



**Population Health  
Research Institute**  
HEALTH THROUGH KNOWLEDGE

[www.phri.ca](http://www.phri.ca)



**Hamilton  
Health  
Sciences**

**McMaster  
University**  
HEALTH SCIENCES





# PHRI History

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**Founded in 1999 as a joint research institute of  
McMaster University  
&  
Hamilton Health Sciences Corporation**

**Evolved from the Preventive Cardiology and Therapeutics Research  
Program (established in 1992)**

# Mission Statement

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*“To conduct trans-disciplinary research to improve major health outcomes in common and neglected conditions affecting Canadians and populations across the world”*



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# Philosophy & Mandate

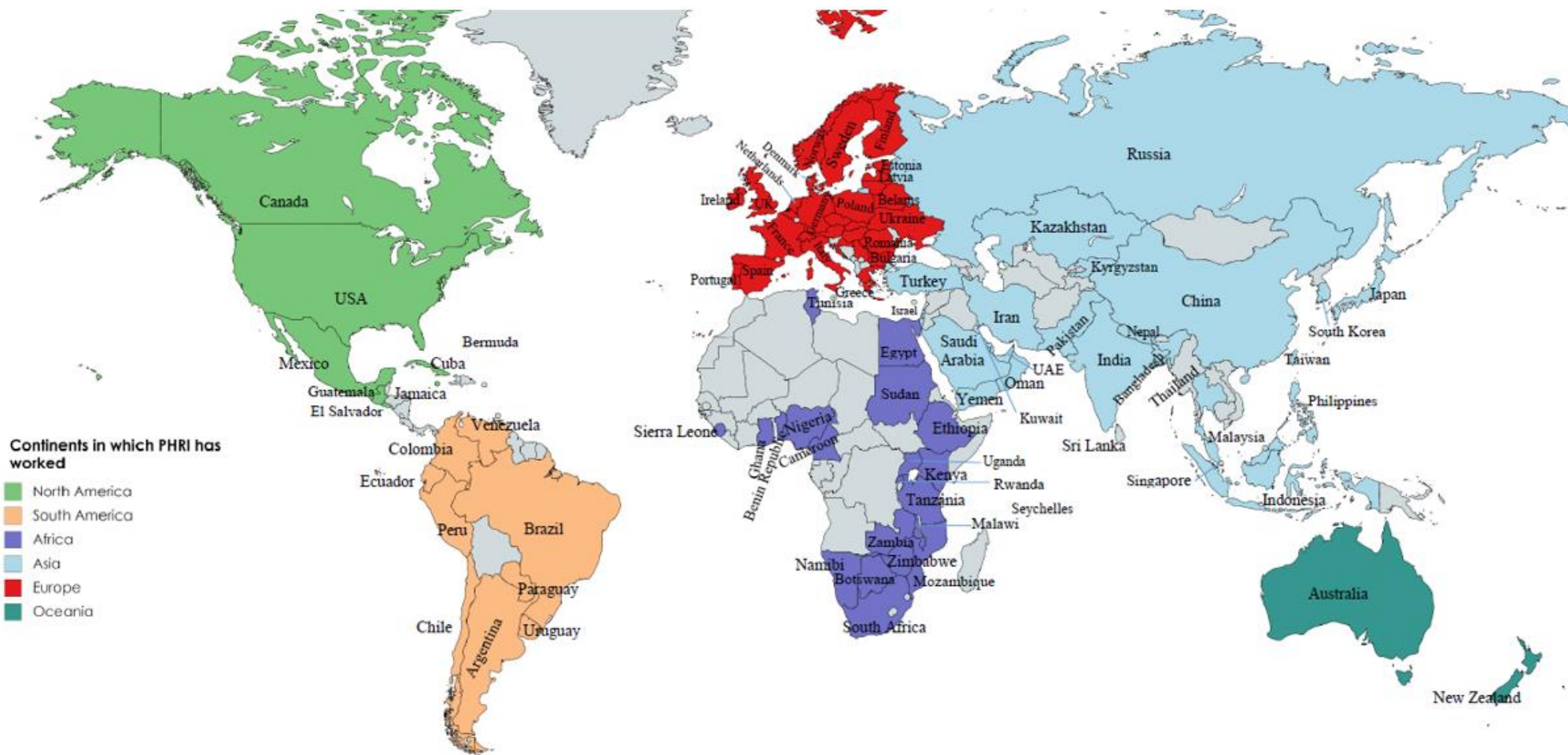
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- Design & conduct large simple randomized trials & major studies into the causes and prevention of CVD and to answer clinically important questions
- Provide leadership in international health research
- Educate and enhance clinical research skills of Canadian and international health researchers
- Build international capacity for global research programs



# Global network

## > 1,600 sites in 101 countries across 6 continents



### AFRICA

Benin Republic, Botswana, Cameroon, Egypt, Ethiopia, Ghana, Kenya, Malawi, Mozambique, Namibia, Nigeria, Rwanda, Seychelles, Sierra Leone, South Africa, Sudan, Tanzania, Tunisia, Uganda, Zambia, Zimbabwe

### ASIA

Bahrain, Bangladesh, China, Hong Kong, India, Indonesia, Iran, Israel, Japan, Kazakhstan, Kyrgyzstan, Kuwait, Malaysia, Nepal, Oman, Pakistan, Philippines, Qatar, Russia, Saudi Arabia, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, Turkey, UAE, Yemen

### EUROPE

Austria, Belgium, Belarus, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Macedonia, Netherlands, Norway, Poland, Portugal, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine, UK

### NORTH AMERICA

Bermuda, Canada, Cuba, El Salvador, Guatemala, Jamaica, Mexico, USA

### OCEANIA

Australia, New Zealand

### SOUTH AMERICA

Argentina, Brazil, Chile, Colombia, Ecuador, Paraguay, Peru, Uruguay, Venezuela

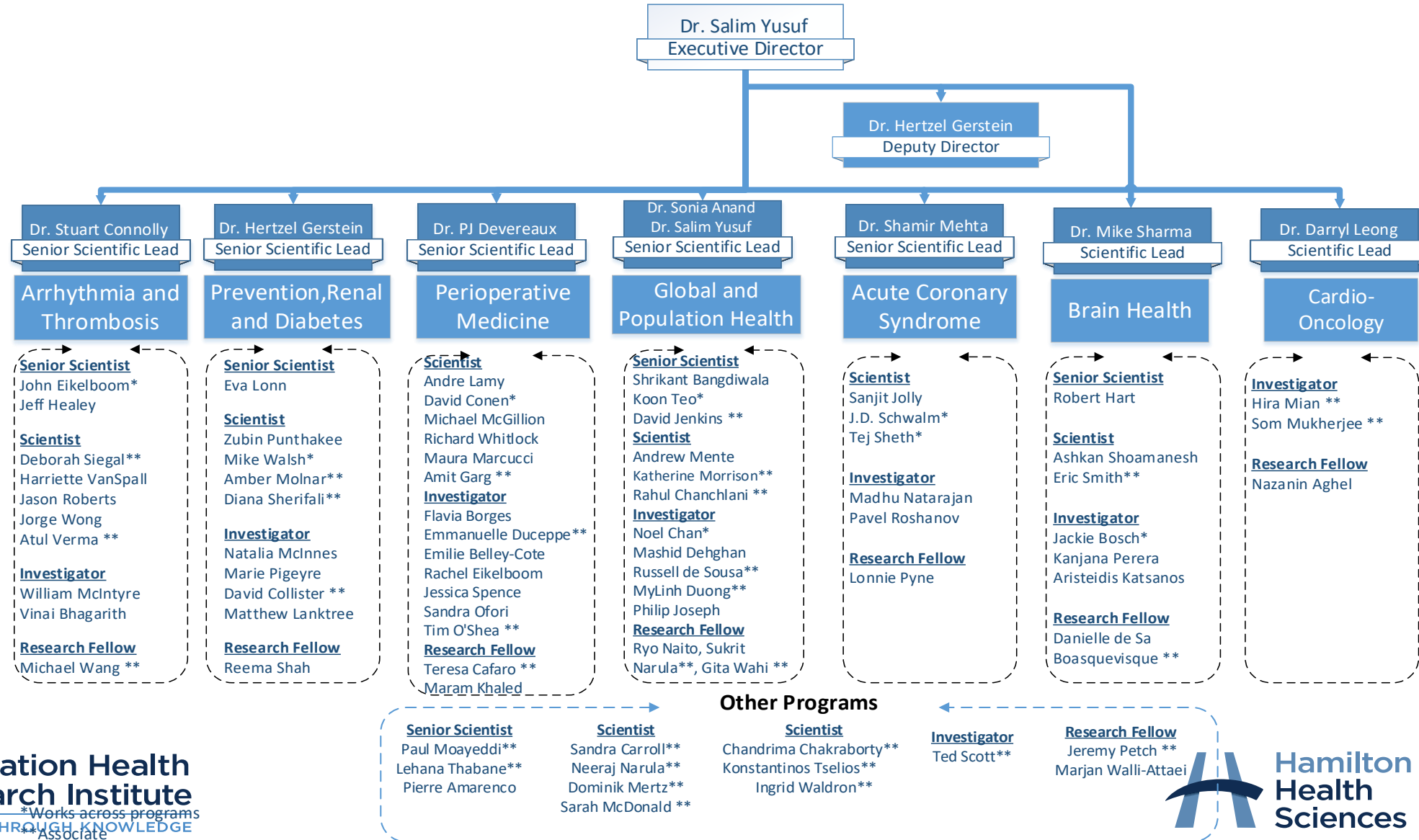
# Staff & Researchers (2022)

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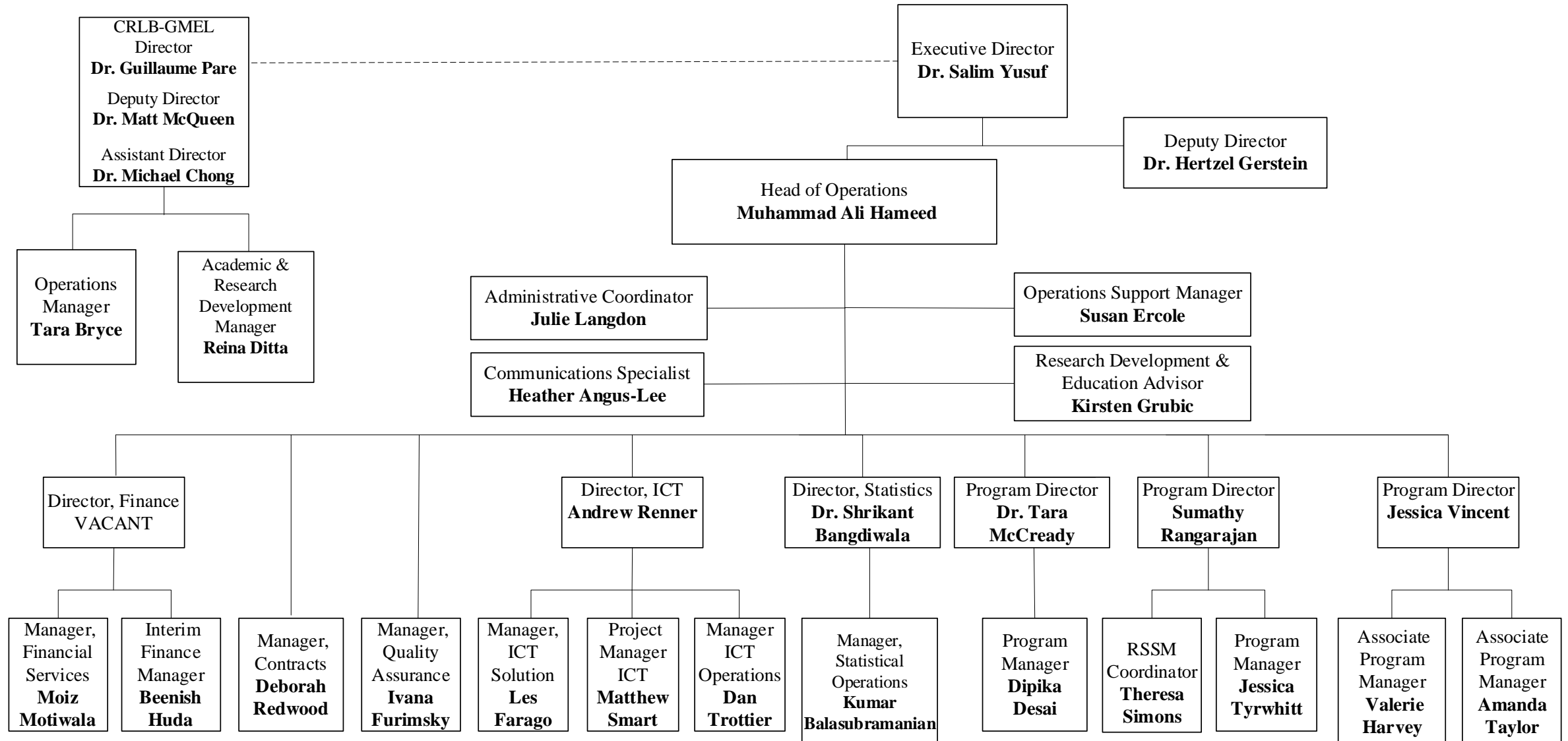
Researchers	66
Programs and Study Teams	175
ICT	47
Statistics and Data Management	31
Finance	16
Contracts	11
Administration, HR and Education	5
DSU & QA	7
Director & HOO	2
<b>Total</b>	<b>360</b>



# Scientific Organization



# Management Team





# Keys to PHRI's Success to Date

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- **Deep & broad range of expertise spanning many disciplines**
  - Clinical: Cardiology, endocrinology, surgery, nephrology, neurology, hematology, rehabilitation, geriatrics, infectious disease, nursing, etc.
  - Health: Nutrition, ethnicity, genetics, proteomics, metabolomics, physiology
  - Methodology: Study design, multiplex lab analyses, core lab
  - Management: Science, operations, sites, committees, sample transfer, drug dist'n, etc
  - Data: Collection, entry, storage, transfer
  - Statistics: DSMB, trial analyses, regulatory agencies, Bayesian approaches
  - Contracts: International interactions with sites, suppliers, companies
  - Pharma: Contacts, experience & relationships, regulatory submissions
  - ICT: Data storage, backup, integrity
  - Finance: Budgeting, managing budgets up to ~100,000,000 over many years
  - Dissemination: Speaking, publishing, dealing with the press



# Keys to PHRI's Success to Date

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- Largest biobank in Canada (~4M aliquots in N=0.5M people)
- Global network of collaborators
- Peer mentorship re career, research, etc.
- A culture of transdisciplinary interactions & resource sharing
- Open to accepting any researcher from new disciplines
- Autonomy within HHS & McMaster
  - *Freedom to design/manage studies in the way most suited to the question*
  - *Use of overages from one PI/study/study team to*
    - *Cover deficits in others (e.g. from all peer-reviewed grants)*
    - *Fund research chairs & some stipends to protect time*
    - *Seed funding for new research programs (internal & external)*



# Study Designs Used & Interventions Tested

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## Study Designs

- *Parallel group, placebo-controlled double blind RCT*
- *PROBE*
- *Factorial designs*
- *Cluster and Cluster cross over*
- *Stepped wedge*

## Interventions Tested

- *Drugs*
- *Vitamins*
- *Surgery types, timing*
- *Follow-up approaches*
- *Devices*



# Scientific Themes

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## Randomized Trials

- Heart diseases
- Stroke & brain health
- Diabetes, obesity, metabolic health
- Health systems (Models of care)
- Kidney diseases
- Perioperative risk & risk reduction
- Cardiac & noncardiac surgery
- Infectious diseases
- Neglected diseases

## Disease Registries

- *Acute coronary syndrome*
- *Atrial fibrillation, stroke*
- *Rheumatic heart disease*

## International Population Studies

- Cohorts
- Case-control
- Birth cohorts
- Environment (air quality, climate, tobacco)
- Genetics & biomarkers





# Some Specific Examples

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## RCTS

- Vitamins (E, folic acid, B6, B12, D, Omega 3 FA, thiamine)
- Vaccines (Influenza, mycoplasma immunotherapy)
- Health system approach (BP control by non-MDs in LMIC)
- Strategies (improved INR control, multiple vs. single coronary intervention)
- Safety (PPI to prevent GI bleeds with antithrombotics)
- Devices (ICD, single v dual chamber P-maker, new stents)
- Cardiac Surgery (steroids, off vs on pump, LA occlusion to prevent strokes in AF)
- Noncardiac surgery (Beta blockers for CVD, tranexamic acid to reduce bleeding)
- Models of care (post-op home care with RAM)
- Polypill



# Some Specific Examples

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## Case-Control Studies

- MI (INTERHEART, 28,000 from 52 countries)
- Stroke (INTERSTROKE, 25,000 from 36 countries)
- Bleeding (INTERBLEED)

## Cohort Studies

- PURE (N=202,000 from 1000 urban & rural communities in 27 countries, f/u > 12y)
- KIRAN (N=900,000 in India using proportionate random sampling)
- Birth Cohort (N=3000)

## Disease Registries

- Heart Failure (INTERCHF of 5000 in 10 countries, & GCHF of 23,000 in 40 countries)
- Perioperative patients (VISION in 50,000 people)
- Rheumatic heart disease (INVICTUS in 13000 people)



# Neglected & Rare Diseases

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- Chagas Disease: BENEFIT trial of benznidazole in 2700 people X 6 y
- TB Pericarditis: IMPI trial of steroids &/or vaccine in 1200 people X 1 y
- Rheumatic Heart Disease: INVICTUS RCT of NOAC vs VKA in 4500  
INVICTUS Registry in 13000
- Stroke Care Capacity/Rehab: OSCAIL in Africa/Asia
- Arrhythmogenic RV Cardiomyopathy: repurposed drug (J Roberts)



# New/Emerging Areas

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- Infections Disease/COVID (J Eikelboom)
- Accelerating Clinical Trials Consortium (PJ Devereaux)
- Arrhythmogenic RV Cardiomyopathy (New Drug Development - J Roberts)
- Cardio-oncology (D Leong)
- Brain Health and healthy aging (R Joundi, M Sharma, D Leong, Yusuf)
- Pediatric Obesity & Energy Expenditure (K Morrison)
- Bariatric Surgery and the Microbiome (A Doumouras)
- Biomarker and genomics discovery program ( STRIVE: Gui Pare)
- New models of care using advanced remote monitoring( VICTOR: M McGillion)





# Key Achievements/Recognitions

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- > 5500 publications
- > 350,000 participants enrolled worldwide in >150 RCTs
- >1,500,000 participants enrolled in all PHRI studies
- > 27 publications with >1000 citations
- > 14 studies have supported regulatory approvals globally
- Trained and mentored > 120 scientists from around the world
- 5 PHRI researchers named as top 1% of cited authors worldwide (1 named the most cited in Canada)



# Studies that → Regulatory Approval of Drug

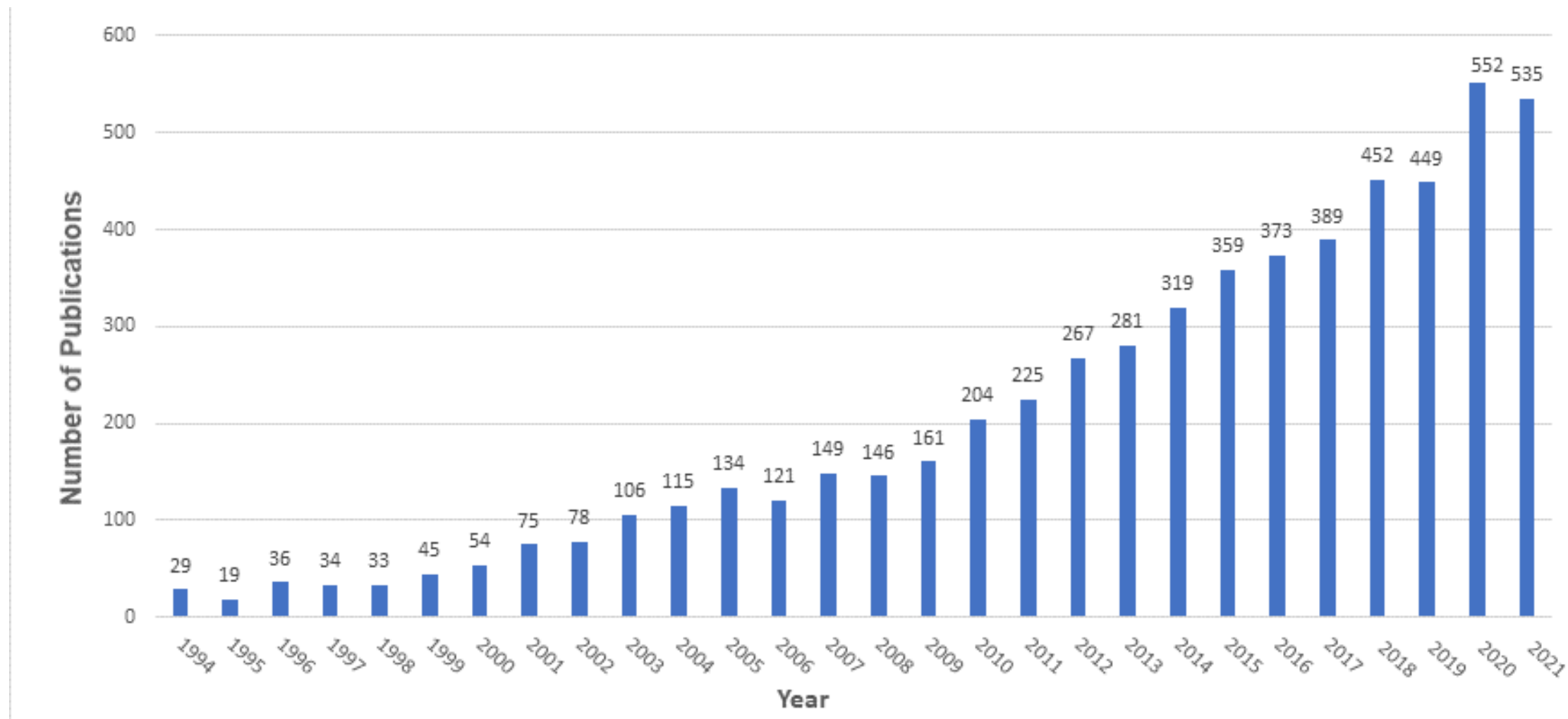
Study Name	Drug	Indication
HOPE	Ramipril	Secondary CV prevention
RESOLVD / CHARM	Candesartan	Heart Failure
	Metoprolol CR	Heart Failure

*Note that these & many other trials have also directly caused changes in international clinical practice guidelines*

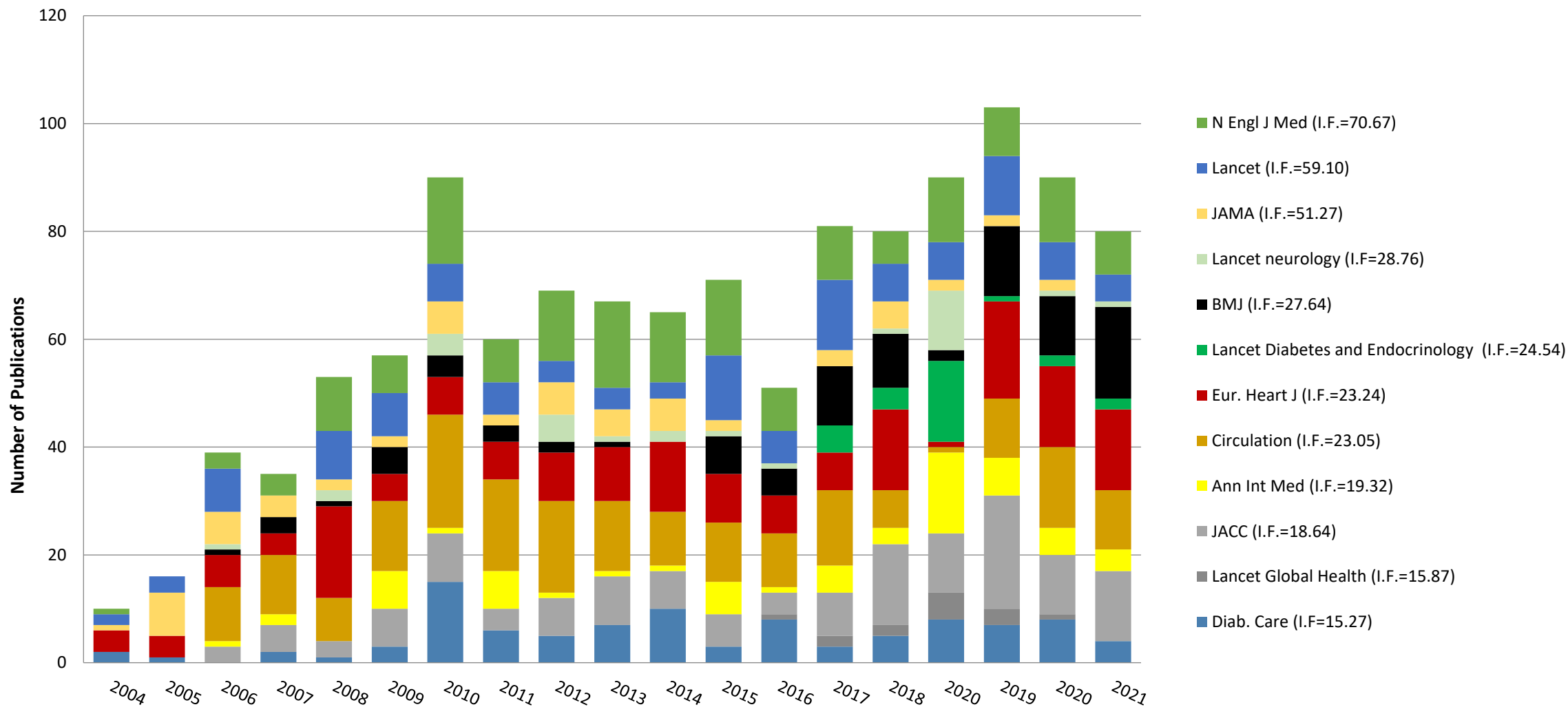
ONTARGET / TRANSCEND	Telmisartan	Prevention of CV Disease
RE-LY	Dabigatran	Prevention of Stroke in AF
AVERROES	Apixaban	Prevention of Stroke in AF
COMPASS	Rivaroxaban	CAD / PAD
REWIND	Dulaglutide	Primary prevention of MACE, stroke
ANNEXa-4	Andexanet Alfa	Anti-coagulation reversal for life-threatening bleed



# Publications Until 2021



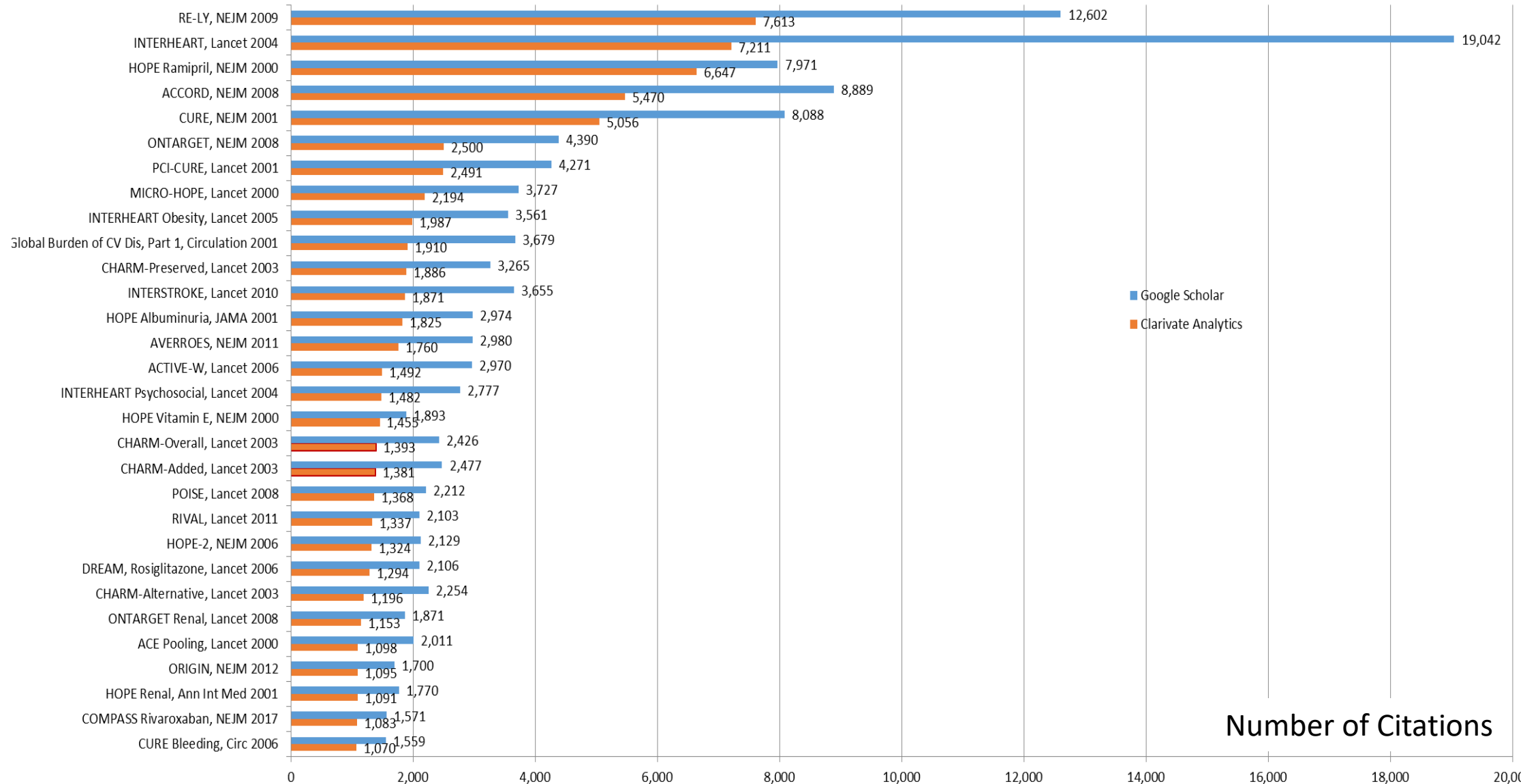
# High Impact Publications





# Publications with > 1000 Citations

As of Jan 1, 2022



# Summary

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- PHRI's research spans a broad spectrum of health
- It has identified:
  - *New therapies to prevent & manage a broad range of diseases*
  - *New ways to detect diseases*
  - *New biomarkers for drugs & diseases*
  - *Diet, environmental, & epidemiologic risk factors for diseases*
  - *New paradigms of disease*
- It has transformed health care in Canada & globally over 20 years
- Contributed to benefitting tens of millions of people globally



# Comparison of the cumulative impact of different interventions on CVD mortality

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Type of cardiovascular disease intervention	Cumulative CVD averted, 2023-2050
Primary + secondary prevention FDCs/polypill (with aspirin), 90% coverage*	<b>140 million</b>
Primary + secondary prevention FDCs (without aspirin/polypill), 90% coverage	<b>120 million</b>
Hypertension treatment, 80% coverage	61 million
Full implementation of WHO tobacco control policies by 2023	20 million





# Population Health Research Institute

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HEALTH THROUGH KNOWLEDGE

Explore new areas & new approaches...

Seek out new cures & new paradigms...

And boldly go where no one has gone before!