



Division of Clinical Research & Training

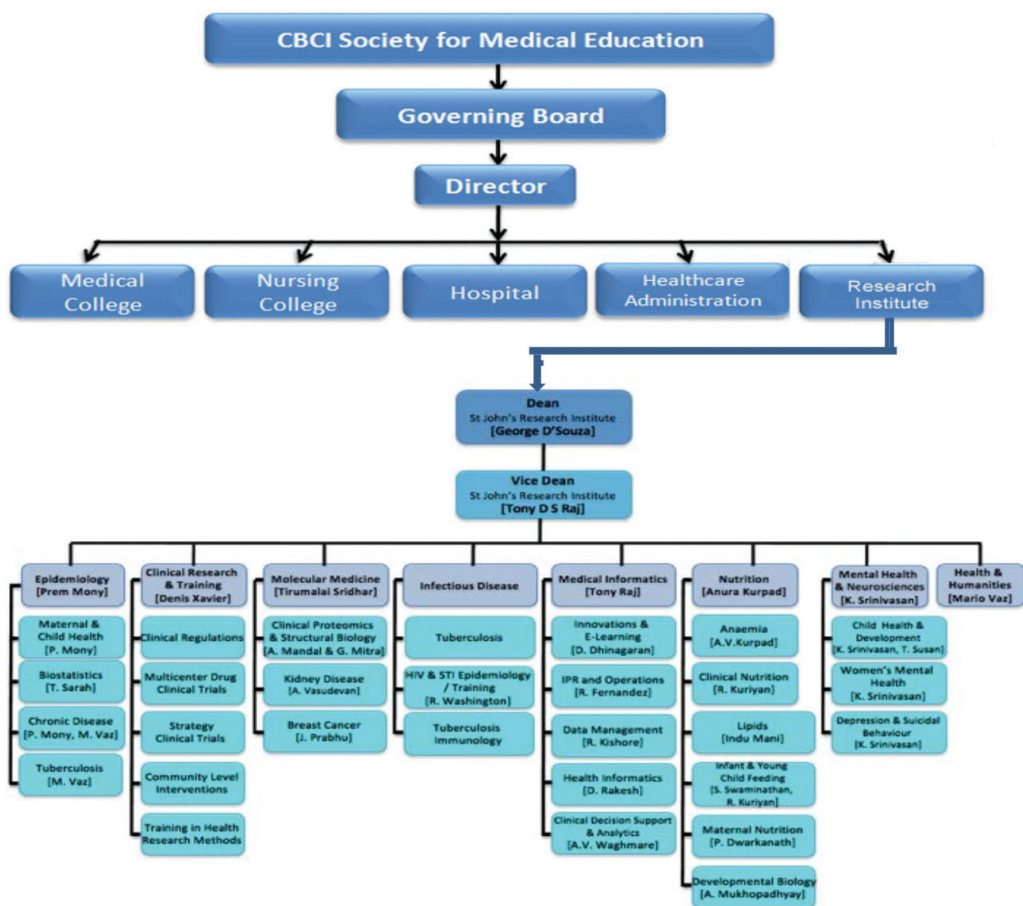


St. John's Research Institute
Bangalore, India

Division of Clinical Research & Training

Our Mission

- To develop and conduct Clinical Research with special relevance to India and other developing countries
- To achieve world class research standards at 'realistic' costs
- To transform knowledge to better health through advocacy and policy change



Division of Clinical Research & Training

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About us

The Division of Clinical Research and Training is a part of St. John's Research Institute, established in the year 2000. The St. John's Research Institute (**SJRI**) is one of four institutions of the St John's National Academy of Health Sciences. The other institutions are St. John's Medical College Hospital with **1200 beds**, St. John's Medical College ranked one among the **top ten Medical Colleges** in India and St. John's College of Nursing.

From its inception 50 years ago (in 1963) St. John's set before it an ideal of excellence in academic training as well as service to society.

In 2000, St. John's commitment to excellence in research led to setting up an Institute dedicated to research and capacity development.

The Research Institute has 8 Divisions:

1. **Clinical Research and Training**
2. **Epidemiology and Biostatistics**
3. **Health and Humanities**
4. **Infectious Diseases**
5. **Medical Informatics**
6. **Mental Health and Neurosciences**
7. **Molecular Medicine**
8. **Nutrition**

The Division of Clinical Research and Training designs and conducts national and international clinical trials and observational studies in cardiovascular disease (CVD). Our collaboration includes about 200 institutions - the largest network of academic clinical researchers in India. We have recruited more than 60,000 subjects in different studies in just over a decade. Most of these are investigator-initiated studies funded

by peer-reviewed grants while some are supported by Industry.

Our studies have been published in leading journals including the Lancet, JAMA, NEJM, Nature Cardiovascular, American Heart Journal, Circulation, European Heart Journal, Indian Heart Journal, JAPI, etc. (See Pages)

To focus on **knowledge translational research and training in health research methods**, we recently formed the Indian Cardiovascular Research and Advocacy Group (ICRAG) in collaboration with McMaster University, Canada and three other Institutions in India (Rajah Muthaiah, Annamalai Nagar, Mahatma Gandhi Institute, Sevagram and Fortis Escorts Hospital, Jaipur). We are recognised as a Center of Excellence by the National Heart Lung Blood Institute (NHLBI) National Institute of Health (NIH, USA) and United Health to counter chronic diseases in developing countries.

Our Team

DCRT has a dedicated and highly qualified Team for the conduct of Clinical Research. The team is led by **Dr. Prem Pais** and **Dr. Denis Xavier**.



Dr. Prem Pais M.D.,
Professor of Medicine
Chief Mentor, Division of Clinical Research & Training

Dr. Prem Pais, is one of India’s eminent clinical researchers in preventive cardiology. He is on the review board of the Indian Council of Medical Research (ICMR) and a reviewer of the Davidson’s Textbook of Internal Medicine. He is the steering committee member and Principal Investigator of several large registries, case control studies and clinical trials that have identified risk factors and defined the evidence for the treatment of cardiovascular disease. Dr. Pais is the co-chair of the NIH Centre of Excellence to counter chronic diseases in developing countries.



Dr. Denis Xavier M.D., M.Sc (Clin Epi)
Vice Dean (PG)
Professor and Head of Pharmacology, SJMC
Head, Division of Clinical Research & Training

He has helped understand the risk factors for CVD (INTERHEART, INTERSTROKE case control studies), practice patterns and outcomes in CVD (CREATE, INSPIRE, RELY registries) and the effect of antiplatelet, anticoagulants, antihypertensive, lipid lowering drugs and a Polypill (POISE, VITATOPS, PROFESS, ASPIRE, OASIS, TIPS, TIPS-3, TIPS-K, HOPE-3, ARISTOTLE, RECREATE, AVVEROES). He was the Principal Investigator of the ‘Centre of Excellence’ award by the NHLBI (NIH, USA) and United Health under their Global Health Initiative program

Academic Collaborators:

 COLUMBIA UNIVERSITY	 DUKE UNIVERSITY	 National Institutes of Health Fogarty International Center		
 Population Health Research Institute	 Royal Perth Hospital	 STANFORD UNIVERSITY	 THE GEORGE INSTITUTE for Global Health	 THE UNIVERSITY OF SYDNEY

(2009-2014). He conducted knowledge translational studies and managing comprehensive training programs for about 1100 health professionals in health research methods. He was the Principal Investigator of the SPREAD trial evaluating the impact of community health worker based interventions in the secondary prevention of acute coronary syndromes (14 centers, 800 patients) and co-investigator of the PREPARE trial, a cluster RCT evaluating the impact of community health workers in primary prevention among rural communities. He was also the Principal Investigator of INSPIRE a 10,500 patient Stroke Registry from all regions of India.



Dr. Padmini Devi M.D.,

Associate Professor of Pharmacology, SJMC

Co Investigator for MARS and AMEND program. A core member of the Health Research Methodologies training team. Her areas of interest include diabetes and cardiovascular research.



Dr. Atiya Faruqui, MD

Associate Professor of Pharmacology, SJMC

Co-investigator in observational studies in cardiovascular disease- FRIENDS Study (primary care physicians) and SPECTRUM (secondary and tertiary care physicians); VISION Study (A cohort study in Peri-operative cardiac Ischaemia). She is currently involved in areas of health promotion, coordinating the development of a website, as well as working with primary care physicians.



Dr. Mangala Rao, MD

Assistant Professor of Pharmacology, SJMC

Co-investigator of a Systematic Review of all the cardiovascular studies conducted in India, involved in an observational study in primary care physicians (FRIENDS). She is the Project officer for the multi centric POISE 2 (PeriOperative Ischemic Evaluation) trial. She is currently involved in looking at the practice patterns for chronic diseases among primary care physicians.

Government Collaborators:



Dr. Deepak Kamath M.D.,

Assistant Professor of Pharmacology, SJMC

Co-Investigator for the TIPS-3 polypill trial and IMPACT-AF. He is also the trial manager for APOLLO, HOPE-3 and other large trials.



Godfreeda Denis

B.Sc (Microbiology), MSc (Clinical Trials & Regulatory affairs)

Senior Coordinator in the Division of Clinical Research and Training from 2001. Her interest includes coordination of multicentre drug trials, registries and observation studies in Cardiovascular disease. She also heads the monitoring group.



Nandini Mathur

M.Sc (Microbiology)

Senior Study Coordinator from 2004 and has experience in coordinating large multicentre randomized clinical trials, case control studies and registries. She is also the program coordinator of the Health Research Methodologies & Training under mentorship program conducted by the NIH-NHLBI-United Health funded Centre of Excellence as well as of Pfizer's Preferred Research Centre.



Our Contribution

Clinical Research

1. Generated evidence from a developing country on risk factors and practice patterns for Acute MI
 - Indian Case control study and INTERHEART
 - CREATE Registry
2. Generated evidence on risk factors and treatments for Stroke
 - INTERSTROKE, INSPIRE
3. Contributed to Global RCTs that have impacted clinical practice
 - CREATE Study – use of LMWH & GIK in Acute MI
 - OASIS 5 & 6 – use of fondaparinux in ACS
 - RELY, ARISTOTLE - Novel anticoagulants in atrial fibrillation

Trials in Health System Research

- PRoFESS – largest secondary stroke prevention study
- POISE 1 & 2 –largest clinical trials evaluating treatments in perioperative ischemia
- TIPS -1, 2 & 3 –RCTs evaluating a “Polypill”
- PREPARE-Randomized trial evaluating primary prevention strategies at the community level.
- SPREAD - Randomized trial evaluating post discharge interventions in ACS patients.

Training

- Research methodology course for medical professionals
- Trial management course for research coordinators
- Clinical training for Biomedical Industry

Industry Collaborators:

Our Capacity for Clinical Research

- At about 200 sites across the country and about 500 investigators.
- Team of trained & experienced coordinators and research assistants, about 50 at St. John's and 500 across the country.
- Capacity to coordinate large multicentre global clinical trials
- Regulatory Approval - National & International



Clinical Research Assistants

- Investigational Product – Importation, storage, redistribution & accounting
- A State of the Art Storage facility which is access controlled and temperature controlled to store
- The store distributes drugs and materials to over 500 sites across India.
- Sample Storage



Clinical Trial Supplies

- A Bio-repository for long term storage of biological samples. It has the capacity to store 80,000 samples.



Sample Storage

❖ Data Management

- Develop Case Report Forms
- Set up database
- Handle data from over 100 sites (receive forms, enter data, generate queries, resolve queries, rolling database lock)



Data Management Team

❖ Bio Statistics

- Consultant for - study design and methodologies, Questionnaire preparation and database development
- Carries out - Sample size calculation, Randomization schedule preparation, Data quality checks, Statistical analysis and result interpretation and contribute to manuscript preparation.



Bio Statistics Team

Two dedicated servers that can support databases. It has facilitated remote data capture for global multicentre clinical trial. Over 15 Years trained 150 sites across the country in data capture, supported central databases with resolution of queries in case report forms.

We have licensed **Promasys**, a versatile database management system. This uses the study life cycle concept, creates data capture forms, build edit checks and overall enhances efficiency in data management.



Data Server

Research Training at DCRT

We conduct various training programs in Health Research Methods for physicians and Research management for research support staff. We are a National Institutes of Health (NIH, USA) Centre of Excellence (CoE) to conduct training in health research methods. We are also recognized as a Preferred Research Centre (PRC) by Pfizer, to conduct training in clinical research.

To date, we have trained 1188 participants from 60 institutions spread across 33 cities in 7 countries.

1. Two-year Research training through mentorship (2009, 2011, 2011-2013)
2. Two week course in Health Research Methodology (2009, 2011)
3. Two week course in Advanced Health Research Methodology (2010, 2012)
4. Six months in Undergraduate Research Mentorship (2009, 2010, 2011, 2012, 2013)
5. Three days course in Clinical Research Management (2011, 2013)
6. Three days course in Research Methodology & Good Clinical Practice for physicians (2010, 2012)
7. One week International course in Health Research Methodology & Evidence Based Medicine (2013, 2014, 2015)



8. One day Nurses Research Workshop in collaboration with Global Research Nurses network (2013)
9. Three day course on Data Management and Biostatistics for health professionals (2014).

10. Two days workshop for setting up Non-Communicable diseases Prevention and Training units (NPTU's) (2014)
11. Three days training program on clinical diabetes and Health Research Methodology (2014, 2015)
12. One day program on Accreditation for Clinical Research-Awareness and expectation (2015)
13. One week seminar on World Heart Federation emerging leader think tank seminar (2016)
14. One week International course in Health Research Methodology & Evidence Based Medicine (2016)

Most of our training is conducted in collaboration with PHRI, McMaster

University, Canada. We initiated a undergraduate medical student's mentorship program at MGIMS, Sevagram and at St. John's which completed 6 batches (2009-2015).

We are a pre vetted site for the Fogarty Fellowship program. Health professionals can apply to conduct research at St. John's with financial and technical support from the Fogarty center based in the USA.

The PRC activities at St. John's are overseen by a Steering Committee which includes members from St. John's and Pfizer India Ltd. The training activities include two short-term courses for Clinicians in Health Research Methods and Good Clinical Practice (GCP), and Site Research Coordinators in Clinical Research Management and GCP.



Year 2009 No of participants - 24



Year 2010 No of Participants - 33



Year 2011
No of Participants - 31



Year 2012
No of Participants - 29

Ongoing Studies

1. TIPS-3 - A clinical trial of polypill in primary prevention setting to reduce cardiovascular outcomes (Global – 5000/India– 2000)
2. MACE Registry- A nation wide observational study in Acute Coronary Syndrome (ACS) (India-10,000+)
3. AMEND PHASE II- An ongoing program (research, patient management strategies) to prevent & manage CVDs in India (India-10,000)
4. STABILITY-RCT to evaluate the effects of chronic treatment with darapladib in high-risk patients with chronic CHD(Global – 15,828/ India-398)
5. IMPACT- A clustered randomized controlled trial to improve stroke in patients with atrial fibrillation by improving treatment with anticoagulants (Global –1800/ India-494)
6. HF-CHW- Health workers to enhance adherence to treatment and self care among heart failure patients (India-30)
7. ODYSSEY- A phase III trial to evaluate the lipid lowering efficacy of a monoclonal antibody that blocks PCSKA receptors (Global-18,000/ India-521)
8. MANAGE- Randomized clinical trial of Dabigatran in peri operative myocardial infraction (Global-1750/ India- 250)
9. CANTOS- RCT of subcutaneous canakinumab in the post-MI with elevated hsCRP (Global- 17,200/ India-1,200)
10. PROGRESS- Policy and peer mentor intervention proGrams on cardiovascular disease at work Sites in 3 South Asian countries (India- 3,000)
11. AUGUSTUS- Apixaban versus Vitamin K Antagonist in Patients with Atrial Fibrillation and Acute Coronary Syndrome and/ or Percutaneous Coronary Intervention (Global 4,600/ Inida- 400)
12. TREAT- Compare ticagrelor with clopidogrel in STEMI patients treated with fibrinolytic therapy within 24 hours (Global- 4,000/ India-600)
13. BP Home Monitoring- Perception of patients and healthcare providers on patients' self management of blood pressure: A pilot mixed methods study (Global- 150/ India- 25)
14. PANACEA-HF- Piloting a quality improvement intervention for optimal medical management of patients with chronic Heart failure (India- 230)

Completed Studies

1. HOPE-3 - A trial to evaluate the safety and efficacy of rosuvastatin and cadesartan/hydrochlorothiazide and their combinations in middle aged people, who are at intermediate risk for vascular events (Global-11,000/India - 2000)
2. MACE Registry - A nation wide observational study in Acute Coronary Syndrome (ACS) (India - 10,000+)
3. VISION - A large cohort study to evaluate major vascular events in patients undergoing non-cardiac surgery (Global- 40,000/India - 4000, JAMA 2012)
4. AMEND - An ongoing program (research, patient management strategies) to prevent & manage CVDs in India (India - 10,000)
5. INSPIRE - An observational study to determine etiologies, clinical practice patterns and outcomes of strokes in India (India - 10,500)
6. SPREAD - A randomized trial comparing post discharge interventions by CHWs to standard care in ACS patients (India - 800)
7. ICMR - A case control study to study the risk factors for AMI in Indians (India - 2000)
8. INTERHEART - A case control study of risk factors for AMI in all regions of the world (Global-29,972 / India - 3000, Lancet 2004 / JAMA 2006)
9. CREATE - RCT of Reviparin and or GIK Vs placebo in AMI (Global - 20,201/India - 8060, JAMA 2004 / AHJ 2004)
10. POISE - Metoprolol vs placebo in Peri Operative Ischemia (Global -8351/India - 777, Lancet 2008)
11. CURRENT - RCT of standard vs high dose of clopidogrel in unstable angina or non-ST segment elevation (Global - 25000 /India -2250)
12. PrePare-Aclusterrandomizedtrial to evaluate primary prevention strategies at the community level to promote treatment adherence to prevent cardiovascular disease (India - 27,000)
13. CREATE ACS Registry - To examine the treatment patterns and outcome of ACS patients in India (Global and India - 20,468, Lancet 2008)
14. POISE - Metoprolol vs placebo in Peri Operative Ischemia (Global - 8351/India - 777, Lancet 2008)
15. PRoFESS - RCT of Dipyridamole, Clopidogrel & Telmisartan in ischemic stroke (Global - 20,333 /India - 1,620, NEJM 2008)
16. TIMACS - RCT of timing of Intervention in ACS (Global - 3031 /India - 31, AHA 2008)
17. OASIS 5 - RCT of fondaparinux Vs enoxaparin in unstable/non-ST-segment elevation MI (Global-20,078 /India - 522, NEJM 2006)

18. OASIS 6 - RCT of Fondaparinux Vs placebo in STEMI (Global-12,092 /India -1444, JAMA 2007)
19. RELY - RCT of dabigatrin Vs warfarin in atrial fibrillation (Global - 18113 /India - 578, NEJM, Lancet)
20. VITATOPS - RCT of multi-vitamins vs placebo in secondary stroke prevention (Global - 8167 /India - 1421, Int J of Stroke, 2007)
21. AVVEROES - RCT of apixaban Vs ASA to prevent stroke in atrial fibrillation patients who had failed or are unsuitable for Vit- K antagonist (Global - 5000 /India- 203, NEJM 2011)
22. ARISTOTLE - RCT to evaluate apixaban in preventing stroke and systemic embolism in atrial fibrillation (Global - 18,000/ India- 601, NEJM 2011)
23. RECREATE - RCT of Intensive insulin therapy targeting normoglycemia in acute MI (Global - 287/India - 273, Diab Care 2011)
24. RIVAL - RCT of radial versus femoral PCI Access in Unstable Angina or Myocardial Infarction (Global - 7000/India - 340, JAMA 2012)
25. INTERSTROKE - A case control study to determine the importance of conventional and emerging risk factors for stroke (Global - 24,000/India - 5000, Lancet 2011)
26. APOLLO-A randomized controlled trial of aliskiren in the prevention of major cardiovascular events in elderly people (Global - 11,000/ India - 1600)
27. APPRAISE 2 - A trial to evaluate apixaban in patients with recent ACS (Global - 10,000/India - 1078)
28. RELY-AF Registry - An observational study to determine predisposing conditions & regional variations in atrial fibrillation/ flutter (Global -15,000/India - 2500)
29. ASPIRE - A randomized controlled trial of low-dose aspirin after initial anticoagulation to prevent the recurrence of venous thromboembolism (Global - 2000/India - 400)
30. FRIENDS - A Prospective Study of Practice Patterns and Outcomes in Chronic Disease in an Urban Family Practice Setting (India - 2000)
31. SPECTRUM - Situational analysis of the practice patterns in cardiovascular disease in all regions of India (India - 1300)
32. OASIS-8/ FUTURA - RCT to evaluate standard Vs low dose adjunctive i.v. UFH in patients undergoing PCI (Global - 2000 / India - 500, JAMA 2010)
33. MARS - A five arm RCT of amlodipine + metoprolol XL & amlodipine as individual components in Indians (India - 400, Blood Pressure 2011)

34. POLYCAP - A 9 arm RCT of a POLYCAP Vs its components in subjects with at least one CV risk factors (India – 2053, Lancet 2009)
35. TIPS-K - RCT of low strength polycap & of low strength K+ supplementation in patients with stable CVD/ ischemic heart disease (India –500)

Abbreviations:

ACS: Acute Coronary Syndrome, CHW: Community Health Worker, CVD: Cardio Vascular Disease, RCT: Randomized Controlled Trial, AMI: Acute Myocardial Infarction, MI: Myocardial Infarction, STEMI: ST-Elevation MI, UFH: Unfractionated Heparin, ASA: Aspirin, PCI: Percutaneous LMWH: Low Molecular Weight Heparin GIK: Glucose Insulin Potassium Intervention, K+: Pottassium)

Selected Publications

1. Pais P, Pogue J, Jayprakash S, Yusuf S, et al; Risk factors for acute myocardial infarction in Indians: case-control study. *Lancet* 1996. PMID: 8709733.
2. Yusuf, S., Hawken, S., Ôunpuu, S., Dans, T., Avezum, A., Lanas, F., Pais P et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study, *Lancet* 2004 - 937-952. PMID:15364185
3. Yusuf S, Mehta SR, Pais P, Xavier D, et al; CREATE-ECLA investigators and steering committee. Challenges in the conduct of large simple trials of important generic questions in resource-poor settings: the CREATE and ECLA trial program evaluating GIK (glucose, insulin and potassium) and low-molecular-weight heparin in acute myocardial infarction. *AmHeart J*. 2004 Dec;148(6):1068-78. PMID:15632895.
4. Yusuf S, Mehta SR, Xavier D, Pais P, Zhu J, Liu L, et al; CREATE Trial Group Investigators. Effects of reviparin, a low-molecular-weight heparin, on mortality, reinfarction, and strokes in patients with acute myocardial infarction presenting with ST-segment elevation. *JAMA*. 2005 Jan 26;293(4):427-35. PMID: 15671427.
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6. Yusuf S, Hawken S, Ounpuu S, et al; INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet*. 2005 PMID: 16271645.
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10. Cook D, Moore-Cox A, Xavier D, et al; Randomized trials in vulnerable populations. *Clin Trials*. 2008; PMID: 18283082.
11. Oldgren J, Wallentin L, Afzal R, Pais P, Xavier D, Yusuf S; OASIS-6 Investigators. Effects of fondaparinux in patients with ST-segment elevation acute myocardial infarction not receiving reperfusion treatment. *Eur Heart J*. 2008 PMID: 18084015.
12. Xavier D, Devereaux PJ, Pais P, Yusuf S. Polypharmacotherapy for primary prevention of cardiovascular disease. *Indian Heart J*. 2008 PMID: 19359761.
13. Xavier D, Pais P, P J Devereaux, Changchun Xie, D Prabhakaran, K Srinath Reddy, Rajeev Gupta, Prashant Joshi, Prafulla Kerkar, S Thanikachalam, K K Haridas, T M Jaison, Sudhir Naik, A K Maity, Salim Yusuf et al; CREATE registry investigators. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. *Lancet*. 2008 PMID: 18440425.
14. Devereaux PJ, Yang H, Yusuf S, Xavier D, Pais P, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. *Lancet*. 2008 May PMID: 18479744.
15. Sacco RL, Diener HC, Yusuf S, Pais P et al; PROfESS Study Group. Aspirin and extended-release dipyridamole versus clopidogrel for recurrent stroke. *N Engl J Med*. 2008 PMID: 18753638.
16. Yusuf S, Diener, Pais P, et al; PROfESS Study Group. Telmisartan to prevent recurrent stroke and cardiovascular events. *N Engl J Med*. 2008 Sep 18;359(12):1225-37. Epub 2008 Aug 27. PMID: 18753639; Central PMCID: PMC2714258.
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