

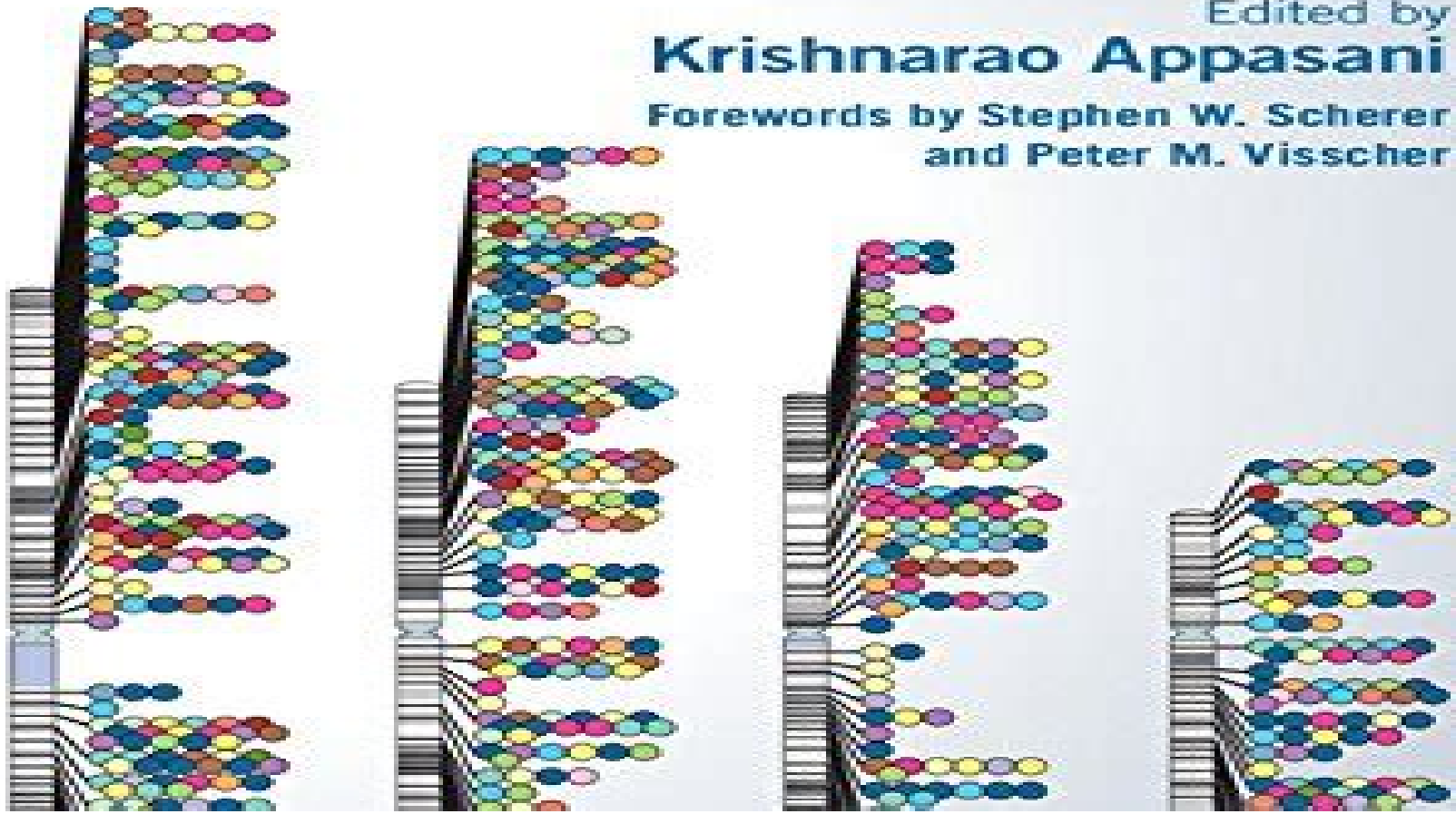
# Genome-Wide Association Studies

From Polymorphism to Personalized Medicine

Edited by

**Krishnarao Appasani**

Forewords by Stephen W. Scherer  
and Peter M. Visscher



# Genome Wide Association Studies Polymorphism Personalized Ebook

**Hoi-Man Emily Wong, 王慧文**

## **Genome Wide Association Studies Polymorphism Personalized Ebook:**

*Clinical Anesthesia, 7e: Print + Ebook with Multimedia* Paul Barash, Bruce F. Cullen, Robert K. Stoelting, Michael Cahalan, Christine M. Stock, Rafael Ortega, 2013-02-07 Clinical Anesthesia Seventh Edition covers the full spectrum of clinical options providing insightful coverage of pharmacology physiology co existing diseases and surgical procedures This classic book is unmatched for its clarity and depth of coverage This version does not support the video and update content that is included with the print edition Key Features Formatted to comply with Kindle specifications for easy reading Comprehensive and heavily illustrated Full color throughout Key Points begin each chapter and are labeled throughout the chapter where they are discussed at length Key References are highlighted Written and edited by acknowledged leaders in the field New chapter on Anesthesia for Laparoscopic and Robotic Surgery Whether you re brushing up on the basics or preparing for a complicated case the digital version will let you take the content wherever you go [Tratado de Psicofarmacología \(eBook online\)](#) Michel Salazar Vallejo, 2014-09-09 De f cil lectura y alto contenido cient fico el Tratado de Psicofarmacolog a Bases y aplicaci n cl nica es una obra dirigida no s lo a psiquiatras y profesionales de las neurociencias sino al resto de especialidades m dicas principalmente a m dicas de atenci n primaria residentes psic logos cl nicos y profesores Igualmente los estudiantes de ltimos cursos de medicina y enfermer a especializada encontrar n en esta obra cualquier aspecto relacionado con la pr ctica totalidad de las prescripciones en psiquiatr a **Harrison's Principles of Internal Medicine 19/E (Vol.1 & Vol.2) (ebook)** Dennis L. Kasper, Anthony S. Fauci, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson, Joseph Loscalzo, 2015-04-17 The landmark guide to internal medicine updated and streamlined for today s students and clinicians The only place you can get ALL the great content found in the two print volumes AND the acclaimed DVD in one convenient resource Through six decades no resource has matched the authority esteemed scholarship and scientific rigor of Harrison s Principles of Internal Medicine Capturing the countless advances and developments across the full span of medicine the new 19th edition of Harrison s provides a complete update of essential content related to disease pathogenesis clinical trials current diagnostic methods and imaging approaches evidence based practice guidelines and established and newly approved treatment methods Here are just a few of the outstanding features of the new Nineteenth Edition Content is practically organized around two basic themes education and clinical practice The teaching and learning sections cover foundational principles cardinal manifestations of disease and approach to differential diagnosis the content devoted to clinical practice focuses on disease pathogenesis and treatment NEW chapters on important topics such as Men s Health The Impact of Global Warming on Infectious Diseases Fatigue and many more Critical updates in management and therapeutics in Hepatitis Coronary Artery Disease Ebola Virus Disease Multiple Sclerosis Diabetes Hypertension Deep Vein Thrombosis and Pulmonary Embolism Acute and Chronic Kidney Disease Inflammatory Bowel Disease Lipoprotein Disorders HIV and AIDS and more Increased number of the popular Harrison s clinical algorithms clinically relevant radiographic examples spanning hundreds of diseases clinical

pathological images in full color crystal clear full color drawings and illustrations and helpful tables and summary lists that make clinical application of the content faster than ever Outstanding multi media resources including practical videos demonstrating essential bedside procedures physical examination techniques endoscopic findings cardiovascular findings are available for easy download Supporting the renowned coverage are supplemental resources that reflect and assist modern medical practice more than 1 000 full color photographs to aid visual recognition skills hundreds of state of the art radiographs from plain film to 3D CT to PET Scans beautiful illustrations that bring applied anatomy and processes to life the renowned Harrison s patient care algorithms essential summary tables and practical demonstrative videos In addition several digital atlases highlight noninvasive imaging percutaneous revascularization gastrointestinal endoscopy diagnosis and management of vasculitis and numerous other issues commonly encountered in clinical practice Acclaim for Harrison s Covering nearly every possible topic in the field of medicine the book begins with a phenomenal overview of clinical medicine discussing important topics such as global medicine decision making in clinical practice the concepts of disease screening and prevention as well as the importance of medical disorders in specific groups e g women surgical patients end of life The extensive chapters that follow focus on a symptom based presentation of disease and then illness organized by organ system Numerous tables graphs and figures add further clarity to the text Written by experts in the field this book is updated with the latest advances in pathophysiology and treatment It is organized in a way that makes reading from beginning to end a logical journey yet each chapter can stand alone as a quick reference on a particular topic Doody s Review Service reviewing the previous edition of Harrison s

**Pandemic of Diabetes and Prediabetes: Prevention and Control, An Issue of Endocrinology and Metabolism Clinics of North America, EBook** K M Venkat Narayan,2021-08-17 Provides in depth clinical reviews on diabetes and prediabetes prevention and control providing actionable insights for clinical practice Presents the latest information on this timely focused topic under the leadership of experienced editors in the field Authors synthesize and distill the latest research and practice guidelines to create these timely topic based reviews In this issue of Endocrinology and Metabolism Clinics guest editor K M Venkat Narayan brings considerable expertise to the topic of diabetes and prediabetes

**Harrison's Principles of Internal Medicine 19th Edition and Harrison's Manual of Medicine 19th Edition (EBook)VAL PAK** J. Larry Jameson,Anthony S. Fauci,Dennis L. Kasper,Stephen L. Hauser,Dan L. Longo,Joseph Loscalzo,2017-11-18 SPECIAL OFFER SAVE WHEN YOU PURCHASE HARRISON S PRINCIPLES OF INTERNAL MEDICINE 19e ALONG WITH THE COMPANION HARRISON S MANUAL This dollar saving Harrison s bundle includes these two great resources Harrison s Principles of Internal Medicine Nineteenth Edition Through six decades no resource has matched the authority esteemed scholarship and scientific rigor of Harrison s Principles of Internal Medicine Capturing the countless advances and developments across the full span of medicine the 19th edition of Harrison s provides a complete update of essential content related to disease pathogenesis clinical trials current diagnostic methods and imaging

approaches evidence based practice guidelines and established and newly approved treatment methods Here are just a few of the outstanding features of the Nineteenth Edition Presented in two volumes Volume 1 is devoted to foundational principles cardinal manifestations of disease and approach to differential diagnosis Volume 2 covers disease pathogenesis and treatment NEW chapters on important topics such as Men s Health The Impact of Global Warming on Infectious Diseases Fatigue and many more Critical updates in management and therapeutics in Hepatitis Coronary Artery Disease Ebola Virus Disease Multiple Sclerosis Diabetes Hypertension Deep Vein Thrombosis and Pulmonary Embolism Acute and Chronic Kidney Disease Inflammatory Bowel Disease Lipoprotein Disorders HIV and AIDS and more Increased number of the popular Harrison s clinical algorithms clinically relevant radiographic examples spanning hundreds of diseases clinical pathological images in full color crystal clear full color drawings and illustrations and helpful tables and summary lists that make clinical application of the content faster than ever Access to outstanding multi media resources including practical videos demonstrating essential bedside procedures physical examination techniques endoscopic findings cardiovascular findings and more The package also includes Harrison s Manual of Medicine Nineteenth Edition Harrison s Manual of Medicine is a concise bedside resource derived from content found in Harrison s Principles of Internal Medicine Nineteenth Edition Perfect for use at the point of care the Manual presents clinical information covering key aspects of the diagnosis clinical manifestations and treatment of the major diseases that are likely to be encountered in medical practice Presented in full color and incorporating an efficient blend of succinct text bullet points algorithms and tables Harrison s Manual of Medicine Nineteenth Edition covers every area of clinical medicine including Etiology and Epidemiology Clinically Relevant Pathophysiology Signs and Symptoms Differential Diagnosis Physical and Laboratory Findings Therapeutics Practice Guidelines

*The Road from Nanomedicine to Precision Medicine* Shaker. A Mousa,Raj Bawa,Gerald F. Audette,2020-01-06 The enormous advances in nanomedicine and precision medicine in the past two decades necessitated this comprehensive reference which can be relied upon by researchers clinicians pharmaceutical scientists regulators policymakers and lawyers alike This standalone full color resource broadly surveys innovative technologies and advances pertaining to nanomedicine and precision medicine In addition it addresses often neglected yet crucial areas such as translational medicine intellectual property law ethics policy FDA regulatory issues nano nomenclature and artificial nano machines all accomplished in a user friendly broad yet interconnected format The book is essential reading for the novice and the expert alike in diverse fields such as medicine law pharmacy genomics biomedical sciences ethics and regulatory science The book s multidisciplinary approach will attract a global audience and serve as a valuable reference resource for industry academia and government

**Harrison's Principles and Practice of Internal Medicine 19th Edition and Harrison's Principles of Internal Medicine Self-Assessment and Board Review, 19th Edition (EBook)Val-Pak** J. Larry Jameson,Anthony S. Fauci,Dennis L. Kasper,Stephen L. Hauser,Dan L. Longo,Joseph Loscalzo,Charles Weiner,2017-11-18 SPECIAL OFFER SAVE WHEN YOU

**PURCHASE HARRISON S PRINCIPLES OF INTERNAL MEDICINE 19e ALONG WITH THE COMPANION BOARD REVIEW BOOK** This dollar saving Harrison s bundle includes two great resources Harrison s Principles of Internal Medicine Nineteenth Edition Through six decades no resource has matched the authority esteemed scholarship and scientific rigor of Harrison s Principles of Internal Medicine Capturing the countless advances and developments across the full span of medicine the 19th edition of Harrison s provides a complete update of essential content related to disease pathogenesis clinical trials current diagnostic methods and imaging approaches evidence based practice guidelines and established and newly approved treatment methods Here are just a few of the outstanding features of the Nineteenth Edition Presented in two volumes Volume 1 is devoted to foundational principles cardinal manifestations of disease and approach to differential diagnosis Volume 2 covers disease pathogenesis and treatment NEW chapters on important topics such as Men s Health The Impact of Global Warming on Infectious Diseases Fatigue and many more Critical updates in management and therapeutics in Hepatitis Coronary Artery Disease Ebola Virus Disease Multiple Sclerosis Diabetes Hypertension Deep Vein Thrombosis and Pulmonary Embolism Acute and Chronic Kidney Disease Inflammatory Bowel Disease Lipoprotein Disorders HIV and AIDS and more Increased number of the popular Harrison s clinical algorithms clinically relevant radiographic examples spanning hundreds of diseases clinical pathological images in full color crystal clear full color drawings and illustrations and helpful tables and summary lists that make clinical application of the content faster than ever Access to outstanding multi media resources including practical videos demonstrating essential bedside procedures physical examination techniques endoscopic findings cardiovascular findings and more The package also includes Harrison s Principles of Internal Medicine Self Assessment and Board Review Based on the content of Harrison s Principles of Internal Medicine Nineteenth Edition this full color study aid is essential for Internal Medicine Board certification or recertification maintenance of certification or as a refresher for any internal medicine examination Reflecting the accuracy currency and wide scope of Harrison s this complete review of internal medicine delivers more than 1 000 extremely challenging review questions many of which utilize realistic patient scenarios including radiographic and pathologic images Each question is accompanied by explanations for correct and incorrect answers These explanations which are derived from and cross referenced to Harrison s Principles of Internal Medicine Nineteenth Edition are one of the most effective ways to learn and teach internal medicine They are designed to bolster your understanding of pathophysiology epidemiology differential diagnosis clinical decision making and therapeutics You will also find a beautiful full color atlas

### **Single Nucleotide Polymorphism and Copy Number Variant**

**Genotyping for Genome Wide Association Studies** Eleni Giannoulatou,2010 [Genomic and Precision Medicine](#)

Geoffrey S. Ginsburg,Huntington F Willard,Sean P. David,2017-03-30 Genomic and Precision Medicine Primary Care Third Edition is an invaluable resource on the state of the art tools technologies and policy issues that are required to fully realize personalized health care in the area of primary care One of the major areas where genomic and personalized medicine is

most active is the realm of the primary care practitioner Risk family history personal genomics and pharmacogenomics are becoming increasingly important to the PCP and their patients and this book discusses the implications as they relate to primary care practitioners Presents a comprehensive volume for primary care providers Provides succinct commentary and key learning points that will assist providers with their local needs for the implementation of genomic and personalized medicine Includes a current overview on major opportunities for genomic and personalized medicine in practice Highlights case studies that illustrate the practical use of genomics in the management in patients **Genomic and Precision**

**Medicine** Geoffrey S. Ginsburg, Huntington F Willard, 2017-11-17 Genomic and Precision Medicine Cardiovascular Disease Third Edition focuses on the applications of genome discovery on the broad spectrum of cardiovascular disorders Each chapter is organized for the application of genomics and personalized medicine tools and technologies to a Risk Assessment and Susceptibility b Diagnosis and Prognosis c Pharmacogenomics and Precision Therapeutics and d Emerging and Future Opportunities in the field Presents a comprehensive volume written and edited by cardiovascular genomic specialists Covers succinct commentary and key learning points that will assist providers with their local needs for the implementation of genomic and personalized medicine into practice Provides an overview on major opportunities for genomic and personalized medicine in practice Includes case studies that highlight the practical use of genomics in the management of patients

**Robust Approaches for Performing Meta-analysis of Genome-wide Association Studies to Identify Single Nucleotide Polymorphisms and Copy Number Variations Associated with Complex Traits** Pimphen Charoen, 2013

**Efficient Design and Analysis of Genome-wide Association Studies** Emrah Kostem, 2013 The recent advances in genomic technologies have made it possible to collect large scale information on genetic variation across a diverse biological landscape This has resulted in an exponential influx of genetic information and the field of genetics has become data rich in a relatively short amount of time These developments have opened new avenues to elucidate the genetic basis of complex diseases where the traditional disease study approaches had little success In recent years the genome wide association study GWAS approach has gained widespread popularity for its ease of use and effectiveness and is now the standard approach to study complex diseases In GWAS information on millions of single nucleotide polymorphisms SNPs is collected from case and control individuals SNP genotyping is cost effective and due to their abundance in the genome SNPs are correlated to their neighboring genetic variation which makes them tags for genomic regions Typically each SNP is statistically tested for association to disease and the genomic regions tagged by the significant SNPs are believed to be harboring the functional variants contributing to disease In order to reduce the cost of GWAS and the redundancy in the information collected an informative subset of the SNPs or tag SNPs are genotyped Typically the genomic regions harboring the significantly associated tag SNPs may be large and contain many additional polymorphisms At this stage of the study it may not be clear which specific genes or polymorphisms are in fact most strongly associated to disease We present a novel framework for

designing cost effective follow up association studies to further characterize such regions by genotyping additional SNPs to identify all the associated polymorphisms This identification of all associated polymorphisms provides a catalog of all possible functional variants and the values of the actual association statistics at these polymorphisms may provide information to identify causal variants We present the utility of our method in identifying significant associations and causal variants using simulated and real GWAS datasets Although GWAS have been widely used to study associations of SNPs to disease phenotypes there has been growing interest in applying the GWAS approach to high throughput biological phenotypes such as gene expression In these studies the goal is to identify genomic regions that affect gene expression levels known as expression quantitative trait loci eQTL A challenge in applying GWAS to eQTL studies is that there are tens of thousands of measurements each representing the expression level of one gene for each sample tested as opposed to values for one or two clinical traits This results in a tremendous computational burden when performing the analysis requiring computation for billions of tests and demands substantial computational resources We present a novel two stage approach to efficiently identify all of the significant associations without testing all the SNPs In the first stage a small number of informative SNPs across the genome are tested Based on their observed associations our approach locates the regions that may contain significant SNPs and only tests additional SNPs from those regions We demonstrate that this method increases the computational speed of eQTL studies by a factor of ten and can be applied to reduce the computational burden of a wide range of association statistics Finally we develop a novel approach to address a problem that has been of fundamental interest to geneticists for decades The contribution of genetics to a trait termed as heritability is often measured by the amount of variation in the trait that is due to genetics Heritability quantifies the role of genetics in a trait and provides insight about disease etiology Traditionally heritabilities were estimated in studies of individuals with known relatedness such as classical twin studies Recently estimating the heritability of a trait from unrelated individuals using GWAS data and further partitioning the heritability into the contributions of genomic regions has received a lot of attention Existing methods partition the heritability by jointly estimating the contributions of all regions However these methods are computationally intractable and may be inaccurate when the number of regions is large In this work we present an alternative approach that partitions the total heritability into the contributions of an arbitrary number of regions while performing these computations in parallel We demonstrate that our method is more accurate and computationally efficient than existing approaches

### **Methods To Analyze Genetic Associations With Complex Traits In Diverse Populations** Keenan

Anderson-Fears,2024 The growth of large scale genome wide association studies GWAS in the first decade of the new millennium resulted in a plethora of genetic association signals Early researchers were quick to point out the novelty and potential power in the ability to map specific mutations within the genome to disease outcomes with the results being the genesis of the phrase Personalized Medicine By the end of the decade however a new problem had arisen and association



studies were now left scrambling for answers Dubbed the Missing Heritability problem the single nucleotide polymorphisms SNPs associated in each study were only able to account for a relatively small proportion of the genetic heritability of any given disease Through the years many possible resolutions have been put forward from epigenetics being the driver of heritability to all phenotypes being misdiagnoses and each individual phenotype the result of completely different causes By 2010 a resolution was tentatively reached under the understanding that traits were complex and highly polygenic being affected by hundreds possibly thousands of SNPs with additive effects Follow up studies on such traits as schizophrenia addiction and educational attainment have helped to support this understanding with increasing sample size leading to increasing numbers of SNPs identified However as increasingly diverse populations were genotyped and began to be included in association studies linkage disequilibrium began to become a concern and by 2015 with the release of linkage disequilibrium score regression LDSC became part of the standard pipeline for association studies Along with LDSC came a suite of tools that allowed for expanded or easy analysis such as plink for association analysis and popcorn for genetic correlation between traits Additionally as increasing amounts of data in the form GWAS began to accrue in the later half of the 2010s meta analysis became a popular method to increase sample size and identify novel variants all in an attempt to close the gap in heritability In 2018 a multi trait meta analysis method was released named MTAG which was able to meta analyze multiple GWAS across correlated traits borrowing strength across phenotypes Even still the lack of proportional representation within genomic data sets combined with LD differences between ethnic populations has led in part to poor health outcomes for underrepresented populations However today we understand that genetic variants are often shared between traits or ancestries and jointly analyzing data sets via meta analysis across different traits and ancestries will likely improve power Following in the footsteps of previous generations we aim to take advantage of the wealth of GWAS data available and by including multiple traits and multiple ancestries we propose a new method for multi trait and cross ancestry meta analysis that significantly improves power across populations Additionally we show new work in the realm of candidate gene studies as a preamble to our method on the associations between respiratory syncytial virus acute respiratory failure and mutations in surfactant genes in the lungs Our new method uses a variable number of principal components from a genetic correlation matrix as covariates in a meta regression model to account for phenotype heterogeneity and adjusts for sample overlaps using residual correlation from LDSC To test the effectiveness of our new method we compiled the largest multi ancestry SLE data set consisting of GWAS summary statistics for 740 000 individuals in six different ancestries for 14 autoimmune diseases For many of these diseases both genetic and environmental risk factors are shared with many precursors to the diseases only becoming highly specific immediately prior to development of final stages These similarities in triggers have made specification in testing arduous and gives the perfect testing grounds for our method To test our method with those available we compare our method with the multi trait analysis of genome wide association MTAG method

using Popcorn for genetic correlation as well as a standard fixed effect meta analysis Our results show that IMAC outperforms MTAG in simulation with controlled type 1 error compared to MTAGs conservative type 1 error and higher statistical power across all scenarios of heritability 0.1 and sample sizes 20 000 50 000 and 100 000 On real world data IMAC using a single principal component with a p value cutoff of 0.2 identifies 57 81 105 127 and 134 novel loci compared to MTAGs 61 61 30 28 and 29 across five correlation sets Our findings highlight the importance of including multi ancestry and multi trait information together which along with increasing sample sizes increases power for rare variant detection and has the potential to reduce health disparities

*Genetic Matching by Ancestry in Genome-wide Association Studies* Diana Luca, 2008

**Genome-Wide Association Analyses on Complex Diseases** Hoi-Man Emily Wong, 2017-01-26 This dissertation Genome wide Association Analyses on Complex Diseases From Single nucleotide Polymorphism to Copy Number Variation by Hoi man Emily Wong was obtained from The University of Hong Kong Pokfulam Hong Kong and is being sold pursuant to Creative Commons Attribution 3.0 Hong Kong License The content of this dissertation has not been altered in any way We have altered the formatting in order to facilitate the ease of printing and reading of the dissertation All rights not granted by the above license are retained by the author

**Abstract** Complex diseases unlike Mendelian diseases are often characterized by genetic heterogeneity and multifactorial inheritance involving defects in genes from the same or multiple alternative pathways Many congenital diseases and psychiatric disorders are complex diseases and incur heavy health care burden on the society With the advancement in high throughput genotyping technologies and the availability of the human single nucleotide polymorphism SNP catalogue genome wide association study GWAS has been widely used to investigate the genetic component of complex diseases Copy number variations CNV can also be identified using the data from the same SNP array Aiming to identify more disease susceptibility loci for complex diseases separate GWAS using a case control design were conducted on anorectal malformations ARMs and schizophrenia ARMs are rare congenital diseases with heterogeneous phenotypes which could probably be explained by the genetic heterogeneity among patients while schizophrenia is a common psychiatric disorder that is well known for its multigenic inheritance The GWAS studies on ARM and schizophrenia included 4 369 patients N 363 controls N 4 006 and 1 231 Han Chinese patients N 381 controls N 850 respectively The two studies were mainly focused on investigating the contribution of rare CNVs to the diseases involving analyses on global CNV burden rare CNV association protein protein interaction PPI network pathway and chromosomal aberrations The associations of SNPs with ARMs were also examined Apart from elucidating the genetic components in these two diseases a systematic analysis on four CNV detection programs CNV partition PennCNV QuantiSNP and iPattern was also undertaken In the study of schizophrenia a new approach in CNV filtering which was based on latent class analysis was adopted to gather information from multiple CNV prediction programs The study of ARMs revealed 79 genes which were disrupted by CNVs in patients only In particular a de novo duplication of DKK4 an antagonist of WNT signaling was identified

and addition of Dkk4 protein was demonstrated to cause ARMs in mice Another 10 genes uniquely disrupted in ARMs patients are also related to WNT signaling Interestingly this pathway was also significantly inferred by CNV in patients with schizophrenia A different set of genes related to WNT signaling was disrupted in ARMs patients and patients with schizophrenia WNT signaling is crucial for the development of multiple parts in the embryo The contribution of different WNT signaling pathways at different development stages may vary Apart from the WNT signaling pathway other genes with biological relevance were also implicated in the two studies through gene network and pathway analyses The results from these two GWAS studies support our existing understanding of complex diseases that defects in various interacting genes could contribute to the same disease In summary the CNV results from the two studies have demonstrated the genetic heterogeneity nature of these two complex diseases The findings also uncovered a set of putative disease candidate genes which can be used as reference materials for future genetic research for ARMs and schizophrenia DOI 10.5353/th.b5053409

Subjects Abnormalities Human Genetic a **Polymorphisms** Wasana Sukhumsirichart,2018 Polymorphism or variation in DNA sequence can affect individual phenotypes such as colour of skin or eyes susceptible to diseases and respond to drug vaccine chemical and pathogen It occurs more often than mutations frequency 1% The common polymorphism is single nucleotide polymorphism SNP which is a single base change in a DNA sequence that occurs most commonly in the human genome SNPs have been used as molecular markers in a wide range of studies Genome wide association studies GWAS searches for SNPs that occur more frequently in person with a particular disease than in person without the disease and pinpoint genes or regions that may contribute to a risk of disease This topic describes about polymorphisms SNPs GWAS linkage disequilibrium LD minor allele frequency haplotype method for SNP genotyping and application of SNPs and genome wide association study in human diseases and drug development

**Towards Leveraging Short Tandem Repeats for Large Scale Genome-Wide Association Studies** Shubham Saini,2021 Most of the efforts in human genetics are directed towards identifying and characterizing genetic variants that impact human traits achieved by examining relationships between traits and variants A Genome Wide Association Study GWAS quantifies statistical association between genetic variation and phenotypes These statistical associations can tell us about the biological mechanisms affecting the phenotype and can allow us to predict the phenotype from genetic information in a clinical setting However the majority of GWAS datasets have been generated with commodity genotype arrays of single nucleotide polymorphism SNP that fail to explain the majority of heritability for many complex traits even with large sample sizes One compelling hypothesis explaining the missing heritability dilemma is that complex variants such as multi allelic repeats not in strong linkage with common SNPs are important drivers of complex traits but are largely invisible to current analyses Short tandem repeats STRs consisting of repeated motifs of 1-6bp in tandem comprise more than 3% of the human genome Multiple lines of evidence support a role of STRs in complex traits particularly in neurological and psychiatric phenotypes However existing technologies have not

allowed for systematic STR association studies To overcome these challenges we recently generated a reference STR SNP haplotype panel that enables imputation of STR genotypes into SNP genotypes available for most GWAS cohorts Our imputation pipeline achieves a high concordance and can be used to impute nearly 500 000 STRs genome wide Next we leveraged our reference haplotype panel to impute STRs into GWAS data for more than 50 000 samples from the Psychiatric Genomics Consortium PGC to perform a genome wide analysis of associations between STR lengths and schizophrenia In this dissertation I demonstrate an end to end pipeline for conducting large biobank scale GWAS using STRs that serves as one of the initial studies which researchers can find useful for incorporating complex variants into their analysis

A Network-based Approach to Prioritize Results from Genome-wide Association Studies (GWAS) in Multigenic Traits Nirmala Akula,2009

**Assessing Rare Variation in Complex Traits** Eleftheria Zeggini,Andrew Morris,2015-08-13 This book is unique in covering a wide range of design and analysis issues in genetic studies of rare variants taking advantage of collaboration of the editors with many experts in the field through large scale international consortia including the UK10K Project GO T2D and T2D GENES Chapters provide details of state of the art methodology for rare variant detection and calling imputation and analysis in samples of unrelated individuals and families The book also covers analytical issues associated with the study of rare variants such as the impact of fine scale population structure and with combining information on rare variants across studies in a meta analysis framework Genetic association studies have in the last few years substantially enhanced our understanding of factors underlying traits of high medical importance such as body mass index lipid levels blood pressure and many others There is growing empirical evidence that low frequency and rare variants play an important role in complex human phenotypes This book covers multiple aspects of study design analysis and interpretation for complex trait studies focusing on rare sequence variation In many areas of genomic research including complex trait association studies technology is in danger of outstripping our capacity to analyse and interpret the vast amounts of data generated The field of statistical genetics in the whole genome sequencing era is still in its infancy but powerful methods to analyse the aggregation of low frequency and rare variants are now starting to emerge The chapter Functional Annotation of Rare Genetic Variants is available open access under a Creative Commons Attribution 4 0 International License via link [springer.com](http://springer.com)

*On Considering Epistasis in Genome Wide Association Studies* Noffisat Oyindamola Oki,2012

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