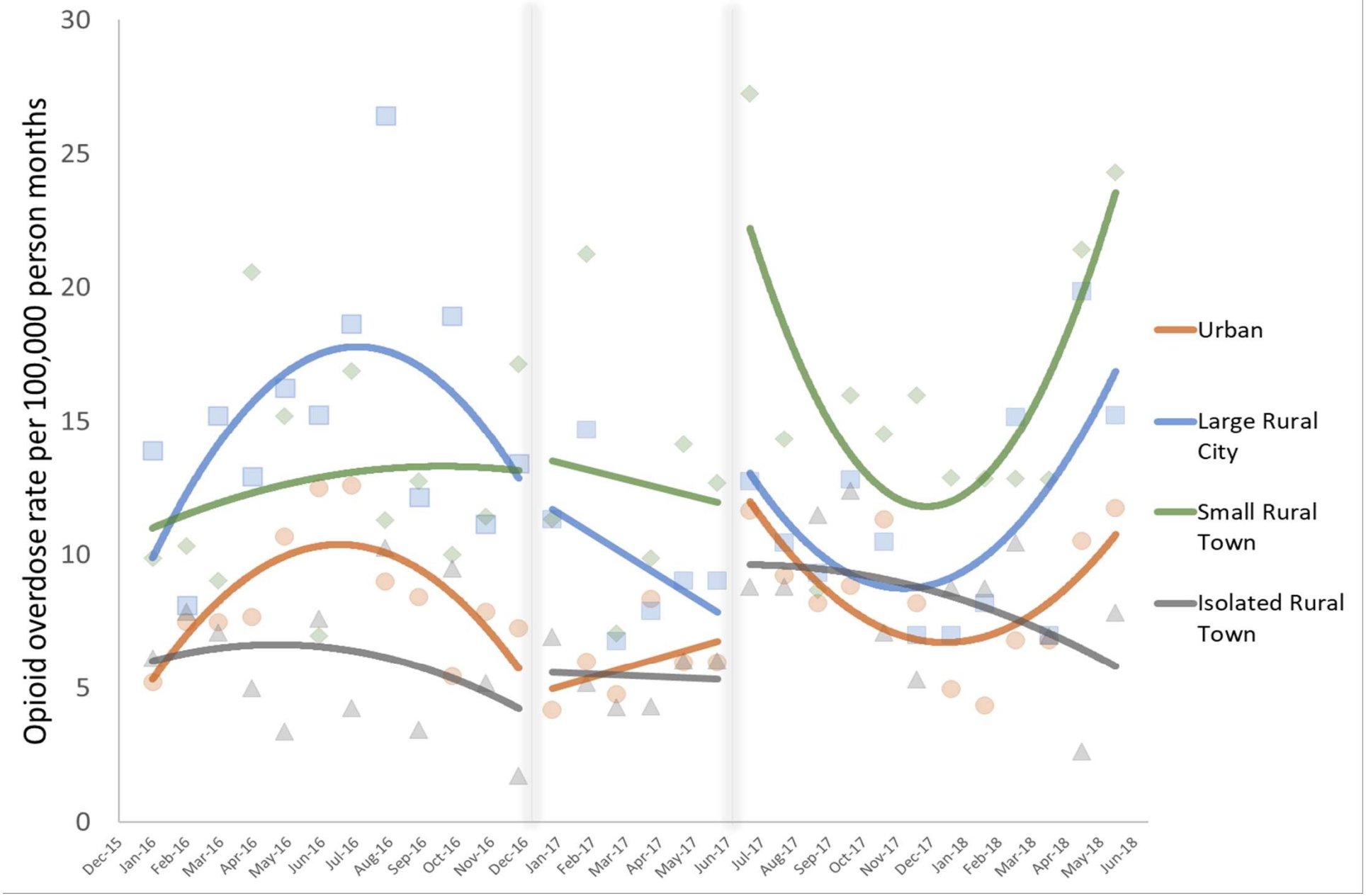
Opioid Overdose Rates by Rurality

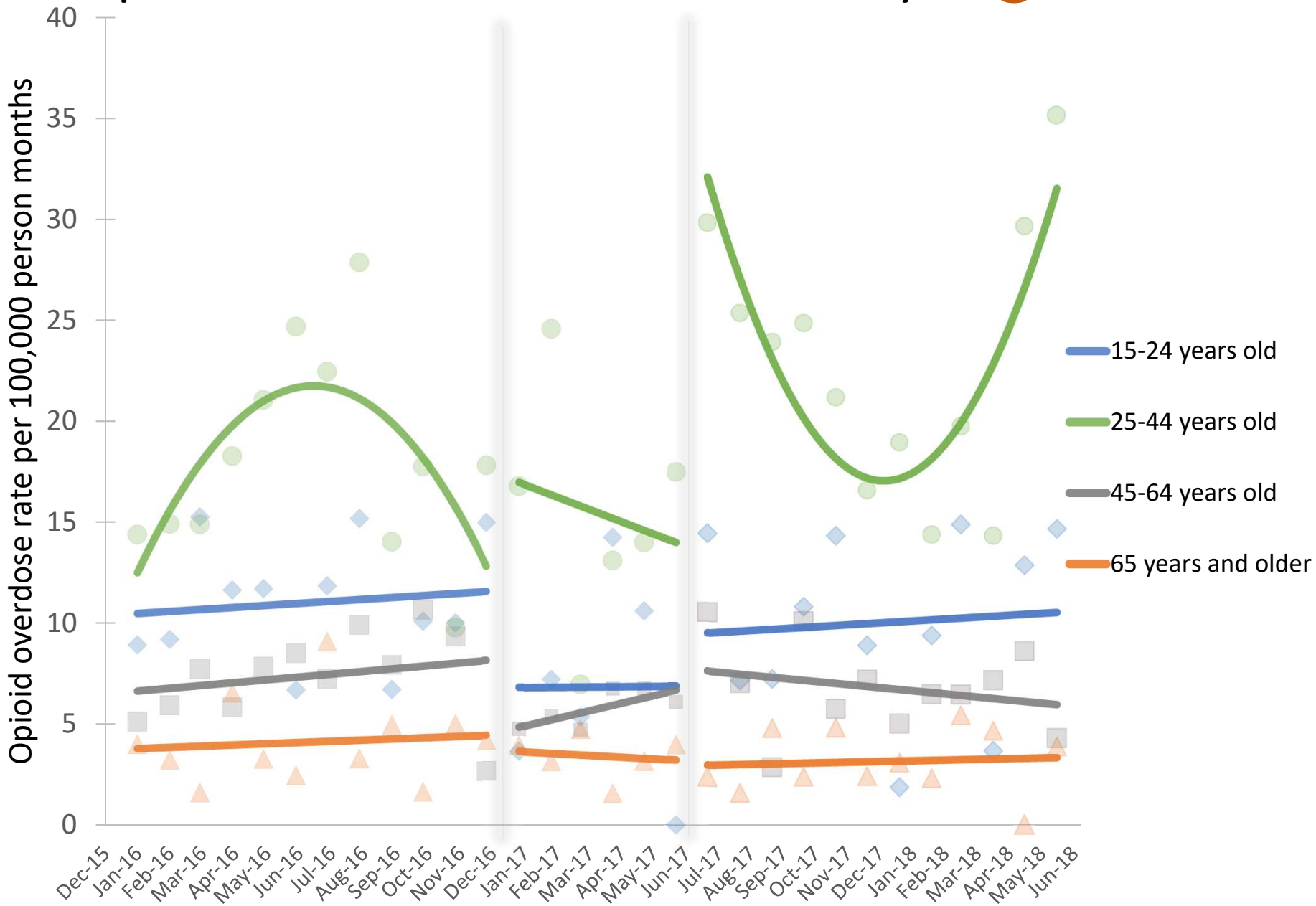


Rurality Category	Example Towns
Urban	Burlington, Winooski, Colchester, Essex Junction, Milton, Jericho, Charlotte, Richmond, St. Albans, North Hero, Stowe, Waterbury
Large Rural City	Rutland, Barre, Montpelier, Quechee, White River Junction, Bennington
Small Rural Town	Middlebury, Brattleboro, Castleton, Windsor, Vernon, Franklin
Isolated Rural Town	Ludlow, Woodstock, Randolph, Derby, Norwich, Randolph

Opioid Overdose Rates by Rurality



Opioid Overdose Rates by Age



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Hospital Utilization for Opioid Overdose

Next Steps:

1. Share and Learn with Community Stakeholders
2. Refining Analyses and Publishing Results

THANKS