

## Article

# The Cholesterol Paradox in Long-Livers from a Sardinia Longevity Hot Spot (Blue Zone)

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**Abstract:** **Background/Objectives:** Hypercholesterolemia is commonly viewed as a risk factor for coronary heart disease; however, several studies have reported an inverse relationship between cholesterol levels and cardiovascular mortality, particularly in older adults. This “cholesterol paradox” challenges the conventional understanding of lipid metabolism. Despite often being dismissed as a result of reverse causality, the precise causes of this paradox remain poorly understood. This study aimed to investigate the potential existence of the cholesterol paradox in a long-lived population from central Sardinia, Italy. **Methods:** We recruited 168 baseline nonagenarians (81 males, 87 females) from the longevity Blue Zone area in 2018 and followed them until December 2024. The lipid profile was determined for all participants according to current guidelines, and its impact on survival was analyzed with Kaplan–Meier curves and Cox proportional hazards regression models. **Results:** The median total cholesterol was 199.5 (range 89–314) mg/dL in males and 202.5 (range 89–324) mg/dL in females. Survival time was significantly longer in participants with LDL cholesterol (LDL-C) above 130 mg/dL compared to that in nonagenarians with LDL-C lower than 130 mg/dL ( $3.82 \pm 1.88$  years vs.  $2.79 \pm 1.56$  years,  $p < 0.0001$ ). Cox regression analysis revealed a significant reduction in the hazard ratio (HR) for mortality in participants with mild hypercholesterolemia (LDL-C  $\geq 130$  mg/dL) compared to that in those with normal cholesterol (OR 0.600, 95%CI 0.405–0.891). **Conclusions:** In the long-lived population examined, the cholesterol paradox was unlikely to be a reflection of reverse causality. Our results challenge the common view that longevity is invariably associated with low cholesterol levels. Furthermore, moderate hypercholesterolemia does not preclude the oldest adult from attaining advanced ages, contrary to common belief.

**Keywords:** cholesterol paradox; blue zone; longevity; Sardinia; elderly

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## 1. Introduction

Cardiovascular disease, the leading cause of mortality in high-resource countries, is often attributed to several risk factors, (including sex, family history, hypertension, cigarette smoking, obesity, and dyslipidemia [1]), which independently increase the probability of atherosclerosis development. The notion that high blood cholesterol is one of the primary factors for cardiovascular risk owes much to the work of Alexander Ignatowski, Nikolai Anichkov, and Semen Chalotov in the first two decades of the last century, when

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**United States. Bureau of the Census**



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**Psychopharmacology Abstracts** ,1970      **Marriage Licenses of Frederick County, Maryland** Margaret E. Myers,2009-05-01 About 7 500 couples listed by bride and groom      **Federal Register** ,1983-03      *Pediatric Hepatology and Liver Transplantation* Lorenzo D'Antiga,2019-04-29 This book is the first to provide balanced examination of both pediatric liver disease and liver transplantation two topics that are inherently related given that most chronic liver disorders eventually require organ replacement The different forms of liver disease encountered in the pediatric age group are first discussed in a series of disease specific chapters that have a reader friendly uniform structure covering pathophysiology diagnostic and treatment algorithms clinical cases and transition to adult care Key topics in the field of liver transplantation are then addressed Examples include indications and contraindications surgical techniques and complications immunosuppression in pediatric liver transplantation acute and chronic rejection and allograft dysfunction and CMV and EBV infection in transplant recipients long term graft injury and tolerance A section on pediatric hepatology across the world includes chapters presenting the features and management of pediatric liver disease in South America Africa and Asia A closing section considers what the future holds for pediatric liver disease and its management including novel genetic testing cell therapy and gene therapy *Pediatric Hepatology and Liver Transplantation* will be of value for a range of practitioners from residents making their first approach to pediatric liver disease through to specialists working in transplantation centers

A Photographic Atlas for the Microbiology Laboratory Michael J. Leboffe,Burton E. Pierce,2012-01-01 Intended to act as a supplement to introductory microbiology laboratory manuals This full color atlas can also be used in conjunction with your own custom laboratory manual      *FDA's Regulation of Carcinogenic Additives* United States. Congress. House. Committee on Government Operations. Human Resources and Intergovernmental Relations Subcommittee,1987      Index Medicus ,2001      **Principles of Hepatic Surgery** Silvio Marcio Pegoraro Balzan,Vinicius Grando Gava,2016-03-21 Principles of Hepatic Surgery introduces the reader to current trends in Liver surgery knowledge and practice This reference book covers liver surgery fundamentals as well as cutting edge progress in this exciting surgical specialty Contributions have been written by expert hepatic surgeons from major medical centers around the world Key features include Information organized into five comprehensive sections i Liver Anatomy and Perioperative Care ii Approach to Malignant Hepatic Disease iii Approach to Benign Hepatic Disease iv Technical Aspects of Liver Resections and v Liver Transplantation Over 350 illustrations Truly effective didactic text with logical clear explanations giving readers a pleasant reading experience Commentary sections written by experts for specific surgical cases Principles of Hepatic Surgery is a valuable reference for both novice hepatologists and practicing liver surgeons      Designer World Avrohom Katz,1994 Do we truly appreciate the breath taking miracles of nature and the wisdom inherent in all of the universe Rabbi Katz opens our eyes to the wonders of our Creator and the intricacy of His world      **Edinburgh Medical Journal** ,1925      **Diseases of the Liver and Biliary**

**System in Children** Deirdre A. Kelly, 2017-03-20 This market leading book with comprehensive coverage of the entire spectrum of liver disease in children returns with 12 brand new chapters covering key areas in liver transplantation viral hepatitis and liver disease in infancy Authored by the world's leading hepatologists and pediatricians and expertly edited by Deirdre Kelly it covers the entire topic from pathology to diagnosis and clinical management and in all stages of childhood from the unborn baby through to infancy and from childhood to the transition into adolescence Hepatologists pediatricians and gastroenterologists of all levels will find it an essential tool to consult time and time again

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*Quarterly Cumulative Index to Current Medical Literature. V. 1-12; 1916-26*, 1918

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**Transplantation of the Liver** Ronald W. Busuttil, Goran B. Klintmalm, 2014-12-24 Drs Busuttil and Klintmalm present Transplantation of the Liver 3rd Edition which has been thoroughly revised to offer you the latest protocols surgical approaches and techniques used in this challenging procedure Encompassing today's expert knowledge in the field this medical reference book is an ideal single source for authoritative up to date guidance on every imaginable aspect of liver transplantation Consult this title on your favorite e reader conduct rapid searches and adjust font sizes for optimal readability Access valuable pearls pitfalls and insights from Dr Ronald Busuttil and Dr Goran Klintmalm two of the world's preeminent experts in liver surgery Understand today's full range of transplantation techniques with complete step by step descriptions of each and access the background information and management options for each hepatic disease entity Take advantage of detailed discussions of everything from pathophysiology and patient and donor selection to transplantation anesthesia and operative procedures immunosuppression postoperative care and ethical issues Overcome your toughest challenges in liver transplantation Many new and thoroughly revised chapters include Deceased Organ Donation after

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