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Assessment of Prevention Research Measuring Leading Risk Factors and Causes of Mortality and Disability Supported by the US National Institutes of Health

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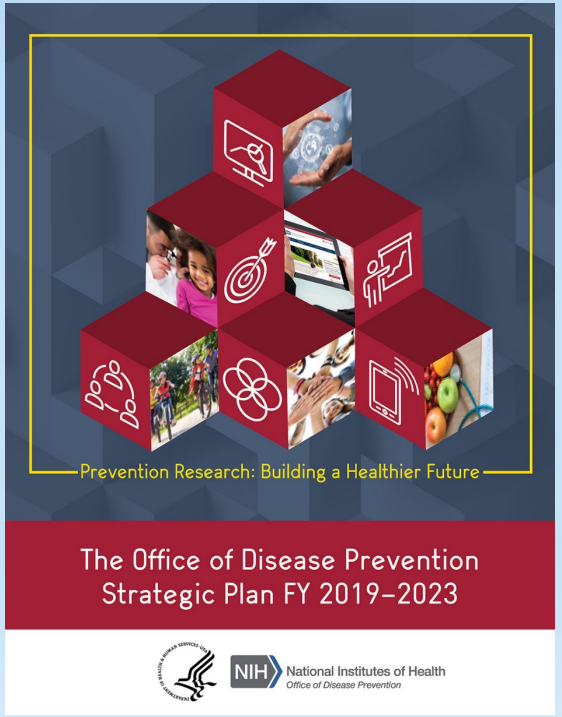
Office of Disease Prevention

Council of Councils
January 24, 2020

National Institutes of Health
Office of Disease Prevention

Strategic Priority I

- Systematically monitor NIH investments in prevention research and assess the progress and results of that research.
  - ODP defines prevention research to include primary and secondary prevention in humans, together with relevant methods development.
  - ODP's definition includes research designed to promote health; to prevent onset of disease, disorders, conditions, or injuries; and to detect, and prevent the progression of, asymptomatic disease.
  - Prevention research includes studies for:
    - Identification and assessment of risk and protective factors,
    - Screening and identification of individuals and groups at risk,
    - Development and evaluation of interventions to reduce risk,
    - Translation, implementation, and dissemination of effective, preventive interventions into practice, and
    - Development of methods to support prevention research.



Selection of Activity Codes

- ODP worked with staff from many ICs to identify activity codes likely to support NIH prevention research that met ODP's definition.
  - Basic and preclinical research were excluded.
  - Awards for community services, facilities, infrastructure, loan repayment, meetings, planning, and training were excluded.
  - Intramural research was excluded to focus on extramural research.
  - Contracts proved too difficult to code using our methods.
  - Methodological research was included only if it yielded products that were applicable to prevention research without additional development.

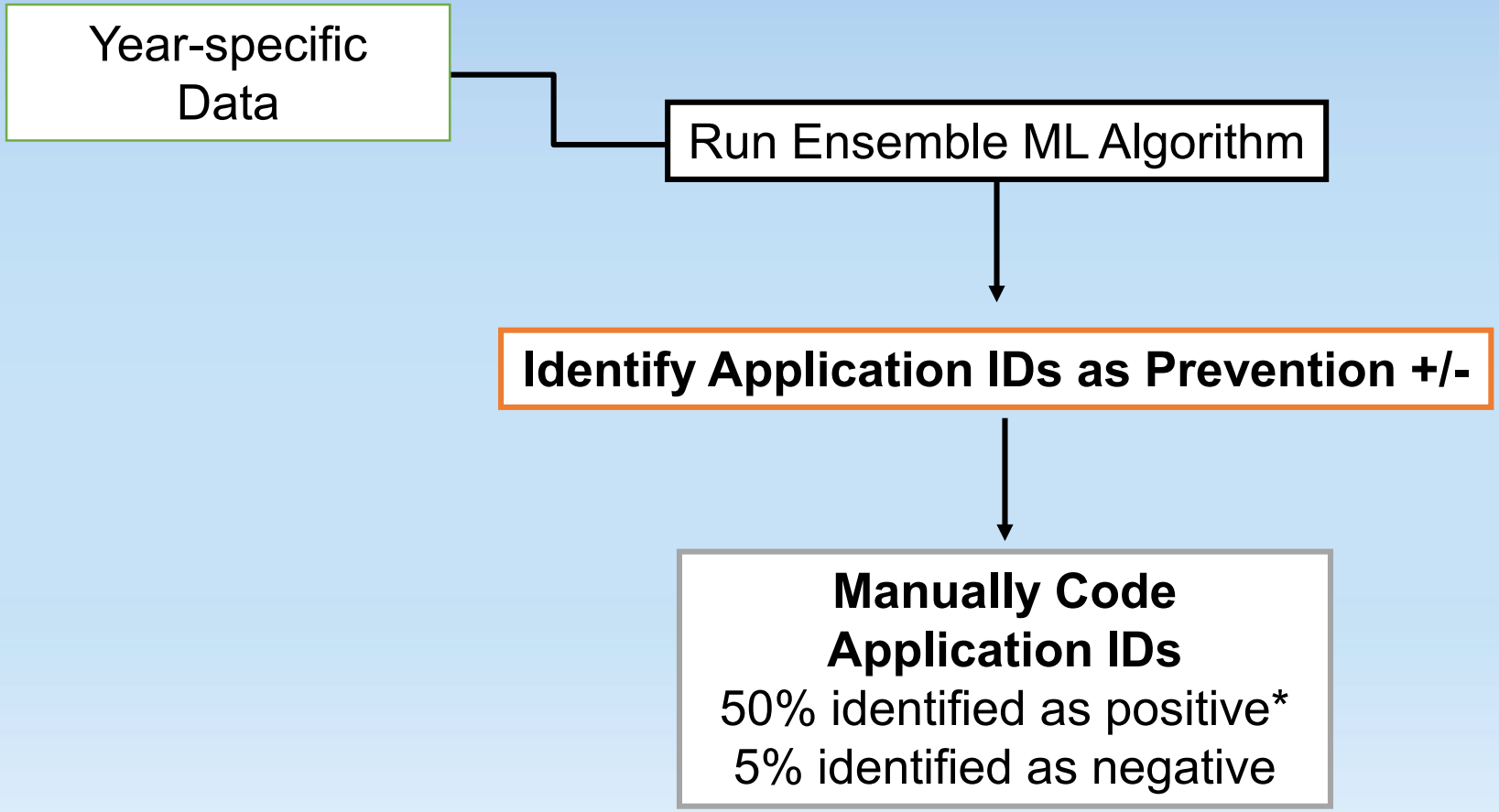
  - We included all remaining R, P, and U activity codes with at least 500 awards across FY12-17 or at least $500M awarded across FY12-17.
  - Several of these activity codes involved awards with multiple subprojects; as a result, we sampled Application IDs (Appl IDs) instead of awards.

Portfolio Coverage by These 12 Activity Codes

Awards and Costs	All Activity Codes	R, P, U Activity Codes	Research R, P, U Activity Codes	ODP's Selected Activity Codes	% Research R, P, U Activity Codes
Total Awards	111,626	68,757	63,381	58,104	91.7%
Total Costs	$57.5 B	$32.6 B	$30.6 B	$25.7 B	84.1%

- All figures based on Type I, 2, and 9 awards from FY12-17, excluding parent awards for projects with sub-awards to avoid double counting.

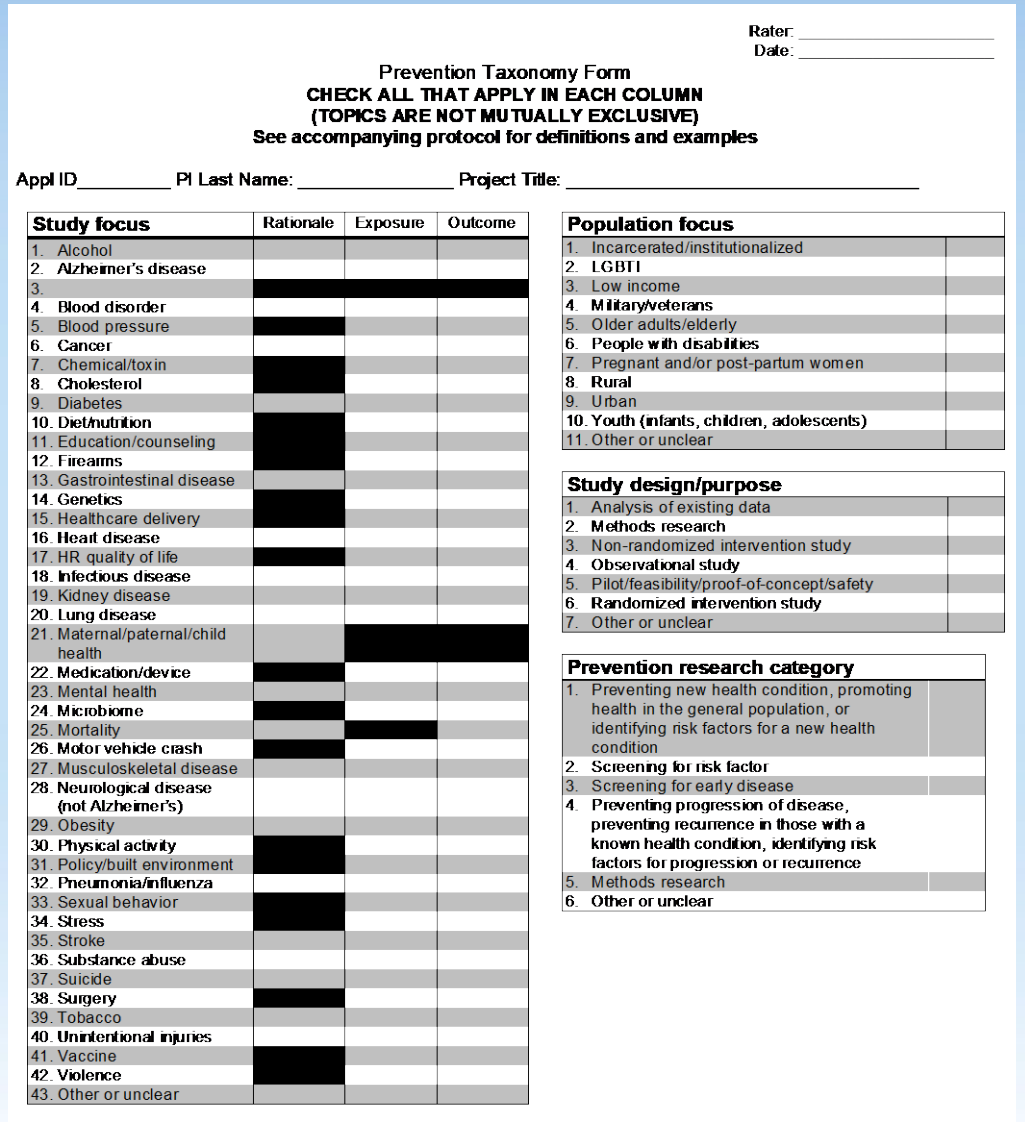
Sampling of Application IDs



* 100% of 1R01s identified as positive were manually coded

Coding Based on a Prevention Research Taxonomy

- A classification system to characterize projects or subprojects on:
  - Study Focus
    - Rationale
    - Exposures
    - Outcomes
  - Population focus
  - Study design/purpose
  - Prevention research category
- 128 topics, 29-page protocol
  - Applied to title, abstract, public health significance
- Input from the PRCC



Rater: _____
Date: _____

Prevention Taxonomy Form
CHECK ALL THAT APPLY IN EACH COLUMN
(TOPICS ARE NOT MUTUALLY EXCLUSIVE)
See accompanying protocol for definitions and examples

Appl ID_____ PI Last Name: _____ Project Title: _____

Study focus	Rationale	Exposure	Outcome
1. Alcohol			
2. Alzheimer's disease			
3.	■	■	■
4. Blood disorder			
5. Blood pressure	■		
6. Cancer			
7. Chemical/toxin	■		
8. Cholesterol	■		
9. Diabetes			
10. Diet/nutrition	■		
11. Education/counseling	■		
12. Firearms	■		
13. Gastrointestinal disease			
14. Genetics	■		
15. Healthcare delivery	■		
16. Heart disease			
17. HR quality of life	■		
18. Infectious disease			
19. Kidney disease			
20. Lung disease			
21. Maternal/paternal/child health		■	■
22. Medication/device	■		
23. Mental health			
24. Microbiome	■		
25. Mortality		■	
26. Motor vehicle crash	■		
27. Musculoskeletal disease			
28. Neurological disease (not Alzheimer's)			
29. Obesity			
30. Physical activity	■		
31. Policy/built environment	■		
32. Pneumonia/influenza			
33. Sexual behavior	■		
34. Stress	■		
35. Stroke			
36. Substance abuse			
37. Suicide			
38. Surgery	■		
39. Tobacco			
40. Unintentional injuries			
41. Vaccine	■		
42. Violence			
43. Other or unclear			

Population focus	
1. Incarcerated/institutionalized	
2. LGBTI	
3. Low income	
4. Military/veterans	
5. Older adults/elderly	
6. People with disabilities	
7. Pregnant and/or post-partum women	
8. Rural	
9. Urban	
10. Youth (infants, children, adolescents)	
11. Other or unclear	

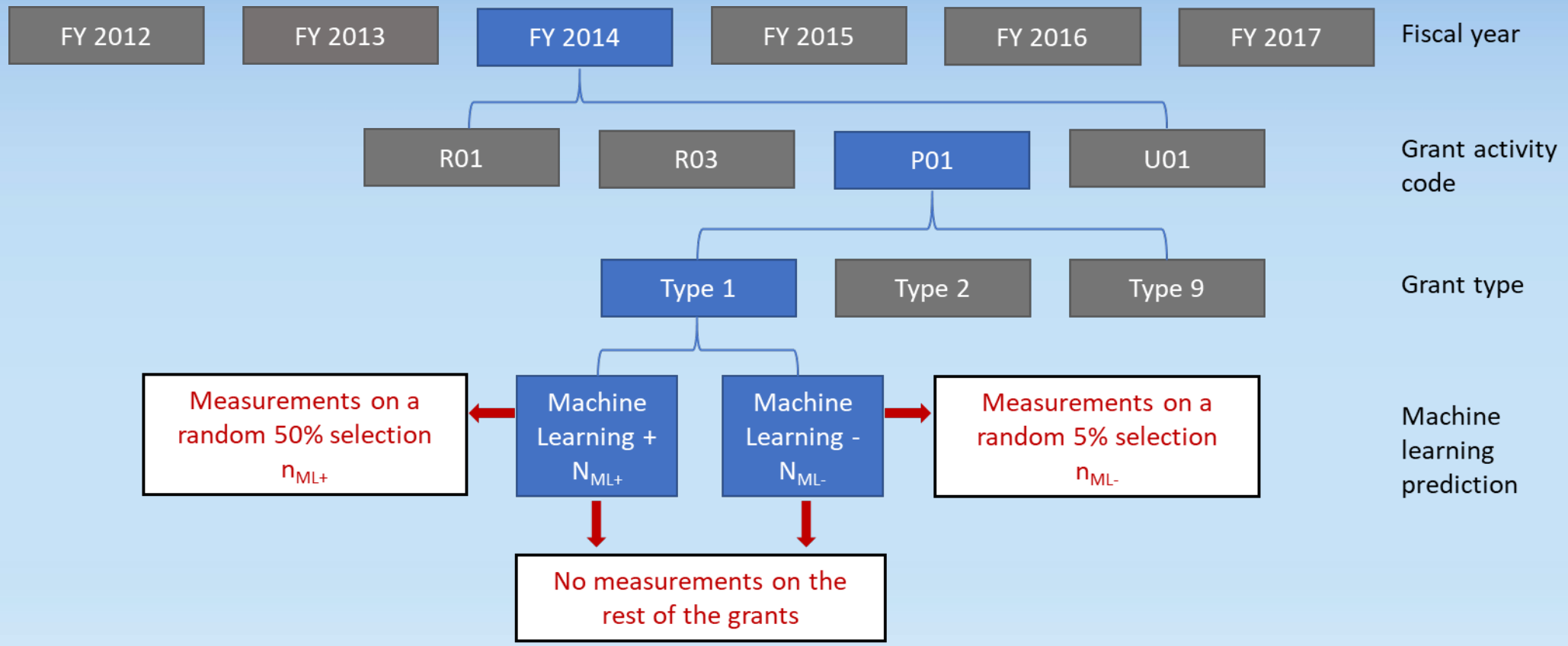
Study design/purpose	
1. Analysis of existing data	
2. Methods research	
3. Non-randomized intervention study	
4. Observational study	
5. Pilot/feasibility/proof-of-concept/safety	
6. Randomized intervention study	
7. Other or unclear	

Prevention research category	
1. Preventing new health condition, promoting health in the general population, or identifying risk factors for a new health condition	
2. Screening for risk factor	
3. Screening for early disease	
4. Preventing progression of disease, preventing recurrence in those with a known health condition, identifying risk factors for progression or recurrence	
5. Methods research	
6. Other or unclear	

Team-Based Coding

- Coders
  - Contract staff: MPH grads led by a PhD epidemiologist
  - 2 months training in groups of 3-4
  - Overseen by ODP staff
- 3-person teams coded abstracts using iPads
  - Each person coded independently, then the team resolved disagreements to generate a set of consensus codes for each Application ID
  - ODP coded 10-20% of the abstracts weekly for QC using the same methods
  - ODP reconciled discrepancies with the contract coding teams
- Average interrater agreement was 0.86.

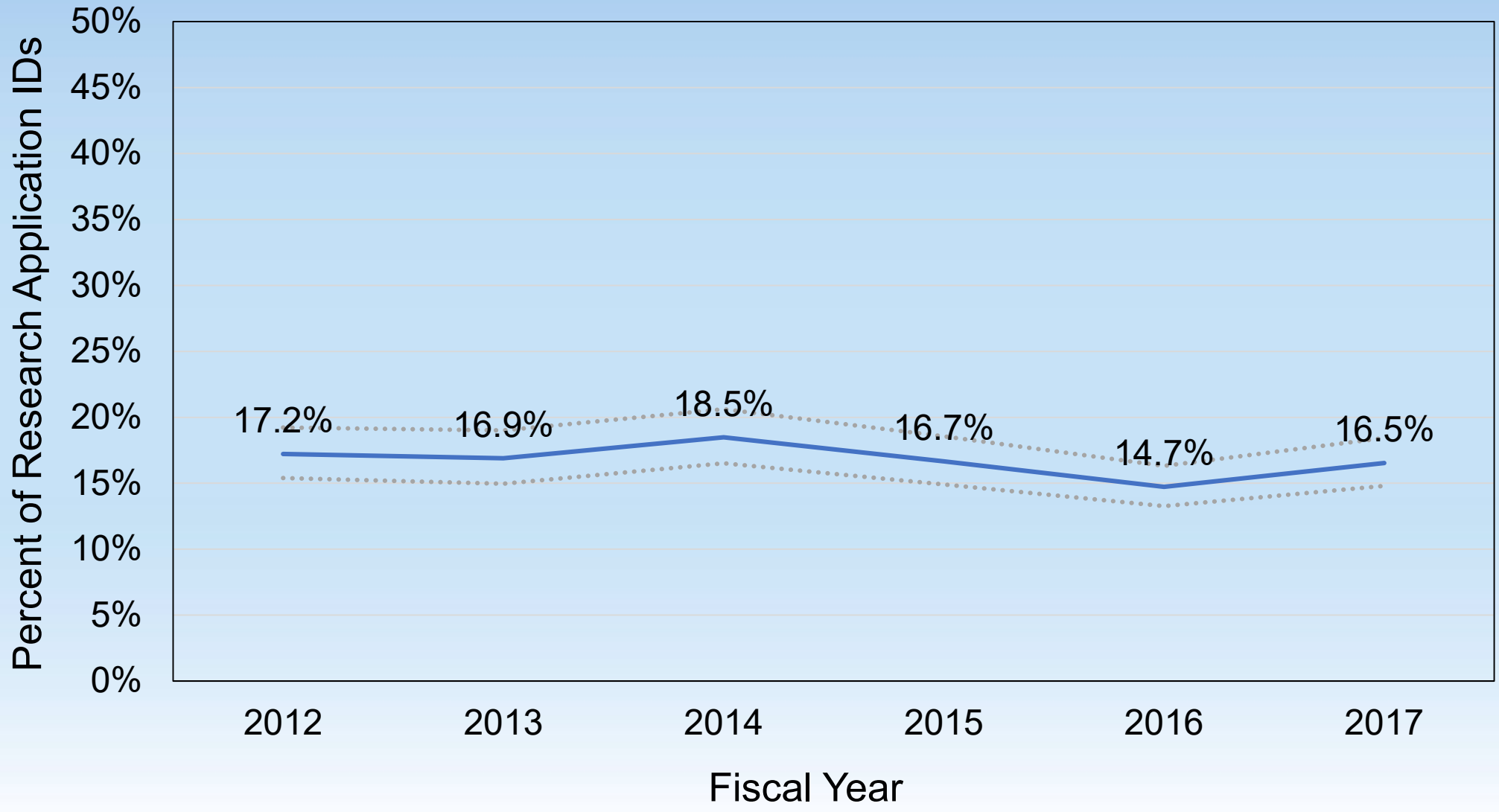
Weighting



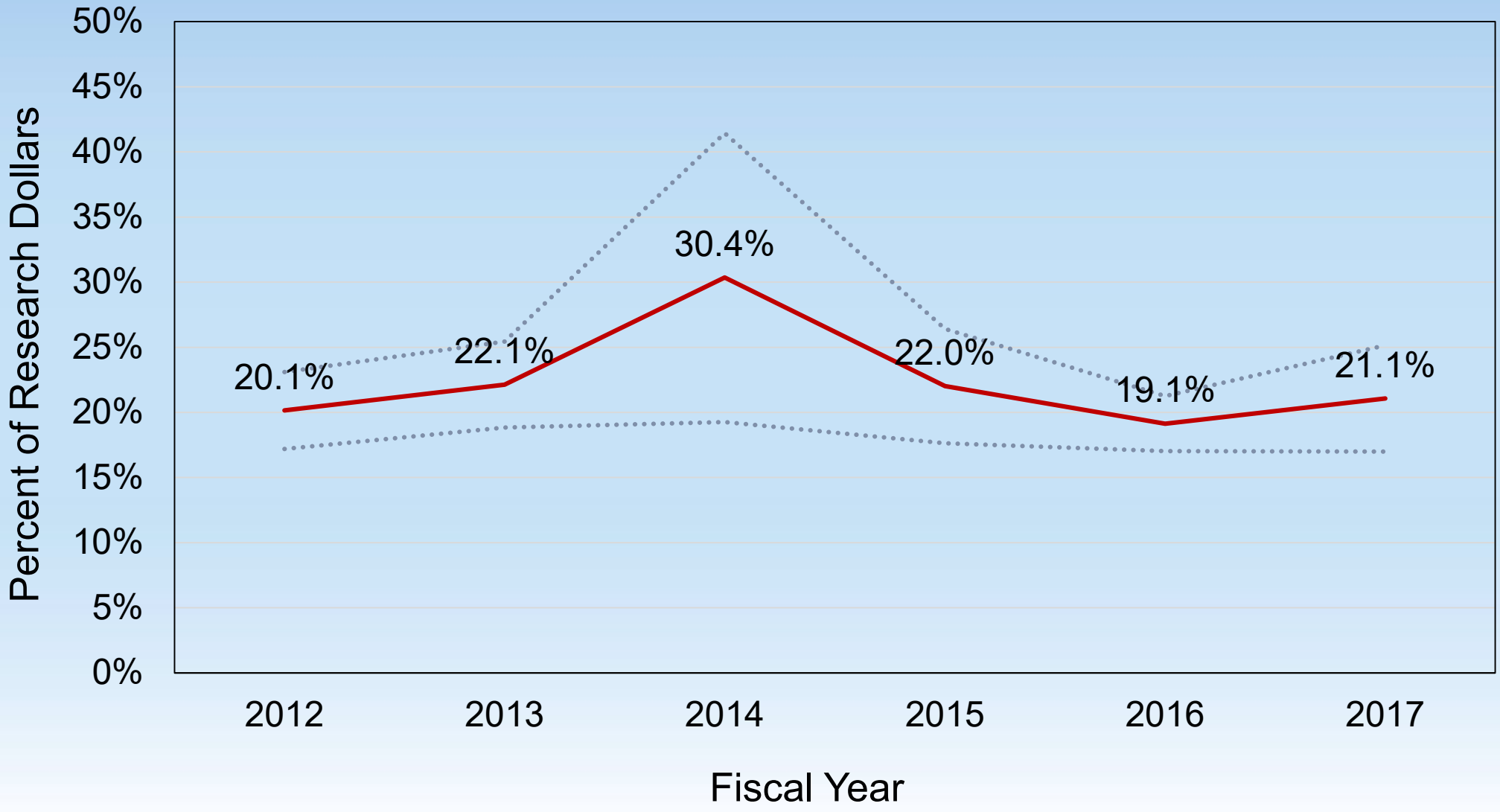
Weights for FY14, P01, type 1, Machine Learning + = $N_{ML+/}\, n_{ML+}$

Weights for FY14, P01, type 1, Machine Learning - = $N_{ML-/}\, n_{ML-}$

Primary and Secondary Prevention Research in Humans: FY12-17



Primary and Secondary Prevention Research in Humans: FY12-17



American Journal of
Preventive Medicine

RESEARCH ARTICLE

NIH Primary and Secondary Prevention Research in Humans During 2012–2017

David M. Murray, PhD,[1] Jennifer Villani, PhD, MPH,[1] Ashley J. Vargas, PhD, MPH,[1] Jocelyn A. Lee, PhD, MPH,[1] Ranell L. Myles, PhD, MPH, CHES,[1] Jessica Y. Wu, PhD,[2] Patricia L. Mabry, PhD,[3] Sheri D. Schully, PhD[1]

Am J Prev Med 2018;55(6):915–925. Published by Elsevier Inc. on behalf of American Journal of Preventive Medicine.

Follow-Up

- 74% of deaths in the U.S. are attributable to 10 well-known causes.[a]
- 57.3% of deaths and 42.1% of Disability-Adjusted Life Years lost in the U.S. are attributable to 10 well-known risk factors.[b]
- How does NIH prevention research address these causes and risk factors?
  - ODP staff worked through the database of 11,082 coded awards to revise coding for the leading risk factors and causes of death to be consistent with the definitions used by CDC and GBD.
  - ODP then repeated the portfolio analysis, focused on projects that included an exposure or outcome that was a leading risk factor or cause of death.

[a] Centers for Disease Control (CDC) report Mortality in the United States, 2017. Accessed April 4th, 2019. https://www.cdc.gov/nchs/data/databriefs/db328_tables-508.pdf#4.

[b] U. S. Burden of Disease Collaborators, Mokdad AH, Ballestros K, et al. The State of US Health, 1990-2016: Burden of Diseases, Injuries, and Risk Factors Among US States. *JAMA.* 2018;319(14):1444-1472.

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Assessment of Prevention Research Measuring Leading Risk Factors and Causes of Mortality and Disability Supported by the US National Institutes of Health

Ashley J. Vargas, PhD, MPH, RDN; Sheri D. Schully, PhD; Jennifer Villani, PhD, MPH; Luis Ganoza Caballero, MD, MPH; David M. Murray, PhD

JAMA Network Open. 2019;2(11):e1914718. doi:10.1001/jamanetworkopen.2019.14718

NIH Primary and Secondary Prevention Research in Humans vs. Leading Risk Factors for DALYs Lost in the U.S.

Leading Risk Factors - DALYs Lost	NIH prevention research portfolio, % projects (95% CI)	NIH prevention research portfolio, % dollars (95% CI)	GBD,[a] % attributable DALYs lost
Any Top 10 Risk Factor - DALYs	31.4 (29.6-33.3)	30.3 (26.6-33.9)	42.1
1) High body mass index	5.3 (4.7-6.0)	6.5 (3.7-9.4)	11.6
2) Tobacco	6.6 (5.8-7.6)	5.4 (4.5-6.3)	11.1
3) Dietary risk	7.8 (7.0-8.8)	6.7 (5.7-7.7)	10.4
4) High fasting plasma glucose	4.6 (3.9-5.4)	6.6 (3.7-9.6)	9.7
5) High systolic blood pressure	2.7 (2.2-3.3)	3.1 (2.3-3.9)	8.0
6) Drug use	7.3 (6.4-8.2)	7.6 (6.0-9.2)	6.5
7) Alcohol use	5.6 (4.9-6.4)	4.1 (3.6-4.7)	4.2
8) High LDL cholesterol	1.8 (1.4-2.3)	2.0 (1.3-2.6)	4.0
9) Impaired kidney function	1.6 (1.0-2.3)	1.6 (1.0-2.3)	3.1
10) Occupational risks	0.3 (0.1-0.4)	0.2 (0.1-0.3)	2.5

[a] The top 10 leading risk factors for Disability Adjusted Life Years (DALYs) lost in the U.S. for 2016 are from a recent Global Burden of Disease (GBD) publication: U. S. Burden of Disease Collaborators, Mokdad AH, Ballestros K, et al. The State of US Health, 1990-2016: Burden of Diseases, Injuries, and Risk Factors Among US States. *JAMA.* 2018;319(14):1444-1472.

NIH Primary and Secondary Prevention Research in Humans vs. Leading Risk Factors for Deaths in the U.S.

Leading Risk Factors for Death	NIH prevention research portfolio, % projects (95% CI)	NIH prevention research portfolio, % dollars (95% CI)	GBD,[a] % attributable deaths
Any Top 10 Risk Factor for Death	34.0 (32.2-35.9)	32.5 (28.9-36.2)	57.3
1) Dietary risk	7.8 (7.0-8.8)	6.7 (5.7-7.7)	19.1
2) Tobacco	6.6 (5.8-7.6)	5.4 (4.5-6.3)	17.8
3) High systolic blood pressure	2.7 (2.2-3.3)	3.1 (2.3-3.9)	17.4
4) High body mass index	5.3 (4.7-6.0)	6.5 (3.7-9.4)	13.9
5) High fasting plasma glucose	4.6 (3.9-5.4)	6.6 (3.7-9.6)	13.6
6) High total cholesterol	1.8 (1.4-2.3)	2.0 (1.3-2.6)	8.4
7) Impaired kidney function	1.6 (1.0-2.3)	1.6 (1.0-2.3)	6.3
8) Alcohol/drug use	11.2 (10.2-12.4)	10.2 (8.5-11.8)	5.6
9) Air pollution	1.4 (1.1-1.6)	1.4 (0.9-1.8)	3.8
10) Low physical activity	5.0 (4.4-5.7)	4.3 (3.7-4.8)	3.3

[a] The top 10 leading risk factors for death in the U.S. for 2016 from a recent Global Burden of Disease (GBD) publication: U. S. Burden of Disease Collaborators, Mokdad AH, Ballestros K, et al. The State of US Health, 1990-2016: Burden of Diseases, Injuries, and Risk Factors Among US States. *JAMA.* 2018;319(14):1444-1472.

NIH Primary and Secondary Prevention Research in Humans vs. Leading Causes of Deaths in the U.S.

Leading Causes of Death	NIH prevention research portfolio, % projects (95% CI)	NIH prevention research portfolio, % dollars (95% CI)	CDC,[a] % attributable deaths
Any Top 10 Leading Cause of Death	25.9 (24.0-27.8)	28.2 (24.8-31.5)	74.0
1) Heart disease	4.2 (3.3-5.2)	4.8 (3.2-6.4)	23.0
2) Cancer	11.9 (10.5-13.4)	11.3 (9.2-13.4)	21.3
3) Accidents	1.7 (1.2-2.4)	1.7 (1.1-2.4)	6.0
4) Chronic lower respiratory disease	1.8 (1.4-2.3)	2.0 (1.3-2.7)	5.7
5) Stroke	2.7 (2.2-3.4)	3.3 (2.3-4.3)	5.2
6) Alzheimer's disease	2.0 (1.4-2.6)	3.2 (1.9-4.6)	4.3
7) Diabetes	3.6 (3.0-4.2)	4.5 (3.4-5.6)	3.0
8) Influenza/Pneumonia	0.5 (0.2-1.0)	0.7 (0.1-1.3)	2.0
9) Kidney disease	1.4 (0.9-2.2)	1.4 (0.8-2.0)	1.8
10) Suicide	0.7 (0.5-0.9)	0.7 (0.5-0.9)	1.7

[a] The top 10 leading causes of death in the U.S. for 2017 from the Centers for Disease Control (CDC) report Mortality in the United States, 2017. https://www.cdc.gov/nchs/data/databriefs/db328_tables-508.pdf#4. Accessed April 4th, 2019.

NIH Primary and Secondary Prevention Research in Humans Involving Multiple Risk Factors or Causes of Death in the U.S.

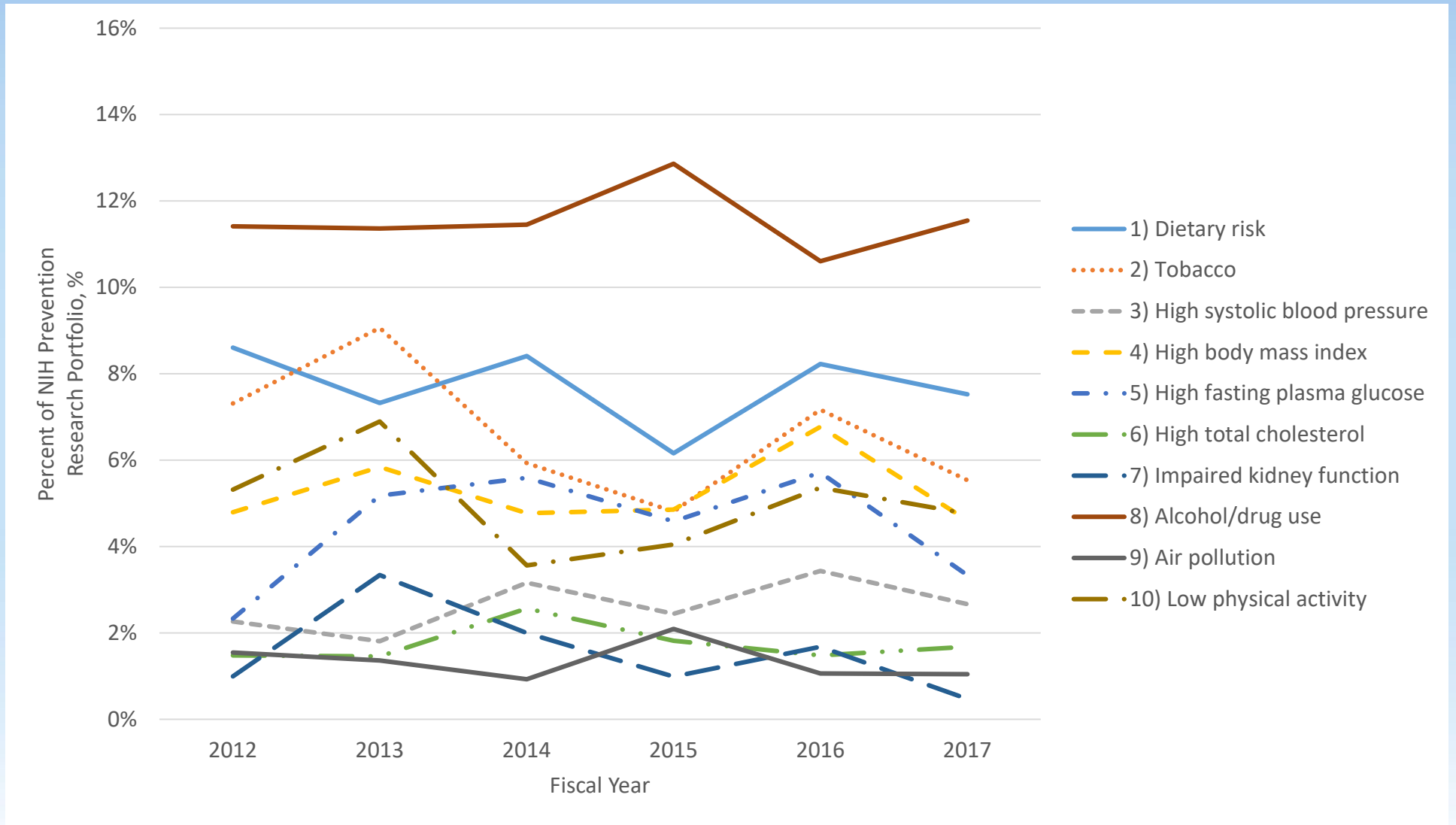
- 3.3% (95% CI, 2.6-4.1) of prevention research projects measured more than one leading cause of death as an exposure or outcome.
- 8.8% (95% CI, 7.9-9.8) of prevention research projects measured more than one leading risk factor for death as an exposure or outcome.
- 24.6% (95% CI, 22.5-26.9) of prevention research projects included a randomized intervention designed to address a leading risk factor or cause of death.

The Rest of the NIH Prevention Research Portfolio?

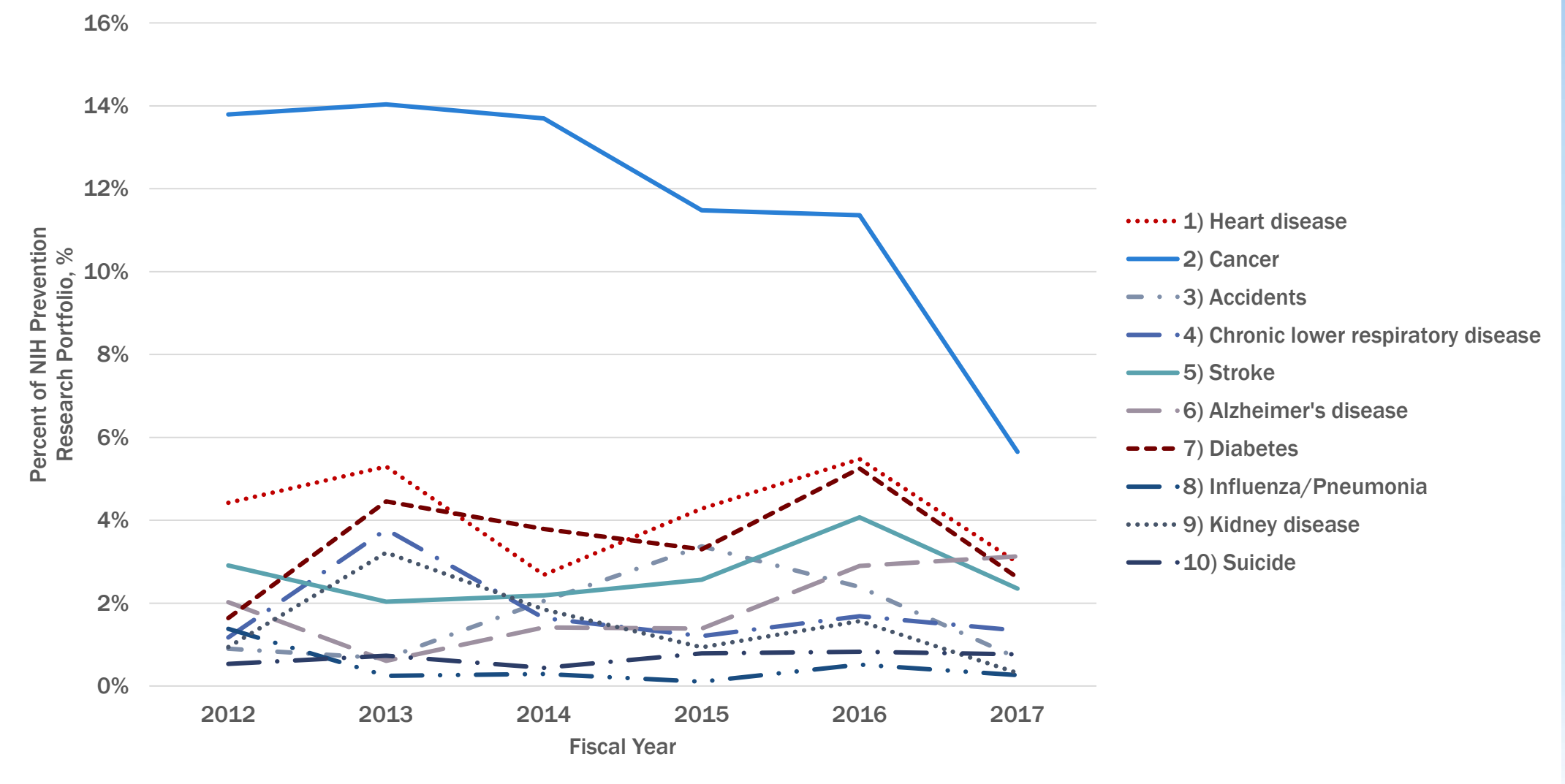
Study exposure and/or outcome	Portfolio, % (95% CI)	Study exposure and/or outcome	Portfolio, % (95% CI)
1) Other	86.0 (83.4-88.4)	14) Sexual behavior	2.8 (2.3-3.4)
2) Genetics	32.0 (28.8-35.4)	15) Chemical/toxin[c]	2.6 (1.9-3.5)
3) Infectious disease[a]	16.7 (14.4-19.2)	16) Violence	2.6 (1.9-3.5)
4) Education/counseling	12.3 (10.9-13.9)	17) Musculoskeletal disease	2.5 (1.6-3.7)
5) Medication/device	11.6 (9.4-14.1)	18) Policy/built environment	2.3 (1.8-2.8)
6) Mental health	10.7 (8.9-12.7)	19) Mortality	2.0 (1.6-2.5)
7) Healthcare delivery	10.0 (8.5-11.6)	20) Kidney disease[d]	1.7 (1.0-2.9)
8) Neurological disease[b]	9.5 (7.6-11.9)	21) Lung disease[e]	1.4 (0.8-2.3)
9) HRQOL	5.6 (4.5-7.0)	22) Heart disease[f]	1.2 (0.9-1.6)
10) Stress	4.0 (3.1-5.2)	23) Surgery	1.2 (0.6-2.2)
11) Vaccine	3.1 (2.0-4.8)	24) Stroke[g]	0.6 (0.4-0.9)
12) Microbiome	3.0 (2.0-4.4)	25) Blood disorder	0.5 (0.3-0.8)
13) GI disease	3.0 (1.8-4.9)	26) Firearms	0.2 (0.1-0.3)[h]

[a] This category does not include pneumonia/influenza. There is a separate category below for pneumonia/influenza.
[b] This category does not include Alzheimer's disease. There is a separate category below for Alzheimer's disease.
[c] This category includes chemical/toxins beyond air pollution and beyond the Global Burden of Disease definition of air pollution.
[d] This category includes congenital kidney defects and urinary tract infections which are not in the CDC definition of Kidney disease.
[e] This category includes cystic fibrosis, pulmonary fibrosis, lung injuries, and pulmonary hypertension which are not the CDC definition of chronic lower respiratory disease.
[f] This category includes congenital heart disease which is not in the CDC definition of heart disease.
[g] This category includes Venous Thromboembolic Disease and unspecified stroke risk factors which are not in the CDC definition of stroke.
[h] Fewer than 10 research projects were manually coded in this category which may make estimates from these data unstable

Trends in prevention research measuring leading risk factors for death in the U.S.



Trends in prevention research measuring leading causes of death in the U.S.



Summary of Findings

- During FY12-17, 16.7% of NIH research supported by extramural grants and collaborative agreements focused on primary and secondary prevention in humans, together with methods development to support that research.
  - 51.4% of that portfolio, or 8.6% of the total NIH research portfolio, addressed a leading risk factor or cause of death.
  - 31.4% of that portfolio, or 5.2% of the total NIH research portfolio, addressed a leading risk factor or cause of disability.
  - 3.3% of that portfolio, or 0.6% of the total NIH research portfolio, measured more than one leading cause of death as an exposure or outcome.
  - 8.8% of that portfolio, or 1.5% of the total NIH research portfolio, measured more than one leading risk factor for death as an exposure or outcome
  - 24.6% of that portfolio, or 4.1% of the total NIH research portfolio, included a randomized intervention that addressed a leading risk factor or cause of death.

Discussion Questions

- How should NIH respond to these findings?
  - Should the prevention research portfolio be reshaped to emphasize projects that address the leading risk factors and causes of death and disability?
  - Should the prevention research portfolio be reshaped to emphasize projects that address multiple risk factors or causes of death and disability in the same study?
  - Should the prevention research portfolio be reshaped to emphasize the development and testing of preventive interventions to address the leading risk factors and causes of death and disability?
  - Other advice?

Acknowledgments

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Charlene Liggins, Lead
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Erin Ellis
Natasha Oyedele

Past ODP Team
Sheri Schully (AoU)
Jen Villani (NIDA)
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GBD Team
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National Institutes of Health
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