

Towards a new normal: Why boosting CV health is critical

Opportunities for healthcare systems to build back better for patients in Europe

May 2022





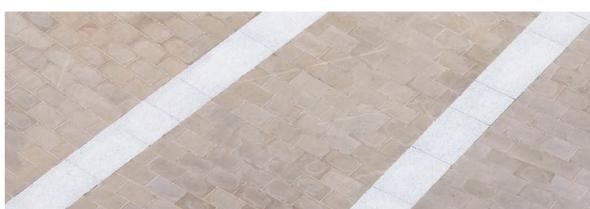
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Foreword (EFPIA)

Every day, 5,000 Europeans lose their lives due to Europe's number-one killer: cardiovascular diseases (CVDs), such as heart attacks or strokes. And the pandemic has made it worse: CVD was the tinder that allowed COVID-19 to burn through the global population, drastically inflating the number of preventable deaths. The millions of people with undetected CVDs were five times more likely to die than others. So, while COVID-19 didn't create the problem, it did draw attention to what had been an existing challenge for decades.

That is why EFPIA has commissioned this report with the health experts of PwC. We wanted to understand the impact of the pandemic on the 60 million CVD patients living in the European Union and the lessons we could learn from this health emergency. Ultimately, we're looking for recommendations about how European healthcare systems could be built back better and become more resilient for the next crisis.

With the pandemic not yet over, we see the next stress test coming from the war in Ukraine. First and foremost, this will play out in Ukraine itself, but then also in its neighbouring countries and further to the west. We know that the outcomes for CVD patients in Central Eastern European (CEE) countries have been worse than for their western counterparts. While treatable mortality sits at 16 cases per 100,000 inhabitants in France, the same score is at 105 or more in CEE countries. So, once we see refugees from the war integrate into their host countries, we need to make sure that we can offer them better outcomes as well as earlier diagnosis and elevate the level of CVD care to reduce the burden.

As a pharmaceutical industry's federation we've made the pledge to build the evidence for good policy decisions in the field of cardiovascular diseases. This report is the first piece in a forthcoming series designed to create more intelligence to inform better CVD policy. Please watch out for an analysis of international policy best practices for better outcomes to be published soon.

No matter what we develop, we want to do so in partnership and close alignment with our stakeholders in the European health ecosystem. Here we'd especially like to refer to the European Alliance for Cardiovascular Health (EACH), a platform of like-minded organisations advocating for a stronger focus on CVD as a key health issue to be addressed in Europe in the coming years. For this report we're proud to acknowledge that many of our partners in EACH agreed to contribute.

We want to thank all the experts, not only for spending their time and passing on knowledge and ideas for this report, but also ultimately for sharing the passion to improve the lives of CVD patients and prevent as many heart attacks, strokes and other CV-related events as possible.

Last but not least, the EFPIA CVD Network stands for promoting equal access and fast uptake of innovative medicines, pursuing state-of-the-art science and knowledge in CVD treatment. We believe that secondary prevention needs to receive more attention. Did you know that one in two heart attacks are repeat episodes? We need to stop this vicious cycle for patients and give them access to treatments and rehab opportunities – no matter where they live in Europe.

We hope you will find this report helpful in assessing the threat cardiovascular diseases poses to European society. Thank you for reading and engaging.

The EFPIA CVD Network

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The EFPIA CVD Network consists of eight pharmaceutical companies fighting to reduce premature mortality in Europe through better data, better access to treatments, better health literacy, higher awareness and a focused collaborative effort to save tens of thousands of lives in the coming years.

Executive Summary

Progress made to contain the burden of cardiovascular disease (CVD) has recently been slowing down. Mortality rates, after a significant decrease over the last few decades, has lately started plateauing, if not increasing. It is clear that CVD doesn't affect each European country to the same extent. Rather, there are worrying divergences in the burden of disease observed within and across countries. This diverse pattern makes CVD outlook uncertain, and meanwhile contribute to growing inequalities in the European region.

On top of this, the COVID-19 pandemic has deeply disrupted care for CVD patients. At the same time, the underlying chronic CVD burden complicated the management of the COVID-19 crisis by challenging

healthcare systems' ability to cope with the demand for care. The pandemic also amplified health disparities, showing that socially disadvantaged members of society disproportionately bear the brunt of both chronic diseases, and acute crises. In light of these observations, there's an obvious need for European countries to identify strategies to create more resilient and equitable healthcare systems.

We argue that better CV population health can provide a key lever for boosting health system resilience and equity. Based on existing evidence, we've formulated actionable recommendations, grouped into three key areas, to activate this lever.





Area 1: Strengthen population screening

- 1. Broaden screening programmes for genetic and metabolic risk factors: Today, the CVD burden remains largely undetected, resulting in the highest number of avoidable deaths from non-communicable diseases (NCDs) across Europe. Systematic screening for metabolic and genetic risk factors could improve early disease detection and management, when combined with personalised medical advice. Countries should define local goals and regularly measure progress around CVD detection and management.
- 2. Simplify access to screening, especially for vulnerable populations: To be successful, a screening programme must reach as many members of the target population as possible. That means it's crucial to engage individuals that are typically reluctant to seek care. Therefore, population-wide screening should be matched with 'concentrated' interventions (i.e. focused on risk groups) to ensure equitable access across the population.

Area 2: Ensure treatment initiation, maintenance and follow-up for at-risk patients

- 3. Gear the system towards rewarding outcomes: The implementation of CVD guidelines falls short in many settings, leaving a significant proportion of disease burden undetected, undertreated or mismanaged. In response, systems should reward adherence to clinical guidelines and the achievement of the associated health goals through, for example, financial incentives, benchmarking systems and/or public reporting.
- 4. Strengthen digital health and information sharing: Digital health can help manage CVD risk drivers, monitor patients remotely and even contribute to cardiac rehabilitation. To fully realise this potential, however, both financial and procedural integration are key. Some European countries are setting new policy trends around sharing medical information across the healthcare system as well as introducing financial incentives for e-health delivery. Other European countries should follow suit.

Area 3: Foster data-driven decision-making

5. Collect/leverage data to drive CVD insights, support clinical decision-making, value-based care delivery and inform CVD policy-making: Enhanced CVD data collection could significantly improve population CV health promotion and management. Data can help predict disease trajectories, support personalised interceptive medicine, inform value-based agreements and guide CVD policy. Europe has already articulated its ambition to create a shared space for health data. And CVD-specific initiatives, such as the pan-European CVD registry EuroHeart, are already underway. Efforts in the CVD area should be intensified and scaled up, enabling the Europe-wide collection and use of clinical, epidemiological and economic data on CVD.

How CVD affects Europe

Cardiovascular disease (CVD) is the major cause of mortality and morbidity across the continent, affecting almost 60 million patients¹ in the European Union and, notably, causing 1.24 million acute coronary events in wider Europe each year.^{2.3} CVD accounts for almost one-third of all premature deaths,⁴ and is responsible for 23% of all disability-adjusted life years (DALYs) measured across Europe, exceeding the burden caused by all other non-communicable diseases (NCDs), including cancer (15% of DALYs).^{5,6} CVD also imposes a significant financial burden, costing the EU an estimated 210 billion euros per year.⁶

Progress in containing the CVD burden has recently been slowing down, and to some extent even reversing. Overall mortality rates, after decreasing significantly over the past decades, have lately started plateauing, or even increasing again in some countries.⁵ In parallel, the time spent living with a CVD condition has extended.^{2,7} Multiple factors are to blame for these trends, and particularly an intersection of demographic, socioeconomic and environmental changes, not fully addressed in terms of disease management policies across Europe.⁸

Importantly, CVD doesn't affect each European country to the same extent. Rather, CVD displays worrying divergences within and across countries, which contributes to growing inequalities and an uncertain outlook when it comes to CVD burden management. A closer look reveals particularly troublesome differences between Eastern Europe and the rest of the continent (Figure 1).

> CVD doesn't affect each European country to the same extent. Rather, CVD displays worrying divergences within and across countries, which contributes to growing inequalities and an uncertain outlook.

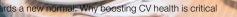
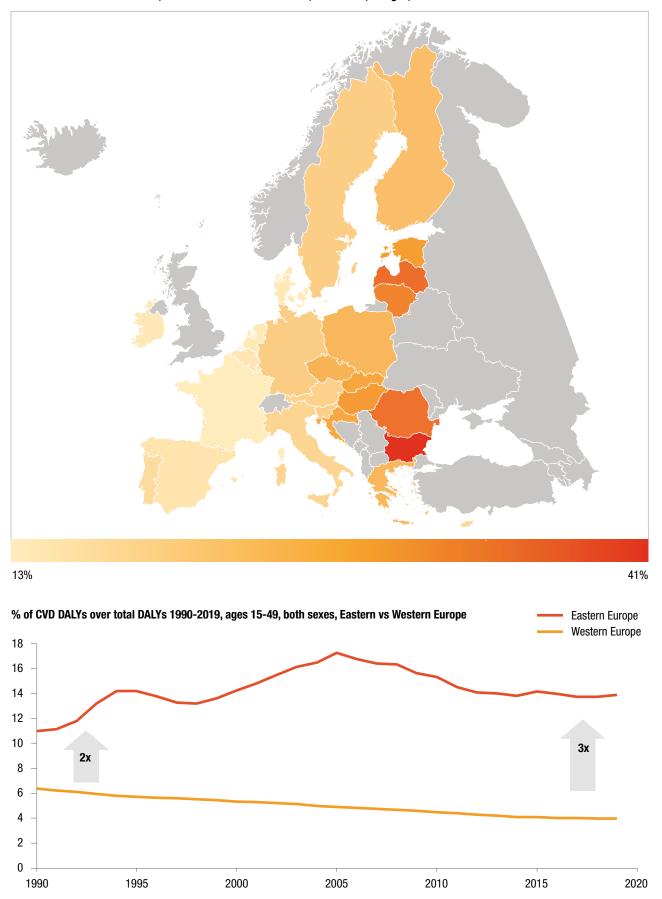


Figure 1: Europe displays a pattern of disease burden characterized by an East-to-West gradient (upper figure). Such divergences are becoming even wider among the youngest fraction of the population, with the rate of burden attributed to CVD growing in Eastern Europe over the past decades, while steadily decreasing in Western Europe (lower figure).

Cardiovascular disease burden, % of total DALYs across the EU, both sexes, all ages, 2019

Source: GBD 2019. PwC analysis.



At the same time, many CVDs are preventable or, at least, manageable with appropriate interventions, often more so than other major NCDs. Overall, about 70% of the CVD burden is attributable to risk factors that can be controlled or modified, such as hypertension (responsible for 22% of CVD cases), high cholesterol (8%) or diabetes $(5\%)^9$ (Figure 2).

Therefore, despite the availability of effective approaches to controlling metabolic and other risk factors, ischemic heart disease is still responsible for more than 150,000 deaths per year across Europe. It's the health condition that causes the highest number of avoidable deaths before the age of 75 across Europe.¹⁰

Figure 2: Risk factors for cardiovascular disease

Sources: GBD 2019, Martinez-Garcia 2021, Schultz et al. 2018, Yusuf et al 2020. PwC analysis

CVD is influenced by a variety of risk factors, from metabolic to behavioural to socio-economic ones





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The interplay of CVD and COVID-19

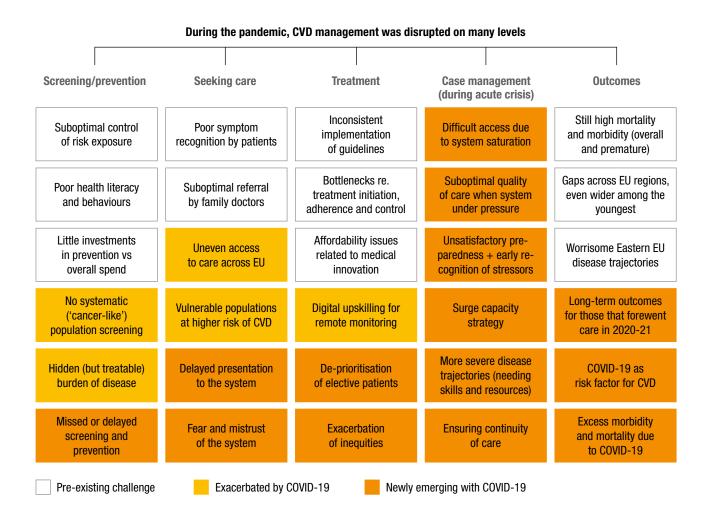
CVD patients represented one of the most vulnerable groups of patients during the pandemic, as they were impacted in at least three ways. First, COVID-19 led to significant disruptions of CVD care across Europe. Second, it might, going forward, contribute to the rise of CVD-related Long COVID. Third, pre-existing CVD has raised the risk for severe COVID-19 trajectories, thus complicating pandemic management.

The impact of COVID-19 on CVD patients

The full extent of the consequences the COVID-19 pandemic had on CVD patients remains to be fully documented and described. COVID-19 has disrupted care and damaged health outcomes, creating new

challenges and exacerbating existing ones. This was clearly seen during the peak of each wave in 2020-21 and in the subsequent acute response phases **(Figure 3)**.

Figure 3: Impact of COVID-19 on CVD care pathway (PwC analysis)



In terms of acute effects, the evidence for CV-specific excess mortality determined by COVID-19 is building. Different European countries recorded excess CV mortality during the pandemic, but it appears that the specific context and the ability of the system to cope with the increased demand of healthcare played a key role in triggering such excess death.^{11,12}

European experts fundamentally agree on two main potential determinants of long-term consequences for CVD patients. The first is the missed identification of CVDs or CVD risk factors owing to lockdowns, overwhelmed care services and fear of infections, all of which prevented people from accessing screening and diagnostic services as usual. For example, data from Danish national registries show a 47% decline in reported new-onset atrial fibrillation during the 2020 lockdown compared to 2019.¹³ Similarly, UK data demonstrate that, during the first wave, emergency calls to ambulance services were reduced by 10% for strokes, 39% for myocardial infarction and 26% for acute coronary syndrome, only partially bouncing back in May 2020.¹⁴ The second potential long-term determinant is delayed patient presentation to the system, determined by missed early detection, or simply due to the patient's choice to deprioritise health matters. For example, myocardial infarction has been reported at a later stage than usual by 60% of healthcare professionals.¹⁵ These delays are likely, in the future, to trigger increased mortality and shorter life expectancy.¹⁶

Looking ahead, the combined effect of the two factors mentioned above is likely to lead to more severe disease trajectories for CV patients. Early data already suggests that delays in seeking care and declines in hospital admissions can result in worse health outcomes.¹⁷ Based on UK mortality data, it's further estimated that the indirect effects of COVID-19 on CV mortality (i.e. effects due to disruption of care) are going to be delayed yet significant, having led to between 50,000 and 100,000 excess deaths within the first year of the pandemic.¹⁸

The spectre of Long COVID CVD

Long COVID, the long-term complications resulting from a COVID-19 infection, is likely to pose an additional burden on public health.

Recently, there have been concerns raised that COVID-19 may cause delayed CVD complications, which have the potential of increasing future demand for care. Data from the US shows that patients affected by COVID-19 have an increased risk of experiencing heart failure, atrial fibrillation and myocarditis (73%, 79% and 422% increased likelihood, respectively) 30 days to 1 year after acute infection.¹⁹

Of note, the extent of Long COVID from a population health perspective, beyond their impact on the clinical history of each affected individual, has yet to be determined: the number of patients affected by such events, in the timescales we can observe today, remains unclear.²⁰



The impact of CVD burden during a pandemic

The existing CVD burden across the population also complicated the management of the COVID-19 crisis, especially by challenging healthcare systems' ability to cope with care demand.

It was obvious very early as the COVID-19 crisis unravelled that pre-existing CVD and other chronic conditions increased the risk of severe disease for people infected with the SARS-CoV-2 virus. During the first six months of 2020 we saw that, while 25% of COVID-19 patients had an underlying CVD diagnosis, this proportion increased to 35% among people affected by severe COVID-19 requiring hospitalisation and represented 44% of all COVID-19 deaths (**Figure 4**).²¹ In addition, socially disadvantaged members of society are at markedly higher risk of both CVD and of adverse COVID-19 outcomes.²² For example, Swedish women with only primary school education were 51% more likely to die from COVID-19 compared with women having completed secondary education (**Figure 4**).²³

The interplay between acute infection, underlying chronic conditions and social factors led experts to speak about COVID-19 as an 'acute-on-chronic health emergency' – highlighting how the chronic disease burden drove a large part of COVID-19 mortality.²⁴

Figure 4: COVID-19 outcomes given pre-existing CVD, CVD risk factors and social disadvantage

CVD	Risk x-fold higher for COVID-19 outcome	Severe Disease	Hospitalisation or ICU stay	Mortality
	Cerebrovascular accident/disease	••	••••	••••
Pre-existing	Arrythmia	•••	•••	••••
re-ex	Heart failure	•••	•	••••
	Coronary heart disease	••	••	••
10	Risk x-fold higher for COVID-19 outcome	Severe Disease	Hospitalisation or ICU stay	Mortality
factors	Obesity	•	•••	•
10	Chronic kidney diagoog			

(0				
CVD risk factors	Obesity	•	•••	•
	Chronic kidney disease	••	••	••
	Hypertension	••	••	•
	Diabetes	•	•	•

	Risk x-fold higher for COVID-19 outcome	Severe Disease	Hospitalisation or ICU stay	Mortality
disadvantage	Ethnic minority	n/a	n/a	••
advar	Immigrant (from low-income country)	•	•	•
	Deprivation	•	n/a	•
Social	Low income	•	n/a	•
	Low education	n/a	n/a	•

Source: PwC analysis.

Upper table: estimates based on systematic literature review conducted by EFPIA CVD Network; middle and lower tables: estimates based on targeted literature review indicative estimates of effect only. Target period: March 2020 and November 2021. The shades of red reflect the numerical extent of the increased risk (continuous colour scale).

Risk 1-2x	•
Risk 3-5x	••
Risk 5-10x	•••
Risk >10x	••••









Improving CV population health to build equitable and resilient systems

Why we need resilient systems

The pandemic disrupted healthcare delivery to CVD patients and at-risk individuals along the entire care pathway: prevention efforts were neglected, opportunities to detect conditions early were missed and patients with established CVD struggled to get the care they needed.

COVID-19 has therefore exposed the limited resilience of several healthcare systems during a health emergency. Going forward, European health systems need to keep preparing for future health crises, whether unforeseen or slowly building up over time.

Europe is in the grip of a demographic change, in particular population growth and ageing. In 2050, 130 million Europeans will be over 65, and 27 million over 85.²⁵ Because of that, it's expected that healthcare systems will face a growing number of chronic and multi-morbid patients.^{26, 27} In particular, evolving disease patterns will pressure systems and force them to reshape their care delivery models. For example, ever more common musculoskeletal disorders will call for rehabilitation services, while the growing burden of neurological conditions will require long-term inpatient care.^{28, 29}

Also, CVD-related healthcare demand in Europe is bound to grow and transform over the coming decades. While advanced projections about the evolving CVD burden for Europe are lacking, it's reasonable to assume that CVD care will become more resource intensive, as the result of a growing fraction of multi-medicated and frail patients.³⁰

Relatedly, some underlying factors, such as diabetes and obesity, are on the rise. For example, 20% or more of the population in most European countries will be living with obesity by 2025, rising all the way to an average of 31% in many countries by 2037.^{31,32}

On another note, climate-sensitive health risks (e.g. heat stress, malnutrition or infectious disease transmission) related to rising temperatures and natural disasters are expected to escalate over the next decades. Europe is experiencing ever more intense heat waves, which have already led to an increase in heat-related mortality by 33% from 2000 to 2018.^{33, 34}

However, the need for European healthcare systems to prepare for the evolving demand of care isn't just driven by long-term developments. Instead, short-term shocks, similar to COVID-19, are also likely to become more frequent going forward, thus boosting healthcare demand and stretching healthcare services even further.

As humans interact ever more closely with the natural environment, emerging infectious diseases resulting from animal-to-human spill-overs, such as COVID-19, are expected to become more frequent and, potentially, more lethal.^{35, 36} Some models predict that there is a 47-57% chance of another global pandemic as deadly as COVID-19 in the next 25 years.³⁷

What's more, geopolitical conflicts and frictions may result in medical emergencies that put additional stress on health systems, potentially over sustained periods of times. For example, the current crisis in Ukraine, with millions of refugees displaced across EU countries, is already demanding increased attention to manage the rise of potential health issues and minimise disruptions around the delivery of health services.³⁸

Finally, the demands on healthcare are intrinsically changing due to increasing patient expectations around care standards/levels as well as patient empowerment, coupled with technological advancements.

Together, 'short-term shocks' and 'accumulated stress' have the potential to stretch European healthcare systems to a breaking point from a care delivery and financing perspective.³⁹ This makes it essential to improve health system resilience to cope with future healthcare demand.

Why we need equitable systems

It's well documented that socially disadvantaged individuals (i.e. people with low educational attainment, income and employment levels) are exposed to higher risks of chronic diseases, increased prevalence of CVD risk factors, such as smoking or obesity, as well as higher incidence of CVD events (e.g. heart attacks).^{40,41,42}

Furthermore, vulnerable individuals suffering from NCDs are disproportionally likely to die prematurely.⁴³ With respect to CVDs specifically, a study published in The Lancet found that CVD accounted for 39% of the total mortality disparity between low and high educational groups in eight Western European countries.^{42,44}

Recently, we also learnt that social disadvantage goes hand-in-hand with a higher risk of COVID-19 infection, as well as a risk of severe and fatal COVID-19 outcomes.^{45,46} Importantly, these dynamics are closely intertwined and

reinforce each other. CVDs and risk factors raise the risk of adverse COVID-19 outcomes; conversely, people suffering from COVID-19 are at peril of developing CVDs months after acute infection (as illustrated in the section The interplay of CVD and COVID-19, p. 10).¹⁹

The convergence of these forces, i.e. an acute stressor such as COVID-19 acting on top of underlying chronic diseases, determines a 'syndemic' situation, i.e. an 'aggregation of diseases on a background of social and economic disparity, resulting in the exacerbation of the adverse effects of each separate disease'.⁴⁷

Therefore, there's a definite need for a more equitable healthcare system with the potential to buffer the effects of a syndemic, or any other crisis potentially affecting the population.



Resilience and equity in the European policy context

In the context of COVID-19 recovery and mitigation, European decision-makers and stakeholders understandably positioned improved equity and resilience at the top of the list of priorities for future healthcare systems. For example, the EU4Health initiative as well as the vision around the prospective European Health Union speak about fostering more resilient health systems, as does World Health Organisation (WHO) Europe in its recent strategy for sustainable development.^{48,49,50}

In parallel, the European Commission set an overarching goal for the reduction of inequalities when it comes to their plan to reduce the burden of NCDs.⁵¹

Prominent among the key strategic investments envisaged to build up resilience are usually pandemic preparedness, international coordination, supply chain and infrastructural investments to reinforce healthcare delivery. Interestingly, disease prevention and health promotion are also considered by European stakeholders as key dimensions for improved health and resilience, as demonstrated by the important role assigned to Europe's Beating Cancer Plan as a flagship initiative to save lives through prevention.⁵² European decision-makers and stakeholders positioned improved equity and resilience at the top of the list of priorities for future healthcare systems.

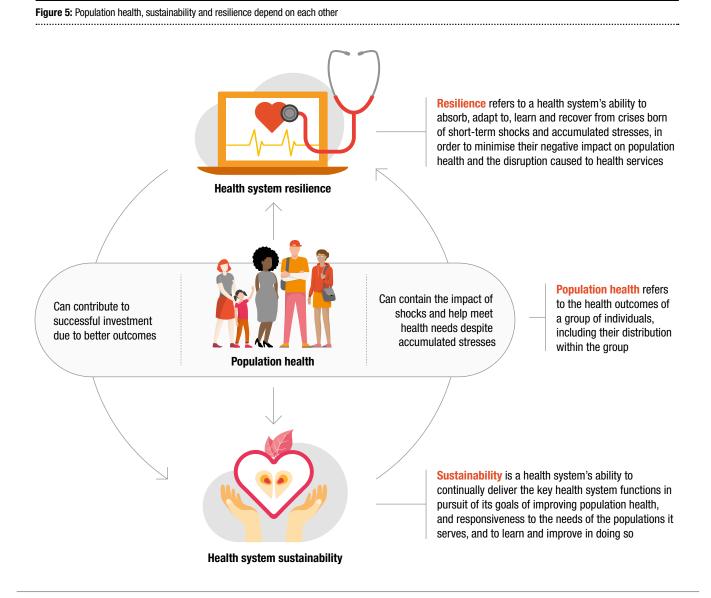


Population CV health as a lever for achieving stronger systems

Better population health has the potential to support the achievement of resilience and equity goals, as outlined in these pages.

Typically, system resilience is understood as the ability of a system to meet population health goals in line with the evolving health needs. At the same time, population health represents a 'proactive element' that facilitates resilience. Good baseline health constitutes an element of strength and an advantage in the face of health threats. This concept has been acknowledged – though somewhat forgotten – over the years, starting from the Declaration of Alma-Ata (1978), and serving later as a founding principle of the vision around the UN's Sustainable Development Goals.⁵³ Overall, proactively managing population health via prevention and health promotion initiatives will create systems that are in better shape to face future crisis. Importantly, supporting population health is also a sustainable approach to increased resilience, able to set in motion a positive loop for an even stronger system response in a crisis⁵⁰ (Figure 5).





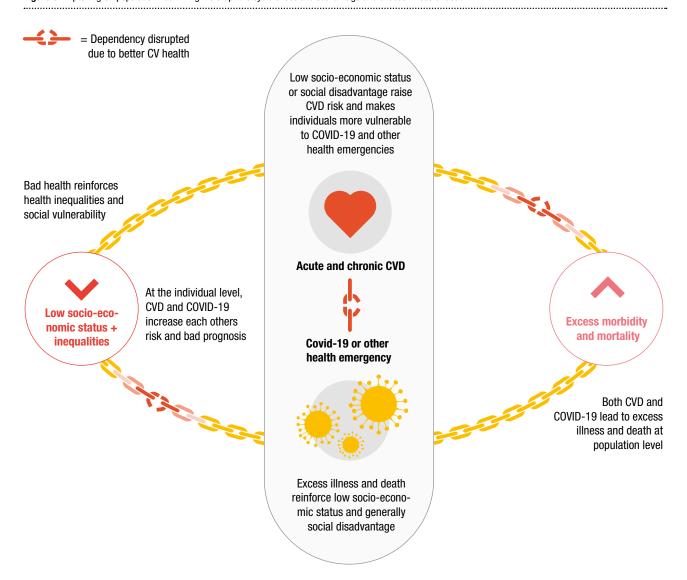
Sources: Source: PwC analysis.

Definitions of resilience and sustainability from the Partnership for Health Sustainability and Resilience (2021). Definition of population health from Kindig and Stoddard (2003).

Second, improved population health can also promote equity by disrupting the vicious cycle where inequities, co-morbidities and adverse health outcomes trigger each other **(Figure 6)**. Better population health – understood as referring both to the health outcomes of a given population as well as their distribution – will serve as a 'circuit-breaker' and help contain adverse outcomes and the ever-widening inequalities suffered by the most vulnerable segments of society. Containing NCD mortality is already a European and global health priority.⁵⁴ In Europe, CVD represents the most burdensome set of conditions affecting the population, yet they are preventable and treatable.⁹ This means that considerable improvement of European CV health can potentially be achieved via population-wide CV prevention and management measures, with upsides on individual and population health outcomes, and consequently strengthening of healthcare systems.

Filling the gap in 'CVD control' is both feasible and needed, and should be set as a priority from a public health and policy perspective in Europe.

Figure 6: Improving CV population health might disrupt the cycle of social disadvantage and excess illness or death



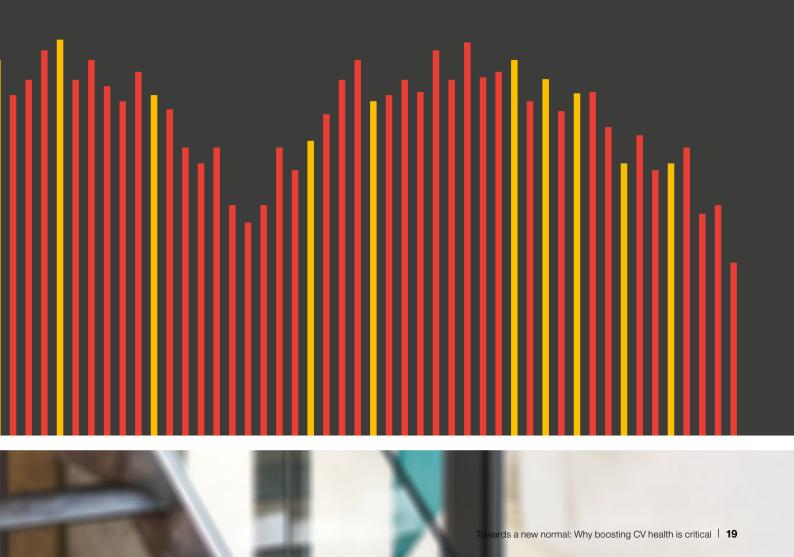


Strategic options for better CV population health

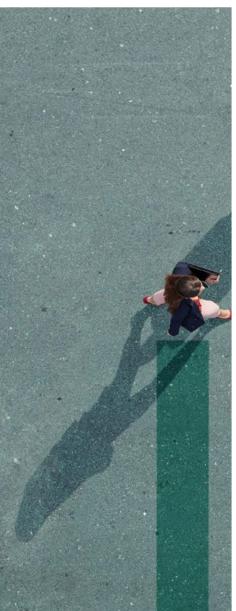
In this section, we develop recommendations for boosting CV population health across Europe. Our proposals are categorised into three key strategic areas:

- 1. strengthen population screening,
- 2. ensure treatment initiation, maintenance as well as follow-up for at-risk patients and
- 3. foster data-driven decision-making.

Importantly, these recommendations work best in concert. For example, early detection of CVDs without successful transition into appropriate disease management won't help address the CVD burden and improve outcomes at population level.









Key messages

- Each country's healthcare system to systematically and proactively detect and manage people's risk of developing CVD and elevated risk of progressing to severe cardiac events.
 - Each country to spell out ambitious, yet feasible goals for CVD management policy through national plans, supported by clear and tangible key performance indicators (KPIs) aligned at European level.
- Decrease the individual risk of developing disabling or fatal CV conditions.
 - Prevent the need for acute specialist care and/or hospitalisation.
 - Detect and manage the 'invisible' CVD burden by triggering lifestyle changes and seeking medical advice early on.
 - Assess CV population health baseline to pinpoint areas of greatest need and tailor public health plans.
 - Improve overall health management of individuals affected by multiple conditions.

In Europe today, a considerable proportion of the CVD burden remains undetected⁵⁵, and this is compounded by the lack of systematic and large-scale screening programmes.^{56,57} Instead, CV conditions and uncontrolled risk factors are typically detected only via voluntary health screenings or as secondary findings to other health issues.

This is in marked contrast to preventive approaches in oncology, with screening run for some cancer types by many European countries.^{58,59} This discrepancy is due to multiple factors. First, unlike most cancers, it may take decades before subclinical or chronic CVD forms progress to cause disabling or life-threatening episodes, such as a stroke or heart attack.⁶⁰ Also, only a fraction of the population at risk actually develops a severe condition (this being a key consideration for any population screening). These factors overall lower the perceived feasibility and urgency of identifying subjects at risk of developing CVDs.

Not only that, slow progression and poor predictability also considerably complicate evidence generation, as the long-term outcomes that are measured today are the results of clinical studies which were designed several decades ago, when e.g. the treatment standards, the care delivery model, the risk factors being assessed or the target population were very different from today.⁵⁷ Moreover, data from randomised studies on primary prevention are lacking for Eastern Europe. Insights from Western Europe are hard to generalise to the entire European region, given differences in healthcare systems and the relative burden of CVD (e.g. prevalence and risk factor patterns). As a result, findings are both hard to interpret and difficult to act on.⁵⁷

Last, CVDs are traditionally seen as driven by lifestyle choices (e.g. smoking or poor eating habits), and are therefore often deemed a matter of individual responsibility. But that is a significant simplification. There's a wide range of risk factors, that overlap and interact with CVD such as metabolic conditions (e.g. high blood pressure, high cholesterol, diabetes, obesity), socio-economic status (e.g. income, education) or environmental features (e.g. air pollution), which are largely driven by systemic factors, in addition to individual ones. And more than 30% of CVD risk is driven by genetic factors, the early identification of which is crucial for lifelong management of hardcoded risk factors.⁶¹

In fact, data shows that, across Europe, CVD results in the highest number of premature deaths that could have been treated, and are the second group of diseases in terms of preventable premature deaths. These numbers make a compelling case for better CVD detection and management.^{10,62,63}

First recommendation: broaden screening programmes for genetic and metabolic risk factors

Health systems should empower people to make positive decisions about their health and enable them to manage their individual risks, whether through lifestyle changes, advice from a healthcare professional, or through medical treatment. To do that, uncontrolled CVD risk factors or subclinical CVD detection should be strengthened to offer people the best chance of managing their health effectively, and limit the number of avoidable, premature deaths caused by CVDs.

As population-level screenings are context-specific interventions, many local variables play a role. These include demographics, risk-factor patterns, care delivery models, financing and so on. All these make it hard to offer generalised insights about the cost-effectiveness of screenings across Europe.^{57,64} As a consequence, the optimal screening approach (e.g. target population,

tests, interventions in scope, time horizon and outcome measurements) should be defined locally.

With that in mind, some simple approaches offer great potential for preserving people's health, and are likely to show a positive ratio between the costs and benefits. For example, measuring hypertension is a simple procedure that can be conducted in primary care and community settings. Despite causing half of all CVD-related ill health, disability and deaths, hypertension remains undetected in almost 30% of people living in high-income countries.^{2,65} That is a significant missed opportunity, given that high blood pressure, once detected, can be managed and lowered through lifestyle changes and/or medical treatment, decreasing the risk of later acute CV episodes.

A 2015 meta-analysis published in The Lancet, covering research conducted on more than 600,000 people over 50 years, showed that every 10-mmHg reduction in systolic blood pressure reduces the risk of major acute CVDs by 20%, of coronary heart disease by 17%, of strokes by 27% and of heart failure by 28%. This, in the populations studied, led to a significant 13% reduction in all-cause mortality.⁶⁶

In line with the available evidence, many professional societies are openly supportive of systematic blood pressure screening, or more generally CV risk screening, in the general population or in targeted subpopulations with a higher risk of CVD such as people with diabetes or obesity.^{67,68,69}

Systematic CVD screening shows promise across Europe. Successful screening schemes for metabolic risk factors are currently being run in the UK and Italy (Case Study 1). Slovenia universally screens its children for familial hypercholesterolemia (FH), a common inherited genetic condition that results in significantly elevated cholesterol levels and raises the risk for early cardiovascular disease, especially coronary heart disease (Case Study 2). Crucially, these programmes don't stop at detection, but also transition patients successfully to CVD management, whether achieved through behavioural counselling or pharmacological interventions.

Other relevant examples are the testing of low-density lipoprotein (LDL) cholesterol, blood glucose, body mass index and of albuminuria, a marker for chronic kidney disease. These tests can also be performed rather easily in primary care and community settings, and offer comparable upsides. To illustrate, high LDL cholesterol is responsible for almost 30% of all CVD-related ill health, disability and deaths in Europe.² Despite that, data suggests that most adults don't know their LDL-C levels or never had them tested.⁷⁰ This points to another missed chance, as high LDL cholesterol can be managed very effectively. For patients on a statin therapy, for example, each 1 mmol/L (38.6 mg/dL) reduction in LDL-C results in a 20-25% lower global CV risk.^{71,72}

Importantly, CVD detection and management require goal setting and outcome measurement at national level. For example, the NHS England Long Term Plan, published in 2019, articulates the goal to prevent 150,000 strokes, heart attacks and dementia cases over the next 10 years.73 The Heart-Brain alliance, a German initiative launched in November 2021, calls for a 30% reduction in CV events by 2030.74 Outside Europe, the US Million Hearts initiative by the US Centers for Disease Control and Prevention (CDC) and the Centers for Medicare & Medicaid Services (CMS) aims at averting one million heart attacks and strokes in five years.⁷⁵ Finally, the Japanese plan for promotion of measures against cerebrovascular and cardiovascular diseases aims to extend healthy life expectancy by three years until 2040 (compared to 2016).76

Similar goals should be devised in all European initiatives, ideally coherently with a Europe-wide call for action. The alignment of goals and KPIs would be instrumental to 'make healthy life expectancy more equitable' across the region.⁷⁷

Overall, strengthening systematic screening for metabolic and genetic risk factors has the potential to increase the detection of silent risk factors or conditions, and to successfully manage them via personalised counselling or medical advice.





Case Study 1 Screening for CVD risk factors

The NHS Health Check

The NHS Health Check, started in 2009, is a UK population-wide programme for the prevention of CVDs and other chronic non-communicable diseases.⁷⁸ The programme relies on simple measurements of blood pressure, weight/body mass index (BMI) and cholesterol, performed by a GP, nurse or healthcare assistant in a primary care, pharmacy, community or workplace setting. These checks, repeated every five years, target adults aged between 40 and 74 without pre-existing conditions. After six years of the programme, there's evidence that subjects have been able to better control their CV risk factors (blood pressure (BP), weight, smoking), and reduce their individual risk of experiencing an acute CV event.⁷⁹

Cardio50 & Young50

Cardio 50 is CVD prevention programme, established in Italy in 2014.⁸⁰ It aims to identify asymptomatic individuals aged 50+ with hypertension, high blood sugar and/or high cholesterol, and then enrol them in a structured primary prevention programme, featuring counselling on smoking cessation, healthy diet and physical activity.

The pilot showed promising results, being able to identify high blood pressure and/or high blood sugar in 12% of the study population.

The programme has been recognised as a best practice by the European Commission and is now – under the label 'Young 50' – being rolled out in Romania, Lithuania and Luxembourg.⁸¹



Case Study 2 FH screening

Detecting genetic risk factors: FH screening in Slovenia

Familial hypercholesterolemia (FH) is a common inherited genetic condition with a prevalence of 1 in 200 to 250 people around the world, and 2.5 million affected people in Europe.⁸² FH affects cholesterol metabolism, determining high levels of low-density lipoprotein (LDL) cholesterol in the blood, a risk factor for CVDs.

FH is a silent condition, nonetheless it leads to premature morbidity and mortality due to the underlying atherosclerotic cardiovascular disease.⁸³ Individuals with untreated FH have an over ten-fold elevated risk of cardiovascular complications.⁸⁴ Despite the high FH burden, the disease remains underdiagnosed and undertreated.⁸⁵ According to recent numbers, only 10% of people born with FH are diagnosed and treated.⁸³

FH screening is highly effective. Governmentsupported FH programmes that feature universal paediatric screening have substantially improved recognition and treatment, reducing premature CVD by as much as 76%.⁸⁴ In addition, FH screening is also very cost-effective, with a cost of roughly 5,000 euros per quality-adjusted life year (QALY), well below typical thresholds.⁸⁶ Further, a recent study from the UK highlighted the cost-effectiveness potential of electronic screening criteria for identifying FH patients within primary care.⁸⁷

Despite that, FH screening programmes are seldomly implemented in Europe, with Slovenia being a notable exception. Slovenia's programme follows a two-step approach. The first step consists of universal hypercholesterolemia screening in preschool children (age 5-6) at their programmed visit at the primary care paediatrician. In a second step, there's genetic FH screening in children referred to tertiary care level (i.e. the lipid clinic at the University Children's Hospital Ljubljana) according to clinical guidelines, with additional cascade screening of family members and further clinical care as required.⁸⁴ Both steps are reimbursed nationally.⁸³ In 2021, the Slovenian screening programme, along with the Czech and the Dutch ones, have been recognised as a public health 'Best Practice' by the European Commission, making its emulation across the continent more likely in the future.

2

Second recommendation: simplify access to CVD screening, especially for vulnerable populations

The success of any screening programme relies on its capacity to reach the entire target population. It's crucial, therefore, to engage members of society that are reluctant to seek care or don't interact with the healthcare system consistently. Data shows that socioeconomic vulnerability correlates with both lower participation in CV health checks and a higher risk of developing CVDs.^{88,89}

Research points to several barriers that prevent people from accessing CVD screening in primary care settings. These range from personal characteristics (e.g. socioeconomic status, age, sex or ethnicity) and attitudes (e.g. expectations about outcomes, importance of health) to purely practical reasons (e.g. how the invitation is made, the time or costs involved).⁹⁰

Based on social approaches, population-wide screenings should be matched with 'concentrated' interventions to maximise equitable access for the entire population.⁹¹⁹²

To increase participation in screening programmes, especially among hard-to-reach groups, policy-makers should design-in ways to lower barriers to participation, by focusing on local hurdles.⁹⁰ That may mean, for example, involving influential figures within less engaged communities to inform people about CVD screening, or, more generally, integrate screening efforts into wider 'social prescribing' initiatives.^{93,94,95} Of note, these approaches are particularly valuable in the context of integrated or patient-centric approaches to care **(Case Study 3)**.

Finally, the success of cancer screening programmes may offer some useful lessons. Dedicated solutions to encourage participation may include one-onone education, personal reminders, use of tailored communication channels, but also measurement and reward of screening provider performance.⁹⁶





Case Study 3 Farmers Have Hearts

Making CVD screening more accessible: Farmers Have Hearts

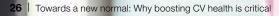
Farmers Have Hearts illustrates one of the approaches that allow the concentration of healthcare interventions on a population traditionally reluctant to seek care.

Farmers Have Hearts is a tailored workplace intervention programme, led by the Irish Heart Foundation since 2009.⁹⁷ Its aim is to target Irish farmers, who are at disproportionate risk of developing heart disease, yet often hard to reach. At local farmers' markets, nurses perform a free, 30-minute CVD health check (involving taking blood pressure, cholesterol, glucose etc.) and provide lifestyle advice. Early results look encouraging, with 64% of the farmers manifesting the intention to meet their doctor more regularly, and 48% already making lifestyle changes.⁹⁸









Area 2

Ensure treatment initiation, maintenance and follow-up for at-risk patients

Key messages

- Enable counselling and treatment according to care standards of eligible at-risk individuals, chronic disease patients and those with a history of acute events; ensure regular monitoring and follow-up over time.
- Decrease the risk of acute CV events and treatable mortality by acting in a timely fashion.
 - Decrease the risk of repeat acute CV events by achieving and maintaining metabolic targets indicated in clinical guidelines.
 - Provide patients with the support they need to manage their condition over time.
 - Ensure evidence-based care in line with guidelines.
 - Foster equitable care across all people in need.

Clinical guidelines are crucial to ensuring quality care, as they provide a standardised approach to decision-making. In CV medicine, regularly updated guidelines cover a broad range of aspects related to the management of acute and chronic conditions, including all stages of prevention and care, different target populations and disease profiles, as well as different types of interventions and technologies.⁹⁹

Despite the efforts of scientific societies to develop standardised decision-making tools and algorithms, the implementation of clinical guidelines falls short in many settings.¹⁰⁰ For example, in Western Europe, it's estimated that around 71% of individuals with hypertension are diagnosed, but only 61% receive treatment, and 40% achieve control. In comparison, in Central and Eastern Europe, only 52% are treated and just 19% reach control.65 Similarly, only 16% of European patients with established CVD achieve the LDL-C control target of 1.8 mmol/L as recommended in the 2016 guidelines issued by the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). And since the target was decreased to 1.4 mmol/L in 2019, the percentage might be even lower.¹⁰¹ These numbers show unequivocally that guideline implementation is far from ideal, resulting in a significant proportion of disease burden left undetected - at least until it manifests in acute and severe forms - and an even larger proportion undertreated or mismanaged.

'Therapeutic inertia' is observed all along the care pathway, from the management of risk factors to the moment an individual is clinically eligible to start medical treatment. It may also occur when therapy intensification would be required because treatment goals aren't met – e.g. when lifestyle modifications are insufficient to control hypertension or new anti-hyperglycemic therapies that demonstrated CV risk reduction are not utilised.¹⁰²

The failure to manage or treat CV conditions is a missed opportunity to improve people's health and wellbeing. For example, patients whose hypertension medications aren't managed in line with the expected standard of care are up to 33 times less likely to achieve blood pressure control compared to patients that are treated effectively.¹⁰² Similarly, a one year delay in treatment intensification in people with type 2 diabetes is associated with an increased risk in myocardial infarction, heart failure and stroke.

Therapeutic inertia arises for many reasons and may be related to clinician, patient, healthcare system and policy/regulatory factors.¹⁰² For example, healthcare professionals might lack the time and information to manage complex patients and multiple comorbidities calling for intricate regimens. Their training may not be able to keep up with evolving guidelines. Alternatively, healthcare professionals may experience a shortage of resources impacting on their ability to follow patients, or there could be concerns related to healthcare spend or reimbursement/out-of-pocket costs.^{100,103}

Patients themselves may also struggle to stick to their treatment, which negatively impacts health outcomes. For example, patients with diabetes and heart conditions that don't adhere to their prescribed treatment are almost twice as likely to die of their ailments compared to those that do adhere.¹⁰⁴ Poor adherence can happen for many reasons, including the extent to which healthrelated information is understood and used (so-called 'health literacy'), complicated medication regimes, socioeconomic context, personal beliefs, and inadequate communication between patient and healthcare professionals across the healthcare system.¹⁰⁵ Whatever the reason, the result is that up to 31% of people diagnosed with confirmed diabetes, hypertension, or high cholesterol never fill their first prescription. Of those who do, only 50% to 70% take their medications regularly. Finally, fewer than half of these patients continue taking their medication for two years, and therefore 'adhere' diligently to the prescribed treatment course.104

Last, therapeutic inertia may also stem from healthcare system financing and governance – as opposed to just the clinician- or patient-driven factors listed above. For example, few countries in Europe systematically measure adherence to guidelines or employ adherencerelated quality or performance indicators.¹⁰⁴ This is therefore a potential area for improvement, and initiatives in this direction may generate opportunities in terms of increased transparency about real-life treatment outcomes, as well as boosted system efficiency and effectiveness.

In the same vein, European systems may consider opportunities stemming from incentivising and rewarding the achievement of target outcomes for CVD patients. Europe still largely operates fee-for-service models that link payment of healthcare providers to services rendered. Value-based models that link reimbursement to the value of care delivered could help achieve improved outcomes for CVD patients.¹⁰⁶

Making sure that guidelines are implemented and that target outcomes are achieved should be measured and rewarded by designing appropriate system incentives, which can sustainably shift health behaviours.



3

Third recommendation: gear the system towards rewarding outcomes

In the context of an ageing population and rising incidence of chronic diseases, boosting adherence to the standard of care is going to be increasingly important to improve chronic patient management and contain the risk of deteriorating population health. Therefore, adherence to clinical guidelines, or more appropriately, achievement of desired health goals, should be expected and rewarded.

While rarely an implemented approach, Sweden paves the way around the creation of such incentives in Europe. SWEDEHEART, the national CVD registry, measures an array of quality indicators, including guideline adherence and resulting health outcomes, and publishes individual hospital performance annually **(Case Study 4)**. Since doing so, the worst-performing hospitals have increased their quality scores by 40%, narrowing the gap to the best performers significantly.¹⁰⁷ Second, reimbursement or other financial incentives could be linked to target outcomes. For example, the US Medicare Hospital Readmissions Reduction Program (HRRP), a value-based purchasing programme that links reimbursement to hospital care quality, results in significantly fewer re-hospitalisations of CVD patients, therefore proving the potential of these schemes in CV medicine **(Case Study 5)**.¹⁰⁸

Similar approaches should be tested out and scaled up in Europe, mindful of the lessons learnt so far around the implementation of such schemes.¹⁰⁹ For example, France has been piloting Territorial Hospital Groups as integrators of services that are responsible for the health of a given regional population. The scheme responds to the so-called 'Triple Aim' – better health, better care and at the best cost for a given population – and can represent a suitable platform for the roll-out of incentives related to achieving population health goals.¹¹⁰



Case Study 4 SWEDEHEART

Collecting real-world CVD data

As of now, the most comprehensive approach to real-word data collection on CVDs in Europe is represented by SWEDEHEART, the Swedish CVD registry, formed in 2009 by merging four national registries.¹¹¹ SWEDEHEART was set up specifically to develop evidence-based therapies for acute and chronic CVDs, but also to monitor the quality of care and to develop risk prediction tools. To give an idea of the extent of the effort, SWEDEHEART's sub-registry for Secondary Prevention after Heart Intensive Care Admission (SEPHIA), covers over 100,000 post-acute myocardial infarction patients, including their gender, age, risk factors and pharmacological treatment etc. Overall, SWEDEHEART has proven the ability to shape clinical practice via registry-based studies, as evidenced by the 49 scientific publications achieved in 2020 alone.112

Incentivising the achievement of desired health outcomes

SWEDEHEART also plays a crucial role in incentivising quality of care. For example, SEPHIA measures the percentage of patients achieving blood pressure, LDL cholesterol, glucose, smoking, diet, exercise and further goals – as a readout for guideline adherence.¹⁰⁷ This measurement is one of the key performance indicators for a hospital that are published annually, which, in the local settings, is accepted as a way to promote public accountability and healthy competition on outcomes.

The results speak for themselves: since starting to publish quality of care data, improvement rates in the average quality-index score rose from 13% to 22% per year.¹⁰⁷ By leveraging public reporting in this manner, system incentives are aligned with the goal of providing the best care according to the clinical guidelines.¹⁰⁹



Case Study 5 Hospital Readmissions Reduction Program

Linking CVD care outcomes to reimbursement

The Hospital Readmissions Reduction Program (HRRP) was rolled out in the United States in 2012. It's a Medicare value-based purchasing programme that connects reimbursement specifically to hospital care quality. CMS, the public payer, can reduce payments to healthcare providers by up to 3%, in case of excess readmissions and poor comparative performance. This scheme includes outcome measurement related to three CVDs, i.e. myocardial infarction, heart failure and bypass operations.¹¹³ A recent assessment confirmed that the programme has been able to significantly reduce hospitalisation rates, with a positive 'spill-over effect' to other conditions, without penalising vulnerable hospitals and patients.¹⁰⁸



4

Fourth recommendation: strengthen digital health and information sharing

It's widely acknowledged that remote medicine, and more generally digital health, made a significant difference during the COVID-19 crisis.¹¹⁴ The European Observatory on Health Systems and Policies stated that "digital health tools hold the potential to improve the efficiency, accessibility and quality of care".¹¹⁵ In the aftermath of the crisis, the use of such solutions has persisted in care pathways, connecting patients with healthcare professionals and payers, and collecting real-world as well as real-time data – even though this innovation often remains limited to pilot programmes.¹¹⁶

In CV medicine, digital health has been used mostly for remote monitoring of patients and to provide ad hoc support.¹¹⁷ Digital health solutions have the potential to help manage a wide array of underlying CVD risk drivers, such as hypertension, diabetes, smoking, overweight/ obesity and physical inactivity. In addition, digital health applications can contribute to monitoring and cardiac rehabilitation. For example, telemedicine has been effective in reducing re-hospitalisation and in improving quality of life for heart failure patients.¹¹⁸

To make the shift to digital stick in the future, integration – from both a procedural and financing perspective – is key. Germany blazed a trail with the 'Digital Care Act', establishing an accelerated pathway for patient-focused, low-risk e-health applications.¹¹⁹ Since September 2020, 31 e-health interventions have been reimbursed, including an application ('Rehappy') geared towards post-ischemic stroke care, and many others targeting CVD risk factors, such as diabetes.¹²⁰

Nor are other European countries lagging far behind.¹²¹ Belgium has set up the 'Health Validation Pyramid' to evaluate the quality and effectiveness of mobile-health applications (though none have yet been reimbursed at the time of writing).¹²² Similarly, France has announced plans to replicate Germany's rapid market access pathway for digital therapeutics.¹²³ In addition to digital health, other approaches can drive improved treatment initiation and maintenance, including increased uptake – and integration into local protocols and Electronic Health Record (EHR) systems – of decision support for healthcare professionals to navigate guidelines efficiently and manage multi-morbidity.^{100,102} For example, the Acute Cardiovascular Care (ACVC) Clinical Decision-Making Toolkit, developed by the European Society of Cardiology, offers clear, app-based algorithms to help practitioners treat acute CVDs.¹²⁴

Finally, the involvement of community-level healthcare professionals could contribute to lowering some of today's barriers. In the US, for example, the combination of health promotion by barbershops and on-site pharmacists for medication management demonstrably lowered blood pressure in non-Hispanic black men.¹²⁵ Also, improved data flows across care settings could help pharmacists and nurses monitor and follow up prescription refilling, especially for the most vulnerable people. For example, in France, the dossier pharmaceutique, a confidential electronic medication record set up in 2007 and continuously expanded since, allows community pharmacists and other healthcare professionals to review patients' medication history, thus improving coordination and limiting safety risks.¹²⁶

In sum, digital health tools show promise in advancing CV medicine. However, their adoption and continued use needs to be incentivised appropriately by lowering barriers to reimbursement and facilitating integration into existing health data infrastructure.

«Digital health solutions have the potential to help manage a wide array of underlying CVD risk drivers, such as hypertension, diabetes, smoking, overweight/obesity and physical inactivity.»



Foster data-driven decision-making

Key messages

What?	 Collect and leverage data to generate actionable
	insights, support clinical decision-making and inform
	policy-making.

- Reward outcome-based clinical decision-making.
 - Predict risks and proactively manage people's health.
 - Leverage data to identify and treat patients with CVD and modifiable risk factors.
 - Deliver sustained quality of care in CVD and multimorbid patients.
 - Design policies that are effective at promoting wellbeing and good health behaviours.

Europe has articulated its ambition to create a shared space for health data: the European Health Data Space (EHDS). The vision is to combine data from a range of sources to improve healthcare delivery, conduct research and drive evidence-based policy-making.¹²⁷ The EHDS will offer a way to address healthcare-related 'implementation problems' by generating context-specific and demand-driven insights, based on multidimensional, real-world and real-time data.^{128,129}

Crucially, the EHDS will build on ongoing efforts in multiple therapeutic areas. Steady progress has been made in NCDs, such as cancer, haemophilia, multiple sclerosis and cystic fibrosis.^{130,131,132} For example, the European Network of Cancer Registries has been in operation since 1990, formally supported by the European Commission since 2012. This international registry developed an ad hoc platform to facilitate harmonised data collection, as well as disseminate aggregated indicators of the cancer burden in Europe.¹³³ The European Medicines Agency is also supporting these efforts, with a particular focus on transparency, accessibility of data for public health purposes, independence and sustainability.¹³⁴

As of now, the most comprehensive approach to realword data collection on CVDs in Europe is represented by SWEDEHEART, the Swedish CVD registry, formed in 2009 by merging four national registries. But other efforts to scale up CVD registries across Europe are already underway. For example, the EuroHeart initiative was launched in 2019 and has already established registries in Estonia, Romania and several other countries **(Case Study 6)**.

5

Fifth recommendation:

collect new and leverage existing data to drive CVD insight, support clinical decision-making as well as valuebased care delivery and inform CVD policy-making

Precision public health is an emerging discipline that sits at the crossroads between Big Data analytics used to inform precision medicine, and traditional population health management approaches.¹³⁵ Increasing and expanding CVD data collection is a promising field of application, which could have a powerful impact on several aspects related to CV health promotion and management.

First, real-world data can help assess disease trajectories, i.e. forecast how CV risk evolves based on the underlying pattern of risk factors over time.¹³⁶ For example, a recent systematic study showed that specific temporal patterns of molecular indicators correlate with morbidity and mortality outcomes in people with diabetes and hypertension.¹³⁷ These findings have implications for population health, as they enable the identification of subsets characterised by similar underlying risk patterns (so-called 'risk populations') and the appropriate action to manage their risks. Such predictive studies can also benefit from a multidimensional approach. For example, matching clinical indicators to socioeconomic status indicators can help identify vulnerable populations with the greatest need. During the COVID-19 crisis, an integrated health data system in Massachusetts was able to pinpoint 'medically and socially complex' individuals at higher risk of severe COVID-19 outcomes. In response and as part of a public health containment measure, their underlying chronic health issues could then be proactively addressed.¹³⁸

Second, CVD events can be predicted not only using 'traditional' risk score models, but also – and increasingly accurately – via machine learning and Artificial Intelligence (AI) powered algorithms fed by real-world data. For example, some conditions, such as coronary artery disease, heart failure or strokes, can now be predicted by processing routine cardio imaging and ECG with machine learning-based algorithms.¹³⁹ Thinking further ahead to the future of CV medicine, single-cell multi-omic approaches, relying heavily on Big Data and AI, will allow CVD 'interception' before any cell damage occurs.¹⁴⁰ Combined with existing technologies, interceptive medicine will be able, for example, to automate the analysis of imaging data and intercept myocardial infarctions, or to personalise heart failure treatment based on individual 'omic' patterns of expression.¹⁴¹

Third, real-world data collection enables the implementation of value-based payment models, i.e. models that reward healthcare providers for the 'value' they deliver. In this context, value can mean high-quality care, improved patient experience, multidisciplinary coordination, cost-conscious behaviour, prevention and improved population health.¹⁰⁶

Some of these programmes – such as the Hospital Readmissions Reduction Program (see p. 26, Third recommendation: gear the system towards rewarding outcomes) – are explicitly geared towards improving CVD care, and are already popular in the US. The American Heart Association is an advocate of the move away from fee-for-service models in CVD care, highlighting that value-based models are better suited to rewarding longterm support, care coordination, remote monitoring, and embedding of social care.¹⁴²

There are relatively few examples of value-based payment models applied to chronic diseases in Europe, but there are encouraging results coming from systems that reward primary care physicians based on quality of care, including patient satisfaction, clinical guideline adherence and disease management.¹⁴³ «Europe is well positioned to build on existing data initiatives by intensifying and scaling up efforts in the CVD area.»

Finally, real-world data is needed for evidenceinformed policy-making. In this context, the recently launched World Heart Observatory represents a milestone achievement. As a CVD knowledge hub, the Observatory curates, aggregates and visualises data on cardiovascular conditions, biological risk factors, social determinants of health, health systems and policy responses. Its aim is to become a comprehensive, trusted tool for CVD policy-making around the globe.¹⁴⁴

Even though it often does, real-world data collection should not stop at epidemiological, social and policy data. Rather, data on the cost of CV care is also highly valuable, informing health-economic assessments (e.g. cost-benefit analysis) and guiding policy-making on best buys. As a result, economic indicators around CVD should be gathered as systematically as possible going forward.

Overall, Europe is well positioned to build on existing data initiatives by intensifying and scaling up efforts in the CVD area. A pan-European CVD registry and related outcomes of data collection and research would enable health systems to drive individual and population-level CVD insights and predict future CVD risk. It could also support better decision-making around CVD and accelerate value-based delivery of CVD and, more generally, chronic disease care.



Case Study 6 EuroHeart

Scaling up real-world CVD collection across Europe

Efforts to scale up CVD registries across Europe are already underway. Led by the European Society for Cardiology, the EuroHeart initiative (which stands for European Unified Registries On Heart Care Evaluation and Randomised Trials) was launched in 2019 and has already established registries in Estonia, Romania and several other countries.¹⁴⁵

The initiative's aim is to define common indicators for quality of care and provide easily accessible, realtime, harmonised patient data across participating countries, including data on therapy, interventions and devices.¹⁴⁶ The registry will cover four common disease areas (namely Acute Coronary Syndrome, heart failure, valve disease and atrial fibrillation) and also feature integrated tools for device surveillance and randomised clinical trials. Ultimately, the initiative is designed to benefit patients, citizens and the planning of healthcare investments. For example, it might make it easier to identify patients whose risk factors aren't controlled properly.

Interfaces and synergies

The ambition to realise a European Health Union and improve NCD control will require robust screening approaches, quality care and systematic outcome collection. The recommendations made in this paper align well with European goals and initiatives, as outlined below.

The 'Healthier together: EU Non-communicable Diseases Initiative' calls for effective actions and policies to reduce the burden of major NCDs, with CVDs as one of its main areas of focus.⁵¹ Similarly, the European Economic and Social Committee (EESC) has recently called for an EU mission to address the needs of patients with NCDs impacted by the COVID-19 pandemic, and especially those suffering from CVD.¹⁴⁷ In line with these goals, our recommendations concentrate on systemic approaches to contain the CVD burden. These include targeting the entire population at risk for improved disease management; designing systemic incentives to foster quality care and collecting multidimensional data to predict and manage cardiovascular risk at both individual and population level.

Just like 'Healthier together', the 'Health in All Policies' initiative targets health inequalities. These disparities are known to drive the manifestation of CVDs via risk factors, but are, conversely, also reinforced by underlying disabling conditions, including chronic CVDs. We argue that containing the CVD burden will also have the added benefit of reducing health inequalities (see Improving CV population health to build equitable and resilient systems, p.14).

The proposed 'European Health Data Space', alongside its pathfinder programme 'DARWIN EU' and the broader 'Digital Europe Programme', will foster better access to, and exchange of, multidimensional health data across Europe with the aim of supporting healthcare delivery, health research and policy-making.^{148,149} Integrated CVD registries will enable the collection of deep insights around the most burdensome set of conditions in Europe. CV health management and promotion depend heavily on data availability and flow, which is particularly important given the typical CV patient profile: suffering from multiple morbidities, often advanced in age, dealing with multiple healthcare professionals in different settings and being treated simultaneously on multiple fronts. Preliminary assessments of the new 'Pharmaceutical Strategy' outline the need for Europe to take advantage of innovation promptly, and in particular, to harness technologies such as gene editing, gene sequencing and Al.¹⁵⁰ Scaling up CVD data collection and related insight generation, as discussed in the Section AREA 3 Foster data-driven decision-making, is instrumental to achieving this goal.

The 'Recovery and Resilience Facility' aims to mitigate the economic and social impact of the COVID-19 pandemic and better prepare society for the future by increasing healthcare systems' resilience.¹⁵¹ In line with this mission, we suggest better population CV health as a proactive approach to increasing healthcare system resilience. Decreasing the burden of CVDs has the potential to contain the need for resource-intensive care required by vulnerable segments of the population, such as seniors as well as chronic and multi-morbid patients in emergency settings. The saved healthcare resources can then be deployed elsewhere, thus boosting resilience across the entire system (see Improving CV population health to build equitable and resilient systems, p. 14).

Finally, our recommendations complement the priorities listed in the 'Action Plan for the Prevention and Control of Noncommunicable Diseases in the WHO European Region 2016–2025'.⁷⁷ Its main goal is to reduce premature mortality from NCDs and to avoid disability by focusing on health promotion measures via highly cost-effective interventions. Our recommendations display a similar intent and focus on a population health management approach to detect and support individuals in whom CV conditions or risk factors have already manifested.



Afterword PwC

We're grateful to EFPIA and the CVD Network, an impressively committed working group, for giving us the opportunity to collaborate on this impactful subject. We'll take away with us many interesting readings, brainstorming sessions and discussion insights, especially around the ideas of population health, system resilience and equity.

Some of what we've learnt during this study was quite unexpected and surprising, and we would like to share those with the readers.

Making the case for CVD early detection and

management is difficult. The simple reason is that the evidence that we need to prove the case *today* should've been collected *30 years ago*, when the disease understanding, the disease management options, the medical products and technologies, as well as the policy priorities, were very different from today. Other NCDs are much more straightforward to track: they progress fast, they're debilitating, and they're expensive to treat. CVDs are largely invisible, and the risk of severe sickness builds up slowly over time. Yet the consequences are highly significant for individuals and populations alike. This is one of the main reasons why we placed considerable emphasis on data and outcome collection. We strive to make the case for both existing and future patients, so that they can get the care they need. «Improving health outcomes will make it easier for people to be productive and achieve their life goals – the best predictors of healthy lives.»

Acute CVD events are neither unpredictable nor unpreventable. On the contrary, risk factors and prognostic patterns are very well characterised. While medical professionals may not be able to predict the exact moment a stroke will hit, they can identify people at risk of having one – and a lot can be done to decrease or manage their risk of disease. It was interesting to learn that 70% of CVD (and 90% of strokes!) are, to a large extent, preventable, yet not much is done to manage the risk.

Having a CV condition is not shameful. While a large part of the disease burden could be prevented by personal choices, individuals can't be held responsible for all preventative steps. Rather, prevention requires a shift at the level of healthcare systems and, more broadly, in patterns of socio-economic determinants. This is why this report privileged systemic recommendations, for example incentives and financing, as well as population health measures, rather than individually targeted actions.

We are convinced that improving CV health outcomes will make it easier for people to be productive and achieve their life goals – the best predictors of healthy lives.

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Useful definitions

- Morbidity: the number or proportion of clinically ill persons, typically measured through incidence (i.e., the number of newly diagnosed cases over a certain period of time) and prevalence (i.e., the proportion of people in a population who have disease at a given time).
- Mortality: the number or proportion of deaths resulting from a disease within a given period of time, usually expressed per 100 000 population.
- Avoidable mortality: deaths that could have been avoided through optimal quality healthcare interventions (more specifically, treatable mortality), or through preventive care (more specifically, preventable mortality).
- **Premature mortality:** deaths occurring before the expected age of death for a certain population. The threshold age can be arbitrarily defined. For example, ESC Statistics call a death premature when occurring before 70 years of age.
- **Risk factor:** any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or incurring an injury. Risk factors can be modifiable (e.g., metabolic, lifestylerelated, environmental), or non-modifiable (e.g., genetic, age).
- At-risk (or, risk) population: a group of people within the general population that can be defined by a pattern of features, and that displays an increased susceptibility to develop a given pathological condition.
- **Population attributable fraction:** as per the WHO definition, it is the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were reduced to an alternative ideal exposure scenario. For example, high cholesterol, a metabolic risk factor, is responsible for almost 21% of the CVD burden in high-income countries.
- **Population health:** refers to the health outcomes of a group of individuals, including their distribution within the group. As an academic discipline, population health is concerned with health outcomes, patterns of health determinants and policy implications.

- **Population health management:** an approach to improving population health that leverages data-driven identification of at-risk populations.
- **Prevention:** a set of actions and interventions taken to avoid the manifestation or progression of a disease. According to the WHO, primary prevention aims to prevent a disease from ever occurring (e.g., via healthy diet); secondary prevention is about early detection of subclinical forms of the disease (e.g., hypertension management); tertiary prevention is about avoiding complications and promoting better quality of life for those living with the disease. Preventive actions can focus on an individual or on entire populations.
- Screening: a systematic programme that invites a target population (defined, e.g., by age, sex, or a specific risk profile) to regularly undertake a diagnostic test (e.g., blood pressure measurement) to detect a disease, or the presence of risk factors for a disease. A screening programme is based on some principles: it addresses a recognised health problem; the health problem has a well-characterised early phase in which preventive action can take place; an intervention (e.g., behavioural counselling, or a medication) for individuals testing positive is available; the cost of screening offers an advantage compared to the cost of later care.
- Chronic CV condition vs acute CV event: many CVDs are long-term conditions, appearing in symptomatic or asymptomatic forms. If not managed, those can progress towards more severe stages over time. Occasionally, a sudden and severe event can take place, resulting in a visible drop in the health status of a person. For example, Coronary Artery Disease, a condition that results from the accumulation of fatty deposits in arteries, can have long stable periods, but can manifest acutely at any time if these deposits rupture, leading to strokes and heart attacks.

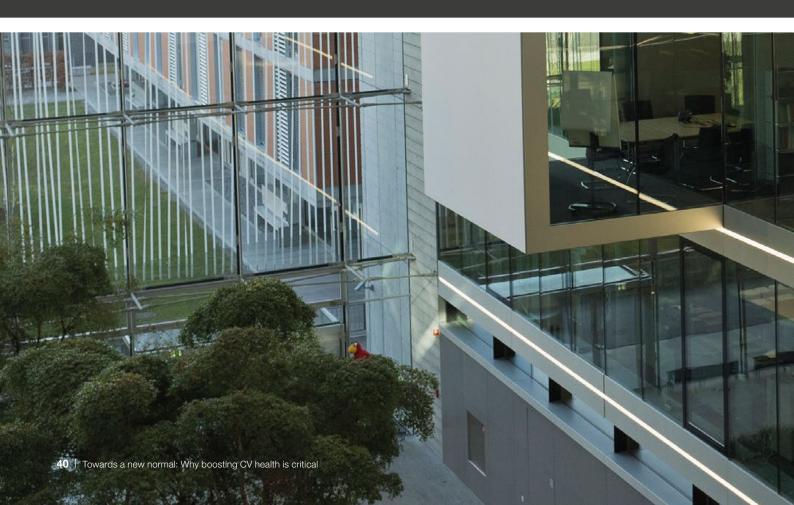


About this research

This report is the result of an independent assessment, based on a strategic options development and analysis (SODA) approach, conducted by PwC between November 2021 and March 2022.

The context assessment was largely based on individual expert discussions (see Acknowledgements) conducted with cardiologists, patient groups, civil society and public health/policy experts around the cardiovascular disease burden, the impact of COVID-19 and syndemic aspects. PwC framed findings around the patient care pathway to highlight existing needs, those exacerbated by the pandemic, as well as new ones. All key findings were verified based on a targeted, peer-reviewed literature search. Statements that could not be verified were excluded from the assessment or indicated in the report as 'expert opinion'.

Emerging challenges and themes were discussed and prioritised with EFPIA CVD Network member representatives during a series of workshops. PwC and the EFPIA team jointly defined the expected impact and goals of the policy recommendations to formulate, as per the SODA approach. Then, PwC identified a set of potential policy areas and solutions, and assessed them via targeted literature review for their ability to meet impact and goals. Finally, a shortlist of options was compiled, organised in three policy areas (screening, treatment, data) and included in a broader narrative. Policy options and/or the full narrative were reviewed in March 2022 by all the experts identified for discussion in the initial project phase.





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References and notes

1	Expressed as the number of prevalent cases across the European Union (as per Global Burden of Disease study).	
2	Global Burden of Disease 2019 [Internet]. 2019 [cited March 30, 2022]. Available from: https://ghdx.healthdata.org/gbd-results- tool.	
3	Informa Datamonitor Healthcare: Prevalent cases of Coronary Artery Disease in Europe [Internet]. 2022 [cited March 30, 2022]. Available from: https://service.datamonitorhealthcare.com/.	
4	i.e. death happening before 70 years of age.	
5	Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, et al. European Society of Cardiology: cardiovascular disease statistics 2021. European Heart Journal. 2022;43(8):716-99.	
6	European Heart Network: Cardiovascular Disease Statistics [Internet]. 2017 [cited March 30, 2022]. Available from: https://ehnheart.org/cvd-statistics/cvd-statistics-2017.html.	
7	The prevalence decrease was just 7% from 1995 to 2019 (age-standardised prevalence per 100 000 population).	
8	Based on expert opinion and PwC analysis.	
9	Yusuf S, Joseph P, Rangarajan S, Islam S, Mente A, Hystad P, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet. 2020;395(10226):795-808.	
10	Eurostat: Preventable and treatable mortality statistics [Internet]. 2021 [cited March 30, 2022]. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Preventable_and_treatable_mortality_statistics.	
11	Voci D, Fedeli U, Farmakis IT, Hobohm L, Keller K, Valerio L, et al. Deaths related to pulmonary embolism and cardiovascular events before and during the 2020 COVID-19 pandemic: An epidemiological analysis of data from an Italian high-risk area. Thromb Res. 2022;212:44-50.	
12	Wadhera RK, Shen C, Gondi S, Chen S, Kazi DS, Yeh RW. Cardiovascular Deaths During the COVID-19 Pandemic in the United States. J Am Coll Cardiol. 2021;77(2):159-69.	
13	Holt A, Gislason GH, Schou M, Zareini B, Biering-Sørensen T, Phelps M, et al. New-onset atrial fibrillation: incidence, characteristics, and related events following a national COVID-19 lockdown of 5.6 million people. European Heart Journal. 2020;41(32):3072-9.	
14	Charlton K, Limmer M, Moore H. Incidence of emergency calls and out-of-hospital cardiac arrest deaths during the COVID-19 pandemic: findings from a cross-sectional study in a UK ambulance service. Emergency Medicine Journal. 2021;38(6):446.	
15	Pessoa-Amorim G, Camm CF, Gajendragadkar P, De Maria GL, Arsac C, Laroche C, et al. Admission of patients with STEMI since the outbreak of the COVID-19 pandemic: a survey by the European Society of Cardiology. European Heart Journal - Quality of Care and Clinical Outcomes. 2020;6(3):210-6.	
16	Hinde S, Harrison A, Bojke L, Doherty P. Quantifying the impact of delayed delivery of cardiac rehabilitation on patients' health. European Journal of Preventive Cardiology. 2020;27(16):1775-81.	
17	ESC Press Office: Worse outcomes observed after heart attacks during pandemic compared to previous year [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.escardio.org/The-ESC/Press-Office/Press-releases/worse-outcomes-observed-after-heart-attacks-during-pandemic-compared-to-previous.	
18	Banerjee A, Chen S, Pasea L, Lai AG, Katsoulis M, Denaxas S, et al. Excess deaths in people with cardiovascular diseases during the COVID-19 pandemic. European Journal of Preventive Cardiology. 2021;28(14):1599-609.	
19	Xie Y, Xu E, Bowe B, Al-Aly Z. Long-term cardiovascular outcomes of COVID-19. Nature Medicine. 2022;28(3):583-90.	
20	Barda N, Dagan N, Ben-Shlomo Y, Kepten E, Waxman J, Ohana R, et al. Safety of the BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting. New England Journal of Medicine. 2021;385(12):1078-90.	
21	Thakur B, Dubey P, Benitez J, Torres JP, Reddy S, Shokar N, et al. A systematic review and meta-analysis of geographic differences in comorbidities and associated severity and mortality among individuals with COVID-19. Sci Rep. 2021;11(1):8562.	
22	Stirbu I, Looman C, Nijhof GJ, Reulings PG, Mackenbach JP. Income inequalities in case death of ischaemic heart disease i the Netherlands: a national record-linked study. Journal of Epidemiology and Community Health. 2012;66(12):1159.	
23	Drefahl S, Wallace M, Mussino E, Aradhya S, Kolk M, Brandén M, et al. A population-based cohort study of socio- demographic risk factors for COVID-19 deaths in Sweden. Nature Communications. 2020;11(1):5097.	
24	The Lancet: Latest global disease estimates reveal perfect storm of rising chronic diseases and public health failures fuelling COVID-19 pandemic [Internet]. 2020 [cited March 30, 2022]. Available from: https://www.healthdata.org/news-release/lancet-latest-global-disease-estimates-reveal-perfect-storm-rising-chronic-diseases-and.	
25	Eurostat: Ageing Europe - statistics on population developments [Internet]. 2021 [cited March 30, 2022]. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Ageing_Europestatistics_on_population_developments.	
26	Baré M, Herranz S, Roso-Llorach A, Jordana R, Violán C, Lleal M, et al. Multimorbidity patterns of chronic conditions and	

geriatric syndromes in older patients from the MoPIM multicentre cohort study. BMJ Open. 2021;11(11):e049334.

- 27 Laires PA, Perelman J. The current and projected burden of multimorbidity: a cross-sectional study in a Southern Europe population. Eur J Ageing. 2018;16(2):181-92.
- 28 Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T. Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10267):2006-17.
- 29 GBD Dementia Forecasting Collaborators: Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050 An analysis for the Global Burden of Disease Study 2019. Lancet Public Health. 2022;7(2):e105-e25.
- 30 Amini M, Zayeri F, Salehi M. Trend analysis of cardiovascular disease mortality, incidence, and mortality-to-incidence ratio: results from global burden of disease study 2017. BMC Public Health. 2021;21(1):401.
- 31 Pineda E, Sanchez-Romero LM, Brown M, Jaccard A, Jewell J, Galea G, et al. Forecasting Future Trends in Obesity across Europe: The Value of Improving Surveillance. Obesity Facts. 2018;11(5):360-71.
- 32 Janssen F, Bardoutsos A, Vidra N. Obesity Prevalence in the Long-Term Future in 18 European Countries and in the USA. Obesity Facts. 2020;13(5):514-27.
- 33 Romanello M, van Daalen K, Anto JM, Dasandi N, Drummond P, Hamilton IG, et al. Tracking progress on health and climate change in Europe. Lancet Public Health. 2021;6(11):e858-e65.
- 34 Watts N, Amann M, Arnell N, Ayeb-Karlsson S, Beagley J, Belesova K, et al. The 2020 report of The Lancet Countdown on health and climate change: responding to converging crises. Lancet. 2021;397(10269):129-70.
- 35 Hassell JM, Newbold T, Dobson AP, Linton Y-M, Franklinos LHV, Zimmerman D, et al. Towards an ecosystem model of infectious disease. Nature Ecology & Evolution. 2021;5(7):907-18.
- Prof. Sarah Gilbert Vaccine vs the Virus: This race, and the next one [Internet]. Oxford University. 2021 [cited March 30, 2022]. Available from: https://www.ox.ac.uk/news/2021-12-07-professor-dame-sarah-gilbert-delivers-44th-dimbleby-lecture.
- The Next Pandemic Could Come Soon and Be Deadlier [Internet]. Center for Global Development. 2021 [cited March 30, 2022]. Available from: https://www.cgdev.org/blog/the-next-pandemic-could-come-soon-and-be-deadlier.
- 38 UNHCR Operational Data Portal: Ukraine Refugee Situation [Internet]. UNHCR. 2022 [cited March 30, 2022]. Available from: https://data2.unhcr.org/en/situations/ukraine.
- 39 Wharton G, Gocke D, McGuire A, Sturm T. The Partnership for Health Sustainability and Resilience Interim Report of the Pilot Phase [Internet]. 2021 [cited March 30, 2022]. Available from: https://www3.weforum.org/docs/WEF_PHSSR_Interim_Report_ of_the_Pilot_Phase.pdf.
- 40 Mair FS, Jani BD. Emerging trends and future research on the role of socioeconomic status in chronic illness and multimorbidity. Lancet Public Health. 2020;5(3):e128-e9.
- 41 Davari M, Maracy MR, Khorasani E. Socioeconomic status, cardiac risk factors, and cardiovascular disease: A novel approach to determination of this association. ARYA Atheroscler. 2019;15(6):260-6.
- 42 Schultz WM, Kelli HM, Lisko JC, Varghese T, Shen J, Sandesara P, et al. Socioeconomic Status and Cardiovascular Outcomes: Challenges and Interventions. Circulation. 2018;137(20):2166-78.
- 43 Lago Peñas S, Rivera B, Cantarero D, Casal B, Pascual M, Blázquez-Fernández C, et al. The impact of socioeconomic position on non-communicable diseases: what do we know about it? Perspectives in Public Health. 2021;141(3):158-76.
- 44 Huisman M, Kunst AE, Bopp M, Borgan JK, Borrell C, Costa G, et al. Educational inequalities in cause-specific mortality in middle-aged and older men and women in eight western European populations. Lancet. 2005;365(9458):493-500.
- 45 OECD: Health at a Glance [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.oecd-ilibrary.org/content/ publication/ae3016b9-en.
- 46 Frank J, Abel T, Campostrini S, Cook S, Lin VK, McQueen DV. The Social Determinants of Health: Time to Re-Think? Int J Environ Res Public Health. 2020;17(16).
- 47 Horton R. Offline: COVID-19 is not a pandemic. The Lancet. 2020;396(10255):874.
- 48 European Commission: EU4Health 2021-2027 a vision for a healthier European Union [Internet]. 2021 [cited March 30, 2022]. Available from: https://ec.europa.eu/health/funding/eu4health-2021-2027-vi
- 49 European Commission: European Health Union Protecting the health of Europeans and collectively responding to cross-border health crises [Internet]. 2019 [cited March 30, 2022]. Available from: https://ec.europa.eu/info/strategy/ priorities-2019-2024/promoting-our-european-way-life/european-health-union_en#lessons-from-the-coronavirus-pandemic.
- 50 Pan-European Commission on Health and Sustainable Development: Drawing light from the pandemic Rethinking strategies for health policy and beyond [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.euro.who.int/__data/assets/ pdf_file/0015/511701/Pan-European-Commission-health-sustainable-development-eng.pdf.
- 51 European Commission: Healthier Together Initiative [Internet]. 2022 [cited March 30, 2022]. Available from: https://ec.europa.eu/health/non-communicable-diseases/overview_en.

- 52 European Commission: A cancer plan for Europe [Internet]. 2021 [cited March 30, 2022]. Available from: https://ec.europa.eu/ info/strategy/priorities-2019-2024/promoting-our-european-way-life/european-health-union/cancer-plan-europe_en.
- 53 WHO Europe: Strengthening resilience a priority shared by Health 2020 and the Sustainable Development Goals [Internet]. 2017 [cited March 30, 2022]. Available from: https://www.euro.who.int/__data/assets/pdf_file/0005/351284/resilience-report-20171004-h1635.pdf.
- 54 WHO: Saving lives, spending less the case for investing in noncommunicable diseases [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.who.int/publications/i/item/9789240041059.

55 Consider, for example, structural heart disease. See, (51).

- 56 d'Arcy JL, Coffey S, Loudon MA, Kennedy A, Pearson-Stuttard J, Birks J, et al. Large-scale community echocardiographic screening reveals a major burden of undiagnosed valvular heart disease in older people: the OxVALVE Population Cohort Study. Eur Heart J. 2016;37(47):3515-22.
- 57 European Heart Network: Early detection of cardiovascular disease [Internet]. 2021 [cited March 30, 2022]. Available from: https://ehnheart.org/publications-and-papers/publications/1304:cvd-screening-2021.html.
- 58 European Commission: Cancer screening Improving cancer prevention across the EU [Internet]. [cited March 30, 2022]. Available from: https://ec.europa.eu/info/research-and-innovation/strategy/support-policy-making/scientific-support-eupolicies/group-chief-scientific-advisors/cancer-screening_en.
- 59 As of 2020, 25 EU countries featured population-based screening for breast cancer in their national cancer control plans; 22 countries screen for cervical cancer; 20 countries screen for colorectal cancer.
- 60 Xu X, Mishra GD, Dobson AJ, Jones M. Progression of diabetes, heart disease, and stroke multimorbidity in middle-aged women: A 20-year cohort study. PLoS Med. 2018;15(3):e1002516.
- 61 Zeng L, Talukdar HA, Koplev S, Giannarelli C, Ivert T, Gan L-M, et al. Contribution of Gene Regulatory Networks to Heritability of Coronary Artery Disease. J Am Coll Cardiol. 2019;73(23):2946-57.
- 62 Marquina C, Talic S, Vargas-Torres S, Petrova M, Abushanab D, Owen A, et al. Future burden of cardiovascular disease in Australia: impact on health and economic outcomes between 2020 and 2029. European Journal of Preventive Cardiology. 2021.
- 63 It applies even before factoring in data around the productivity impact of CVDs. See, for example, (57).
- 64 Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016;37(29):2315-81.
- 65 NCD Risk Factor Collaboration: Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019 - a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet. 2021;398(10304):957-80.
- 66 Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. The Lancet. 2016;387(10022):957-67.
- 67 Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies With the special contribution of the European Association of Preventive Cardiology (EAPC). European Heart Journal. 2021;42(34):3227-337.
- 68 Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). European Heart Journal. 2019;41(1):111-88.
- 69 World Heart Federation: ROADMAP FOR HYPERTENSION Informing health systems approaches to CVD by prioritizing practical, proven, cost-effective action [Internet]. 2021 [cited March 30, 2022]. Available from: https://world-heart-federation. org/cvd-roadmaps/wp-content/uploads/sites/3/2021/04/WHF_Hypertension-Roadmap-WEB.pdf.
- 70 Catapano AL, Wiklund O. Think Again About Cholesterol Survey. Atheroscler Suppl. 2015;20:1-5.
- 71 Cardoso R, Blumenthal RS, Kopecky S, Lopez-Jimenez F, Martin SS. How Low to Go With Lipid-Lowering Therapies in a Cost-effective and Prudent Manner. Mayo Clin Proc. 2019;94(4):660-9.

72 These reductions apply after one year of statin use.

- 73 The NHS Long Term Plan A Summary [Internet]. 2019 [cited March 30, 2022]. Available from: https://www.longtermplan.nhs. uk/wp-content/uploads/2019/01/the-nhs-long-term-plan-summary.pdf.
- 74 Herz-Hirn-Allianz: Ehrgeizige Ziele gegen Todesursache Nummer 1 [Internet]. 2022 [cited March 30, 2022]. Available from: https://www.aerztezeitung.de/Wirtschaft/Herz-Hirn-Allianz-Ehrgeizige-Ziele-gegen-Todesursache-Nummer-1-424695.html.
- 75 About Million Hearts 2027 [Internet]. 2022 [cited March 30, 2022]. Available from: https://millionhearts.hhs.gov/about-millionhearts/index.html.

- 76 Kuwabara M, Mori M, Komoto S. Japanese National Plan for Promotion of Measures Against Cerebrovascular and Cardiovascular Disease. Circulation. 2021;143(20):1929-31.
- 77 WHO Europe: Action Plan for the Prevention and Control of Noncommunicable Diseases in the WHO European Region 2016– 2025 [Internet]. 2016 [cited March 30, 2022]. Available from: https://www.euro.who.int/__data/assets/pdf_file/0008/346328/ NCD-ActionPlan-GB.pdf.
- 78 NHS UK: What is an NHS Health Check? [Internet]. 2019 [cited March 30, 2022]. Available from: https://www.nhs.uk/ conditions/nhs-health-check/what-is-an-nhs-health-check-new/.
- 79 Alageel S, Gulliford MC. Health checks and cardiovascular risk factor values over six years' follow-up: Matched cohort study using electronic health records in England. PLoS Med. 2019;16(7):e1002863.
- 80 CHRODIS+ EU: A Sustainable, Active, Primary Prevention Strategy for Cardiovascular Diseases in Italy for Adults 50+ - 'Projects Cuore and Cardio 50' [Internet]. 2017 [cited March 30, 2022]. Available from: http://chrodis.eu/wp-content/ uploads/2017/03/projects-cuore-and-cardio-50.pdf.
- 81 Young 50: Transferring the CARDIO 50 experience to other member states [Internet]. 2019 [cited March 30, 2022]. Available from: https://www.young50.eu/.
- 82 Hu P, Dharmayat KI, Stevens CAT, Sharabiani MTA, Jones RS, Watts GF, et al. Prevalence of Familial Hypercholesterolemia Among the General Population and Patients With Atherosclerotic Cardiovascular Disease. Circulation. 2020;141(22):1742-59.
- 83 Representatives of the Global Familial Hypercholesterolemia Community: Reducing the Clinical and Public Health Burden of Familial Hypercholesterolemia: A Global Call to Action. JAMA Cardiology. 2020;5(2):217-29.
- 84 Groselj U, Kovac J, Sustar U, Mlinaric M, Fras Z, Podkrajsek KT, et al. Universal screening for familial hypercholesterolemia in children: The Slovenian model and literature review. Atherosclerosis. 2018;277:383-91.
- 85 Vallejo-Vaz AJ, Stevens CAT, Lyons ARM, Dharmayat KI, Freiberger T, Hovingh GK, et al. Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC). The Lancet. 2021;398(10312):1713-25.
- 86 Pelczarska A, Jakubczyk M, Jakubiak-Lasocka J, Banach M, My liwiec M, Gruchała M, et al. The cost-effectiveness of screening strategies for familial hypercholesterolaemia in Poland. Atherosclerosis. 2018;270:132-8.
- 87 Jones M, Akyea RK, Payne K, Humphries SE, Abdul-Hamid H, Weng S, et al. Cost-Effectiveness of Screening Algorithms for Familial Hypercholesterolaemia in Primary Care. J Pers Med. 2022;12(3).
- 88 Dryden R, Williams B, McCowan C, Themessl-Huber M. What do we know about who does and does not attend general health checks? Findings from a narrative scoping review. BMC public health. 2012;12:723-.
- 89 Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, et al. Socioeconomic status and risk of cardiovascular disease in 20 low-income, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. The Lancet Global Health. 2019;7(6):e748-e60.
- 90 de Waard A-KM, Wändell PE, Holzmann MJ, Korevaar JC, Hollander M, Gornitzki C, et al. Barriers and facilitators to participation in a health check for cardiometabolic diseases in primary care: A systematic review. European journal of preventive cardiology. 2018;25(12):1326-40.
- 91 Kypridemos C, Allen K, Hickey GL, Guzman-Castillo M, Bandosz P, Buchan I, et al. Cardiovascular screening to reduce the burden from cardiovascular disease: microsimulation study to quantify policy options. BMJ. 2016;353:i2793.
- 92 Michael Marmot TA, John Bell, Carol Black, Patricia Broadfoot, Julia Cumberlege, Ian Diamond, Ian Gilmore, Chris Ham, Molly Meacher, Geoff Mulgan. Fair Society, Healthy Lives - The Marmot Review. 2010.
- 93 Groenenberg I, Crone MR, van Dijk S, Ben Meftah J, Middelkoop BJC, Assendelft WJJ, et al. Determinants of participation in a cardiometabolic health check among underserved groups. Prev Med Rep. 2016;4:33-43.
- 94 NHS: Social Prescribing [Internet]. [cited March 30, 2022]. Available from: https://www.england.nhs.uk/personalisedcare/ social-prescribing/.
- 95 John Jagan: Social prescribing as a way of tackling health inequalities in all health settings [Internet]. 2022 [cited March 30, 2022]. Available from: https://www.england.nhs.uk/blog/social-prescribing-as-a-way-of-tackling-health-inequalities-in-all-health-settings/.
- 96 Wang GX, Baggett TP, Pandharipande PV, Park ER, Percac-Lima S, Shepard J-AO, et al. Barriers to Lung Cancer Screening Engagement from the Patient and Provider Perspective. Radiology. 2019;290(2):278-87.
- 97 Van Doorn D, Richardson N, Meredith D, McNamara J, Osborne A, Blake, C. Farmers Have Hearts Cardiovascular Health Programme - Detailed Baseline Report [Internet]. 2020 [cited March 30, 2022]. Available from: https://www.teagasc.ie/media/ website/publications/2020/Farmers-Have-Hearts---Detailed-Baseline-Report.pdf.
- 98 Van Doorn D, Richardson N, Osborne, A. Farmers Have Hearts: Irish Heart Foundation Health Checks 2013/14 Evaluation Report Summary [Internet]. 2017 [cited March 30, 2022]. Available from: http://irishheart.ie/wp-content/uploads/2017/01/ FHH_report_Summary_final_13th_May.pdf.
- 99 Guidelines 2002 to 2021 [Internet]. [cited March 30, 2022]. Available from: https://www.escardio.org/Guidelines.
- 100 Uchmanowicz I, Hoes A, Perk J, McKee G, Svavarsdóttir MH, Czerwińska-Jelonkiewicz K, et al. Optimising implementation of European guidelines on cardiovascular disease prevention in clinical practice: what is needed? Eur J Prev Cardiol. 2020:2047487320926776.

- 101 Bruckert E, Parhofer KG, Gonzalez-Juanatey JR, Nordestgaard B, Arca M, Giovas P, et al. Proportion of High-Risk/Very High-Risk Patients in Europe with Low-Density Lipoprotein Cholesterol at Target According to European Guidelines: A Systematic Review. Adv Ther. 2020;37(5):1724-36.
- 102 Dixon DL, Sharma G, Sandesara PB, Yang E, Braun LT, Mensah GA, et al. Therapeutic Inertia in Cardiovascular Disease Prevention. J Am Coll Cardiol. 2019;74(13):1728-31.
- 103 Verhestraeten C, Heggermont WA, Maris M. Clinical inertia in the treatment of heart failure: a major issue to tackle. Heart Failure Reviews. 2021;26(6):1359-70.
- 104 Khan R, Socha-Dietrich K. OECD: Investing in medication adherence improves health outcomes and health system efficiency. 2018.
- 105 Simon ST, Kini V, Levy AE, Ho PM. Medication adherence in cardiovascular medicine. BMJ. 2021;374:n1493.
- 106 Cattel D, Eijkenaar F. Value-Based Provider Payment Initiatives Combining Global Payments With Explicit Quality Incentives: A Systematic Review. Med Care Res Rev. 2020;77(6):511-37.
- 107 The Economist Intelligence Unit: Healthcare in Sweden Reaching the next level [Internet]. 2019 [cited March 30, 2022]. Available from: https://impact.econ-asia.com/perspectives/sites/default/files/value-basedhealthcareinswedenreachingthenext level.pdf.
- 108 Gai Y, Pachamanova D. Impact of the Medicare hospital readmissions reduction program on vulnerable populations. BMC Health Serv Res. 2019;19(1):837-.
- 109 Busse RKNPDQWOfEC-o, Development EOoHS, Policies WHO. Improving healthcare quality in Europe : characteristics, effectiveness and implementation of different strategies. 2019.
- 110 Malone A, Gomez S, Finkel S, Chourchoulis D, Morcos E, Loko MA, et al. Population health management in France: specifying population groups through the DRG system. BMC Health Serv Res. 2021;21(1):733.
- 111 Jernberg T, Attebring MF, Hambraeus K, Ivert T, James S, Jeppsson A, et al. The Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART). Heart. 2010;96(20):1617-21.
- 112 Annual Report 2020 (English) [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.ucr.uu.se/swedeheart/ dokument-sh/arsrapporter-sh/1-swedeheart-annual-report-2020-english-2/viewdocument/3140.
- 113 Center for Medicare & Medicaid Services (CMS): Hospital Readmissions Reduction Program (HRRP) [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/ Readmissions-Reduction-Program.
- 114 EPRS (European Parliamentary Research Service): The rise of digital health technologies during the pandemic [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.europarl.europa.eu/RegData/etudes/BRIE/2021/690548/EPRS_ BRI(2021)690548_EN.pdf.
- 115 Fahy N, Williams G A. Use of digital health tools in Europe: before, during and after COVID-19 (European Observatory on Health Systems and Policies) [Internet]. World Health Organization. Regional Office for Europe. 2021 [cited March 30, 2022]. Available from: https://apps.who.int/iris/handle/10665/345091.
- 116 From pilot to scale: How to make digital health stick [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.pwc. ch/en/publications/2021/digitalhealth.pdf.
- 117 Neubeck L, Hansen T, Jaarsma T, Klompstra L, Gallagher R. Delivering healthcare remotely to cardiovascular patients during COVID-19 : A rapid review of the evidence. Eur J Cardiovasc Nurs. 2020;19(6):486-94.
- 118 European Heart Network: What is the value of digital tools for cardiovascular patients? [Internet]. 2020 [cited March 30, 2022]. Available from: https://ehnheart.org/publications-and-papers/publications/1285:digital-tools-cardiovascular-patients.html.
- 119 ZS Consulting: Digital Health in Europe who is paying for it and why it matters [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.zs.com/content/dam/pdfs/Digital-health-in-europe-wp.pdf.
- 120 DiGa-Verzeichnis [Internet]. 2021 [cited March 30, 2022]. Available from: https://diga.bfarm.de/de/verzeichnis?type=%5B%5D.
- 121 Where is the money in digital health? The roadmap to digital health app reimbursement in Europe [Internet]. 2022 [cited March 30, 2022]. Available from: https://research2guidance.com/where-is-the-money-in-digital-health-the-roadmap-to-digital-health-app-reimbursement-in-europe/.
- 122 mHealth Belgian platform for mobile applications that are CE-marked as a medical device [Internet]. 2022 [cited March 30, 2022]. Available from: https://mhealthbelgium.be/apps.
- 123 France to enable rapid market access for digital therapeutics [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.healthcareitnews.com/news/emea/france-enable-rapid-market-access-digital-therapeutics.
- 124 European Society for Cardiology: ACVC Clinical Decision-Making Toolkit [Internet]. 2018 [cited March 30, 2022]. Available from: https://www.escardio.org/Education/Practice-Tools/Clinical-Decision-Making-Toolkit.
- 125 Victor RG, Lynch K, Li N, Blyler C, Muhammad E, Handler J, et al. A Cluster-Randomized Trial of Blood-Pressure Reduction in Black Barbershops. New England Journal of Medicine. 2018;378(14):1291-301.
- 126 Ordre National des Pharmaciens: What is the Pharmaceutical Record [Dossier Pharmaceutique]? [Internet]. 2019 [cited March 30, 2022]. Available from: http://www.ordre.pharmacien.fr/Qui-sommes-nous/Qu-est-ce-que-l-Ordre/The-French-Chamberof-Pharmacists/What-is-the-Pharmaceutical-Record-Dossier-Pharmaceutique.

- 127 European Commission: European Health Data Space [Internet]. 2019 [cited March 30, 2022]. Available from: https://ec.europa. eu/health/ehealth-digital-health-and-care/european-health-data-space_en.
- 128 Peters DH, Adam T, Alonge O, Agyepong IA, Tran N. Implementation research: what it is and how to do it. Bmj. 2013;347:f6753.
- 129 Theobald S, Brandes N, Gyapong M, El-Saharty S, Proctor E, Diaz T, et al. Implementation research: new imperatives and opportunities in global health. Lancet. 2018;392(10160):2214-28.
- 130 Noone D, O'Mahony B, Peyvandi F, Makris M, Bok A. Evolution of Haemophilia Care in Europe: 10 years of the principles of care. Orphanet Journal of Rare Diseases. 2020;15(1):184.
- 131 German Multiple Sclerosis Society: Improving Multiple Sclerosis Management in Europe: Better Outcomes with Better Data [Internet]. 2014 [cited March 30, 2022]. Available from: https://www.msregister.de/en/forschung/eurems/.
- 132 European Cystic Fibrosis Society (ECFS): ECFS Patient Registry Introduction [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.ecfs.eu/ecfspr.
- 133 European Network of Cancer Registries: Welcome to the ENCR [Internet]. 2012 [cited March 30, 2022]. Available from: https:// www.encr.eu/registries-network.
- 134 European Medicines Agency: Observations and recommendations on patient registries. Patient Registries Workshop; 2016 October 28, 2016.
- 135 Roberts MC, Fohner AE, Landry L, Olstad DL, Smit AK, Turbitt E, et al. Advancing precision public health using human genomics: examples from the field and future research opportunities. Genome Medicine. 2021;13(1):97.
- 136 Koohi F, Ahmadi N, Hadaegh F, Safiee S, Azizi F, Khalili D. Trajectories of cardiovascular disease risk and their association with the incidence of cardiovascular events over 18 years of follow-up: The Tehran Lipid and Glucose study. Journal of Translational Medicine. 2021;19(1):309.
- 137 Wang Y, Wan EYF, Mak IL, Ho MK, Chin WY, Yu EYT, et al. The association between trajectories of risk factors and risk of cardiovascular disease or mortality among patients with diabetes or hypertension: A systematic review. PLoS One. 2022;17(1):e0262885.
- 138 Salina Bakshi MM, Katherine H. Schiavoni MM, Lucas C. Carlson MM, Trina E. Chang MM, Amy O. Flaster MM, Brent P. Forester MDM, et al. The Essential Role of Population Health During and Beyond COVID-19. The American Journal of Managed Care. 2021;27(3).
- 139 Krittanawong C, Virk HUH, Bangalore S, Wang Z, Johnson KW, Pinotti R, et al. Machine learning prediction in cardiovascular diseases: a meta-analysis. Sci Rep. 2020;10(1):16057-.
- 140 Rajewsky N, Almouzni G, Gorski SA, Aerts S, Amit I, Bertero MG, et al. LifeTime and improving European healthcare through cell-based interceptive medicine. Nature. 2020;587(7834):377-86.
- 141 Lifetime: Strategic Research Agenda [Internet]. 2020 [cited March 30, 2022]. Available from: https://lifetime-initiative.eu/wp-content/uploads/2020/08/LifeTime-Strategic-Research-Agenda.pdf.
- 142 McClellan MB, Bleser WK, Joynt Maddox KE. Advancing Value-Based Cardiovascular Care: The American Heart Association Value in Healthcare Initiative. Circ Cardiovasc Qual Outcomes. 2020;13(5):e006610.
- 143 Hayen A, van den Berg MJ, Struijs JN, Westert Gert GP. Dutch shared savings program targeted at primary care: Reduced expenditures in its first year. Health Policy. 2021;125(4):489-94.
- 144 World Heart Federation: World Heart Observatory aims to advance knowledge and improve health [Internet]. 2022 [cited March 30, 2022]. Available from: https://worldheartobservatory.org/2022/02/01/world-heart-observatory-aims-to-advance-knowledge-and-improve-health/.
- 145 European Society for Cardiology: Euroheart [Internet]. 2019 [cited March 30, 2022]. Available from: https://www.escardio.org/ Research/euroheart.
- 146 Wallentin L, Gale CP, Maggioni A, Bardinet I, Casadei B. EuroHeart: European Unified Registries On Heart Care Evaluation and Randomized Trials: An ESC project to develop a new IT registry system which will encompass multiple features of cardiovascular medicine. European Heart Journal. 2019;40(33):2745-9.
- 147 European Social and Economic Committee: Opinion on European Missions [Internet]. 2021 [cited March 30, 2022]. Available from: https://webapi2016.eesc.europa.eu/v1/documents/EESC-2021-05466-00-00-AS-TRA-EN.docx/content.
- 148 European Medicines Agency: Data Analysis and Real World Interrogation Network (DARWIN EU) [Internet]. 2021 [cited March 30, 2022]. Available from: https://www.ema.europa.eu/en/about-us/how-we-work/big-data/data-analysis-real-world-interrogation-network-darwin-eu.
- 149 DG Communications Networks, Content and Technology: Strategic Plan 2020-2024 [Internet]. 2020 [cited March 30, 2022]. Available from: https://ec.europa.eu/info/system/files/cnect_sp_2020_2024_en.pdf.
- 150 European Commission: Combined Evaluation Roadmap/Inception impact assessment: EU Pharmaceuticals Strategy [Internet]. 2021 [cited March 30, 2022]. Available from: https://ec.europa.eu/info/law/better-regulation/have-your-say/ initiatives/12963-Revision-of-the-EU-general-pharmaceuticals-legislation_en.
- 151 European Commission: The Recovery and Resilience Facility [Internet]. 2021 [cited March 30, 2022]. Available from: https:// ec.europa.eu/info/business-economy-euro/recovery-coronavirus/recovery-and-resilience-facility_en#the-recovery-and-resilience-facility.





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