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## NATIONAL STRATEGIC PLAN FOR CARDIOVASCULAR HEALTH

2024 | 2027

Coordinator: Prof. Ciro Indolfi

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*President: Dott. Fabrizio Oliva*

# National Strategic Plan for Cardiovascular Health 2024–2027

*Edited by:*
*Alberto Polimeni, Stefania Paolillo, Pietro Scicchitano*

*Text revision:*
*Alessandro Navazio*

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# ACRONYMS

| | |
|---|---|
| **AIFA** | Italian Medicines Agency |
| **ANMCO** | National Association of Hospital Cardiologists |
| **BES** | Fair and sustainable wellbeing |
| **FIC** | Italian Federation of Cardiology |
| **FSN** | National Health Fund |
| **IRPEF** | Personal income tax |
| **ISTAT** | Italian National Statistical Institute |
| **LEA** | Essential Levels of Care |
| **PNE** | National Outcomes Programme |
| **PNP** | National Prevention Plan |
| **SDO** | Hospital Discharge Card |
| **SICI-GISE** | Italian Society of Interventional Cardiology |
| **SSN** | Italian National Health Service |

# INTRODUCTION

Cardiovascular diseases, the leading cause of death and among the main causes of disability in Italy, Europe, and worldwide, represent one of the major public health challenges for the coming years. The aging population characteristic of western countries and the exposure to cardio-metabolic risk factors will increasingly heighten the burden of these diseases, with significant consequences on the sustainability and resilience of healthcare systems.

In Italy there is no national strategic plan such as the oncology plan aimed at cardiovascular health, although our country is at moderate cardiovascular risk, unlike Spain and France which are at low risk.

The current demographic and epidemiological context is helping to bring attention to this varied and heterogeneous group of diseases. To address the socio-economic burden of cardiovascular diseases, whose cost in Europe alone has reached 282 billion euros, national and international institutions have ramped up joint research initiatives. For instance, JACARDI (Joint Action on CARdiovascular diseases and DIabetes), with 53 billion euros – the second highest co-funded joint action ever allocated in Europe – is a four-year program coordinated by the Italian National Institute of Health (ISS) that aims to reduce the incidence of cardiovascular diseases, diabetes, and related risk factors for at least one million European patients.

In this context, there is a need to develop an integrated vision of cardiovascular diseases to implement a series of prevention, diagnosis, treatment, and rehabilitation interventions, both clinical and organizational-managerial, within territorial and hospital care. At the European and national levels, the idea is gaining ground that a specific plan for cardio, cerebro, and vascular diseases, modeled after plans for other major non-communicable chronic diseases, could provide a currently missing overarching vision;  In this regard, for example, the Spanish Government has adopted a national cardiovascular health plan on the "Estrategia en Salud Cardiovascular del Sistema Nacional de Salud". The aim of this plan is to raise awareness among public decision makers to invest in the prevention and treatment of cardiovascular diseases, keeping in mind that ours is the only G7 country in which, compared to 10 years ago, healthcare spending in relation to GDP has decreased and stands as the lowest of the seven countries, with a small and worrying 6.2%.

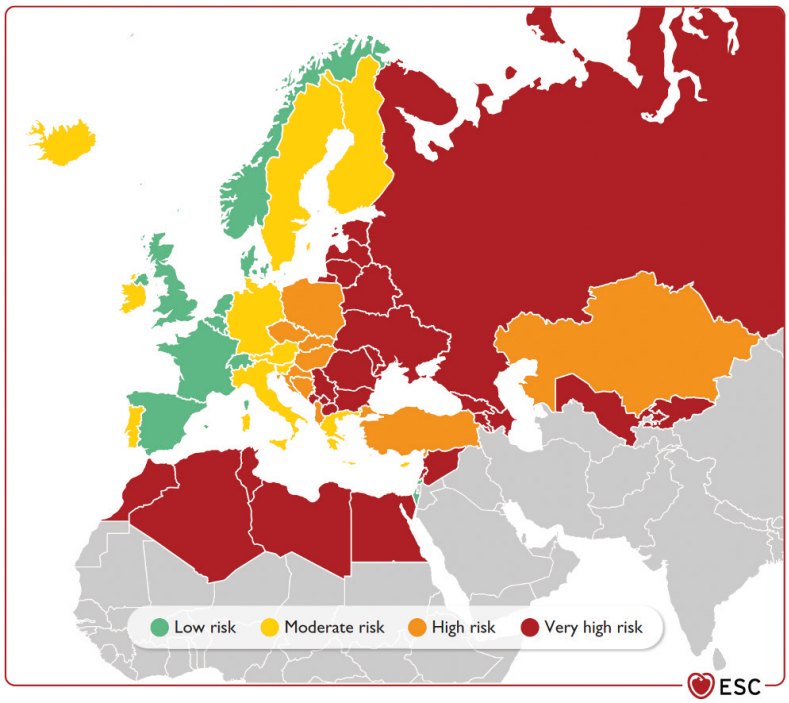
The present Strategic Plan for Cardiovascular Health in Italy 2024-27, developed by the Italian Federation of Cardiology (IFC), with the support of the European Society of Cardiology (ESC) as part of the Advocacy 2024 Project, moves in this direction, promoting investment in prevention and interventions for the care and control of cardio, cerebro, and vascular diseases through a "global" care perspective. The ultimate goal is to contribute to improving the level of cardiovascular health of the Italian population, to bring our nation to a low risk level like France and Spain without forgetting the positive impacts on the healthcare and socioeconomic system such as the reduction of healthcare costs direct and indirect, increase in labor productivity, reduction of social costs.

***Prof. Ciro Indolfi - President of the Italian Federation of Cardiology***

# 01

# IMPACT OF CARDIOVASCULAR DISEASES IN ITALY

Cardiovascular diseases are a significant public health issue worldwide and have a notable impact on our country. This impact is evident in the health of the population and its consequences, including the expenses incurred by the National Health Service (SSN) for treating acute and chronic conditions, the psychological and social effects on patients and their families, the economic burden of work disability caused by these diseases, and the resources required for cardiology research and development.
The cardiovascular risk in Italy is moderate, unlike Spain and France, which are at low risk.



The most recent statistical data published by the Italian National Statistical Institute (ISTAT, Istituto Nazionale di Statistica) (BES, 2023) [1] illustrates a scenario of stability or improvement in most health domain indicators when compared to the previous year and to the pre-pandemic levels in 2019. Despite this, cardiovascular diseases remain the primary cause of death in Italy, accounting for approximately 30% of all deaths (31.7% in males and 37.7% in females). Specifically, there were 746,324 total deaths in Italy in 2020, an increase of 108,496 cases from the 2015-19 average. Mortality in Italy is divided as follows: 227,350 deaths were caused by circulatory diseases (30.4%), 177,858 by cancer (23.8%), 78,673 by COVID-19 (10.5%), and 57,113 by respiratory diseases (7.6%) [2]. Furthermore, when analysing avoidable, i.e. preventable and treatable, mortality, it was observed that at the European level, in 2020, the leading cause of treatable mortality was ischemic heart disease (1.9 per 10,000 residents, accounting for 20.1 percent of the total number of deaths from treatable diseases), followed by colorectal cancer (1.4 per 10,000 residents), breast cancer among women (1.0 per 10,000 residents), and cerebrovascular disease (1 per 10,000 residents) [2]. Ischemic heart disease, including acute myocardial infarction and chronic conditions, is responsible for 9.9% of all deaths in Italy, with 10.8% in males and 9% in females. Cerebrovascular accidents, on the other hand, account for 8.8% of total deaths, with 7.3% in males and 10.1% in females.

These diseases follow the global epidemiological trend in our country. They have a higher prevalence in males compered to females until menopause, when they occur at least 10 years later than in men. Subsequently, women are more affected than men by cardiovascular events, which are often more severe and characterised by a less obvious or often underestimated clinical scenario. For this reason, women typically seek specialistic evaluation later than men, and the long-term consequences of cardiovascular disease may be more noticeable in such individuals.

To end on a positive note, it should be remembered that cardiovascular disease is largely preventable, as it depends not only on non-modifiable risk factors (age, sex, and family history), but also on modifiable factors related to behaviours and lifestyles (smoking, poor diet, sedentary lifestyle), which in turn cause diabetes, obesity, hypercholesterolemia, and hypertension, which are underlying conditions of atherosclerotic cardiovascular diseases. Therefore, it is essential for healthcare professionals managing patients at risk of cardiovascular disease and

those already affected by different forms of the condition to strive to prevent its occurrence and minimise its long-term impact and disability. Similarly, institutions also need to engage in formulating strategic plans for preventing cardiovascular issues, educating the public, providing training, and investing in clinical and preclinical research.

## Strategic framework: the goal of the Strategic Plan for Cardiovascular Health

The goal of the Strategic Plan for Cardiovascular Health is to draft a document shared by experts in the field and institutions aimed at increasing interventions in the prevention, care and control of cardiovascular diseases in our country.

The ultimate goal is to improve the level of cardiovascular health of the Italian population.

The following activities are planned to achieve this goal:

- Promote programmes of knowledge, of health and prevention of cardiovascular diseases throughout Italy at different levels, from schools to workplaces and health facilities, through health education interventions aimed at the population that support the adoption of healthy and sustainable lifestyles and environments;
- Reduce the incidence and prevalence of cardiovascular disease in Italy by implementing prevention programmes, campaigns and actions, enhancing primary care, and improving the overall quality of life and well-being of the population. Increase the availability of advanced treatments and ensure consistent healthcare standards nationwide, eliminating disparities in service quality across different regions;
- Reduce the long-term complications of cardiovascular disease in Italy by improving acute and chronic care, rehabilitation, health restoration, facilitating reintegration into work, and preventing disability.

To achieve this goal, it is essential to have a comprehensive, individual-focused perspective of care, but from a "community" viewpoint that takes into account all factors involved in cardiovascular health. This includes social determinants, health education for the general population, patients, and their families, as well as the training of healthcare professionals.

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# 02

# INEQUALITIES IN CARDIOVASCULAR HEALTH IN ITALY

The Italian National Health Service was de facto established by Law 833 of 23 December 1978. The goal was to renew the national healthcare service provision by implementing principles of fairness and inclusivity, funded by general tax revenues. This initiative aimed to safeguard health as a fundamental right of the individual, as outlined in Article 32 of the Italian Constitution.

In practice, achieving a concrete, fair, and universal implementation of Law 833's provisions has proven to be challenging. This difficulty is primarily due to the irreconcilable differences among the various regional contexts in our country, rather than to issues related to individual characteristics.

Italian healthcare, particularly the services related to cardiovascular health, is affected by various inequalities, all stemming from an unfair management of public health.

Regional, organisational, social, historical, socioeconomic and gender differences are the main factors that lead to inequalities in cardiovascular health in Italy.

## Regional inequalities

Regional divergences in health integrity management are the primary reason for the inequalities found in the cardiovascular disease prevention system in Italy. The structure of the National Health Service and the reforms introduced over the years have undoubtedly made it possible to implement and in some respects improve healthcare organisational aspects. However, they have also triggered an unprecedented process of differentiation among regional areas. In fact, although the introduction of fiscal federalism was an attempt to improve the capacity of regional authorities to meet citizens' health needs and preferences, it also required

them to fund and oversee health service provision, ensuring both affordability and sustainability. Fiscal federalism has made the state responsible for establishing the overall regulatory framework, while enabling regional authorities to pass, within their regions, laws implementing central government's guidelines and to organise public health services and interventions. The funding sources for regional health services include VAT and IRPEF (personal income tax) revenues, along with the equalisation fund. Therefore, any budget deficits in regional health are covered by regional tax revenues. Consequently, the disparity in healthcare management and in individual cardiovascular health across different geographical areas of the country (regions in northern, central, and southern Italy) depends on the financial means of each regional authority.

According to the latest ISTAT data (BES, 2023) [1] in the autonomous provinces of Trento and Bolzano, 5 out of 15 health indicators have achieved the highest values for well-being, making them stand out as particularly successful. On the other hand, Campania and Basilicata tend to have lower scores compared to other regions, with 5 and 4 indicators out of 15 falling into the lowest range, respectively. Moreover, in 2023, the healthy life expectancy indicator at birth was subject to regional differences, i.e. about 4 years lower in the South (56.5 years), compared to the North (60.6 years). After the North-South gap reached its lowest levels in 2021 and 2022 (approx. 2.5 years), the differential returned to pre-pandemic levels (it was 3.9 years in 2019). Mortality rates between 2005 and 2016 were higher in southern regions (Campania, Calabria, Sicily, Sardinia, Molise, and Basilicata) than in northern regions, except for Abruzzo and Apulia [2]. Even the SARS-CoV-2 pandemic did not lead to an increase in the number of available beds. In 2021, the rate of inpatient beds was 3.5 per thousand population [3]. Values higher than the national average are observed in all northern regions, except for Liguria (3.4 per thousand), Veneto (3.3 per thousand) and Friuli-Venezia Giulia (3.4 per thousand); in particular, the highest values are recorded in Piedmont (4.5 per thousand), Valle d'Aosta (4.3 per thousand) and Lombardy (4.2 per thousand). The lowest values for the available beds indicator are observed in the South, particularly in Campania (2.9 per thousand) and Calabria (2.8 per thousand) [3]. Data from the National Outcomes Programme (PNE, Piano Nazionale Esiti 2023) showed a substantial reduction in 30-day mortality rates from heart attack throughout Italy, with values hovering around 7.7%. However, Molise, Apulia, Campania, Sicily and Lombardy show wide intra-regional variability [4]. The same applies to the number of percutaneous coronary artery revascularization (PTCA) inter-

ventions that are performed within 90 minutes in patients with acute ST-elevation myocardial infarction (STEMI), as per international guidelines: again, there is a lot of intra-regional variability and waiting times due to a number of regulatory/organisational conditions ranging from the establishment of the STEMI network, to the rapid interaction between Hub and Spoke centres, to regional logistical difficulties in reaching Hub centres [4]. This variability is not only related to the outcomes of ischemic pathologies. Considering heart failure, a disease with a high socioeconomic impact and hospitalisation rates exceeding 130,000 per year, one realises that Bolzano, Veneto, Molise, and Emilia-Romagna have some of the highest re-hospitalisation rates in Italy.

## Socioeconomic inequalities

Socioeconomic variables used to identify differences in cardiovascular disease prevalence represent a special area when analysing the cardiovascular health status of the Italian population.

Due to the high rate of transcription errors and underreporting (up to 30%) [4], it is rather difficult to evaluate data on the "educational qualification" variable obtained through Hospital Discharge Cards (SDOs, Schede di Dimissione Ospedaliera), it is somewhat obvious that educational level differences can have an impact on cardiovascular health.. The lack of perception of "cardiovascular danger" is accentuated as the social gap grows. A study by Kubota et al. [5] found that among men with education to the primary school level, lifetime cardiovascular risk was 59%, decreasing to 42% among college graduates. Among women, the disparity is even greater, ranging from a 51% risk among the least educated to just 28% among women who have reached the highest level of education [5]. Italian sociodemographic disparities are in line with international data. Petrelli et al. [6] observed that Italian men with a low educational level had a 21% and 17% higher risk of cardiovascular disease and coronary artery disease, respectively, while less educated Italian women had a 41% and 61% higher risk, respectively.

The latest ISTAT data [1] analysed mortality indicators by educational qualification for the first time. In Italy, avoidable mortality, which includes preventable and treatable mortality, between the ages of 30 and 74, is equal to 29.8 deaths per 10 thousand residents, with the preventable mortality component prevailing over the

treatable one. The rate is highly variable according to educational qualification, and is equal to 39.6 deaths per 10,000 residents in the population with a low level of education (primary school certificate or lower), while it drops to 20.3 in the population with the highest level of education (bachelor's degree or higher). Inequality of avoidable mortality by educational qualification is higher in males than in females: less educated males have about 2.3 times higher mortality than the more educated, while among females this ratio is about 1.8. Moreover, when education levels are higher, regional inequalities of avoidable mortality are reduced.

Regarding socioeconomic status as a whole, a study published in JAMA Cardiology estimated that lower status is associated with an incidence rate of myocardial infarction double that of citizens with higher status. Furthermore, the higher incidence of cardiovascular disease in the most disadvantaged classes is apparently 60% due to factors related to socioeconomic status and only 40% due to traditional risk factors [7].

Hence, it is necessary to reach an adequate understanding of the impact of socioeconomic status on cardiovascular risk, with an aim to finding possible solutions to remedy the current significant inequalities.

## Gender inequalities

Cardiovascular disease is the leading cause of mortality in females, yet they often underestimate and do not understand the risk. In fact, according to a study by the Italian Society of Cardiology, women are mainly concerned with oncological diseases, and in particular breast cancer. Worryingly, there has been an increase in female mortality in southern regions, due to both the lack of awareness of cardiovascular risk among women and lack of prevention of risk factors.

In fact, the analysis of PNE data [4] revealed significant gender differences, both in accessing available treatments and in the outcomes. Women who suffered a STEMI gained access to PTCA later than men ($p<0.001$) throughout Italy. Naturally, this behaviour generally results in increased 30-day mortality rates after an episode of acute myocardial infarction (OR=1.07; $p<0.05$).
In fact, care for women with cardiovascular disease is poorer, for example, than hospital care in departments other than cardiology. From a pathophysiological point

of view, it is known that there is different cardiovascular pharmacological management for men and women. Different pharmacokinetic and pharmacodynamic characteristics of cardiovascular drugs have been observed in women [8]. These differences, while often substantial and of considerable importance, are not considered by guidelines that recommend similar titration for both men and women [8].

On the other hand, compared to men, women tend to use healthcare less, as they often put family and its management responsibilities before the proper management of their own health [9].

Therefore, the main aim of health professionals should be to optimise population health management and care by overcoming old stereotypes, promoting greater awareness of the need to look after one's own health, and understanding the pathophysiological basis of individual diversity.

*Table I. Inequalities in cardiovascular health in Italy*

## Causes of differences in cardiovascular health across the country

### 1. Regional causes

Inequality in healthcare provision varies across the country, especially in the southern regions. This highlights a clear "southern healthcare issue" stemming from challenges with re-entry plans, ineffective prevention measures, reduced bed capacity, outdated technologies and facilities in hospitals, as well as a shortage of human resources, in many cases inadequate training and, finaly to the lack of a continuity strategy between hospitals and local areas.

### 2. Socioeconomic and cultural causes

Socioeconomic differences may impact cardiovascular health. Failure to perceive the "cardiovascular danger" and lack of awareness of the effectiveness of prevention as well as the need for swift recourse to hospital facilities, more evident in disadvantaged social classes, are inevitably responsible for increased mortality and morbidity of cardiovascular disease.

### 3. Gender causes

Women are not well informed about the risk of cardiovascular disease, which is their primary cause of death, especially in southern regions. Women, who may experience different symptoms than men, are often reluctant to be hospitalized even when necessary, and drug or interventional therapy is often less effective in their case.

### Possible solutions for a cardiovascular health program in Italy

1. Identify critical geographic areas due to inadequate local prevention, lack of beds, substandard hospitals, outdated technology, and limited human resources.
2. Develop an effective hospital-territory continuity strategy.
3. Conduct social responsibility campaigns and organize targeted programs for the prevention and treatment of cardiovascular diseases, including mandatory screening programs for cardiometabolic risk factors (e.g., hypercholesterolemia, diabetes, obesity, hypertension) across the entire country, with particular focus on critical areas. Pay greater attention to women through the establishment of training and information programs aimed at raising awareness of the risks, more effective gender-specific prevention programs
4. Ensure equitable and timely access to therapies.

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# 03

# PSYCHOLOGICAL, SOCIAL AND ECONOMIC IMPACT OF CARDIOVASCULAR DISEASE

## Morbidity and disabilities of cardiovascular diseases

Circulatory system diseases place a considerable burden on health systems and public budgets. In around 30 years, the number of patients with cardiovascular disease worldwide has almost doubled from 271 million in 1990 to 523 million in 2019 [1]. Overall, the prevalence of cardiovascular disease further increased to 607.64 million cases in 2020, an increase of 29.01% from 2010; the age-standardised prevalence rate reached a value of 7,354.05 per 100,000, an increase of 0.73%. Global trends in disability-adjusted life years (DALYs) and life years lost to cardiovascular disease have also increased significantly: years lived with disability doubled from 17.7 million to 34.4 million over the same period [1,2]. In Europe, 12.7 million new cases of cardiovascular disease were estimated in 2019 with a prevalence of about 113 million people affected [3]. Analysing disability-adjusted life years, there are an estimated 85 million DALYs for cardiovascular disease in Europe, with an average of 4893 age-standardised DALYs per 100,000 people. Disability-adjusted life years for men are almost twice as high as for women and almost four times higher in middle-income countries than in high-income countries [3]. In Italy, on the other hand, the prevalence of individuals affected by cardiovascular disease is 4.4 per thousand [4], with a huge impact not only on healthcare expenditure but also, and above all, on the mental, social, work, and economic state of the affected patients, generating additional management costs related to the emergence of new "disabled" individuals.

## Cardiovascular disease mortality

According to WHO estimates, about 17.9 million people died from cardiovascular disease in 2019, i.e. 32% of all deaths globally, and more than three in four of these deaths occur in low- and middle-income countries [5]. In addition, 85% were due to acute coronary syndromes and strokes. This number rose further in 2022 to reach a grand total of about 19.8 million. Deaths are expected to increase to 24 million by 2030, with an average of more than 66 thousand people per day. However, the age-standardised mortality rate was 239.80 per 100,000 people, which represents a decrease of 12.19% compared to 2010 [2]. Furthermore, although deaths from cardiovascular disease typically rise with age, in 2019, cardiovascular disease accounted for 38% of the 17 million premature deaths (under age 70) caused by cardiovascular diseases [6]. In Europe, cardiovascular disease, in accordance with global data, remains the most common cause of death. They account for about 45% and 39% of female and male deaths, respectively [6,7]. Ischemic heart disease is the most common cause of death from cardiovascular disease, accounting for 38% of all deaths from cardiovascular disease in women and 44% in men, followed by intracerebral haemorrhage and ischemic stroke [3]. 39% of all deaths involve  women compared to men. The standardised mortality rate in European countries for cardiovascular disease was 344 deaths per 100,000 people in 2020, with the rate for men about 1.4 times higher than that for women [3]. These standardised rates are systematically higher for men than for women in all European countries, although gender differences were relatively low for many other causes of death. In Italy, cardiovascular disease remains the leading cause of death, being responsible for 44% of all deaths, with a prevalence higher than the European average (7,499 cases per 100,000 inhabitants) partly due to the particularly high average age of our population [7]. In Italy, there were 746,324 total deaths in 2020, including 227,350 from circulatory diseases (30.4%), 177,858 from cancer (23.8%), 78,673 from COVID-19 (10.5%), and 57,113 from respiratory diseases (7.6%) [8]. Furthermore, when analysing avoidable, i.e. preventable and treatable, mortality, it was observed that at the European level, in 2020, the leading cause of treatable mortality was ischemic heart disease (1.9 per 10,000 residents, accounting for 20.1% of the total number of deaths from treatable diseases), followed by colorectal cancer (1.4 per 10,000 residents), breast cancer among women (1.0 per 10,000 residents), and cerebrovascular disease (1 per 10,000 residents) [2].

## Psychosocial impact on the person and his or her environment

It is now well known how psychosocial factors are implicated in the incidence and prognosis of cardiovascular disease [9]. Indeed, there has been a gradual shift from the traditional biomedical model to the biopsychosocial model in recent years. In other words, the patient is no longer considered as only a passive recipient of medical and pharmacological treatment, but as an individual embedded in a context of relationships and interactions that can affect both the onset and the way the disease is perceived and thus managed during its clinical course: thus, there has been a shift from an approach related to the symptom and the disease to one that places the person at the centre. The relationship between cardiovascular disease and mental disorders is bidirectional. This relationship appears to be mediated by both behavioural and physiological mechanisms, including inflammation, alterations in the autonomic nervous system, neurohormonal factors, and genetic predisposition [10]. After a cardiac event, one can go through states of anxiety, depression, and even develop symptoms typical of post-traumatic stress disorder (PTSD): according to data in the literature, the percentage of patients who develop PTSD is between 19% and 38% of those who have suffered a cardiac arrest, between 16% and 22% of those who have had a myocardial infarction, between 8% and 18% of patients undergoing cardiac surgery, and between 11% and 16% of those who have undergone a cardiac transplant [11]. Failure to adequately intervene in these psychological and emotional aspects may jeopardise the patient's chances of both psychological and physical recovery. People with mental disorders have a shorter life expectancy than the general population, and cardiovascular disease plays a major role in premature deaths in this subpopulation [12]. Cardiovascular disease is often untreated in these patients because they may be related to a high prevalence of modifiable cardiovascular risk factors, underestimation of cardiovascular risk and symptoms.

## Socio-occupational and economic impact

Cardiovascular disease is challenging in terms of healthcare costs and lost productivity due to premature death and stroke [13]. In 2021, healthcare spending on cardiovascular diseases increased to 282 billion euro, 100 billion more than in 2003 (169 billion) [15]. This corresponds to to 2% of the European Union's gross domestic product, with an average per capita expenditure of 630 euro. Specifically, 74% of the estimated 282 billion was for healthcare in the narrow sense (primary care, emergency care, hospitalisations, outpatient care, and drugs) and for so-called informal care (i.e., time taken away from work or one's private life by caregivers of people with a cardiovascular disease), with hospitalisations and drug therapies as the main items of expenditure, while the remainder of the expenditure includes the loss of productivity brought about by premature deaths and disabilities caused by these conditions, as well as for social assistance [14]. Analysing individual cardiovascular diseases, we found that 28% was spent on coronary heart disease and 27% on cerebrovascular disease [16]. As far as Italy is concerned, cardiovascular diseases have a significant impact in socioeconomic terms, which translates into direct and indirect costs to the National Health Service and the social security system amounting to 15% of total health expenditure [15]. In 2021, cardiovascular diseases had an impact on the National Health Service, as direct costs, of about 15 billion euro (2.5 for outpatient services and 12.5 for inpatient admissions), to which we must add about 5 billion euro that can be calculated as lost productivity. In addition, diseases of the cardiovascular system are a major item of expenditure in terms of disability checks provided by the National Institute of Social Welfare (INPS, Istituto Nazionale di Previdenza Sociale), which reached 413,694 in 2001-2015. Annually, more than 750 million euro in indirect costs incurred by the INPS for cardiovascular disease are estimated (with a rising trend) [17].

## Research and innovation in cardiovascular health

The clinical and epidemiological importance of cardiovascular diseases requires further research efforts to deepen our understanding of their causes and mechanisms and their impact on the community, including population health status and clinical management outcomes, as well as approaches to diagnosis and treatments, through innovation, prevention strategies, and appropriate and innovative organisational models.

In 2020, the economic crisis triggered by the pandemic and health containment measures also affected research. According to ISTAT data (www.istat.it), total research and development spending by companies, public institutions, private nonprofit institutions and universities, which amounted to 25.0 billion euro in 2020, decreased by 4.7% compared to 2019. This contraction depended mainly on businesses (-6.8%), but also affected universities (-2.0%) to some extent, while in the public sector spending remained unchanged. Expenditure as a percentage of GDP was 1.51%, up from the previous year (1.46%) due to the marked decline in GDP. However, the improvement was not enough to reach the European target for 2020, which was set at 1.53% for Italy. In 2021 there was an important recovery in business investment (+5.2% over 2020), which, however, was not enough to return to 2019 levels, but fortunately remained steady in 2022. In that year, the EU as a whole spent 352 billion euro on research and development, 6.34% more than in the previous year (331 billion euro). In this overall trend, Italy stands out with a 76.2-million-euro deficit. Spending fell from 25.991 billion in 2021 to 25.915 billion in 2022 (Eurostat data). With the exception of nonprofits and universities, self-funding is confirmed as the main source of R&D spending. Specifically, public institutions finance their industry by 86.5% and domestic enterprises by 82.3%; however, in both industries, self-financing is down compared to 2019 (-0.6 and -3.2 percentage points, respectively). On the other hand, both foreign and government funding increased; in particular, the former mainly in the business sector (+2.7 p.p. compared to 2019), the latter for nonprofit organisations (+6.1 p.p.). Regarding the role of public spending, in 2021, funds earmarked for research and development by central government, regional authorities and autonomous provinces rose by 4.4%, from 11,020 million euro in 2020 to 11,504 million in 2021.

In conclusion, although R&D investment has increased in all industries compared with the pandemic period, our country needs to make a greater effort to reach European standards by aligning itself with other EU countries, particularly in the pursuit of green and sustainable technologies.

## Impact of the COVID-19 pandemic on cardiovascular health

In Italy, the unexpected COVID-19 pandemic caused an unprecedented critical situation in terms of hospitalisations and deaths from cardiovascular diseases [18]. Cardiologists in Italy have been overwhelmed by this unprecedented battle against COVID-19 for several reasons related to the disease itself, the rapid conversion of many hospitals to COVID-19 treatment centres, and the changes in healthcare management caused by the pandemic [19]. The emergency lines (112/118) in some regions were overwhelmed by COVID-19-positive patients, and hemodynamic laboratories have greatly reduced routine non-emergency elective procedures, which have been completely discontinued in the regions with large numbers of infected patients. According to a survey conducted by the Italian Society of Cardiology, a 50% reduction in hospitalisations for acute coronary syndromes was observed during the pandemic, even in regions not heavily affected by COVID-19 [21]. Moreover, it is worth mentioning that this survey also showed that some patients with myocardial infarction with ST-segment elevation arrived at the hemodynamic laboratory with great delay (much longer than the maximum limit of 120 minutes suggested by the guidelines), even in regions with low density of COVID-19 cases where beds were available in coronary care units, but the same is true for patients with myocardial infarction without ST-segment elevation, albeit in a smaller percentage (30% reduction) [19]. This substantial reduction may be due to multiple factors, i.e. partly due to patients' fear of contracting the infection during their hospital stay, lack of availability of local doctors, or the fact that the 118-emergency line was extremely busy managing COVID-19 patients. The rate of hospitalisations for other cardiovascular conditions (heart failure, atrial fibrillation, device malfunction and pulmonary embolism) also decreased during the pandemic period [21]. It is also understood that COVID-19 infection can result in cardiac involvement, in some cases independent of lung disease. An increase in troponin levels related to "non-coronary" myocardial damage has been frequently documented in patients with COVID-19. In addition, type I or type II myocardial infarctions triggered by the inflammatory response of the vi-

rus have also been reported in COVID-19 [22]. In practice, the pandemic created new cardiovascular patients, both because of the outcome of late-treated or even home-managed heart attacks and because of the cardiovascular consequences of the infection itself.

*Table II. Psychological, social and economic impact of cardiovascular disease*

- Circulatory system diseases place a considerable burden on health systems and public budgets. Overall, the prevalence of cardiovascular diseases has further increased: in Italy, this indicator is equal to 4.4 per thousand with an enormous impact not only on healthcare spending, but also and especially on the psychological, social, employment and economic status of affected patients, generating additional management costs related to the emergence of new "disabled" people.
- Cardiovascular disease is costly in terms of healthcare expenditure and lost productivity due to premature death and stroke. By 2021, healthcare spending on cardiovascular disease in Europe has increased to 282 billion euro, 100 billion more than in 2003 (169 billion).
- Cardiovascular disease prevention should not be seen as a cost but rather as an investment and a tool to reduce mortality, disability, and hospital and family costs borne by citizens, contributing to the sustainability of the healthcare system and the growth of the socio-economic system.
- COVID-19 – the most important stress on our healthcare since World War II – could have been an opportunity to reform the National Health Service, but many critical issues remain across the country in terms of prevention, access to care and uniformity of outcomes after an event.

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# 04

# CARDIOVASCULAR RISK FACTORS

The main cardiovascular risk factors can be classified into modifiable and non-modifiable categories. Non-modifiable risk factors include age, sex, ethnicity, and a family history of cardiovascular and autoimmune diseases (e.g., type 1 diabetes). Modifiable and causal risk factors for atherosclerotic cardiovascular disease (ASCVD) include blood lipoproteins containing apolipoprotein-B [with low-density lipoproteins (LDL cholesterol) being the most abundant], arterial hypertension (AH), cigarette smoking, and diabetes mellitus (type 2 diabetes). Another significant risk factor is adiposity (obesity), which increases the risk of cardiovascular disease (CVD) both through conventional major risk factors and other mechanisms. In addition to these, there are many other relevant risk factors, CV risk modifiers, and clinical conditions such as physical inactivity, an unhealthy diet, sleep duration, and even depression.

## Non-modifiable risk factors

### Age

Age is the main cardiovascular risk factor. The incidence and prevalence of cardiovascular diseases – such as ischemic heart disease, heart failure, atrial fibrillation, sudden death, and certain heart valve diseases, particularly aortic stenosis – increase significantly with advancing age. It is recorded that 58% of patients with diseases of the circulatory system are over 65 years old, and of these, 63.3% have at least two cardiovascular risk factors [1]. The prevalence of valvular heart disease reaches 12% in people over 75 years old. This data, contextualised in a society with high-life expectancy and a declining birth rate, poses a major challenge for cardiovascular health in Italy [2].

### Gender

Gender plays a key role in the development of cardiovascular disease, with men tending to experience it on average 6 to 10 years earlier than women. However, the impact and distribution of modifiable cardiovascular risk factors do not differ

significantly between the genders [3]. Cardiovascular disease is the leading cause of death among women, particularly due to cerebrovascular and coronary artery disease [4]. Women have natural protection against atherosclerotic and coronary artery diseases: these occur later than in men, generally leading to lower cardiovascular risk. With advancing age, this benefit diminishes, particularly during menopause, a period when the risk of obesity and hypertension increases, along with lipid levels. Therefore, greater emphasis on exercise and a healthy diet is recommended. Women also have unique cardiovascular risk factors such as early (natural or induced) menopause, oral contraceptive use, prolonged exposure to endogenous oestrogen, polycystic ovary syndrome, gestational diabetes, or pregnancy-related hypertension, which require a targeted approach [5]. In addition, premature births are considered a cardiovascular risk factor because they indicate potential placental insufficiency, a sign of possible endothelial dysfunction. It is also important to note that hormone therapy may increase cardiovascular risk in transgender women [6].

### Genetic factors

In recent years, the role of genetics has grown in importance as a predisposing factor for many cardiovascular diseases, such as familial hypercholesterolemia [8]. Nevertheless, diseases such as hypertension and ischemic heart disease have multifactorial causes: in addition to the genetic factor, predisposing to the onset of the disease, there are other determinants such as the presence of environmental factors or the coexistence of other cardiovascular risk factors. It is important to consider how some gender-related factors can be affected by the interaction between biological sex and social gender. There are also other cardiovascular diseases where genetic factors have been identified, such as dilated cardiomyopathy, peripartum cardiomyopathy, other hereditary cardiomyopathies, or some arrhythmias. Although our understanding of the role of genetics in various cardiovascular diseases is evolving, it is still limited and often inferred indirectly from family history.

## Modifiable risk factors

The prevention of cardio-metabolic risk factors, also highlighted in the National Chronicity Plan and the National Prevention Plan 2020-2025, is an essential component in combating the spread of cardiovascular diseases. Literature and empi-

rical evidence have shown that cardiovascular risk is reversible and that reducing risk factor levels leads to a decrease in both the incidence and severity of events. According to the WHO, by addressing risk factors, especially those that are modifiable, through appropriate lifestyle changes, more than three-quarters of cardiovascular deaths could be prevented. For instance, there is a positive correlation between mortality rates from cardiovascular, cerebrovascular, and vascular diseases and the percentage of individuals who are overweight and do not engage in physical activity, as well as an inverse correlation between adopting a healthy diet and mortality rates.

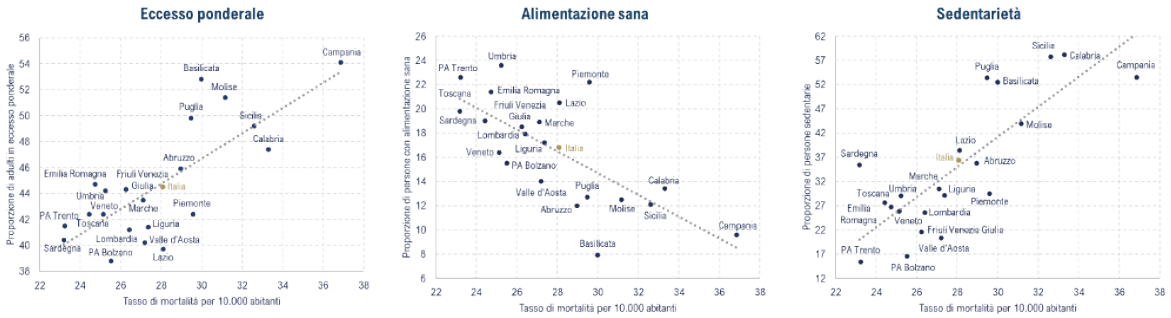



*Figure 1. Comparison of the age-standardized mortality rate for circulatory system diseases and the standardized proportion of overweight individuals aged 18 and over (left), the standardized proportion of individuals aged 14 and over who do not engage in any physical activity (center), and the standardized proportion of individuals aged 3 and over who consume at least 4 servings of fruit and/or vegetables per day (right), 2022 or most recent available data - Source: Meridiano Cardio – The European House-Ambrosetti (2023), "Roadmap towards the National Cardiovascular, Cerebrovascular, and Vascular Plan."*

## Hypercholesterolemia

The causal role of LDL cholesterol (LDL-C) and other apo-B-containing lipoproteins in the development of ASCVD is unquestionably demonstrated by genetic, observational, and interventional studies [9]. The role of LDL-C as a risk factor for ASCVD can be described by the following statements: a prolonged low concentration of LDL-C correlates with a lower risk of ASCVD; the reduction in the risk of cardiovascular disease is proportional to the absolute reduction in LDL-C, regardless of the drugs used for this reduction [10]; and the reduction in LDL-C dependent on the absolute risk of ASCVD and the reduction in LDL-C itself represents an absolute benefit, being beneficial even in patients at high or very high risk [11]. Non-HDL chole-

sterol (HDL-C) encompasses all atherogenic lipoproteins and is calculated as: total cholesterol minus HDL-C. The relationship between non-HDL-C and cardiovascular risk is as strong as that with LDL-C, containing essentially the same information as plasma apoB concentration [12]. Non-HDL-C is used as input data in the SCORE2 and SCORE2-OP risk algorithms. HDL-C is inversely associated with cardiovascular disease risk, but very high levels of HDL-C may indicate increased risk. However, there is no evidence from Mendelian randomization studies or randomized trials showing that as plasma HDL-C increases, the risk of cardiovascular events is reduced [13]. However, HDL-C remains a useful biomarker for refining risk estimation using SCORE2 algorithms. The SCORE2 algorithm cannot be used for patients with genetic lipid disorders, such as familial hypercholesterolemia. Specific LDL-C thresholds and targets are recommended regardless of estimated cardiovascular risk for patients with familial hypercholesterolemia or other rare/genetic lipid disorders. (Specific targets for risk classes + laboratory reports)
It is also necessary to raise awareness among the population about the correct interpretation of laboratory reports and update the relevant alerts: consider an LDL cholesterol target level below 100 mg/dl for individuals with moderate cardiovascular risk, while reducing this threshold to below 70 mg/dl for high-risk patients, below 55 mg/dl for very high-risk patients, and below 40 mg/dl for extreme-risk patients (ESC Guidelines 2019).

In particular, patients with acute coronary syndrome (myocardial infarction or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke, TIA, and peripheral artery disease should aim for an LDL target below 55 mg/dl. Additionally, individuals who have not had an event but have significant atherosclerotic plaque clearly documented via coronary angiography or CT (multivessel coronary artery disease with two major epicardial arteries with stenosis >50%) or carotid ultrasound should also aim for an LDL cholesterol target below 55 mg/dl, in accordance with ESC guidelines.

### Hypertension

Epidemiological studies and randomized trials have confirmed that high blood pressure is a major cause of both atherosclerotic and non-atherosclerotic cardiovascular diseases. (ASCVD and non-ASCVD) corresponding to 9.4 million deaths and 7% of disability-adjusted life years globally [14]. High blood pressure is a risk factor for the development of diseases such as coronary artery disease, heart failure, cerebrovascular disease, atherosclerotic disease of the lower extremities, chronic kidney

disease, and atrial fibrillation. In addition, the risk of death increases linearly with increasing blood pressure values [15]. The benefit of reducing systolic blood pressure depends on the absolute risk and the actual reduction in pressure, considering lower limits dictated by tolerability and safety. The management of hypertension is defined by its category (optimal, normal, normal-high, stage 1 to 3 hypertension, and isolated systolic hypertension), determined by outpatient or home measurements. Studies indicate that the way blood pressure changes throughout life differs between women and men. This could potentially raise the risk of cardiovascular disease at lower pressure levels [16].

### Cigarette smoking

Cigarette smoking is the cause of 50% of preventable deaths among smokers, half of which are due to atherosclerotic cardiovascular disease. Lifelong smokers have a 50% chance of dying from smoking and lose an average of 10 years of life. Smokers under the age of 50 are five times more at risk of cardiovascular disease than nonsmokers [17]. The risk associated with prolonged smoking is greater in women than in men [18]. Smoking is the world's second-largest risk factor for disability-adjusted life years, immediately after high blood pressure [19]. Exposure to second-hand smoke also increases the risk of cardiovascular disease [20], just as the use of some types of vapes is linked to an increased risk of adverse cardiovascular events [21].

In Italy, according to the latest ISTAT data [22], in 2023, the proportion of smokers aged 14 years and older was 19.9%. This proportion is decreasing slightly compared to 2022, but with a markedly increasing trend when compared to 2019 (18.7%). Smoking habits are more prevalent among men than women (23.6% vs. 16.4%); over time the gender gap has become significantly narrower (it was 11.2 percentage points in 2010 and reached 7.2 percentage points in 2023), due to the greater long-term reduction of male smokers compared to female smokers (-4.9 percentage points among men and -2.8 among women between 2010 and 2023). Higher proportions of smokers have been observed among the age group of 20-24 year olds, reaching the highest level among 25-34 year olds (26.9%). In 2023, similar proportions of smokers were observed in the different macroareas of the country, with values standing at 19.7% in northern Italy, 20.1% in southern Italy and 20.2% in central Italy.

## Diabetes mellitus

Type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and prediabetes (pre-DM) are independent risk factors for atherosclerotic cardiovascular disease, approximately doubling the risk depending on the population and therapeutic control [23]. Women with diabetes, especially type 2 diabetes, are noted to have a particularly high risk of cardiovascular outcomes (coronary artery disease, stroke) [24]. Patients with type 2 diabetes tend to have a significantly higher risk of ischemic and vascular mortality, regardless of the presence of other ASCVD risk factors (including dyslipidemia and hypertension), each of which further increases the risk. Therefore, risk stratification for both ASCVD and non-ASCVD cardiovascular disease in diabetic patients is crucial for tailoring treatments proportionate to the patient's risk.

T2DM and prediabetes are common conditions in patients with coronary artery disease (CAD), encompassing both acute coronary syndromes (ACS) and chronic coronary syndromes (CCS), and are associated with worse prognosis. Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance (IR), hyperinsulinemia, and elevated plasma glucose levels. This condition, coupled with traditional cardiovascular risk factors, leads to the development of macrovascular disease even before the onset of manifest diabetes mellitus. The pathophysiological mechanisms supporting the concept of a "glycemic continuum" characterized by elevated fasting glucose levels (IFG: Impaired Fasting Glucose), reduced glucose tolerance (IGT), and overt diabetes mellitus (DM) underlie the pathophysiology of both diabetes and cardiovascular disease. The development of cardiovascular disease (CVD) in the presence of insulin resistance is a progressive process, marked by early endothelial dysfunction and vascular inflammation, foam cell formation, and the subsequent development of lipid streaks. Over the years, this leads to the formation of atherosclerotic plaques, which, with increased inflammatory content, become unstable, resulting in occlusive or sub-occlusive thrombosis. The atheroma in patients with diabetes is richer in lipids, inflammatory mediators, and thrombi compared to that in non-diabetic patients [23a].

Individuals with type 2 diabetes are generally considered at high cardiovascular risk, with a 10-year incidence of cardiovascular disease between 14.7% and 17% and a prevalence of cardiovascular complications between 10.5% and 19.8% [25]. Diabetes accelerates the development of cardiovascular disease, bringing it forward by 20-30 years in women and 15-20 years in men. Mortality from myocardial infarction is higher in diabetics compared to the general population, with a doubling of risk among diabetic women compared to non-diabetic women [26].

Women with type 2 diabetes appear to have an especially high risk of stroke [24]. Patients with type 2 diabetes often have multiple ASCVD risk factors (including dyslipidemia and hypertension), each contributing to an increased risk of both ASCVD and non-ASCVD conditions.

### Obesity

In recent decades, body mass index (BMI) – measured as weight (in kg) divided by height squared (in m^2) – has increased substantially worldwide in children, adolescents and adults [27]. Mendelian randomisation analyses suggest a linear relationship between BMI and mortality in non-smokers and a J-shaped relationship in smokers [28]. In patients with heart failure, there is an obesity paradox, with a lower risk of mortality in patients with higher BMI. A meta-analysis concluded that both BMI and waist circumference are similarly, strongly, and continuously associated with ASCVD and type 2 diabetes [29]. In Italy, 44.6% of 18-year-olds were found to be overweight, according to ISTAT 2023 data [22]. This figure is stable compared to what was recorded in 2022 (44.5%). Men have higher levels of excess weight than women (53.5% vs. 36.1%). This trend is observed in all age groups and is particularly high at middle age, where the proportion of overweight men is about 40% higher than that of women. Excess weight gets higher as age increases and is particularly pronounced in southern regions (49.9% vs. 41% in northwestern regions). Excess weight and obesity are closely related conditions to a sedentary lifestyle. In 2023, the proportion of sedentary people in Italy who stated they did not engage in either sports or physical activity in their free time was 34.2%. Women lead more sedentary lives than men (37.1% vs. 31.2% in total), although the gender gap has been narrowing over time (it was 7.8 percentage points in 2010 and fell to 5.9 percentage points in 2023). As age increases, people's lives become more sedentary: among adolescents and young people up to 24 years old, it affects 2 in 10 people, whereas it reaches almost 7 in 10 people among the population aged 75 years and older [22].

## Cardiovascular risk modifiers

In addition to conventional cardiovascular risk factors listed in risk tables, additional factors or particular individual factors may change the calculated risk. A potential modifier can be taken into account if it improves risk prediction, if there is a clear impact on public health, if it is achievable in daily life, if available infor-

mation shows reduced risk when the modifier demonstrates a positive outcome, and if the literature regarding this potential modifier is not distorted by publication bias. Few modifiers meet all these criteria, and meta-analyses in this field are often subject to considerable publication bias [30]. In addition, there is a general lack of RCTs that determine whether additional risk information leads to better health outcomes. Assessing risk modifiers is particularly important when individual risk is close to a decisional threshold [31].

### Psychosocial factors

According to a dose-response model, there is a correlation between psychosocial stress and the development and progression of ASCVD, independent of conventional risk factors and gender. Psychosocial stress includes stress symptoms and stressors such as loneliness and critical life events. Relative risks (RR) usually range between 1.2 and 2.0 [32]. Psychosocial stress has direct biological effects and correlations with socioeconomic and behavioural risk factors. Only "vital exhaustion" showed improvements in risk re-classification [33]. Guidelines recommend assessing psychological stress in patients with ASCVD [34], and studies have found positive effects of depression screening [35].

### Imaging Techniques

Assessing coronary atherosclerosis by arterial calcium scores (CAC) can change the cardiovascular risk classification, considering conventional risk factors, and is useful in cases of borderline risk [36]. Contrast-enhanced computed tomography (CCTA) identifies coronary stenosis and predicts cardiac events Carotid ultrasonography, despite the lesser extent of evidence compared with CAC, could be considered as a risk modifier [37]. The measurement of arterial stiffness, although predictive, is hampered by technical difficulties and publication bias [38]. The ankle brachial index (ABI) is another possible indicator of cardiovascular risk and is useful for a rapid and economical diagnosis of peripheral arterial disease (PAD).

## Other clinical conditions and lifestyles

### Chronic kidney disease

In the population with chronic kidney disease, cardiovascular disease is the major cause of morbidity and mortality [39]. Cardiovascular diseases in patients with uremia can be assessed with conventional risk factors, although the specific ure-

mic factors must be taken into consideration. The combined effect leads to the so-called "accelerated atherosclerosis" that causes most uremic patients to die from cardiovascular complications even before they reach dialysis. The presence of microalbuminuria or frank proteinuria indicates a cardiovascular risk so high as to be significant even in the general non-uremic population. An improved prognosis can only be achieved with an early and accurate diagnosis.

### Alcohol consumption

There are hypotheses that moderate alcohol consumption is linked to cardiovascular health benefits. [40]. However, the harms caused by alcohol negatively outweigh the possible benefits on cardiovascular health. Alcohol is therefore considered a significant risk factor, being the leading cause of mortality in the 25-49 age group [41]. In Italy, bad alcoholic drinking habits affected 15.6% of the population aged 14 years and above in 2023 [22]. The highest prevalences of at-risk use have been documented in the northern regions, especially in the Northeast (19.4%), compared with the Centre (15.1%) and the South (12.2%); when comparing with 2022, an increase in the prevalence of at-risk consumers was observed in northern regions and conversely a decrease in central regions, further widening regional differences. In southern Italian regions, the situation has been stable for the past two years. The gender differential remained high, with a higher proportion of men with risky drinking habits (21.8% vs. 9.8% of women).

### Diet

An unbalanced diet can trigger health problems that increase the risk of cardiovascular disease. Diets high in saturated fats, sugars and salt can promote the onset of risk conditions such as diabetes, hypertension, dyslipidemia and obesity. Regarding healthy eating habits in Italy, the proportion of the population aged 3 years and above who consumed at least 4 servings of fruits and/or vegetables a day was 16.5% in 2023. This proportion is almost stable compared to the previous year (when it was 16.8%), but remains at significantly lower levels than in 2015-2018, when it reached about 20% [22].

### Physical activity

Physical activity has an important and often superior role to drug therapy in the prevention and treatment of many conditions such as cardiovascular disease, diabetes, cancer, obesity, depression, Alzheimer's, and arthritis. On the other hand, physical inactivity is a persistent public health problem that causes many cardio-

vascular diseases. In fact, 9% of premature deaths can be attributed to physical inactivity, a similar mortality rate can be attributed to cigarette smoking. In addition, physical inactivity is responsible for about 10% of health care costs (a huge figure, amounting to $120 billion annually in the United States) [42].

## Study on physical activity

### Italy, a nation of lazy people

In Italy, 43% of women and 30% of men do not get enough exercise (150 minutes of moderate physical activity per week). This percentage of inactivity is among the highest in EUROPE (Figure 2).

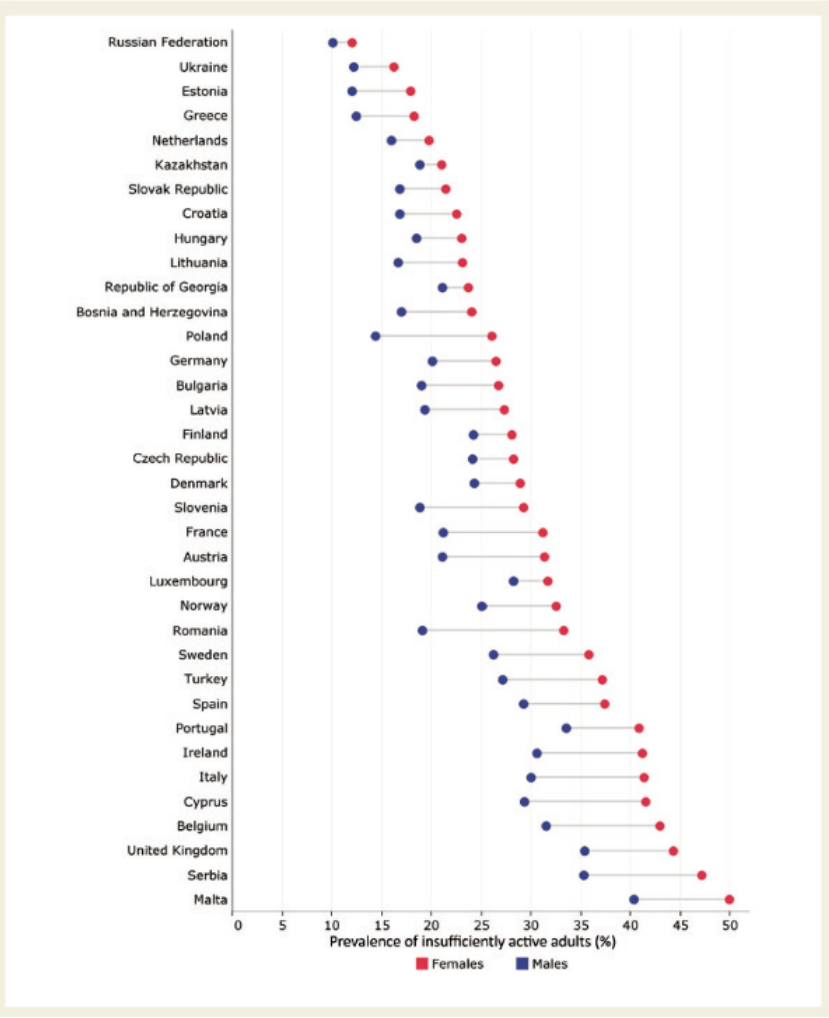
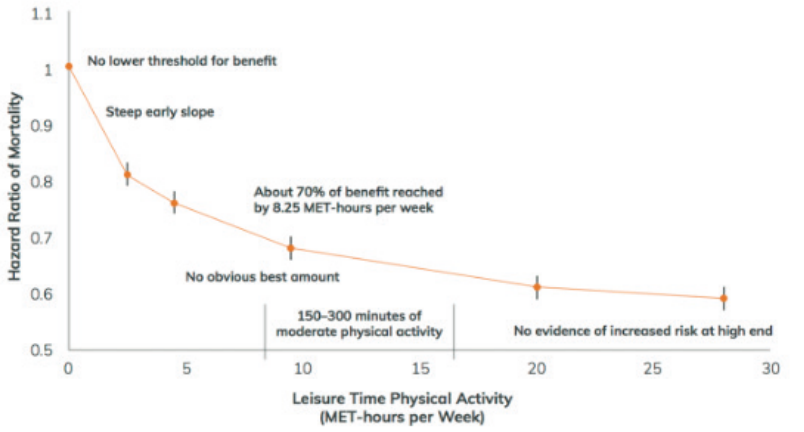



*Figure 2. Prevalence of insufficient active adults in ESC member countries. Modified from European Heart Journal (2017) 0, 1-72 doi: 10.1093.*

To date, many individuals between the ages of 15 and 69 do not meet WHO or Ministry of Health physical activity requirements, which leads to increases in cardiovascular risk factors such as high cholesterol, obesity, diabetes, and hypertension. On the other hand, decreasing sedentary lifestyle and increasing physical activity reduces the risk of cardiovascular disease and type 2 diabetes and protects against risk factors such as hypertension and obesity, as long as the exercise is constant and moderate in intensity. WHO recommends at least 150 minutes of moderate physical activity per week, or 75 minutes of vigorous activity, to reduce the risk of chronic diseases, including cardiovascular disease. Regular exercise of at least moderate intensity can mitigate the risks associated with a sedentary lifestyle in the long term [43].
Exercise has a strongly beneficial effect on the heart and health in general. In fact, a scientific study of more than 300,000 subjects followed for 12 years showed that moderate exercise reduced all-cause mortality by 16-30% compared with inactive subjects [44]. The correlation between physical activity and mortality is shown in Figure 3.




Source: Adapted from data found in Moore SC, Patel AV, Matthews CE. Leisure time physical activity of moderate to vigorous intensity and mortality: a large pooled cohort analysis. PLoS Med. 2012;9(11):e1001335. doi:10.1371/journal.pmed.1001335.

*Figure 3. Correlation between physical activity and mortality. Modified from PLoS Med. 2012;9(11):e1001335. doi: 10.1371/journal.pmed.1001335.*

Aerobic exercise is the recommended type of physical activity as it induces benefits directly proportional to the level of exertion. Aerobic exercise involves moving large muscle groups in a rhythmic manner for a sustained period. It consists of activities that can be done every day such as cycling or brisk walking, gardening, running, jogging, aerobics, and swimming. Moderate-intensity activity is defined as walking at a brisk pace (between 4.8 and 6.5 km/h, or cycling at 15 km/h). Under these conditions, breathing becomes faster but it is still possible to speak in full sentences. On the other hand, vigorous exertion is defined as running, jogging, cycling (with a speed >15 km/h), intense gardening, singles tennis, where breathing becomes very fast and comfortable conversation is no longer possible (Figure 4). One of the recommended types of exercise is power walking, which is walking at a speed above the natural walking range, typically 7 to 9 km/h. To distinguish power walking from jogging and running, at least one foot must maintain contact with the ground the entire time.

**Moderate activity:**

- Brisk walking
- Swimming
- Cycling on flats (<16 km)
- Tennis (double)
- Yoga
- Aquagym

**Intense activity:**

- Jogging
- Swimming
- Cycling (>16 km)
- Tennis (single)
- Kickboxing

*Figure 4. Examples of moderate or intense physical activity*

The World Health Organization (WHO) considers a policy leading to a 10% reduction in the prevalence of physical inactivity in the general population to be strategic, given the rising mortality and health costs of physical inactivity [45]. In fact, there are four harmful behaviours to combat according to WHO: physical inactivity, alcohol, excessive salt use and cigarette smoking. Regarding exercise,

WHO in its strategic plan 2013-2020 (see Figure 3) recommends a policy leading to the redevelopment of dedicated urban areas, educational campaigns for the entire population, physical activity education in schools, and the availability of safe areas in public parks or recreation spaces that encourage physical activity.
To combat pediatric obesity in addition to diet, it is advisable to increase physical activity that is now reduced due to the use of smartphones, games and TV. The latest U.S. exercise guidelines recommend for preschoolers (ages 3 to 5 years) 3 hours a day of physical activity to enhance growth and development. Children and adolescents aged 6 to 17 years should perform one hour of moderate-intense physical activity per day.

In conclusion, physical inactivity is a major risk factor for cardiovascular disease, and in contrast, moderate exercise of 60 minutes 3 times a week (or 150 minutes a week), such as brisk walking (4.8-6 km/hour), lengthens life span and quality of life. Scientific societies, media and institutions must have as a strategic goal the reduction of physical inactivity in the coming years by at least 10% as suggested by the WHO document.

### Lipoprotein(a) or Lp(a)

Lipoprotein(a) is a promising biomarker that can help refine current strategies for assessing the risk of atherosclerotic disease and aortic stenosis. It is elevated in about 20% of the global population and adds value in preventive medicine.
Lp(a) is a low-density lipoprotein (LDL) particle with the addition of apolipoprotein(a) (apo[a]). Etiologically, it may have provided a survival advantage in prehistoric humans by promoting wound healing and reducing bleeding, particularly during childbirth. An individual's Lp(a) level is 80-90% genetically determined. Interestingly, Lp(a) levels remain quite stable throughout a person's life, regardless of lifestyle.
Who should measure this new biomarker?
Primarily, those with a first-degree relative who had premature atherosclerosis (< 55 years in men; < 65 years in women), particularly if labeled as low risk, or patients with severe hypercholesterolemia (LDL-C ≥ 190 mg/dL). It can also help in deciding whether to recommend statins for individuals at intermediate risk or to identify those at risk of developing aortic stenosis. In any case, the new guidelines suggest measuring Lp(a) once in every adult's life to identify those with very high hereditary levels of Lp(a) (> 180 mg/dL), which may indicate a significantly higher risk of atherosclerotic disease. Statins do not reduce Lp(a), whereas PCSK9 inhi-

bitors can reduce it by 30-40%. Studies are ongoing with innovative new drugs aimed at significantly lowering Lp(a), which could be extremely important for the prevention of atherosclerotic disease and aortic stenosis.

### Vulnerability

Vulnerability is a condition defined as a progressive age-related deterioration of physiological systems, which leads to a reduction in reserves of intrinsic functional capacity. This deterioration increases vulnerability to stressors and increases the risk of a range of adverse health outcomes [46]. Vulnerability is closely associated with multivessel coronary artery disease [47] and is a relevant prognostic factor in patients with cardiovascular disease. Evaluation and treatment of vulnerability may predict adverse outcomes in these patients. Given the implications for cardiovascular health, prevention, early diagnosis, and treatment approaches, particularly through multicomponent exercise, are vital. Vulnerability assessment has become a key aspect in determining possible response to treatment, resilience, or ineffectiveness of therapies. This is especially relevant in the era when invasive cardiovascular interventions, such as percutaneous interventions, cardiac surgery, implantation of cardiac devices, and circulatory support systems, have increased. These interventions have become increasingly common in elderly patients, including those in their eighties and nineties.

*Table III. Strategies to reduce the impact of cardiovascular disease*

**To reduce the impact of cardiovascular disease, it is necessary to follow the magnificent seven tips:**

1. Maintain an appropriate body weight
2. Avoid smoking
3. Stay physically active (150 minutes of moderate activity per week)
4. Follow a healthy diet (fish, vegetables and fruits, avoid animal fat and excess calories)
5. Check blood pressure and if greater than 140/90 mmHg take medication
6. Monitor LDL cholesterol levels and maintain them at the target level according to the individual's specific cardiovascular risk. If necessary, use medications to keep LDL levels within the target range
7. Monitor blood glucose levels and, if needed, use medications that reduce cardiovascular risk. Consider the cardiovascular risk associated with elevated blood glucose levels

*Table IV. Possible solutions for a cardiovascular health program in Italy*

1. Promote a policy that leads to the redevelopment of dedicated urban areas and bike paths, educational campaigns for the entire population, physical activity education in schools, and the availability of safe areas in public parks or recreation spaces that encourage physical activity. Promote monitoring of the amount of physical activity actually performed by the NHS, including through the use of computer systems by providing possible forms of rewards for virtuous citizens.
2. Promote through the General Practitioner the measurement for all adult subjects of blood pressure,LDL cholesterol and blood glucose levels and promote, if necessary, lifestyle changes and guideline-recommended therapy.
3. Promote a dietary education program in schools, universities and workplaces.
4. Promote education campaigns among young people to discourage the initial use of cigarette smoking, e-cigarettes and drugs. Provide reward systems to encourage smokers to quit smoking.
5. Promote a cardiovascular risk prevention campaign through a national screening program for individual cardiometabolic risk, assessing hypercholesterolemia, hypertension, obesity, and diabetes.
6. Encourage diabetes prevention by promoting adherence and ensure that individuals at risk have access to innovative therapies for all diabetic patients according to the guidelines.

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# 05

# CARDIOVASCULAR DISEASES

## Ischemic heart disease

As well as being the leading cause of death in Italy [1], ischemic heart disease has also been the most disabling condition in terms of DALYs for the last 3 decades. According to the most recent Global Burden of Disease data (2019), in Italy there are 4,571 total cases per 100,000 population and 530.3 new cases per year per 100,000 population. There were 61,494 deaths from ischemic heart disease (32,504 men and 28,990 women), including 19,753 from acute myocardial infarction. The 1-year mortality rate for acute myocardial infarction IMA was 9.2% (2019) [2].

Thanks to advances in cardiology, the 30-day mortality after hospital admission recorded in 2022 was 7.7%, similar to 2021 and down from 2020 (8.4%) [3].

The COVID-19 pandemic has had a major impact on cardiovascular disease in general and ischemic heart disease in particular. According to data from the National Outcomes Programme (report 2023), following the pandemic, there has been a drastic reduction in hospitalisations for acute myocardial infarction, which were well below the expected values based on the pre-pandemic trend: -12% in 2020 and -9.6% in 2021. In 2022, there was a slight increase in hospitalisations (around 1,200 more than in 2021), approaching pre-pandemic levels [3].

In light of both its epidemiological impact and the operational and organisational challenges faced by healthcare networks and facilities responsible for treating the acute phase and monitoring the post-acute and chronic phase, ischemic heart disease is a vital public health issue in Italy.

### Critical points and gaps in evidence

The organisation of regional networks for the treatment of acute myocardial infarction with ST-segment elevation (STEMI) – as recommended by the Italian Federation of Cardiology (Federazione Italiana di Cardiologia, FIC) and international guidelines – is crucial. The aim is to increase the number of patients undergoing

primary angioplasty and, more generally, coronary reperfusion therapy, speed up the diagnostic-therapeutic process in time-dependent ischemic diseases, and improve prognosis.

The "RETE IMA WEB" Project was launched in 2007 by the Italian Society of Invasive Cardiology (SICI-GISE), in collaboration with the FIC, with the aim of measuring the implementation of STEMI networks in Italy. In 2008, networks across the country were revealed to be inefficient and very uneven, despite a good level of infrastructure [4].

Taking into account Italy's geographical diversity, it is easy to see how well-functioning, easily accessible regional networks responsible for the diagnosis and treatment of the acute phase are of critical importance, and how, particularly in this area, telemedicine and artificial intelligence could play an important role.

On the other hand, there is still a lack of adequate monitoring of post-acute and chronic patients via the organisation of secondary prevention territorial plans and cardiological rehabilitation determined by the risk level of individual patients. Current guidelines emphasise the importance of personalised medicine and the need to tailor treatment strategies to the patient, taking into account gender, age, vulnerability and other risk factors. This approach requires a comprehensive, multidisciplinary, coordinated, patient-centred perspective.

### Goals and actions

Proposals for improving morbidity and mortality rates and the prognosis of patients with ischemic heart disease:

1. Foster primary and secondary prevention activities and campaigns and promote early detection algorithms using artificial intelligence.
2. Improve access to technological and pharmacological innovation.
3. Optimise therapeutic adherence.
4. Implement telemedicine services and other digital health tools.
5. Foster continuity between different care settings (acute and chronic).
6. Encourage the active involvement of the patient [2] and his or her family members.
7. Optimise the use of specific health networks in caring for patients with suspected acute coronary syndrome-STEMI, ensuring access to timely invasive treatment and defining clear strategies for those living in areas without nearby 24/7 accessible hemodynamic rooms.

8. Promote the development of systems for recording and evaluating the quality of healthcare through indicators that ensure good clinical practice, consistency and equity.
9. Establish protocols for standardised action and care (diagnosis, treatment, transport) throughout the geographic area.
10. Promote a training programme for all professionals involved throughout the myocardial infarction care process with the aim of improving and standardising diagnosis and treatment, while also promoting better knowledge of the symptoms of ischemic heart disease in women.
11. Develop and implement a strategic plan of education, communication and outreach for citizens and medical professionals, targeting the most vulnerable groups (elderly patients and women) in particular, to ensure equity in access to diagnosis and treatment and promote more efficient use of emergency systems.
12. Establish key indicators so heart attack care networks can consistently relay information.
13. Develop cardiac rehabilitation and secondary prevention programmes in hospitals and primary care facilities based on patients' risk.
14. Ensure and facilitate the delivery of hospital-based secondary prevention and cardiovascular rehabilitation programmes to patients with ischemic heart disease as soon as possible after suffering an acute event (myocardial infarction, percutaneous revascularisation, or surgery).
15. Implement a training programme for primary care, emergencies and hospital emergencies.
16. Nurture the development of secondary prevention and cardiac rehabilitation units in areas where they are not yet implemented, with standardised resources and activities.
17. Develop interdisciplinary outpatient programmes tailored to the patient's level of risk by fostering the creation of care networks.
18. Incorporate new technology to reinforce the role of the primary care team (general medicine, nursing, physiotherapy) by establishing agile, two-way communication channels between primary care and hospitals (specific applications, electronic consultation, shared health records, apps), which ensure the monitoring and attainment of secondary prevention goals by establishing indicators to assess their effectiveness.
19. Promote education and empowerment in patient and family self-care in coping with chronic disease (healthy lifestyle, adherence to treatment plans and self-monitoring of risk factors) [5].

### Indicators

1. Presence of secondary prevention and cardiac rehabilitation programmes in hospitals and health facilities and percentage of patients receiving secondary prevention and cardiac rehabilitation intervention.
2. Time required to start secondary prevention and cardiology rehabilitation programmes after hospital discharge.
Risk-adjusted in-hospital mortality rate in patients hospitalised for ACS (Acute Coronary Syndrome).
Percentage of patients with ACS with ST segment elevation -STEMI) treated with angioplasty and monitoring the time between diagnosis and invasive treatment.
3. Percentage of patients with ACSwithout ST-segment elevation (NSTEMI) undergoing coronary angiography and monitoring the time between diagnosis and invasive treatment [5].
4. Monitoring the achievement of lipid targets 6 months after an acute coronary syndrome [6]

*Table V. Possible solutions for a cardiovascular health programme in Italy with the aim of reducing ischemic heart disease mortality and morbidity.*

1. Increase perception and treatment of cardiovascular risk factors (Chapter 4).
2. Implement awareness campaigns for the general public such as "every minute counts" to prevent avoidable delays and reduce the pre-hospital mortality of heart attacks. Incentivise calling the national emergency services 118/112 lines and deter patients with suspected myocardial infarction from driving to the hospital. Around 50% of patients who have a STEMI heart attack die before reaching the hospital (preventable deaths).
3. Equipping ambulances with electrocardiographs, telemedicine, and, in the future, artificial intelligence systems (already available), for the diagnosis of STEMI myocardial infarction and other parameters that can be obtained from an electrocardiogram (ejection fraction, patient criticality, left and right ventricular dysfunction, etc.).
4. National systems to evaluate the efficiency of time-dependent networks: simulations of interventions for suspected heart attack, retrospective evaluations of time from first medical contact (FMC) to ECG, ambulance arrival, hospital admission, and door-to-balloon. Evaluation of the suitability of pre-hospitalisation therapy, devices used, etc.

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## Heart failure

### Critical points and gaps in evidence

Heart failure, also known as congestive heart failure, is a condition characterised by the inability of the heart to support the metabolic demands of peripheral tissues or to do so at the cost of increased pressure within the cardiac chambers. It is a chronic disease of great clinical and societal significance, as well as high economic impact, as not just the number of patients, but also their complexity, tends to increase over time [1].

Critical points in the management of heart failure include the need to:

- Organise heart failure care through coordinated multidisciplinary units/programmes with the participation of all professionals involved at all levels, including home care;
- Provide a health care system that can accommodate the sharply rising prevalence of heart failure in the coming years and ever-increasing patient complexity.
- Resolve regional disparities regarding the prescription and dispensing of disease-modifying drugs.

Epidemiological data from Europe and the United States project a 1.5% rise in the prevalence of heart failure in the population by 2030, reaching a rate of 3.5-4.5%, which could lead to an increase of around 200% in the cost of managing the disease, especially in the advanced stage, compared to today. In Italy, in view of the large number of individuals at high cardiovascular risk and the high preva-

lence of ischemic heart disease, the incidence and prevalence of heart failure are progressively rising, alongside healthcare costs and the increasing complexity of care required. Data from the National Outcome Program of the National Agency for Regional Health Services (AGENAS) [1] shows that in Italy, on average, the frequency of hospitalisations for heart failure is high and the rate of readmission within 30 days of discharge is around 14%, with huge disparity between regions.

Gaps in evidence in the management of heart failure include:

- Pathophysiological, diagnostic, and phenotypic framing of specific forms of heart failure, such as preserved ejection fraction, which are widely prevalent in the population but largely underdiagnosed;
- The role of biomarkers in the diagnosis and therapeutic management of heart failure and access to the prescription of NT-Pro BNP by the NHS;
- Treatment plans for patients with preserved or mildly reduced ejection fraction where drugs with proven prognostic benefit are limited;
- Treatment plans for patients with improved ejection fraction where the timing of continuation and/or discontinuation of drug therapy at disease remission is not yet defined;
- Planning of the administration sequence of disease-modifying drugs to patients with reduced ejection fraction heart failure;
- Pharmacological management of patients with severe renal dysfunction;
- Indications for the implantation of implantable devices in patients with preserved or mildly reduced ejection fraction heart failure;
- The advantages of remote disease management with particular regard to home care.

### Goals and actions

To deal with the critical areas of pathology, it is necessary to set general and specific goals and establish a plan of action.

### Critical point 1. Organise heart failure care through coordinated multidisciplinary units/programmes with the participation of all professionals involved at all levels in order to optimise the diagnostic pathway and management of the condition

1. Overall goal: aid the early diagnosis of heart failure in different health care settings (primary, community and hospital care) in order to lessen the evolution of

the disease over time, prevent episodes of acute heart failure, and improve the quality of life of heart failure patients; optimise patient care by specialised facilities in order to manage it effectively.

1.1 Specific goal: develop national protocols on the early diagnosis of heart failure regardless of type, the context in which it is suspected (primary, community or hospital care) and the specialists involved;

1.2 Specific goal: implement a multidisciplinary care network for optimised early diagnosis and prompt care;

1.3 Specific goal: develop nationwide shared protocols for clinical, pharmaceutical, instrumental and follow-up management of heart failure regardless of type and the context in which it is diagnosed (primary, community or hospital care).

Actions to be implemented for the resolution of critical point 1:

- Establish continuing education programmes on heart failure to improve the training of professionals involved in the diagnosis and management of the condition;
- Facilitate nationwide access to specialist outpatient clinics by reducing waiting lists; facilitate access to natriuretic peptide determination, currently not funded by the Italian health service; facilitate access to a level 2 echocardiogram;
- Reduce regional disparities in access to care and reduce healthcare migration;
- Establish a joint hospital/community approach for patients with suspected or confirmed diagnosis of heart failure;
- Establish multidisciplinary care facilities to facilitate patient access to care.

**Critical point 2. Provide a healthcare system that can accommodate the sharp rise in the prevalence of heart failure over the coming years as well as increasing patient complexity.**

1. Overall goal: organise the different levels of care required to manage newly diagnosed heart failure patients as well as complex patients.

1.1 Specific goal: develop nationwide shared protocols to manage complex patients and new cases of heart failure;

1.2 Specific Goal: provide the tools needed to manage complex patients at all levels of care;

1.3 Specific goal: establish a multidisciplinary care network to manage new cases of heart failure and complex patients.

Actions to be implemented for the resolution of critical point 2:

- establish continuing education programmes on newly diagnosed heart failure and decompensated patients with comorbidities to improve the education of professionals involved in the management of the condition;
- establish a joint hospital/community approach for patients with newly diagnosed or multiple diseases;
- establish multidisciplinary care structures to facilitate shared management of complex patients;
- carry out educational activities (workshops, talks, group activities) for patients diagnosed with heart failure and caregivers to improve their symptoms, quality of life, and adherence to both pharmacological and non-pharmacological treatments, promoting self-care.

**Critical point 3. Resolve regional disparities regarding the prescription and dispensing of disease-modifying drugs.**

1. Overall goal: offer equal access to care throughout the different regions of Italy.
   1.1 Specific goal: establish a single system for prescribing and dispensing drugs that impact disease progression.

Actions to be implemented to achieve critical point 3:

- Eliminate regional formularies to standardise access to care;
- Standardise the criteria for prescribing new-generation drugs for the treatment of heart failure (SGLT2i, ARNI) nationwide;
- Establish standardised criteria in the health service on the therapeutic management of heart failure for care units, prioritising indications for the transition between specialised care and emergency and primary care after hospital discharge.

## Indicators

According to the American College of Cardiology/American Heart Association classification, heart failure can be divided into four stages: A, B, C and D [3]. Stage A includes patients with conditions at risk of developing heart failure such as hypertension, diabetes mellitus, and coronary atherosclerosis, but not yet suffering from the condition, in the absence of structural cardiac changes. Stage B patients present structural cardiac changes at risk of developing heart failure. Stage C patients present symptomatic heart failure with instrumental signs of impaired

left ventricular function. Stage D includes patients with refractory heart failure that does not respond to treatment. Indicators related to heart failure can be classified by stage as each phase of the disease has specific requirements and needs. In stage A disease, those involved in the management of patients are GPs and local specialists, particularly cardiologists, nephrologists, diabetologists, and internists. Quality indicators at this stage are aimed at preventing the disease in individuals at high risk of developing it and can be summarised as:

- Percentage of patients identified as being at high cardiovascular risk with a possibility of developing heart failure in the future;
- Establishing and reaching pressure, lipid, and glycaemic targets in order to reduce the risk of long-term complications;
- Assessment of organ damage in patients with cardiovascular risk factors;
- Patient education on diet, physical activity, body weight and blood pressure monitoring, medication compliance, what to do if symptoms deteriorate, individual follow-up plan;
- Left ventricular function assessment at each chemotherapy cycle in cancer patients and within 5 years in subjects with prior chemotherapy exposure;
- Reducing waiting times for making and attending specialist outpatient appointments.

In stage B disease, those involved in the management of patients are general practitioners and local specialists, in particular, cardiologists, nephrologists, diabetologists, and internists, as well as nurses specialised in the management of the disease. At this stage, quality indicators focus on prevention of the disease in high-risk individuals with specific cardiac alterations, as well as the prescription of effective preventive drug treatment:

- Percentage of patients with structural cardiac changes at risk of developing heart failure;
- Prevention of sudden cardiac death;
- Evaluation of left ventricular systolic and diastolic function, carotid atherosclerosis, and presence of proteinuria/microalbuminuria;
- Pharmacological treatment with renin-angiotensin system inhibition, sympathetic nervous system inhibition, statins and antithrombotic drugs in patients with atherosclerosis, anticoagulants in patients with atrial fibrillation;
- Reducing waiting times for making and attending specialist outpatient appointments;

- Overcoming regional disparities in the prescription of drugs to prevent heart failure.

In stage C disease, those involved in the management of patients are GPs and local specialists; in particular, cardiologists with expertise in heart failure, nephrologists with expertise in cardio-renal pathology, diabetologists and internists, as well as nurses specialised in the management of the disease in inpatient and outpatient hospital settings and home care. At this stage, the quality indicators focus on the diagnosis of heart failure, its classification and stage, and prescribing pharmacological treatment effective in modifying the development of the disease and preventing its progression:

- Percentage of patients diagnosed with stage c-level heart failure;
- Classification of the type of heart failure;
- Level 1 multidimensional assessment in patients aged 75 or over for assessment of mental and physical state, cognitive abilities and level of self-sufficiency in terms of individual care needs;
- Inclusion and titration of drugs recommended for the treatment of the type of heart failure diagnosed and prescription rates of individual drugs and combination therapy;
- Primary prevention of sudden death;
- Percentage of patients undergoing clinical and instrumental functional assessment at baseline and in follow-up;
- The use of specific questionnaires to assess quality of life and long-term prognosis;
- Prevention rates of heart failure flare-ups through close monitoring of response to treatment and constant follow-up assessments;
- Reducing waiting times for making and attending specialist outpatient appointments;
- Lowering waiting times for patients who are candidates for invasive procedures;
- Overcoming regional disparities in the prescription of drugs suitable for treating heart failure.

In stage D disease, those involved in patient management are general practitioners and local specialists, in particular: cardiologists with expertise in heart failure and advanced heart failure care; cardiac surgeons; nephrologists with expertise in cardio-renal pathology; palliative care specialists; as well as nurses specialised in the management of the condition in inpatient and outpatient hospital settings and home care. At this stage, quality indicators focus on diagnosing advanced he-

art failure, prescribing pharmacological treatment effective in modifying the development of the disease and preventing its progression, providing palliative care where the disease is no longer responding to standard treatment, and specialist surgery (ventricular assist mechanisms, heart transplant) where the disease is considered refractory:

- Percentage of patients identified as having stage d heart failure;
- Implementation of highly specialised individual care plans agreed upon between the gp and hospital/outpatient clinic where the patient is being treated;
- Implementation of home monitoring systems for symptoms, vital parameters, medication compliance and patient and caregiver education on nutrition, physical activity, weight control, what to do if symptoms deteriorate, individual follow-up plans;
- National implementation of cardiology and respiratory rehabilitation plans;
- Verify pharmacological and non-pharmacological therapy suitable for treating heart failure;
- Percentage of patients identified as requiring referral for specialist surgery (ventricular assist mechanisms, heart transplant, correction of valvulopathy);
- Percentage of patients identified as requiring palliative care referral.

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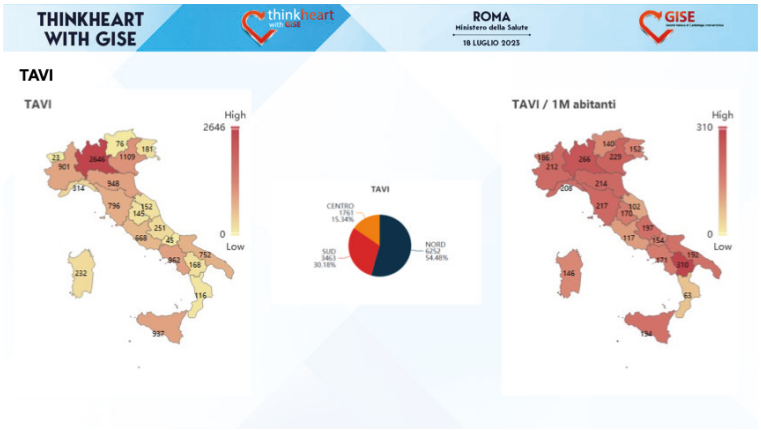
## Valvular Heart Disease

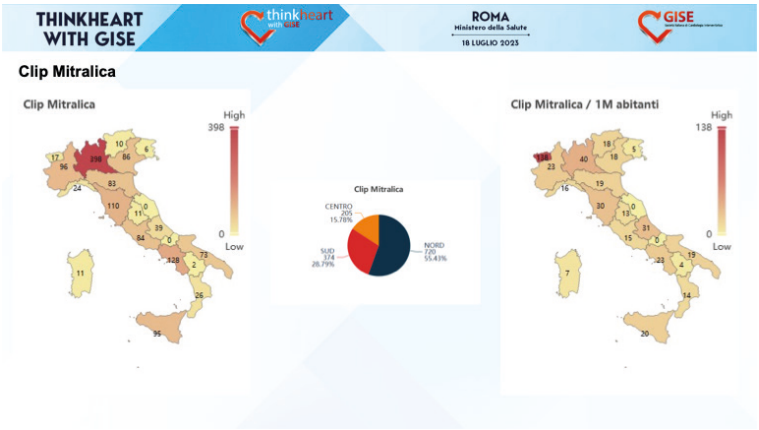
Demographic changes, characterised by an aging population, have led to an inevitable increase in the incidence of valvular heart disease of degenerative etiology in industrialised countries. In contrast, rheumatic etiology still predominates in developing countries. The prevalence of valvular heart disease is higher over the age of 65. Estimates by the Italian National Institute of Statistics (ISTAT) from 2017 demonstrate an incidence of valvulopathy in the elderly at around

12.5%, which could reach 33% in 2040 due to the country's aging population [1]. The most common valvular heart diseases are aortic valve stenosis and mitral insufficiency. There was a 40% increase in surgeries to treat heart valve diseases or disorders between 2010 and 2018, with spikes of 53% for those relating to the aortic valve.
In 2021 there were 33,919 hospitalisations for valvuloplasty or heart valve replacement, up from 29,238 in 2020 (PNE 2021); 9,911 aortic valve replacements with transcatheter approach (TAVI) were performed in the same year. More than 800 million euros is spent each year to treat these patients [1,2]. The latest ESC/EACTS August 2021 guidelines on valvular heart disease, which recommend TAVI for patients aged 75 years and older, also represent an opportunity for the economic sustainability of the healthcare system. The use of TAVI in 90% of patients over 75 would save 52,000 days of hospital inpatient or rehabilitation care annually, estimated at 13 million euro [1-5].




There was a marked increase in valvuloplasty and valve replacement surgeries in the years prior to the pandemic. Following the drastic decline recorded in 2020 (22% lower than expected), in 2022 the recovery which began in 2021 continued, gradually returning to expected levels (-9.3% from pre-pandemic levels, corresponding to around 3,800 fewer hospitalizations). Regarding mortality at 30 days after valvuloplasty or valve replacement surgery, median values were slightly lower in 2022 (2.2%) compared with previous years [3].

Therefore, the increase in average lifespan, the consequent increased incidence of valvular diseases and the simultaneous development of new therapeutic opportunities make these pathologies of important interest in the healthcare sector.




## Critical points and gaps in evidence

Swift diagnosis of valvular heart disease is often hampered by non-specific symptoms. It is necessary to develop protocols for early diagnosis of the disease and use appropriate diagnostic tools. Since it is generally a progressive condition, early diagnosis and the optimisation of the selection and timeframe of the type of treatment (surgical or percutaneous) through a comprehensive multidisciplinary evaluation, is essential. Guidelines highlight the need to increase and improve the use of patient assessment tools (gender, age, frailty) to select the appropriate course of treatment. Among degenerative heart valve diseases, aortic stenosis is the most common primary valvular lesion requiring corrective intervention (surgical or transcatheter), for which guidelines also recommend further research to evaluate its pathophysiological aspects and new therapeutic targets for medical treatment. The treatment of mitral insufficiency has also undergone many changes in recent decades, thanks largely to repair techniques using clips [6]. However, percutaneous mitral valve replacement still requires more evidence and research as opposed to TAVI where the data is more robust. Moreover, the literature shows promising data for the extension of treatment of aortic stenosis with TAVI to patients at low surgical risk as well as in terms of cost-effectiveness [7]. Percutaneous aortic valve prosthesis implantation is currently only possible in hospitals with cardiac surgery departments. However, many studies have demonstrated the low complication rate associated with this procedure, and some ongoing studies present very promising data on TAVI implantation in hospitals without cardiac surgery departments [8].

## Goals and actions

Goals relating to valvular heart disease:

1. Patient education: it is necessary to inform patients about disease-related risks,

help them understand symptoms, and actively involve them in treatment choice;
2. Promote the early diagnosis of valve disease through the development of standardised protocols and guidelines;
3. Design referral protocols for hospital care of patients with suspected valve disease and create a network for follow-up through primary care;
4. Improve knowledge among health professionals of the factors involved in the development of valve disease in order to initiate prevention programmes;
5. Improve the overall approach to patients with valvular heart disease to optimise treatment choice by establishing common criteria agreed by specialists in cardiology, cardiac surgery, geriatrics, and nursing;
6. Establish a process quality control mechanism through mandatory institutional registers and the introduction of new reimbursement strategies such as "pay for performance" [5].

### Indicators

The following indicators can be used with regard to valvular heart disease:
1. Quality of life and impact of treatments on it;
2. Survival rate through statistical analysis of survival and mortality associated with different forms of valvular heart disease;
3. Frequency and duration of hospital admissions, tools that can be correlated to the effectiveness of treatment. 30-day mortality rate from valvuloplasty or heart valve replacement differs according to the valves involved (aorta or mitral) and the procedures (cardiac surgery or transcatheter) [9].
4. Volume of admissions for valvuloplasty or heart valve replacement, categorized by the type of valve (aortic or mitral) and the procedure (surgical or transcatheter) [9].

*Table VI. Critical points and organisational insights in patients with valvular heart disease*

### Critical points and organisational insights in patients with valvular heart disease

- Carry out a national screening program for the diagnosis of treatable heart valve diseases;
- The critical points mainly concern aspects related to the organisational capacity of specialised (hub) and local (spoke) facilities, the waste and inefficiency present in the patient care pathway and the lack of standardised networks. This combination of factors hinders more widespread use of TAVI and percu-

taneous repair of mitral and tricuspid valvulopathy;
- Fifty percent of patients with symptomatic severe aortic stenosis die in 2 years if left untreated. Therefore, it is vital to organise a joint approach between GPs, spoke facilities and hub centres in order to ensure the greatest possible access to innovative transcatheter procedures throughout the country;
- Spread DRGs evenly across the country to avoid a policy of attracting patients to regions where transcatheter procedures are more lucrative;
- Even out the number of interventional procedures per million inhabitants throughout the country so patients are not forced to access healthcare in a different region, which is inconvenient for patients and their families as well as an extra burden on regional governments;
- Assess suitability and outcomes of transcatheter and surgical procedures, through mandatory institutional registers.

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## Arrhythmia

The management and treatment of arrhythmia is an eminent subject on which to concentrate healthcare efforts because of the epidemiological impact, the difficulty of managing it with pharmacological treatment, and the recent boost provided by ablative/interventional technology.

### Critical points and gaps in evidence

Current guidelines on the management of arrhythmia, indications for device implants, as well as on risk stratification of patients at risk of adverse events have a number of critical points and gaps in evidence [1-4]. Accurate screening tools for risk stratification of sudden death in the general population are lacking. Although the field of genetics has made great strides in recent years, there is a lack of objective assessment that can adequately define any genetic variants able to support and predict individual arrhythmic prognosis. Despite the increasingly central role it is taking in cardiovascular diagnostics, cardiac MRI also suffers from a reduced ability to identify the risk of sudden death in subjects with particular pathological conditions such as sarcoidosis, dilated/hypertrophic cardiomyopathy, etc. This stems from the fact that identification of myocardial scarring using gadolinium does not give the clinician the ability to fully discern the patient's incremental risk of lethal arrhythmic degeneration. A consequence of this is the uncertainty in the indications for implantable cardioverter defibrillator (ICD) implantation in primary prevention, which makes it difficult for the clinician/interventionist to reduce fatalities in the general population.

On the other hand, difficulties also arise in the placement of patients with frequent ventricular extrasystole and associated cardiomyopathy [1]: ablative vs. antiarrhythmic treatment are affected by legacy issues and fragmentary literature data especially in apparently asymptomatic subjects. In addition, pharmacological innovation in the field of arrhythmology is stagnant, still using outdated compounds, and at present, nothing new is happening in cardiovascular management. The same uncertainty emerges when considering ion channel disease: the rarity of the condition and the variability of the phenotype and penetrance make the correct stratification of arrhythmic risk and, more importantly, the correct indication regarding implantation of an implantable defibrillator particularly challenging. This also stems from a lack of population screening aimed at identifying subjects and familiar cluster of individuals who are prone to sudden death and

arrhythmic complications, thus to be directed to device implantation for primary prevention purposes.

In fact, there are numerous sticking points related to deciding on the most suitable device to use for pacing, especially when comparing bradyarrhythmias and tachyarrhythmias. While advances in pacemaker algorithms have significantly improved patient outcomes and quality of life, limitations persist. Challenges include optimal pacing site selection, replication of normal cardiac conduction patterns, and biventricular pacing based on the correct identification of "responder sites" [2].

This causes doubts to arise about the invasive treatment of some categories of patients. While life expectancy of less than a year remains a contraindication to defibrillator implantation, it still needs to be established whether the patient's age or vulnerability should be taken into consideration when carrying out careful analysis on the need for the procedure. The ethical/social management of defibrillator implantation is clearly a matter of consensus, although the scientific basis for identifying the benefits is still under investigation and discussion.

Finally, it is crucial not to underestimate the long-standing issue of supraventricular tachyarrhythmias and their management [4]. The use of non-invasive pharmacological treatment remains ambiguous due to the reduced availability of active ingredients on the market at present, as well as their low success rate. Secondly, the choice of non-invasive or invasive assessment of the patient with asymptomatic ventricular pre-excitation remains an issue that needs to be carefully addressed in the literature. Thirdly, unlike ventricular arrhythmias, supraventricular tachyarrhythmias do not have an adequately developed genetic background, which, in turn, makes prognostic stratification of the patient difficult.

### Goals and actions

1. Encourage population screening aimed at early identification of family hereditary arrhythmic diseases, defining risks, prognostic stratification, and outcomes for apparently "normal" patients;
2. Structure dedicated pathways for genetic and hereditary assessment of arrhythmic diseases by creating prespecified networks among clinicians, arrhythmologists, and geneticists to refine the assessment of patients with channelopathies;
3. Identify risk factors and the role of multiparametric imaging in risk stratification of sudden death in the general population;

4. Assess, manage and plan pharmacological and nonpharmacological interventions in patients with ventricular pre-excitation;
5. Develop telemedicine and teleconsultation apparatus for rapid integrated management of arrhythmic events, their complications and information from devices, to make early diagnosis and management of patients.

### Indicators

- Prevalence and incidence of patients with supraventricular and ventricular tachyarrhythmias and their major cardiovascular outcomes;
- Timescale for healthcare delivery structured in standardised diagnostic therapeutic pathways;
- Resource consumption (in terms of fees as well as estimating actual costs) in dedicated pathways for patients with life-threatening arrhythmias with regard to standard-of-care;
- Percentage reduction in sudden cardiac deaths;
- Percentage of subjects correctly assessed as being at high risk for life-threatening arrhythmic disease;
- Percentage reduction in hospitalisations from tachycardiomyopathy/heart failure linked to a failure to control supraventricular/ventricular tachyarrhythmias;
- Nationwide access to interventional procedures and appropriateness and outcome assessment through institutional registers;
- Standardise device and DRG costs across the country.

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# 06

# OTHER CRITICAL POINTS, TARGETS AND INDICATORS FOR IMPROVING CARDIOVASCULAR HEALTH

## Cardiovascular health promotion and prevention, and citizens education

### Critical points

The process of promoting and preventing cardiovascular diseases and educating Italian citizens about them is still an extremely obscure element of the health policy decision-making and management process.

The World Health Organization (WHO) defines health promotion as "the process of enabling people to increase control over, and to improve, their health" [1]. Of course, for this to be possible, it is necessary for citizens to have adequate support through regional governance, as well as to provide further aid for loco-regional treatment facilities to foster autonomy in individual health promotion, and lastly to rethink health services in order to make them more in line with the needs of the population. Such a definition – which should be a corollary to the education of citizens and disease prevention – is not always actionable, thereby contravening the comprehensive application of health promotion principles to the national community.

On the other hand, recent data from the Ministry of Health show a substantial deterioration in the provision of essential levels of care (Livelli Essenziali di Assistenza, LEA) in as many as 12 Italian regions in 2022, with Veneto, Emilia-Romagna and Tuscany currently showing the best levels of management, and a large deficit in Valle d'Aosta, Calabria and Sardinia [2]. This is extremely counterproductive with regard to preventive measures.

The management of cardiovascular prevention remains rather nebulous and controversial. The 2023 Civic Health Report [3] lists access to services (29.6%) as the main concern of citizens in first place, hospital care (15.8%) in second place, prevention (15.2%) in third place, primary care and community healthcare (14.8%) in fourth place, and safety of care (8.5%) in fifth place. The same report indicates a low coverage rate in terms of prevention, health education, screening and vaccination in Italy. The South, in particular, suffers from shortcomings in planning adequate preventive strategies [3]. Add to this the damage caused during the period of sociosanitary anarchy in the pandemic era, and it is easy to understand the sense of gloom regarding healthcare and the consequences of a shameful abandonment of already insubstantial prevention campaigns.

A big sore point is once again the dilemma of waiting lists. While a comparison of 2022 data with 2021 data shows a reduction in waiting lists (from 16.9% in 2021 to 14.6% in 2022), it is important to note that at the same time difficulty in accessing services increased (from 5.8% in 2021 to 12.9% in 2022). All regions suffer from somewhat lengthier waiting and access times for healthcare services, especially in terms of first specialist visits and diagnostic tests [3]. According to a survey by Cittadinanzattiva, citizens waited as long as 60 days for Class B cardiology visits (due within 10 days) and, if the appointment is not given priority, 300 days for a first cardiology visit [3]. Naturally, when this involves cardiovascular medications with a profound impact on patient mortality and morbidity, delays, interruptions, or discontinuations of treatment due to bureaucracy will only increase the incidence of major adverse events [4].Specifically, cholesterol assessment can be performed: A) as a screening on all subjects aged over 40; B) in subjects with cardiovascular disease or cardiovascular risk factors or family history of dysmetabolic diseases, dyslipidemia, or early cardiovascular events. In the absence of elevated values, lifestyle changes or therapeutic interventions, the test should be repeated at 5-year intervals [4]. Considering that atherosclerotic issues often originate in the foetal environment, waiting until age 40 to begin a preventive screening campaign might be too late to effectively lower the incidence of cardiovascular events.

Treatment plans are another source of delay in the administering of LEAs. In the face of an urgent need to control and regulate pharmaceutical prescription to deal with the economic deficit in healthcare, the treatment plan stipulates obligatory specialist appointments, further increasing waiting lists. Of course, when

all this involves medication like cardiovascular drugs with a very high impact on patient mortality and morbidity, their bureaucratic/indirect prolongation, discontinuation or suspension will only increase the incidence of major health outcomes.. Prevention measures, therefore, must first and foremost take into account the need to scale back this notorious trend toward increasing healthcare bureaucracy by finding other ways to control pharmaceutical spending. Although this topic is not sufficiently addressed in institutional settings, credit is due to Italian governance for announcing the National Prevention Plan (NPP) 2020-2025 [5]. In terms of cardiovascular prevention, the 2020-2025 NPP stressed the importance of protecting and promoting physical and mental health from the earliest moments of life with a programme aimed at curbing tobacco use and improving lifestyle through adjusting eating habits and combating obesity. In addition, the NPP aims to consolidate interventions with the purpose of identifying risk conditions for chronic noncommunicable diseases and directing them toward appropriate "caregiving", fostering links with the National Chronicity Plan (NPC) and implementing and extending national coverage of interventions, with particular attention to those targeting patients in vulnerable situations [5].

In this regard, a comprehensive primary prevention programme becomes a key turning point in health promotion in Italy. In fact, intercepting patients at moderate to high/very high cardiovascular risk who have not yet developed events is hardly the preserve of the clinical cardiologist. This is not only in relation to the aforementioned waiting lists, but rather to the lack of educational and preventive campaigns starting with the GP surgery, as well as governmental limitations on the demand for in-depth laboratory/instrumental testing for mass screening of cardiovascular disease. Bearing in mind that the occurrence of adverse cardiovascular episodes is a sign of delayed patient prevention and management, it follows that there is an urgent need to adopt new systems to monitor the cardiovascular health of Italian citizens and, at the same time, improve accessibility to care especially before a cardiovascular event occurs.

There remains, however, the problem of medical human resources required to carry out decision making in cardiovascular prevention. Recent estimates show a shortage of cardiologists amounting to 826 throughout Italy, something that seems to be due primarily to a lack of evaluation and planning in the past few years, but also to the pay gap between specialists in the public and private sector and those also practising abroad – as stated by President of the National Association

of Hospital Cardiologists (Associazione Nazionale Medici Cardiologi Ospedalieri - ANMCO) Dr. Fabrizio Oliva [6]. Obviously, cardiologists throughout Italy – as well as so many other specialists and non-specialists – are committed on a daily basis to coping with the pressures of the system, including in terms of prevention, despite staff shortages. One example is the BRING-UP Prevention and Heart Failure studies implemented recently by ANMCO for coordinated follow-up in secondary prevention of patients at high cardiovascular risk or with heart failure in order to monitor and optimise their management [7,8]. But, as always, these are non-profit studies based on the voluntary research of the clinical cardiologist who is involved beyond his or her commitment to institutional healthcare. Certainly, the creation of appropriate (Preventive)-Diagnostic-Therapeutic-Assistance Pathways (P)DTAPs has become key in promoting the cardiovascular health of citizens by optimising financial resources and availability of facilities. The Apulia Region has launched a dedicated DTAP for the management of dyslipidemia in primary and secondary prevention precisely in an attempt to bring regional economic welfare in line with the health needs dictated and enshrined in international guidelines, with a view to close collaboration between policy makers and governors of public health [9]. The hope is that these strategies can be implemented. They are in any case part of the 2020-2025 NPP and need to be immediately included in the complex field of health promotion.

### "Pay for Performance" or value-based payment

Pay for Performance in the healthcare sector (P4P), also known as value-based payment, includes payment models that link financial incentives/disincentives to provider performance. P4P is part of a broader national strategy to shift healthcare toward value-based medicine. Although the fee-for-service (FFS) system is still in use, P4P pushes providers toward value-based care because it ties reimbursement to outcomes based on objective metrics (mortality, readmission, etc.), proven best practices, and patient satisfaction, thus aligning payment with value and quality of service.

### Performance-based payment and hospital reimbursement

While traditional FFS reimbursement represents a source of income for hospitals, the transition to value-based health programs is rapidly emerging as a new way to deliver healthcare funding. In P4P programs, hospitals are required to pay attention to a wide range of factors that are not incentivized under traditional FFS systems.

There are two basic types of Pay for Performance projects implemented for hospitals. With the first, payers reduce overall FFS payments and use the funds to reward hospitals based on their performance in terms of processes, quality, and efficiency. In the second, hospitals are financially penalized for below-average performance, and the penalties result in direct cost savings for payers or are used to generate an incentive pool.

### Hospital Readmission Reduction Program (HRRP)

Since readmission rates for specific care events vary significantly from hospital to hospital, in the United States, Medicare began penalizing hospitals with higher readmission rates compared to all other acute care hospitals under the Hospital Readmissions Reduction Program (HRRP). In Italy, it is necessary to start by ensuring reliable data through mandatory, institutional, and national registries, which will then allow for strategies to improve quality and assess outcomes.

### Goals and actions

1. Implement policies to intercept the patient at cardiovascular risk at the GP surgery through cardiovascular health education campaigns;
2. Revise the aforementioned Appropriateness Decree in order to create a national preventive cardiovascular screening campaign aimed at reducing the incidence and prevalence of adverse events with the early introduction of pharmacological and nonpharmacological principals in at-risk individuals;
3. Encourage closer collaboration between general medicine and cardiovascular specialists in order to optimise interventions –pharmacological and nonpharmacological – for proper cardiovascular risk management of citizens;
4. Foster interaction between specialists, local pharmacists and regional/state governance to improve the implementation of cutting-edge, clinically proven drug prescriptions by reducing the bureaucratic burden, used as a deterrent to align pharmaceutical spending with health budget caps. In this regard, adherence measures and prescription appropriateness should become a guide for proper management of hospitals and public health;
5. Avoid the health service getting bogged down with unnecessary and repetitive examinations. Evaluate appropriateness of prescriptions; organise information systems to optimise patient flows; evaluate incentive systems for healthcare staff to cut waiting lists; encourage reduction of the bureaucratic burden on doctors so they can devote themselves to clinical activities;
6. Implement the budget for hiring specialist physicians by redesigning staffing

requirement plans not only at the level of loco-regional healthcare, but also at the ministerial level in terms of graduate school fellowships;
7. Reallocate National Recovery and Resilience Plan (NRRP) funds to upgrade hospital instrumentation but also provide incentives for telehealth processes that can overcome the limitations arising from the limited availability of physical resources for carrying out preventive strategies;
8. Define evidence-driven, patient-centred (Preventive)-Diagnostic-Therapeutic-Assistance- (P)DTA pathways for the effective management of all the patient's needs and better management of community resources.

### Indicators

- Reduce the incidence and prevalence of cardiovascular disease in terms of first cardiovascular adverse events or recurrence of events/hospitalisations;
- Reduce the incidence and prevalence of key modifiable risk factors of cardiovascular disease;
- Reduce the deadly impact of cardiovascular disease in Italy;
- Reduce the wait for specialist visits and instrumental examinations by implementing timely systems for tracking prescription appropriateness.

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## Knowledge management, research and innovation

Knowledge management, research and innovation, play a crucial role in healthcare, and contribute to improving its effectiveness, safety and efficiency.

Knowledge management, in the medical field, includes the collection, organisation and sharing of clinical and scientific information. The sharing of best practices, guidelines, clinical protocols and clinical trial results is critical to improving medical practice and promoting innovation. The latter is based on the application of new technology, approaches and solutions to improve the diagnosis, treatment and management of diseases. Examples of innovation include the use of artificial intelligence, telemedicine and precision medicine.

### Critical points

Knowledge management, along with research and innovation are critical for progress in any field, particularly in healthcare. However, some critical points may hinder its development:

- Resistance to change
- Limited financial resources
- Fragmentation of information
- Lack of interdisciplinary collaboration
- Slow adaptation to emerging trends

Unfortunately, poor training of health professionals in research and innovation still appears to be widespread. Research and innovation, particularly those related to cardiovascular issues, should start precisely from health system and citizen needs. Fostering innovation also involves rapid changes that keep pace with new technology. It involves the development of virtual care models, promotion of telemedicine, better management of health data including through the use of artificial intelligence.
The digitalisation process is still a long one with many difficulties, including those linked to geographical differences, and financial issues related to this kind of transformation. Also associated with the aforementioned scenario is a shortage of citizen expertise, and a lack of appreciation for patient outcomes and experiences in institutional relationships.

## Goals and actions

The National Recovery and Resilience Plan (PNRR, Piano Nazionale di Ripresa e Resilienza) in the section Innovation, research and digitisation of the health service [1] also sets its general objectives as enhancing knowledge, research and innovation, enhancing investment in the healthcare system (human, digital, structural, instrumental and technological resources), reinforcing scientific research in biomedical and health fields, and enhancing the structural technological and digital innovation of the health service at central and regional levels. This would ensure the evolution of healthcare delivery, better quality and lower waiting times, as well as make the patient an active participant in clinical care processes.

Regarding the need to orient the training of health professionals toward research and innovation, the following actions can be proposed:
1) Develop training programmes that enable learning of the required skills;
2) Facilitate the development of collaboration between different levels of education, degree and specialised training.

Citizens should also play an active role in the process, acquiring adequate knowledge about cardiovascular health to enable them to be active participants in the process of prevention and treatment. Patients' stories and experiences should be considered valuable sources of growth. Therefore, it is crucial to include patient-reported outcomes and experiences in institutional outcome reporting.

The specific objectives in this area are:

- Use health outcomes to identify needs or problems that require research, development and innovation activities in order to guide Italian projects;
- Create a map of cardiovascular health research, development and innovation needs that assesses previous findings and is periodically updated. Identify for each need the goals to be achieved and the estimated health and economic impacts;
- create a multidisciplinary working group composed of experts in research, innovation and healthcare management, as well as patient associations, to identify initial requirements;
- promote the creation of large national databases by digitalising and sharing data from individual centres;
- foster the use of Artificial Intelligence for better data analysis with huge implications for clinical practice; it is necessary to promote the creation of multidi-

sciplinary working groups with experts in research, innovation and healthcare management;
- Facilitate accessibility of cardiovascular disease patients through e-Health platforms and telemedicine services.

### Indicators

1. Training programmes/courses for professionals in the field of cardiovascular health oriented towards interdisciplinary and integrative approaches;
2. Availability of training programs for patients and caregivers on cardiovascular health;
3. Existence of an updated map of needs related to cardiovascular health;
4. Availability of electronic tools and artificial intelligence systems for healthcare;
5. Scientific publications that reflect commitment to research and knowledge sharing;
6. Distribute the IRCS (Scientific Hospitalization and Care Institutes) homogeneously throughout the national territory for a fair distribution of resources.

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## Equity and gender in cardiovascular health

### Critical points

- Critical point 1. Promote awareness of cardiovascular disease and the importance of self-care in women.
- Critical point 2. Train cardiology health professionals at all levels of care on the specific aspects of diagnosis and treatment of cardiovascular disease in women and gender inequalities.
- Critical point 3. Foster multidisciplinary expertise for the shared management of women's cardiovascular health at all ages of life.

## Goals and actions

### Critical point 1.

1. Overall goal: Integrate gender into health promotion and prevention actions to achieve gender equity.

   1.1 Specific Goal: Raise awareness among women and society in general about the importance of cardiovascular disease in women and the concept of gender-differentiated disease;

   1.2 Improve primary and secondary prevention programs for cardiovascular disease in women.

Actions to be implemented related to Critical Point 1:

- Work with equality policy organisations to promote co-responsibility and investment in public assistance services;
- Prepare health materials on cardiovascular health and gender and make them available to the population, through the education and health centres;
- Develop targeted interventions for primary and secondary prevention of cardiovascular disease specifically targeting women and taking into account their specific characteristics.

### Critical point 2.

1. Overall goal: train healthcare professionals to acquire the skills to detect gender-related differential aspects of cardiovascular disease.

   1.1 Specific objective: design and implement protocols and gender-sensitive procedures;

   1.2 optimize the implementation of guidelines by emphasising the importance of gender-related differential approaches.

Actions to be implemented related to Critical Point 2:

- Adjust clinical, instrumental, and laboratory standards by sex identifying differentiated cut-offs;
- Promote early diagnosis of acute coronary syndrome and facilitate access to emergency facilities;
- Develop early cardiovascular disease prevention protocols differentiated by gender;
- Use differentiated pharmacological approaches based on literature data where available.

### Critical point 3.

1. Overall goal: train healthcare professionals who deal with women's health to acquire the skills to detect gender-related differential aspects of cardiovascular disease.

   1.1 Specific objective: design and implement multidisciplinary care services dedicated to gender medicine;

   1.2 Specific objective: break down cultural, social and economic differences in the management of cardiovascular disease in women to ensure equity of access to care for all women.

Actions to be implemented related to Critical Point 3:

- Establish multidisciplinary outpatient clinics dedicated to gender medicine;
- Prepare health materials on the various multidisciplinary aspects of cardiovascular health in women and make them available to the general public via educational and health centres;
- Develop shared multidisciplinary protocols for gender-differentiated cardiovascular disease management.

### Indicators

- Percentage of annual increase in coverage of primary and secondary prevention interventions in women and comparison with the increase in men;
- Percentage of women accessing elective and acute specialist cardiovascular care compared with data for men;
- Implementation of gender-differentiated cardiovascular disease diagnosis, management and treatment protocols;
- Production of information materials for healthcare personnel and the general public on the differential aspects of cardiovascular disease in women.

# 07

# HEALTH ECONOMICS IN THE CARDIOVASCULAR FIELD

## Critical points in the economic management of healthcare

The very recent publication of the report on the activity of the Italian Court of Audit (13/02/2024) [1] has highlighted the strain on the socioeconomic resilience of the health service. The accounting magistrates write: "The trend, for the past several years, appears slow but steady: from a health service focused on the protection of a constitutionally guaranteed right, to many different regional healthcare systems increasingly based on free market rules. After sustaining the impact of the pandemic, the health service is suffering from a systemic crisis exacerbated by underpaid medical staff leaving [1-2].

In fact, healthcare spending in Italy constitutes a large slice of gross domestic product (GDP) standing at around 170 billion euros, or about 6.7% of GDP for the year 2023 according to data from the 6th GIMBE foundation report on the Italian health service [3]. Of this budget, around 1.41% of GDP – about 33 billion euros – is allocated to pharmaceutical spending [3]. It follows that the identification of critical points in the economic management of healthcare – particularly in the cardiovascular field – is a key area for reducing the financial deficit associated with the health service.

Firstly, it should be reiterated that Italy "spends less on healthcare." Compared with the OECD average, Italian public health spending is 0.3% lower according to GIMSE data for 2022 (6.8% vs. 7.1%) [3, 4]. Italy ranks 13th in terms of healthcare spending compared to other European countries, primarily Germany where it accounts for 10.9% of GDP [3, 4]. Compared to the other G7 countries, Italy has consistently remained last in terms of health financing, with a relentless downward trend witnessed from 2008 to the present linked to cutback policies and/or lack of investment [4]. This, of course, inexorably affects the clinical/practical management of healthcare and, in turn, the perceived inadequacy of the system felt by patients.

In fact, the need to curb health spending recalls a somewhat old but still relevant consideration by Borgonovi, who, in one of his articles, describes the attitude of the state toward the financial pressure of public health as aiming to eliminate "as soon as possible those symptoms" that can prove fatal to the economic organism – almost as if it were a high fever – but without eradicating or modifying the root cause, or rationalising intervention on future socio-economic planning of healthcare in a prudent, objective manner [5].

The focal point in this context is the optimisation of infrastructure and human resources. The balance between the two components is the object of much debate. Countless healthcare facilities across Italy fail to offer a good standard of health and social care due to a lack of funding, resources and space to provide the many complex services required for modern patient care. The building of state-of-the-art, "managerially" complete infrastructure and the closure of others that are outdated, limited and still tied to local management profiles with no prospects for growth is a critical juncture for the future of healthcare. In this regard, NRRP funds earmarked for the strengthening of outreach networks, facilities and telemedicine for community healthcare could open up new prospects for national health management [6]. The risk of the financing dehiscing and becoming unsustainable is at the very least realistic. This stems from two considerations: the first is related to the decision to reinforce the national network, an admirable goal if it were not for the fact that the SARS-CoV2 pandemic exposed difficulties in hospital acute care management that, until that point, were bubbling under the surface, ready to boil over. The second, on the other hand, stems from the observation that, once again, the human worker component – particularly medical executives – do not feature in the resilience process, almost as if the latter should be placed somewhere between tablets used for impersonal teleconsultations and soulless filing cabinets. Therefore, there is a risk of squandering financial resources that could be put to better use in the current straitened circumstances.

Another sore point in healthcare economic management is pharmaceutical spending. The 2022 report of the National Observatory on the Use of Medicines recently published by the the Italian Drug Agency (Agenzia Italiana del Farmaco - AIFA,) showed that regional pharmaceutical spending in Italy costs around 33 million euros (about 1.40% of GDP) [7]. Expenditure on innovative drugs is growing, with a 30% increase in 2022 compared to 2021, exceeding the budget of the national innovative drugs fund (1,100 million euros), by 172 million euros. In 2021, the sur-

plus was even larger (286 million euros), although the budget was less generous (1,000 million euros) [7]. These figures are consistently lower than those of other European countries. Loco-regional recovery plans are leaning toward drastic cuts in pharmaceutical spending. When a pharmaceutical spending recovery plan is to be implemented, several solutions can be adopted: setting spending caps, implementing treatment plans, imposing pharmaceutical/corporate budgets, controlling the way drugs are dispensed, and checking prescription appropriateness [8]. However, each of these solutions has objective limitations. Spending caps without a doubt prevent proper health infrastructure development, as well as the adoption of the most modern equipment and drugs. The negative impact on public health is self-evident. Consider the example of heart failure. The average cost of a stay in intensive care unit (ICU) for a period of not less than 5-7 days is around 14,000–35,000 euros/person to which must be added the costs for dedicated healthcare personnel, loss of work days, reduction in quality of life and physical performance in carrying out previous duties. Recently published data from the PNE report a prevalence of heart failure in Italy of 163,249 hospitalizations in 2023 alone with 30-day mortality of 10.73% and 30-day re-hospitalization for heart failure of 13.01% [9]. If, in line with international guidelines and based on data from trials and clinical observations in the literature, we adopt the new heart failure drugs in all patients, we should be able to achieve a 61% reduction in all-cause mortality and a 64% reduction in cardiovascular mortality and re-hospitalisation for heart failure [10]. Extending the evaluations to a purely socioeconomic sphere – even considering the cost of drug expenditure and without taking into account the cost of device implantation and management or related complications – would result in consistent savings for regional and state coffers both with regard to improved quality of life [11] and reduced costs of hospitalisations [12].

Treatment plans merit similar consideration. By definition, the Treatment Plan (TP), which comes under the purview of AIFA, allows limits on the use of those drugs deemed essential for single pathologies and covered by the health service. This is also to guarantee continuity for patients between the hospital and local services, directing the physician's treatment choices toward more effective and tested molecular drugs [13]. TPs are used for restricted prescription drugs that can be sold to the public on prescription by specialists at health facilities identified by the Italian regions [13]. The need to adhere to dedicated individual centres, to have to fight waiting lists and poorly delineated modes of care, as well as bureaucratic and methodological delays that make it difficult to optimise timeframes in the practical

work environment, all represent an often insurmountable obstacle to the proper implementation of therapy or, in any case, further delay an already deferred use of innovative drugs with an established body of literature. Indeed, the use of TPs becomes more of a deterrent aimed at limiting current healthcare spending, rather than a way to effectively address and potentially impact, in a realistic and non-utopian way, the health prospects of patients. The resulting vision is one of not wanting to consider the reduction of hard endpoints through the immediate adoption of proven molecular drugs, but of letting older, cheaper treatment regimens eke out their presence on the market, inducing an agonising inability to address the health concerns of citizens. And if we considered this for patients with decompensation, or even in secondary prevention after acute coronary and cardiovascular events, the need for pharmacological implementation beyond treatment plans is fundamental in safeguarding both health and state coffers [14].

Another sore point related to the socioeconomic management of health care in Italy is the use of DRGs (Diagnosis Related Groups) in the health service as a classification system based on the homogeneous grouping of diagnoses at the time of discharge, which allows for the economic quantification of resource absorption and remuneration of spending and financing of hospitals [15]. According to a recent report by the Consiglio Superiore di Sanità [15], "the DRG system, as currently conceived, appears to be out of date to adequately describe the activity and performance of hospital facilities, both from a clinical and an economic/financial point of view." However, the current version is unfortunately not aligned with the progressive development of diagnostic and therapeutic capabilities in the cardiovascular field. In fact, the last decade has seen the introduction of new invasive and non-invasive treatment techniques based on the use of methods and instruments not adequately considered by current DRGs. In addition, the DRG fee schedule, which allows for the identification of a "single" principal diagnosis (usually the one with the highest resource absorption), is detrimental in the case of patients with a high level of complexity (e.g., prolonged stays in hospital) or patients treated for more than one condition during the same stay (e.g., valvular pathology and ischemic heart disease, vascular pathology and ischemic heart disease, etc.). [15]. All this hinders the growth prospects and management of cardiology patients as the departmental managerial set-up could be severely limited by a reimbursement system that is unable to provide adequate care to individuals. For example, take Coronarography with fractional flow reserve analysis or imaging (DRG 124-125): extra cost for materials € 1,000 – actual reimbursement € 2,100. This creates an

inconceivable economic disadvantage for a method that – like so many others – is becoming increasingly important in the management of heart patients when the conditions for its use are met [15].

The criticality in the socioeconomic management of healthcare is real and distressing especially for the clinician who has to cope daily on the one hand with a large volume of patients and their frustrations with bureaucratic delays and waiting lists, and on the other with the lack of adequate instrumentation and human/infrastructural resources to be able to work efficiently. Healthcare that is more centred on the socioeconomic management of the doctor–patient relationship would also be desirable for the best use of resources.

## Prescription appropriateness

The critical issue in socioeconomic health management and pharmaceutical expenditure scaling remains the approach to prescriptive appropriateness. Effective monitoring of medication consumption requires analysis of the appropriateness of medication use. This involves identifying indicators that capture both what doctors prescribe and how patients take their medication. In Italy a few years ago, there was an estimated 25 bn euros of waste out of around 112 bn euros from the National Health Fund (22% of total direct spending), roughly 17% of overall healthcare spending, both public and private (amounting to 146 bn euros) [16]. While it is true that most regions have adopted spending caps to recover from healthcare budget deficits, it is also the case that the best way to assess and determine prescription appropriateness remains to be established and defined.

Close collaboration between local pharmacists and prescribing cardiologists/specialists is essential in assessing prescription feasibility and consistency as well as adherence to prescribing guidelines.

The adoption of treatment plans could be an appropriate way to monitor prescription transparency and drug eligibility, provided that there are some changes from the current system:

- All specialist physicians should be able to issue prescriptions. Limiting new drug prescriptions to just a few facilities would hinder their widespread use in everyday medical care. This creates an uneven distribution of access, favouring those few facilities over the many specialists in the area. The resulting discrimination causes work overload for those facilities as well as longer waits for patients.
- Treatment plan renewals should be separate from scheduled appointments, with dedicated agendas managed by a central nurse manager who can direct citizens to the most suitable locations for renewals or initial prescriptions.
- Review – through special committees interacting with the main national scientific societies – drug delivery methods according to scientific evidence and recommendations from international scientific societies, to be able to implement pharmacological innovations in the shortest possible time, avoiding delays that affect the immediate financial profile more than medium- and long-term health planning
- Provide the prescribing doctor with the tools to understand the patient's medical history, facilitating the definitive implementation of national health records as well as making available a national registry and database that can immediately relay the patient's medical, pharmacological and instrumental history. This would allow the clinician to have access to data to ensure they are prescribing the right medication without relying on the often incomplete information provided by the patient.

Problems with correct drug prescription can be included in a more general process of appropriateness in healthcare – particularly cardiovascular care –which is a longstanding issue in healthcare spending. In fact, there has already been some discussion about waiting times for access to instrumental evaluations and specialist appointments. One of the main reasons for this long delay turns out to be the excessive demand for services often unrelated to meaningful primary health indicators. Curbing this trend, however, is by no means easy. It would be extremely difficult to try to define supranational rules in terms of specialist/instrumental prescription. While it is easier to identify controlled administration management protocols for medication, the use of instrumental and specialised examinations is

not as easy to assess. On the other hand, each individual clinical case is different from the other, therefore it is difficult to discern schematically who merits clinical investigation compared to another. Obviously "defensive" medicine and medico-legal litigation do not help in the process of clearing the logjam of healthcare claims, by virtue of the preconceived notion that diagnostic and therapeutic evaluations are central to the clinician's ability to investigate pathological processes. The extension of immunity from prosecution for healthcare workers in Italy until the end of 2024, pending a comprehensive reform of the subject, was addressed in the recent Decreto Milleproroghe (a government decree) [17]. It could well help to attenuate an overly legalistic approach to healthcare, but there remains a long way to go. Nor should we forget that the patient's wishes and requests often influence the clinician's decision-making process in an almost paternalistic approach that oversteps the bounds of scientific rationality. On this point it becomes somewhat abstruse to employ limiting healthcare policies, but behavioural training could bring about possible favourable effects.

In this context, the implementation of appropriate loco-regional and/or national PDTAs becomes a system for trying to classify patients and pathologies as well as possible pathways for the judicious and predetermined implementation of clinical-laboratory-instrumental assessments for the diagnosis and treatment of the disease. This would not only lead to the systematic evaluation of patients in similar situations, but also streamline access to diagnosis and treatment resulting in a real reduction in costs and a positive impact on the healthcare budget.

*Table VII. Health economics in the cardiovascular field*

- After enduring the impact of the pandemic, the health service is suffering from a systemic crisis, often with reduced human resources and exacerbated by underpaid medical staff leaving.
- Scarce funding for health care. Italy ranks 13th in terms of healthcare spending compared to other European countries. Compared with the other G7 countries, Italy has consistently remained last in terms of healthcare funding, with a relentless downward trend.
- Countless healthcare facilities across Italy, often falling short of current legal standards, fail to offer a good standard of health and social care due to a lack of funding, resources and space.
- Streamlining cardiology activities to allow healthcare professionals to focus

on clinical tasks (e.g., removing therapeutic plans, etc.).
- Redesigning the DRG system for the purpose of adequately describing the activity and performance of hospitals, both from a clinical and an economic/financial point of view.

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