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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Council of Councils
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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

|                      | 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

- Year-specific Data
- Run Ensemble ML Algorithm
- Identify Application IDs as Prevention +/-
- Manually Code Application IDs
  - 50% identified as positive*
  - 5% identified as negative

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

Fiscal year: FY 2012, FY 2013, FY 2014, FY 2015, FY 2016, FY 2017

Grant activity code: R01, R03, P01, U01

Grant type: Type 1, Type 2, Type 9

Measurements on a random 50% selection $n_{ML^+}$

Machine Learning + $N_{ML^+}$

Machine Learning - $N_{ML^-}$

Measurements on a random 5% selection $n_{ML^-}$

No measurements on the rest of the grants

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

Percent of Research Application IDs

Fiscal Year

2012 2013 2014 2015 2016 2017

17.2% 16.9% 18.5% 16.7% 14.7% 16.5%
Primary and Secondary Prevention Research in Humans: FY12-17

Percent of Research Dollars

| Fiscal Year | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|------------|------|------|------|------|------|------|
| 2012       | 20.1% | 22.1% | 30.4% | 22.0% | 19.1% | 21.1% |
NIH Primary and Secondary Prevention Research in Humans During 2012–2017

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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.
Original Investigation | Public Health

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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## 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                                    |
## 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                         |
| 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                       |
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       |
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?
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