

BIOGRAPHICAL SKETCH

NAME: **Denis Xavier**

eRA COMMONS USER NAME: DENISXAVIER

POSITION TITLE:

Vice Dean (PG), Professor & Head, Pharmacology,
Head, Division of Clinical Research Training, St. John's Research Institute, Bangalore

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
St. John's Medical College, Bangalore, IN	MBBS	1991	Medicine, Surgery & Obstetrics
St. John's Medical College, Bangalore, IN	MD	1997	Pharmacology
McMaster University Hamilton, Canada	MSc	2007	Clinical Epidemiology & Biostatistics

A. Personal statement.

I am Professor and Head, Department of Pharmacology, Vice Dean - PG and Head, Division of Clinical Research & Training at St. John's Medical College and Research Institute, Bangalore, India. With Dr. Pais I helped set up the Clinical Research Unit at St. John's in 1999 and a large collaboration of Cardiovascular Clinical Investigators in over 180 centers in India. From over 50 studies, we have to date recruited over 95,000 subjects.

In close to 2 decades I acquired the training, developed the expertise and leadership to conduct nation-wide research in cardiovascular research (CVD). After contributing to understand the **burden and risk factors** for CVD (acute myocardial infarction and strokes), I undertook several drug clinical trials with a particular focus on Low and Middle Income Countries. In the last 8 years I have begun work on **health systems** to address critical concerns of health care access. As PI of the 'Centre of Excellence' award by the NHLBI (NIH, USA) (2009-2014) I led 3 knowledge translational studies. I am the Principal Investigator of PROGRESS, funded by the UK-MRC and Wellcome Trust to evaluate innovative strategies to reduce risk of heart disease and strokes at work places in 3 South Asian countries.

Personally I am keen on training the next generation in health research methods and we organize different types of courses and workshops. Since 8 years we trained over 1500 faculty and graduate students from all regions of India and 7 countries in Asia and Africa.

My team and I are set to a conduct a study on generating high quality evidence on controlling hypertension utilizing innovative and low cost strategies. Thereafter to scale up feasible interventions at the national level using multi-stake holder engagement and policy dialogues. This proposal is also an opportunity to train faculty and graduate students in a relatively new, but important area of implementation research from all regions of India.

B. Positions and Honors.

- Vice Dean (Post Graduate), Department of Pharmacology St. John's Medical College, Bangalore, since 2016; faculty at St. John's since 1998
- Professor & Head, Pharmacology, St. John's Medical College, Bangalore, since 2008
- Head, Div of Clinical Research & Training, St. John's since 2014, coordinator since 1999.
- Fellow, Cardiovascular Epidemiology and Prevention World Heart Federation, 2003
- HOPE-Canada Research Scholar, PHRI & McMaster University, Canada 2005-2007.
- Reviewer: Lancet, European Heart Journal, Science Translational Medicine, Indian Council of Medical Research and Drugs Controller General of India
- Chairperson, Narayana Health Academic Ethics Committee.
- Member, Ethics Committee, National Institute of Mental Health and Neurosciences (NIMHANS)

C. Contribution to science

When I started my research career in 1999, there was little knowledge on the rates, treatments and outcomes for cardiovascular disease (CVD) from a national perspective. First I set out to form a team to answer questions at the national level in CVD. We conducted the first large multi center study on treatments and outcomes of acute coronary syndromes among over 20,468 patients in 89 centers in all regions of India (Lancet 2008, Ref-1, Role PI). We also studied the causes of myocardial infarction (INTERHEART) and strokes (INTERSTROKE Refs, 6, 26 Role PI for India). Total subjects in our **observational studies** 52,086. Then I set out to conduct **drug clinical trials** in CVD (over 30, recruiting 35,173).

We also began to research **better systems to treat patients** with CVD, pioneering research on a Polypill (refs 2, 3, 16, 20), and health systems interventions to treat patients with atrial fibrillation (IMPACT – Ongoing support-3, Role PI for India) and reducing CVD risk in worksites (PROGRESS ongoing support-2, role PI).

I led the NHLBI (NIH) **Center of Excellence Program** (completed support-4) with a team of about 185 investigators and research staff across India and completed three knowledge translation studies; a RCT in secondary prevention (SPREAD, Ref 23, role PI), a rural cluster randomized trial in primary prevention (PREAPRE, Ref 18, Role-Co Inv) and a 65 centre stroke study on 11,001 patients, (Role PI, publication being submitted).

I am keen on building research capacity among the next generation. After training in clinical epidemiology and biostatistics at McMaster University in Canada, I set up a 2-week and then a 1-week course in Health Research Methods. This includes lectures, journal clubs, hands-on statistical analysis and project presentations. I also organize shorter courses and longer mentorship based training for young faculty (2-year) and UG students (8-12 months). Since 2008 we trained over 1,500 from all regions of India and 7 other countries in Asia and Africa.

My future focus is to **impact policy changes to improve outcomes in CVD** through high quality research, policy dialogues and other advocacy activities in India and other similar Low and Middle Income countries in Asia and Africa.

D. Selected peer-reviewed publications.

1. **Xavier D**, Pais P, Devereaux PJ, Xie C, Prabhakaran D, Reddy KS, et al. Treatment and outcomes of acute coronary syndromes in India (CREATE): a prospective analysis of registry data. **Lancet**. 2008 Apr 26;371(9622):1435-42.
2. Xavier D, Pais P, Sigamani A, Pogue J, Afzal R, Yusuf S. The need to test the theories behind the Polypill: rationale behind the Indian Polycap Study. **Nat Clin Pract Cardiovasc Med**. 2009 Feb;6(2):96-7.
3. **Xavier D**, Devereaux PJ, Goyal A, Pais P, Yusuf S. Polypharmacotherapy for primary prevention of cardiovascular disease. **Indian Heart J**. 2008 Mar-Apr;60(2 Suppl B):B29-33.
4. O'Donnell MJ, **Xavier D**, Liu L, Zhang H, Chin SL, Rao-Melacini P, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. **Lancet**. 2010 Jul 10;376(9735):112-
5. Pais P, **Xavier D**. Heart failure in India: an area of darkness. **Natl Med J India**. 2011 Jan-Feb;24(1):53.
6. O'Donnell M, **Xavier D**, Diener C, Sacco R, Lisheng L, Zhang H, et al. Rationale and design of INTERSTROKE: a global case-control study of risk factors for stroke. **Neuroepidemiology**. 2010;35(1):36-44.
7. Karthikeyan G, **Xavier D**, Prabhakaran D, Pais P. Perspectives on the management of coronary artery disease in India. **Heart**. 2007 Nov;93(11):1334-8
8. Gupta R, Guptha S, Joshi R, **Xavier D**. Translating evidence into policy for cardiovascular disease control in India. **Health Res Policy Syst**. 2011;9:8.
9. Devereaux PJ, **Xavier D**, Pogue J, Guyatt G, Sigamani A, Garutti I, et al. Characteristics and short-term prognosis of perioperative myocardial infarction in patients undergoing noncardiac surgery: a cohort study. **Ann Intern Med**. 2011 Apr 19;154(8):523-8.
10. Cerqueira MT, Cravioto A, Dianis N, Ghannem H, Levitt N, Yan LL, **Xavier D** et al. Global response to non-communicable disease. **BMJ**. 2011;342:d3823.
11. Lonn E, Bosch J, Teo KK, Pais P, **Xavier D**, Yusuf S. The polypill in the prevention of cardiovascular diseases: key concepts, current status, challenges, and future directions. **Circulation**. 2010 Nov 16;122(20):2078-88.
12. Diener HC, Connolly SJ, Ezekowitz MD, Wallentin L, Reilly PA, **Xavier D**, Yang S, et al. Dabigatran compared with warfarin in patients with atrial fibrillation and previous transient ischaemic attack or stroke: a subgroup analysis of the RE-LY trial. **Lancet Neurol**. 2010 Dec;9(12):1157-63.
13. Yusuf S, Pais P, Afzal R, **Xavier D**, Teo K, Eikelboom J, et al. Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomised trial. **Lancet**. 2009 Apr 18;373(9672):1341-51.
14. Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC, et al. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. **Lancet**. 2008 May 31;371(9627):1839-47.
15. Cook D, Moore-Cox A, **Xavier D**, Lauzier F, Roberts I. Randomized trials in vulnerable populations. **Clin Trials**. 2008;5(1):61-9.

16. **Denis Xavier**, Alben Sigamani, Deepak Y. Kamath, Prem Pais. Polypill Is an Important Strategy for the Prevention of Cardiovascular Disease Risk. **Journal of Clinical and Preventive Cardiology** April 2012.
17. Timothy A. Brighton, John W. Eikelboom, Kristy Mann, Rebecca Mister, Alexander Gallus, Paul Ockelford, Harry Gibbs, Wendy Hague, **Denis Xavier**, Rafael Diaz, Adrienne Kirby, & John Simes Low-Dose Aspirin for Preventing Recurrent Venous Thromboembolism, **New Eng J Med** 2012.
18. Fathima FN, Joshi R, Agrawal T, Hegde S, **Xavier D**, Misquith D, Chidambaram N, Kalantri SP, Chow C, Islam S, Devereaux PJ, Gupta R, Pais P, Yusuf S. Rationale and design of the Primary pREvention strategies at the community level to Promote Adherence of treatments to pREvent cardiovascular diseases. **Am Heart J**. 2013.
19. Devi P, **Xavier D**, Sigamani A, Pandey S, Thomas T, Murthy S, Sharma K, Bosco B, Mehta K, Joshi S, Gupta R, Singh G, Hiremath J, Ds C, Nambiar A, Pais P. Effect of fixed dose combinations of metoprolol and amlodipine in essential hypertension: MARS--a randomized controlled trial. **Blood Press**. 2011 Dec;20 Suppl 2:5-12.
20. Yusuf S, Attaran A, Bosch J, Joseph P, Lonn E, McCready T, Mente A, Nieuwlaat R, Pais P, Rodgers A, Schwalm JD, Smith R, Teo K, **Xavier D**. Combination pharmacotherapy to prevent cardiovascular disease: present status and challenges. **Eur Heart J**. 2014 Feb;35(6):353-64. PubMed PMID:24288261
21. P.J. Devereaux, M. Mrkobrada, D.I. Sessler, A. Sigamani, **D. Xavier**, S. Pettit, S. Chrolavicius, and S. Yusuf et al, for the POISE-2 Investigators. Aspirin in Patients Undergoing Noncardiac Surgery. **The New England Journal of Medicine**, 31 March 2014. PMID: 24679062
22. Mangala Rao, **Denis Xavier**, Padmini Devi, Alben Sigamani, Atiya Faruqui, Rajeev Gupta, Prafulla Kerkar, Rajendra Kumar Jain, Rajnish Joshi, N Chidambaram, Daya Sagar Rao, S Thanikachalam, SS Iyengar, Kiron Verghese, V Mohan, Prem Pais: Prevalence, treatments and outcomes of coronary artery disease in Indians: A systematic review. **Indian Heart Journal**, August 2015.
23. **Xavier D**, Gupta R, Sigamani A, Kamath DY, Devereaux PJ, George N, Joshi R, Pogue J, Pais P, Yusuf S. Community health worker based intervention for adherence to medications and lifestyle after Acute Coronary Syndrome: A randomized controlled trial. **The Lancet Diabetes & Endocrinology** 2016
24. Lonn EM, Bosch J, López-Jaramillo P, Zhu J, Liu L, Pais P, Diaz R, **Xavier D**, Sliwa K, Dans A, et al. Blood-Pressure Lowering in Intermediate-Risk Persons without Cardiovascular Disease. **N Engl J Med** 2016.
25. Yusuf S, Lonn E, Pais P, Bosch J, López-Jaramillo P, Zhu J, **Xavier D**, Avezum A, Leiter LA, et al. Blood -Pressure and Cholesterol Lowering in persons without Cardiovascular Disease **N Engl J Med** 2016.
26. Martin J O'Donnell, Siu Lim Chin, Sumathy Rangarajan, **Denis Xavier**, Lisheng Liu, Hongye Zhang, Prem Pais, Salim Yusuf, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE) **Lancet** 2016.

E. Research Support

Ongoing Research Support

1. 200709IR2-177449-RSB-CEBA-38611, CIHR, Canada, 2008-2015 **Funding:** CD\$5,797,254
Heart Outcome prevention evaluation (HOPE 3): international multi center trial of BP and lipid lowering in moderate risk of CVD with candesartan and rosuvastatin
Role: National Coordinator and Co Principal Investigator for India
2. MR/M019624/1, UK –MRC, DFID and Wellcome Trust 2015–2016; funding GBP136,373
Policy and peermentOr Intervention proGrams on cardiovasculaR disease at work Sites in 3 South Asian countries. PROGRESS
Role: Global Principal Investigator
3. EPM 5814 – DUKE University, BMS-F 2014 – 2016 **Funding:** US \$250,000
An International Multicenter cluster randomized controlled trial to imProve treatment with AntiCoagulanTs in patients with atrial fibrillation. IMPACT
Role: National Coordinator and Principal Investigator for India
4. KDE-133844 PHRI, Boehringer Ingelheim 2014-17; **Funding** CD\$ 223,979
Management of myocardial injury After NoncArdiac surGEry . MANAGE
Role: National Coordinator and Principal Investigator for India

Completed Research Support

1. MCT-50851, CIHR, Canada 2004 - 2007 **Funding:** CD \$5,306,074
PeriOperative ISChemic Evaluation study (POISE study): randomized trial of metoprolol versus placebo in patients undergoing non-cardiac surgery at moderate and high risk of a perioperative cardiac event
Role: National Coordinator and Principal Investigator for India
2. NHMRC and NHF Australia (110267, 403913, 572630, G99P0405, G02P0735, G04P1611) 2000 -2006 **Funding:** AU \$2,708,102
VITAMins TO Prevent Stroke trial (VITATOPS trail): rationale and design of a randomized trial of B- vitamin therapy in patients with recent transient ischaemic attack or stroke
Role: National Coordinator and Principal Investigator for India
3. 570967, NHMRC, Australia 2009 - 2011 **Funding:** AU \$1,916,600
ASPIRE study: Randomized trial examining the efficacy and safety of low-dose aspirin after initial anticoagulation to prevent recurrent venous thromboembolism
Role: National Coordinator and Principal Investigator for India
4. HHSN268200900025C, NHLBI, NIH, 06/08/09-06/07/14 **Funding:** US\$2,656,378
Global Health Activities in Developing Countries to combat Non-Communicable Chronic Cardiovascular and Pulmonary Diseases-Centers of Excellence (COE)
Role: Principal Investigator
5. MOP-119385, CIHR, Canada 2012 - 2016 **Funding:** CD \$3,684,006
PeriOperative ISChemic Evaluation-2 Trial (POISE-2): randomized trial to evaluate clonidine and aspirin in perioperative ischemia
Role: National Coordinator and PI for India