MASTER OF MEDICAL SCIENCE IN CLINICAL INVESTIGATION

A MASTERS DEGREE PROGRAM OFFERED BY HARVARD MEDICAL SCHOOL FOR CLINICAL AND TRANSLATIONAL INVESTIGATORS

hms.harvard.edu/mmsci
The Harvard Medical School Master of Medical Science in Clinical Investigation (MMSCI) is a two-year degree program specifically targeted to attract future world leaders in patient-oriented and translational research. The provision of outstanding training in clinical research and/or laboratory methodology is essential for the future success and development of biomedical sciences and related fields. The MMSCI curriculum embodies this goal, incorporating training in core subjects, such as epidemiology and biostatistics; implementation science, clinical trials; and translational methods such as genetics, immunology and systems biology with an innovative skills-based approach to modern pedagogy.

The primary mission of the MMSCI program, in keeping with the mission of HMS, is to play a key role in the training and development of the best and brightest students from all corners of the globe. The matriculation of students with an MMSCI degree from HMS represents a key milestone for each individual student and the beginning of exciting and productive careers as physician-scientists, clinical scholars and biomedical researchers.

I encourage you to participate in this innovative and prestigious program.

Ajay K. Singh, MBBS, FRCP (UK), MBA
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Program Overview

The Harvard Medical School Master of Medical Science in Clinical Investigation (MMSCI) degree provides world-class training in the methods and conduct of clinical discovery for future leaders in patient-oriented and translational research. This two-year program, which requires students to reside in Boston for its duration, combines innovative forms of pedagogy from leading Harvard faculty with an individual mentored research experience. This program is designed for post-graduate clinician-scientists working in clinical research at the fellowship and junior faculty level (or equivalent). Candidates holding an MD, MBBS, PhD or a comparable academic degree, are eligible to apply.

The MMSCI program provides each student with the unique opportunity to perform cutting-edge research in a Harvard-based laboratory, under the direct supervision of a Harvard mentor. Guided by a dedicated thesis committee, each student must complete two first-author manuscripts based on the work from their individual research projects. The innovative curriculum is specifically designed to deliver the theoretical and practical skills that will complement this mentored research experience.

The central pillars for delivering our fully integrated program consist of three intensive workshops across a two year span. Between each workshop, students will continue to acquire core knowledge and skills by way of longitudinal lectures and a longitudinal seminar series. In addition to the traditional learning of biostatistics, epidemiology and translational methods, our goal is to promote the development of critical thinking skills, writing and presentation skills, and leadership experience.

To complement individual learning and development, the MMSCI program places a core emphasis on practical skills and team-based approaches to clinical and translational research training. Facilitated by continual access to HMS faculty who are leaders in their field, the MMSCI structure is designed to ensure that students are equipped with the necessary tools to launch productive, fulfilling and successful research careers upon graduation.
The MMSCI program is a unique and novel learning experience. It is the perfect combination of learning theoretical concepts as well as their application in real life through a mentored research project with the highest quality faculty. In addition to its high academic profile, this master’s program is enriched by the outstanding faculty that lead it. The faculty display full-time dedication to our needs while encouraging and helping us with our difficulties along the way. The coordination team does a great job organizing every activity and is always ready to help. Finally, my class has given me the opportunity to meet colleagues from all over the world, allowing me to learn from their culture and native practice of medicine, and to become great friends with them.”

- Lourdes Perez-Chada, MD
MMSCI Student, Class of 2018
AFTER COMPLETING THIS PROGRAM, SCHOLARS WILL BE ABLE TO:

1. Construct focused research questions and formulate testable hypotheses
2. Design and implement well-designed clinical and translational research studies
3. Analyze, interpret and present clinical and translational research data

LEARNING MODEL

• **MENTORED RESEARCH EXPERIENCE:** The core feature of the MMSCI program is the mentored research experience in a Harvard-based research group. During the two years of the program, under the guidance of their primary mentor and dedicated thesis committee, each student is required to develop and execute his or her individual research projects. In order to graduate, students must submit and defend a thesis based on their mentored research experience. This should take the form of two original manuscripts (one accepted and one submitted) in which the student is first-author.

• **INTENSIVE WORKSHOPS:** The central pillars of the MMSCI program will consist of three intensive workshops and didactic sessions that are complemented by journal clubs, office hours, computer laboratory classes, team-based projects and presentations.

• **LONGITUDINAL TEACHING:** Between each workshop, further exploration of contemporary research topics will occur at weekly interactive sessions. Novel pedagogic approaches for this longitudinal series include the use of 'flipped classroom' methods, where students review and dissect learning material in advance of facilitated discussions.

• **CONTEMPORARY TOPICS IN CLINICAL INVESTIGATION:** The seminar series is designed to complement the didactic and longitudinal curriculum analyzing a database working in teams: presenting the data in figures and tables in various format (poster, short presentation, and a research presentation), as well as “state-of-the-art” talks.

• **INDIVIDUALIZED LEARNING:** Opportunities for customized learning, including new tracks both in clinical investigation and translational investigation and individualized pathways in clinical trials, comparative research, and implementation science.
Overview

The MMSCI program provides either a choice of the Clinical Investigation (CI) track with one of three optional pathways for individualized learning or the choice of the Translational Investigation Track.

CLINICAL INVESTIGATION (CI) TRACK

This track is co-led by Finnian Mc Causland and Ajay Singh who have extensive experience in both observational research and clinical trials. The track allows customized learning for students through pursuing one of three pathways: comparative research, clinical trials or implementation science.

TRANSLATIONAL INVESTIGATION (TI) TRACK

This track is co-led by Harvard Medical School faculty Rosalyn Adam, PhD and Martina McGrath, MBBCh. Both have extensive experience in bench and translational research. The translational investigation track aims to fill an unmet need in providing training for individuals pursuing a career in basic and/or translational research (i.e. in the T0 to T2 spectrum of translational investigation). Incorporating the translational track within the MMSCI program is consistent with the overall goal to train future global leaders in clinical and translational research. Bringing together students and faculty interested in clinical and translational investigation will ensure diversity of experience, skills and ideas, while promoting collaboration across the spectrum of clinical and translational research.
INNOVATION WITH INTEGRATION

The MMSCI program is specifically designed to ensure that each student is fully prepared to attain and surpass core learning objectives: to stimulate critical thinking, development of practical skills, networking and learning how to deal with uncertainty in patient-oriented research. To achieve these aims, there is a foundational first year where students enrolled in both the clinical or translational tracks learn together. In the second year, beginning with workshop 2, students in each of the tracks then customize their learning along their interests. Theory is reinforced and consolidated with case studies and laboratory exercises, while skills are developed and refined with practice-oriented tasks.

Curriculum

Mentored Research Experience
During the mentored research experience each student will have the opportunity to take the lead on clinical research projects in their individual areas of interest. Working in a Harvard-based laboratory, under the direct supervision of a primary mentor, each student is required to complete a thesis at the end of the program. This must take the form of two original manuscripts that have been submitted to a peer-reviewed journal in which the student is first-author.

The purpose of this requirement is two-fold: 1) To highlight the importance of publishing quality research in peer-reviewed academic journals; and 2) To promote excellence in the practice of scientific communication. Additional guidance and oversight is provided to each student by a thesis committee, that consists of the student, the primary mentor, one external member (i.e. someone who is not in the student’s primary laboratory and who is not directly involved in the student’s research) and a MMSCI program representative.

Clinical Data Science: Design & Analytics I
This course introduces methods for the generation and analysis of data for clinical research through seamless integration of epidemiology, biostatistics and machine learning. The course is structured in three components that correspond to the three main objectives of clinical research: description, prediction and causal inference. The descriptive component introduces different data types and study designs, summary measures (including frequency and occurrence measures) and statistical inference (hypothesis testing, confidence intervals). The predictive component introduces association measures, regression (linear as well as logistic) and other learning algorithms with applications to screening and clinical classification. The causal component introduces a causal inference (counter-factual) framework via randomized clinical trials, which covers survival analyses, sample size calculation, biases and effect heterogeneity. The course emphasizes critical thinking and practical applications, including assignments based on articles published in medical journals and a case study at the end of each week. All methods are taught along with Stata software to implement them.
**Clinical Data Science: Design and Analytics I and II**

This course extends the topics introduced in Design and Analytics I for each of the three goals of clinical research: description, prediction and causal inference. The description sessions discuss data wrangling, data visualization and unsupervised learning with a focus on clustering. The prediction sessions discuss building and evaluation of predictive models via regression and other learning algorithms. The causal inference sessions discuss advanced design of randomized clinical trials (factorial, non-inferiority, adaptive, crossover, cluster-randomized trials) and evidence synthesis using meta-analysis.

**Clinical Data Science: Comparative Effectiveness Research I**

This course introduces causal inference methodology when randomized trials are not feasible. The course focuses on the use of epidemiologic studies, electronic health records and other big data sources for comparative effectiveness and safety research. Key concepts of bias, such as confounding, selection bias and measurement bias are described via causal diagrams. Methods for confounding adjustment, including stratification, outcome regression, propensity scores, matching and standardization are introduced along with an emphasis on formulating well-defined questions in clinical research.

**Clinical Data Science: Comparative Effectiveness Research II**

This course extends the topics introduced in Comparative Effectiveness Research I. The course covers efficient epidemiologic designs such as case-control, case-cohort and case-crossover. It also dives into advanced methods for confounding adjustment (inverse probability weighting, parametric g-formula) for the comparison of sustained treatment strategies and instrumental variable estimation. The course also covers techniques for the secondary analysis of randomized clinical trials in the presence of deviations from protocol.
Drug Development, Safety and Translational Pharmacology
This course will include topics such as: How are Drugs Discovered and Developed, Case Study of the Pre-clinical Stages of Drug Development, Moving a Compound through the Drug Development Process, Good Manufacturing Practices--a Global Perspective, and Overview of Diagnostic Device Development.

Leadership and Teamwork
This course examines different aspects of working with, managing and leading a team. Lectures will discuss the skills and techniques that are needed to manage a talented group of people effectively, pilot successful collaborations within and outside a group, navigate the complexities of the institution and manage the inevitable conflicts that arise in a high-stakes environment.

“The MMSCI program attracts students from all over the world to learn the theory and develop the practical skills necessary to perform patient-oriented research. You will be immersed in an unparalleled learning environment and stimulated to think and ask questions in new and innovative ways”.

- Julie Buring, ScD
Professor of Medicine
Harvard T. H. Chan School of Public Health
Ethics in Clinical Research
This course reviews some common challenges in the conduct of patient-oriented research. Lectures examine the history and evolution of ethical codes and regulations; the role and responsibility of physicians as investigators; the preparation of research protocol applications and informed consent documents; and the challenges of conducting research involving children and adolescents.

Clinical Trials
The goals of this year long pathway comprising of two semester long courses is develop a deep understanding of how clinical trials are conceived, funded, developed (including protocol development and in the case of industry trials, industry approval process), conducted and closed out. Key topics will include different trials designs (including adaptive, point-of-care, pragmatic designs etc), trials in different settings (emergency, pediatrics, cancer, biomarker, device, etc), statistical monitoring of trials, safety issues secondary analysis of clinical trial data, committee organization and management, advanced ethics, post-marketing surveillance studies, and writing up trials for publication. Practical examples mixed with theory will be emphasized.

The course content includes lectures on study design and implementation, including different designs, endpoints, study protocol, study population, recruitment, baseline assessment, randomization, stratification and blinding. Other key issues that are covered include data analysis and sample size and power, treatment regimens and follow-up procedures, and monitoring and interim analysis plans.

Genetic Epidemiology
The goals of this course are to provide clinical researchers with the skills to: address opportunities to incorporate genetic studies to answer specific research questions; understand basic genotyping techniques; understand the basics of genetic study design and analysis; identify and use publically available databases for genetic research; and understand the principles of ethical conduct of genetic research.

Implementation Science
The goals of this year long pathway comprises of two semester long courses is to study factors that impact across multiple levels, including patient, provider, clinic, facility, organization, and often the broader community and policy environments. Topics will include the design of clinical interventions across consumer, provider, and or organizational contexts, including controlled implementation trials and hybrid effectiveness-implementation designs. The ability to conduct both quantative and/or qualitative desgins. Assessment of variations in implementation in different contexts. Developing skills in big data and machine learning methods to capture or assess data on implementation across patient-level processes/outcomes of care and value/return-on-investment measures. Further refinement of implementation strategies involving organizational and/or provider behavior change as these relate to evidence based practice. Development of provider/practice networks to conduct implementation. Learning how to use cross-disciplinary methods that address provider behavior organizational change (e.g., business, economics, policy, operations research. etc.)
TRANSLATIONAL INVESTIGATION

Students within the MMSCI tracks will have the same core courses (Mentored research, Ethics and the IRB, Design & Analytics I & II, Genetic Epi, Leadership and Teamwork and Contemporary Topics in Clinical Investigation); however, the translational investigation track will have the following individual courses:

**Investigative Models for Translational Research**

This course introduces the range of investigative models within the translational research spectrum, with emphasis on the advantages and disadvantages of each system. Introductory sessions focus on developing well-designed research questions and selecting appropriate analytic methods to interpret results. The course will consider both discovery-based hypothesis-generating as well as hypothesis-driven mechanistic studies, illustrating each with case studies. Participants will learn about the various types of model systems used for translational research, from in vitro and ex vivo approaches, to the use of animal models and human biospecimens. Lastly, commonly used bench techniques will be discussed. At the conclusion of this course, participants will have an appreciation for where translational investigation fits within the research spectrum.

**Cell and Molecular Biology in Medicine**

The goals of this course are to provide translational investigators with a broad understanding of the fundamental processes that drive cell function in health and disease. An overview of cell biology is followed by introduction to specific cell functions that play key roles in disease processes, including inflammation, angiogenesis, wound healing and fibrosis. The innate and adaptive arms of the immune system are covered, with focus on cutting edge techniques for immunological investigation. Specific disease entities including diabetes, cancer, cardiovascular and neurodegenerative diseases are explored as examples of studies in cellular and molecular medicine. Case studies will be used throughout to illustrate key points, and the course will conclude with a discussion of the therapeutic exploitation of cell biology in the pursuit of precision and personalized medicine.
Curriculum

TRANSLATIONAL INVESTIGATION

Systems Biology and Omics Analysis

The goals of this course are to introduce participants to fundamental concepts in systems biology and to provide a basis for experiments that generate large genomic, transcriptomic or proteome datasets. An introduction to DNA and RNA sequencing, as well as fundamental concepts in gene expression and regulation, is followed by exploration of experimental design for generation of large datasets and their integration using systems biology principles. Mass spectrometry-based proteomics and related technologies are discussed in the context of biomarker discovery and the course concludes with investigation of the microbiome and its relevance in health and disease. Throughout the course, consideration will be given to the specialized statistical analyses required when using high-dimensional data and how this influences experimental design for omics-based studies.

Translating Innovation into Practice

This course is designed to provide learners with an introduction to the process of translating research innovations into clinical practice. It will examine the design of first in human studies, the process of protecting intellectual property and filing patents, and navigating the regulatory process to bring an innovation to the clinic. Securing funding through industry networks, and how to approach commercializing a discovery are also covered, with case studies throughout.

With this model, all students will have access to individuals with the expertise relevant to their educational and training needs.

“As a clinical trial physician, the ultimate training need is the integration of medicine, translational sciences and most importantly biostatistics and epidemiology. The clinical investigation program has efficiently integrated all of these components especially the epi and stats aspects while the mentored research experience integrates all other components. This is a unique model that is unparalleled, and I can consider this training as one of the most important journeys in my clinical research career at one of the best medical schools in the world”.

- Girish Naik, MBBS
MMSCI Student, Class of 2018
**Program Director**

**AJAY K. SINGH**  
MBBS, FRCP, MBA  
Program Director,  
MMSCI Program  
Senior Associate Dean  
Postgraduate Medical Education  
Harvard Medical School

Dr. Singh, Senior Associate Dean for Postgraduate Medical Education, is a member of the renal division in the Department of Medicine at Brigham and Women's Hospital and an Associate Professor of Medicine at HMS. He completed his undergraduate and medical training at University College London School of Medicine in England and his clinical and research renal fellowship at Tufts-New England Medical Center. He has written more than 200 publications and edited 11 books in nephrology and internal medicine. He has earned international recognition for his work in leading several global clinical trials in nephrology, including the CHOIR study and the ASCEND phase 3 program. His research has been published in the New England Journal of Medicine, Circulation, JASN, Kidney International and Science Translational Medicine. Dr. Singh is a Fellow of the Royal College of Physicians in London, and received his MBA from Boston University.

**Program Co-Director**

**FINNIAN R. MC CAUSLAND**  
MBBCh, MMSc, FRCPI  
Associate Director  
MMSCI Program  
Faculty Director  
Postgraduate Medical Education  
Harvard Medical School

Dr. Mc Causland is a nephrologist at Brigham and Women's Hospital and Assistant Professor of Medicine at HMS. Dr. Mc Causland received his medical degree from University College Dublin, Ireland and completed higher specialist training in nephrology and medicine before joining the Renal Division at Brigham and Women's Hospital. Dr. Mc Causland's major research interest relates to the cardiovascular consequences associated with hemodialysis. He is the Principal Investigator of two ongoing randomized controlled trials related to the dialysate prescription and its effect on hemodynamic stability. He has received funding from the National Institutes of Health, the American Heart Association and the National Kidney Foundation. Dr. Mc Causland received his Master of Medical Science degree in clinical investigation from Harvard Medical School.
Core Faculty

ROSA NY ADAM, PHD
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Associate Professor of Surgery
Harvard Medical School

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Director, The Mongan Institute
Director, Mongan Institute Health Policy Center
Professor of Medicine
Harvard Medical School

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MICHAEL CHO, MD
Assistant Professor of Medicine,
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Director of the Center for Bioethics, Harvard Medical School

DAVID WYPJ
Senior Lecturer on Biostatistics
Department of Biostatistics
Associate Professor of Pediatrics, Harvard Medical School
Director of the Statistics and Data Coordinating Center, Department of Cardiology
Children's Hospital Boston
Who Are We Looking For?

Applicants to the MMSCI program must have an MD, PhD, MBBCh MBBS or equivalent degree. We will consider applications from candidates with a Master’s degree on a case-by-case basis.

Students accepted into the program must demonstrate, through grades and performance in graduate level training, the potential to learn effectively in a challenging educational environment.

Admissions

APPLICATIONS DEADLINES & TUITION INFORMATION
Please visit hms.harvard.edu/mmsci for more in-depth application and tuition information.

“\textit{The MMSCI is a unique program with an innovative approach that integrates different modules covering a wide range of topics relevant to real-life experiences in clinical research. Being taught by world-renowned leaders, with special emphasis on two key components; teamwork and mentorship, this program represents a state-of-the-art opportunity to learn the theory with a direct hands-on experience. I look forward to the upcoming two years along with my fellow students who I consider a second family.}”

- Omar Abu-Qamar, MD
  MMSCI Student, Class of 2018
Master of Medical Science In Clinical Investigation Program

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