
Venerdì 13 Settembre

SESSIONE PLENARIA

MEDICINA DELLA COMPLESSITÀ

***La nuova sfida, integrare la medicina di precisione nella medicina della complessità***

***Enzo Manzato***

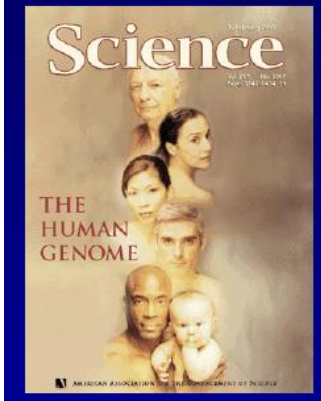
# Current applications of precision medicine: a bibliometric analysis

The terms individualized and personalized medicine have often been used interchangeably with precision medicine in recent literature, thus leading to ambiguity.

Individualized medicine has been defined as a “therapeutic approach tailoring therapy for genetically defined subgroups of patients”. Individualized medicine first arose from a study regarding the structure of the genome, mapping genes and sequencing DNA to emphasize genetic differences between patients.

Personalized medicine, which was first mentioned in published literature in 1971, has been defined as a “broad and rapidly advancing field of healthcare that is informed by each person’s unique clinical, genetic, genomic and environmental information”.

***Per Med 16, 351, 2019***




In February 2001, two papers provided the first detailed look at the nearly complete sequence of the human genome.


Human Genome Project

Prevention

Wellness

Health Promotion

# Current applications of precision medicine: a bibliometric analysis

The most commonly used definitions of precision medicine in the literature were those developed by:

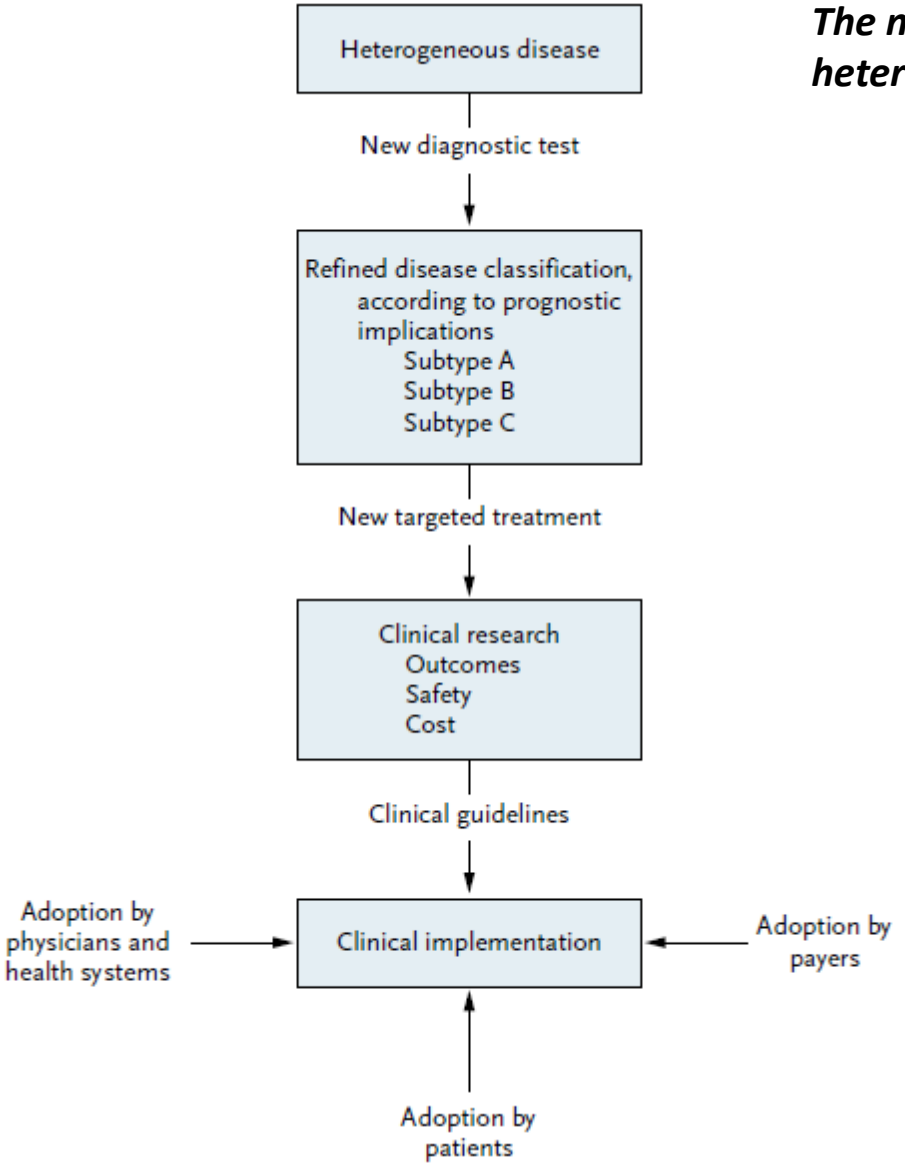
NIH (2018): an emerging approach to disease treatment and prevention that takes each person's variability in genes, environment and lifestyle into account;

US FDA (2013): the right patient with the right drug at the right dose at the right time;

National Research Council (2011): tailoring of medical treatment to the individual characteristics of each patient.

***Per Med 16, 351, 2019***

# Precision Medicine — Personalized, Problematic, and Promising



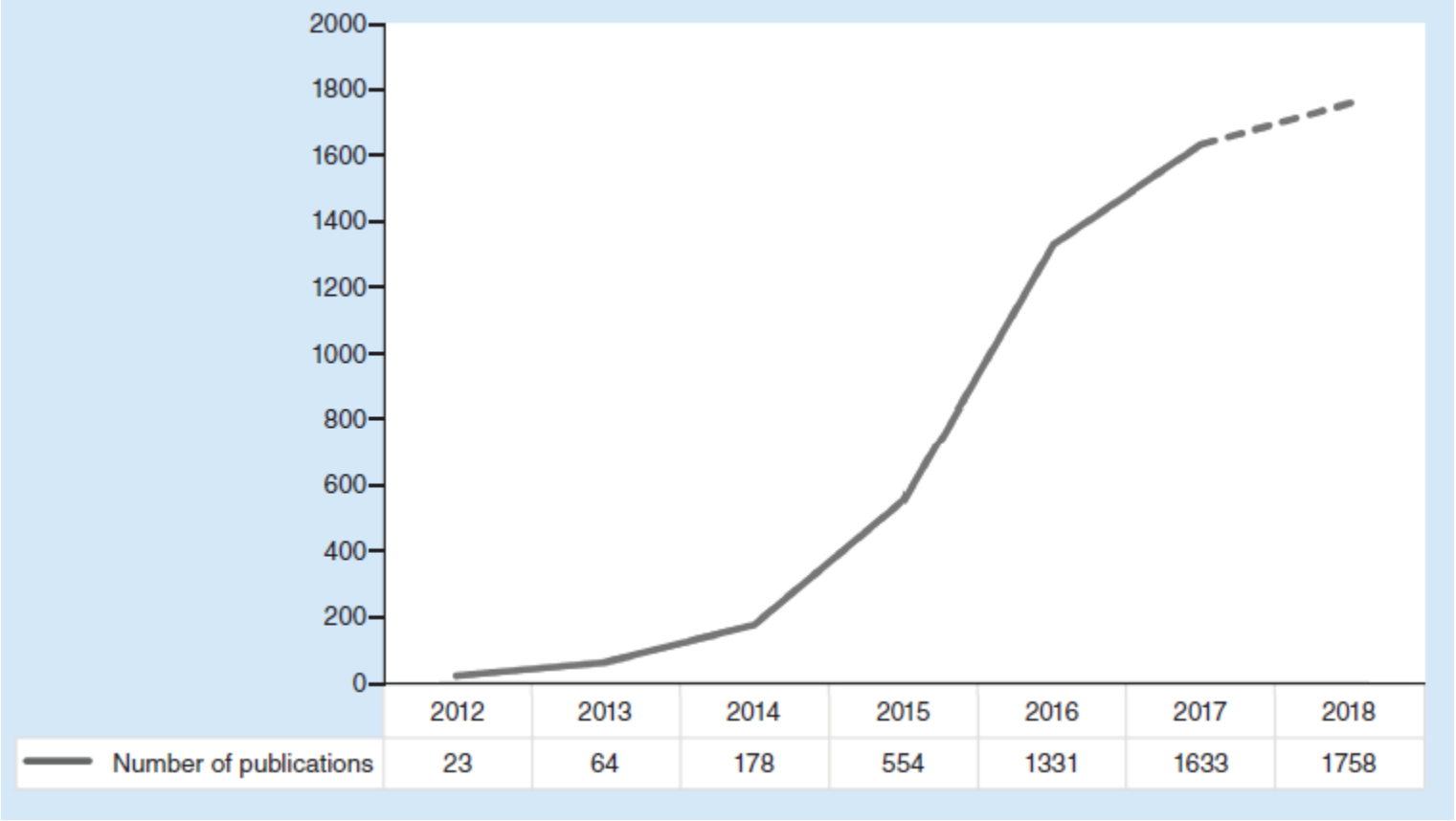

***The need for precision medicine is driven by the heterogeneous nature of many diseases***

***Precision medicine should be viewed as a means of providing the best available health care for a population by identifying the needs and improving the outcomes of individual patients.***

***N Engl J Med 372, 2229, 2015***

# Current applications of precision medicine: a bibliometric analysis

***Trends in the use of the term 'precision medicine' from 2012 to 2018***




| | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
|---|---|---|---|---|---|---|---|
| Number of publications | 23 | 64 | 178 | 554 | 1331 | 1633 | 1758 |

***Per Med 16, 351, 2019***

# Current applications of precision medicine: a bibliometric analysis

***Application of the term precision medicine across the top ten clinical specialty areas***

| Clinical specialty area | Articles, n (%) |
|---|---|
| Oncology | 1060 (33.4) |
| Respiratory | 197 (6.2) |
| Cardiac/cardiovascular | 155 (4.9) |
| Pathology | 146 (4.6) |
| Clinical neurology | 144 (4.5) |
| Immunology | 135 (4.3) |
| Radiology, nuclear medicine and medical imaging | 134 (4.2) |
| Urology and nephrology | 123 (3.9) |
| Endocrinology and metabolism | 112 (3.5) |
| Psychiatry | 100 (3.2) |

***Per Med 16, 351, 2019***

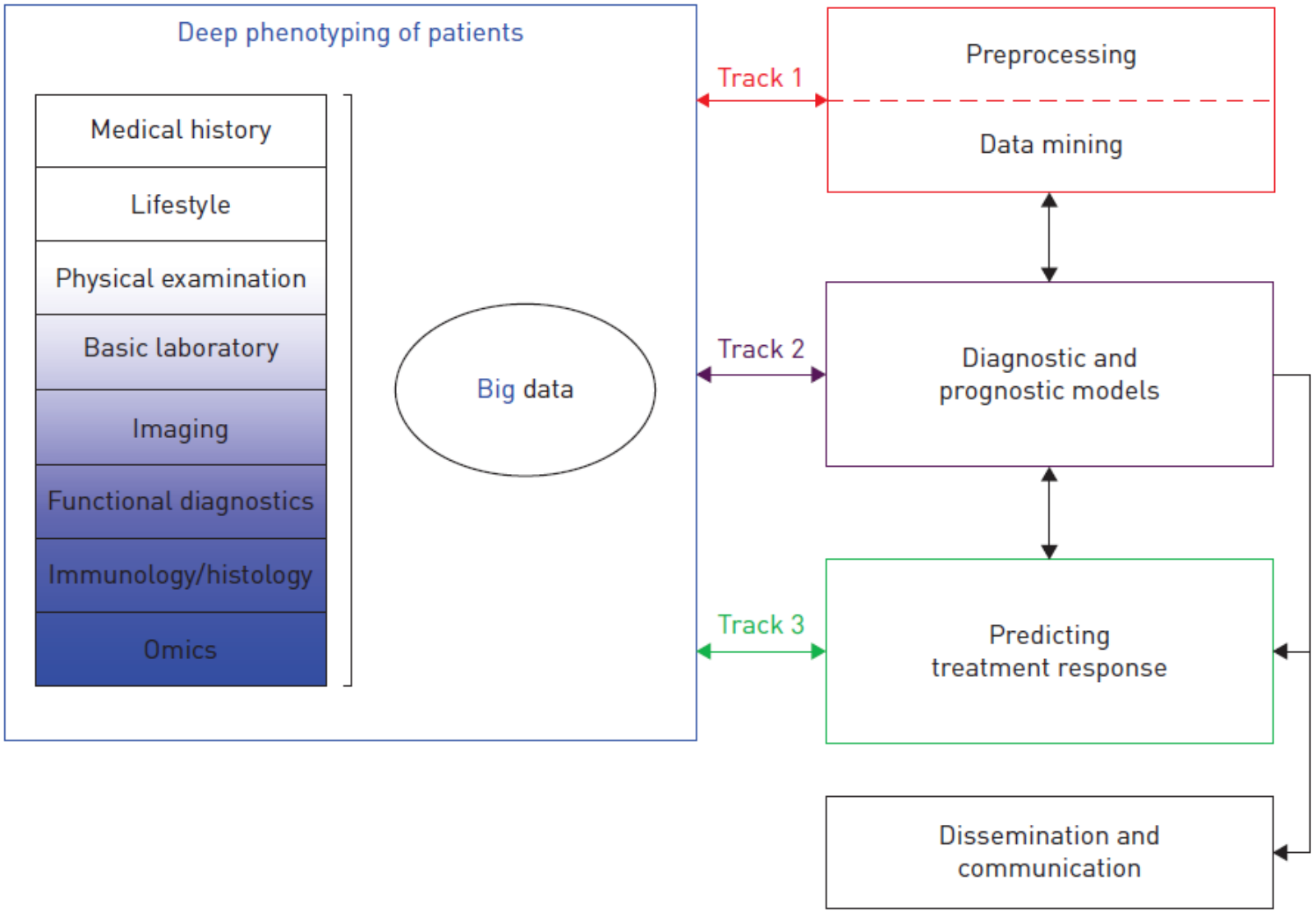
# Precision Medicine — Personalized, Problematic, and Promising

**Table 1. Examples of Conditions in Which Precision Medicine Has Been Used.***

| Medical Field | Disease | Biomarker | Intervention |
|---|---|---|---|
| Cancer | Chronic myeloid leukemia | BCR-ABL | Imatinib[4] |
| | Lung cancer | EML4-ALK | Crizotinib[3] |
| Hematology | Thrombosis | Factor V Leiden | Avoid prothrombotic drugs[5] |
| Infectious disease | HIV/AIDS | CD4+ T cells, HIV viral load | Highly active antiretroviral therapy[6] |
| Cardiovascular disease | Coronary artery disease | *CYP2C19* | Clopidogrel[7] |
| Pulmonary disease | Cystic fibrosis | *G551D* | Ivacaftor[8] |
| Renal disease | Transplant rejection | Urinary gene signature | Antirejection drugs[9] |
| Hepatology | Hepatitis C | Hepatitis C viral load | Direct-acting antiviral agents[10] |
| Endocrine disease | Multiple endocrine neoplasia type 2 | *RET* | Prophylactic thyroidectomy[11] |
| Metabolic disease | Hyperlipidemia | LDL cholesterol | Statins[12] |
| Neurology | Autoimmune encephalitis | CXCL13 | Immunotherapy[13] |
| Psychiatry | Alcohol-use disorder | *GRIK1* | Topiramate[14] |
| Pharmacogenomics | Smoking cessation | *CYP2A6* | Varenicline[15] |
| Ophthalmology | Leber's congenital amaurosis | *RPE65* | Gene therapy[16] |

***N Engl J Med 372, 2229, 2015***

# What is precision medicine?

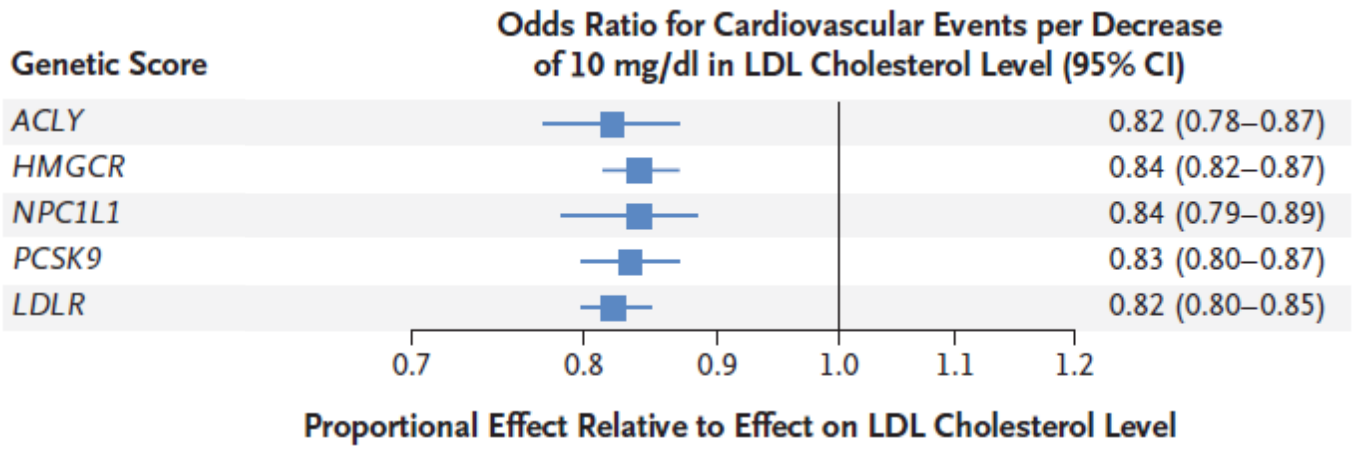



*Eur Respir J 2017; 50:1700391*

# DNA

UN PO' DI SALIVA
E TI DIRÒ CHI SEI

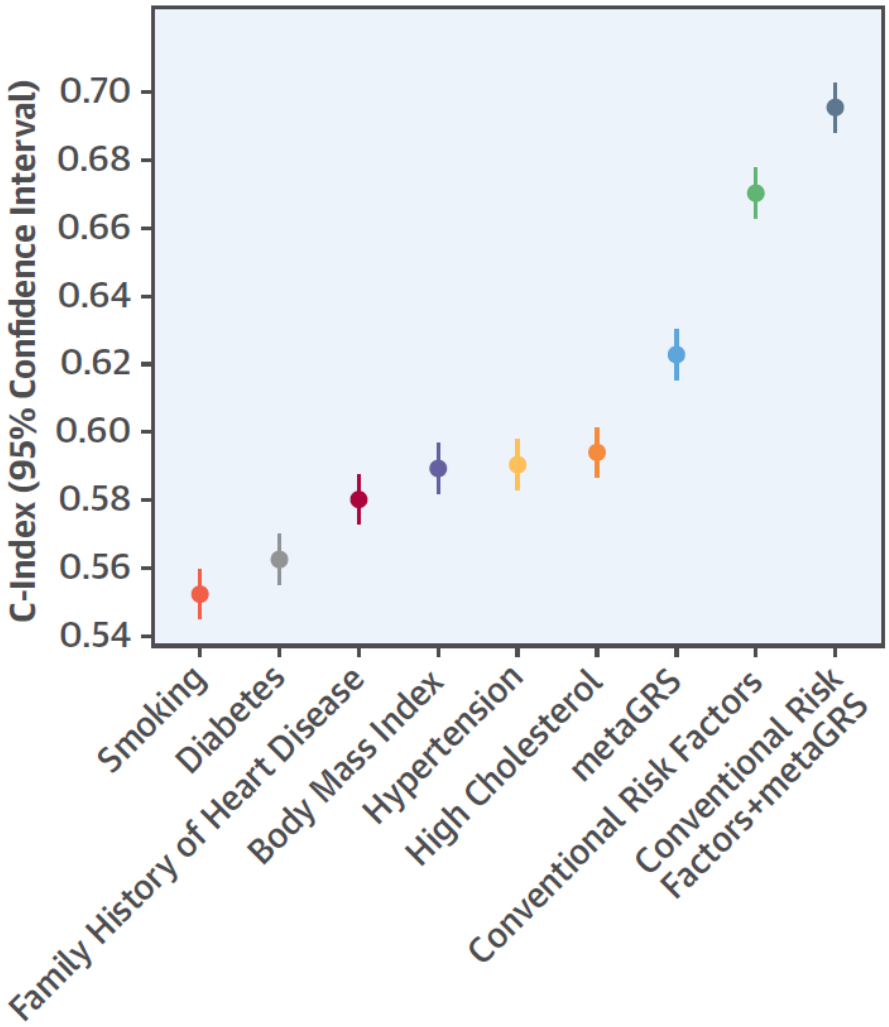
## *Associations of the Genetic Scores with the Risk of Cardiovascular Events*




*N Engl J Med 2019;380:1033*

# Genomic Risk Prediction of Coronary Artery Disease in 480,000 Adults

## Implications for Primary Prevention




***A genomic risk score for coronary artery disease***

- ***Greater association with future coronary artery disease than any single conventional risk factor***
- ***Independent of yet complements conventional risk factors***
- ***Provides meaningful lifetime risk estimates of coronary artery disease***
- ***Quantifiable at or before birth and shows potential for risk screening in early life***

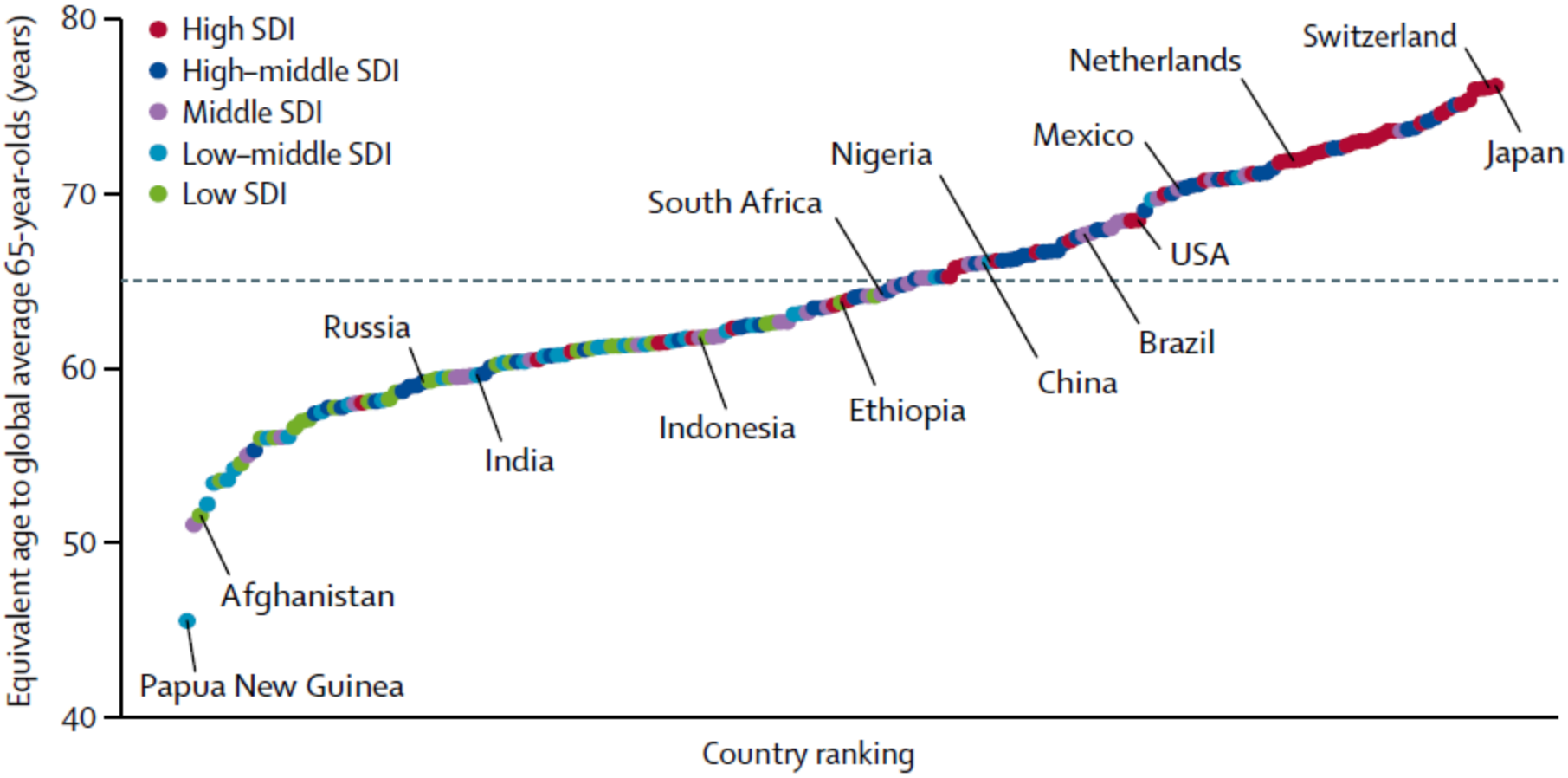
***J Am Coll Cardiol 2018;72:1883***

# Current applications of precision medicine: a bibliometric analysis

Those involved in the development of future precision medicine innovations have a responsibility to ensure they are based on new interdisciplinary methods that take into account all factors that contribute to individual differences in health including genes, environments and lifestyles.

***PerPer Med 16, 351, 2019***

# Measuring population ageing: an analysis of the Global Burden of Disease Study 2017




*Lancet Public Health 2019; 4: e159–67*

# Measuring population ageing: an analysis of the Global Burden of Disease Study 2017

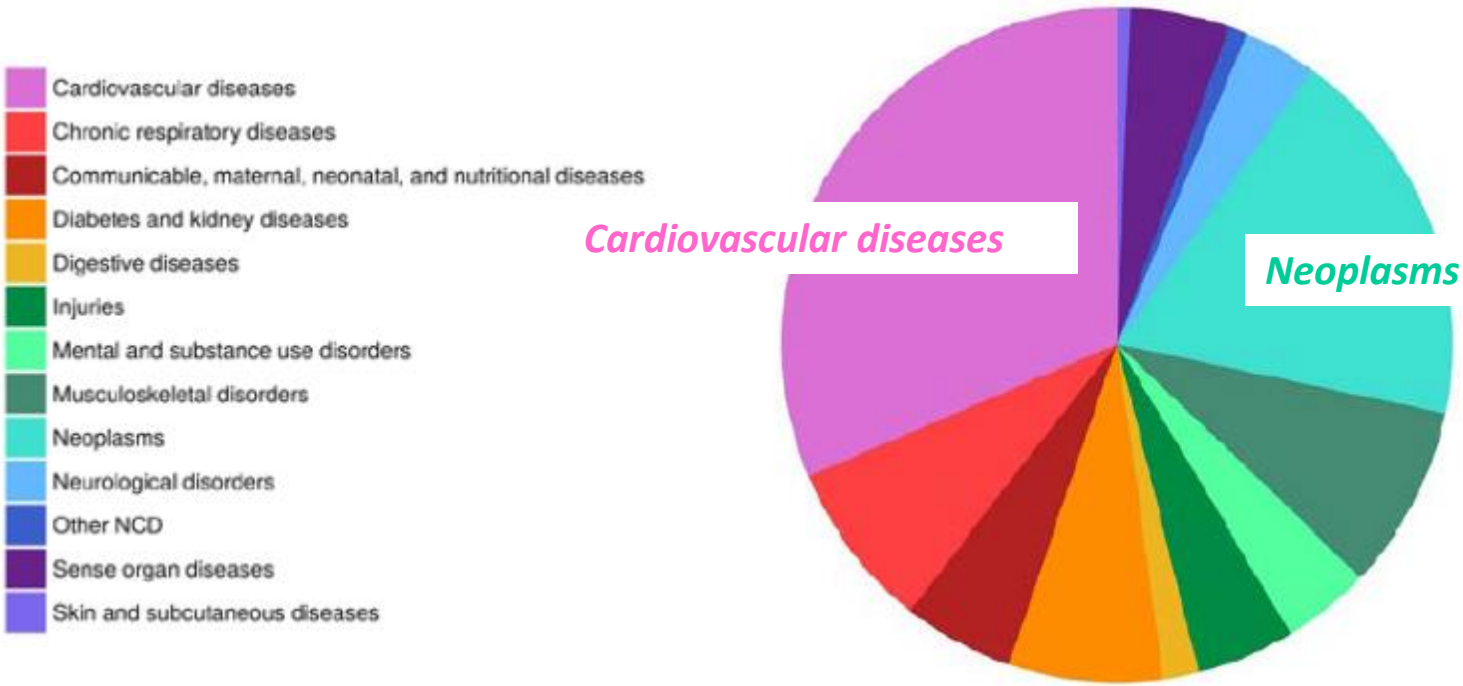
***Sensitivity analysis: 2017 equivalent age to global 65-year-olds***

| Country | 2017 equivalent age to global 65-year-olds (years) | | |
|---|---|---|---|
| | Sensitivity analysis | Original result | Dif (%) |
| Italy | 74.5 (73.5, 75) | 74.8 (74.3, 75.4) | -0.4% |

***Lancet Public Health 2019; 4: e159–67***

# Measuring population ageing: an analysis of the Global Burden of Disease Study 2017

***Distribution of age-related burden at the global level in 2017 measured in disability-adjusted life year (DALYs)***

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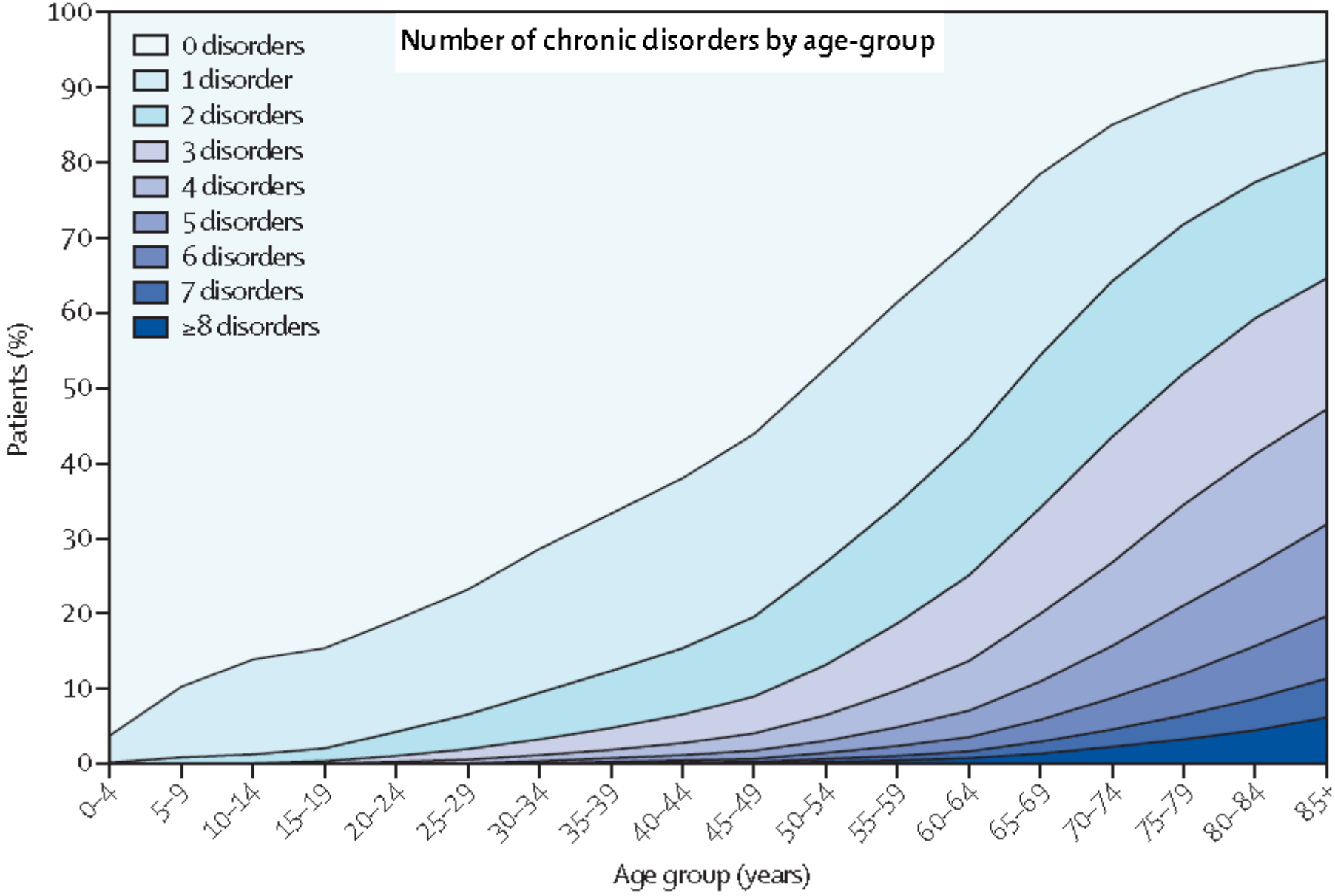
# Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study




*Lancet 2012; 380: 37*

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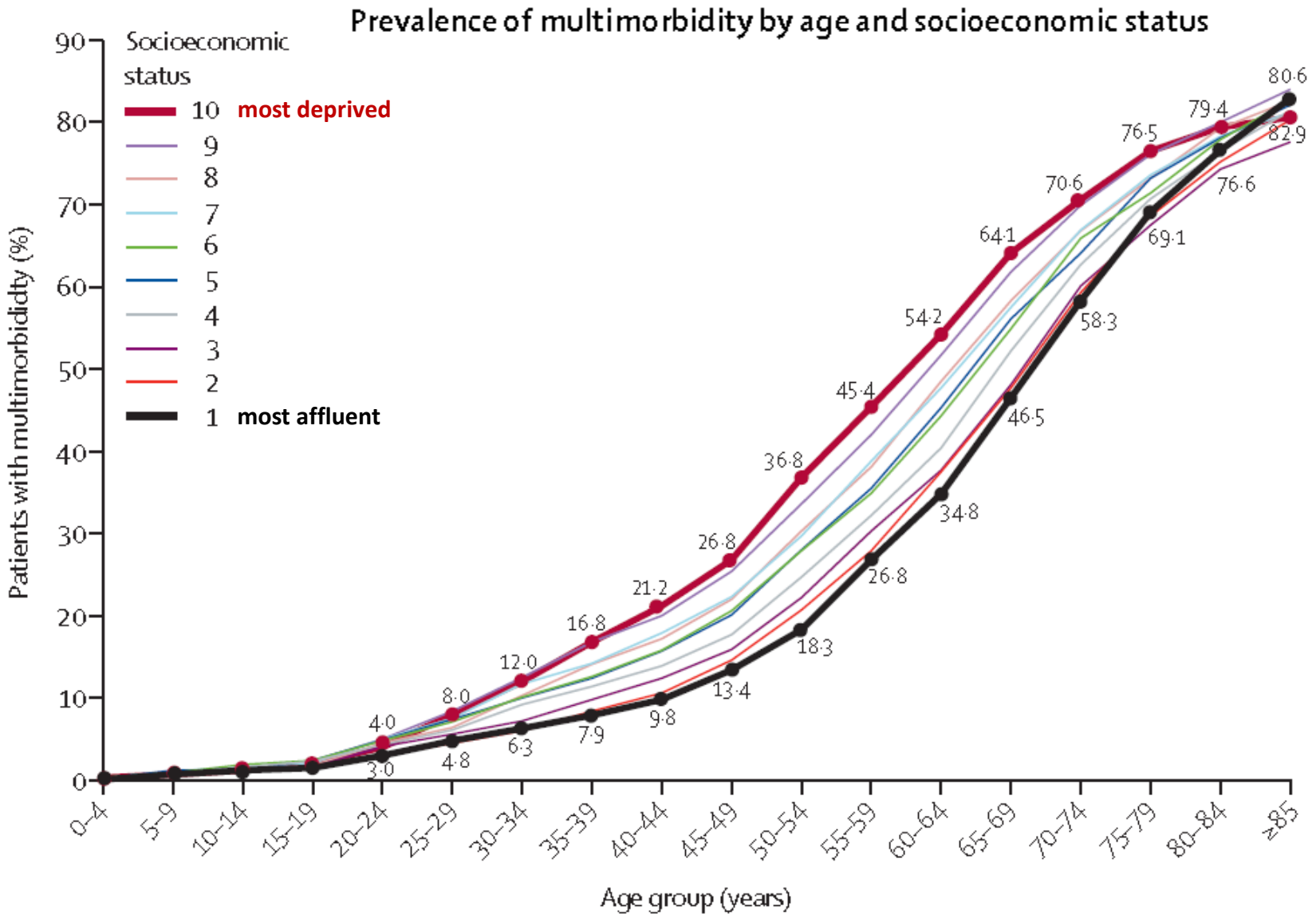


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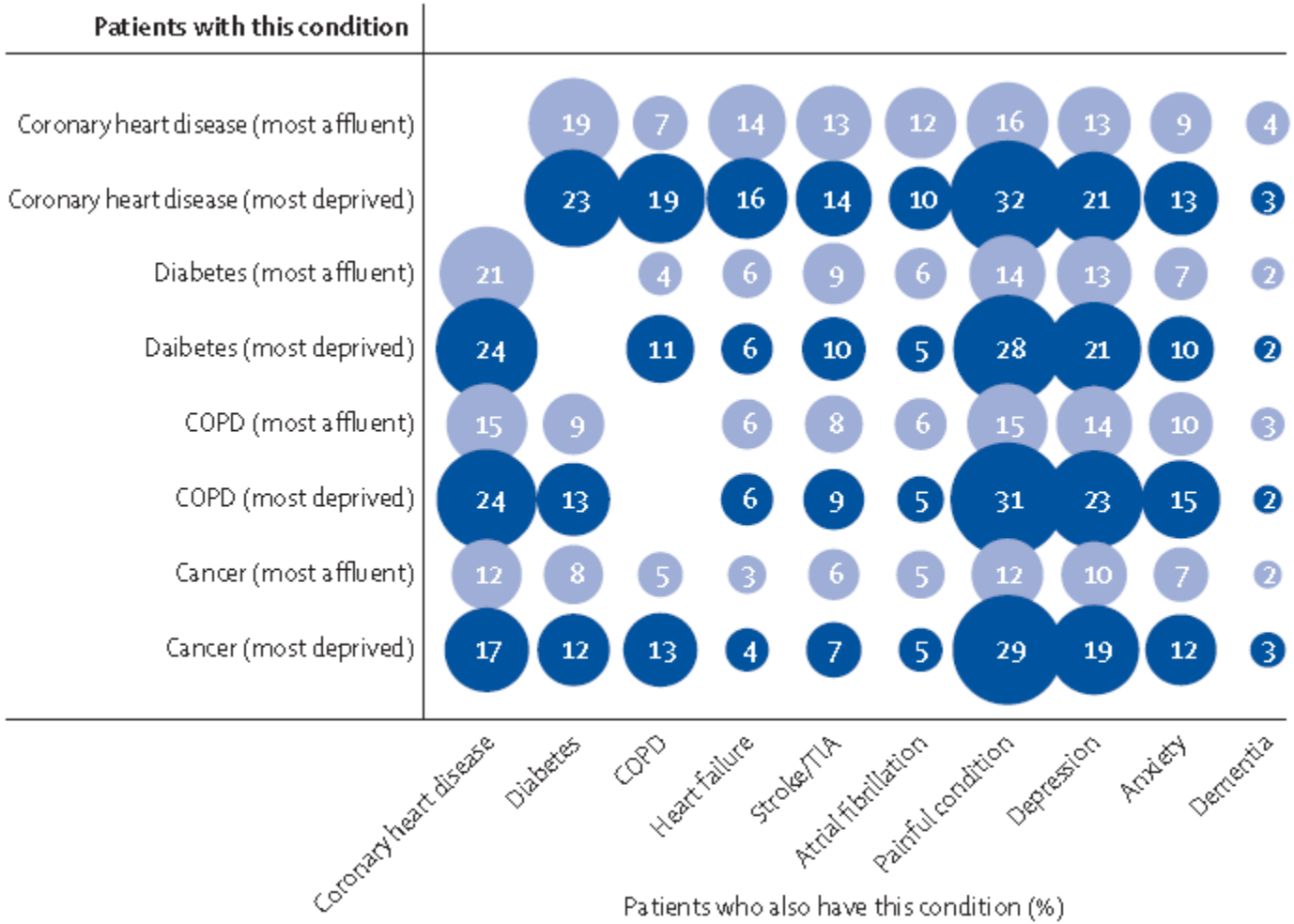


***Lancet 2012; 380: 37***

# 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

## 2. OVERARCHING RECOMMENDATIONS FOR ASCVD PREVENTION EFFORTS

### 2.1. Patient-Centered Approaches to Comprehensive ASCVD Prevention

***RECOMMENDATIONS***

1. ***A team-based care approach is recommended for the control of risk factors associated with ASCVD***

2. ***Shared decision-making should guide discussions about the best strategies to reduce ASCVD risk***

3. ***Social determinants of health should inform optimal implementation of treatment recommendations for the prevention of ASCVD***

***J Am Coll Cardiol 2019; 74: 1376***

# *il signor Giovanni…*

***il malato che contraddistingue il nostro secolo non è affetto da un'unica e definita malattia, acuta e risolvibile nel breve-medio termine, ma è un malato cronico, affetto da più patologie incidenti contemporaneamente***

***il fenotipo clinico risultante è determinato da fattori biologici (malattia-specifici) e da determinanti non biologici (status socio-familiare, economico, ambientale, accessibilità delle cure ecc.), che interagiscono fra di loro in maniera dinamica***

***Gensini GF, M. Fabbri LM, Fini M, Nozzoli C: La Medicina della Complessità Firenze University Press, 2010***

# *il signor Giovanni…*

***la presenza di patologie croniche multiple induce:***

- ***a consultare numerosi specialisti***
- ***alla prescrizione di trattamenti farmacologici multipli***
- ***a ridurre l'aderenza ai trattamenti***
- ***all'aumento di interazioni farmacologiche e di reazioni avverse***
- ***all'aumento ingiustificato dei costi sanitari e sociali***

***Gensini GF, M. Fabbri LM, Fini M, Nozzoli C: La Medicina della Complessità***
***Firenze University Press, 2010***


"CARDIOLOGIA DI PRECISIONE"

# Razionale

Gli attuali progressi nella diagnostica e nel trattamento delle malattie cardiovascolari, integrati da banche dati e dalla possibilità di un inquadramento genetico del singolo soggetto, ci consentono di personalizzare la terapia adattandola alle caratteristiche fenotipiche e genotipiche.

La medicina sta ritornando ad essere sartoriale.