Health First Europe

INSIGHT REPORT:

The Compelling Case for Better Screening and Secondary Prevention in Europe: Lessons From Five Representative Diseases

ACKNOWLEDGEMENTS

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EXECUTIVE SUMMARY

The purpose of this paper is to highlight the value of screening and secondary prevention in general for improving patient safety, the quality of care in healthcare settings and quality of life across Europe. Regular exams and screening tests can detect disease in its earliest stages, dramatically increasing the likelihood of preventing the worst impacts of diseases and restoring patients' health and well-being to their previous state. Increased screening and secondary prevention can also substantially reduce the cost of public health services over the long term.

Europe has many national success stories that could be better shared and implemented across borders. This Insight Report showcases concrete examples and solutions for implementing national screening programmes which have been successful in improving outcomes for patients and society in five representative disease areas: breast cancer, type 2 diabetes, healthcare-associated infections, heart failure, and new-born and severe combined immune deficiency (SCID).

INTRODUCTION

When she presented Europe's Beating Cancer Action Plan more than a year ago, European Commission President Ursula von der Leyen emphasised the critical role of screening and early diagnosis: "Science tells us that 40% of cancer cases are preventable. And yet only 3% of health budgets go into prevention", she said (European Commission, 2018). Unsurprisingly, Europe's Beating Cancer Plan embraces early detection and diagnosis. In many other disease areas, prevention and early diagnosis have not yet a similar attention despite being just as effective, life-saving, life-changing and cost-efficient compared with the cost of failing to catch and treat a disease early.

For Health First Europe and its members, patient safety and prevention have always been at the heart of our core activities. For more than 15 years we have evangelised the public health benefits of screening and other secondary prevention tools as key enablers for saving and improving lives while ensuring the long-term sustainability of our healthcare systems. Indeed, screening and early diagnosis play a critical role in detecting a disease in its earliest stages, even before any symptoms are apparent – but too often the potential of routine screening is neglected, with high costs in individual and public health as a result.

> *"Science tells us that 40% of cancer cases are preventable. And yet only 3% of health budgets go into prevention*

Screening refers to testing healthy individuals to identify those at risk of developing diseases, or those having diseases before any symptoms appear while early diagnosis focuses on detecting problematic health conditions in people as early as possible (WHO Europe, 2021). Common examples of successful screening tools include breast cancer screening using mammography or clinical breast exams and screening for infections ranging from COVID-19 to healthcare associated infections (HAIs) and antibiotic resistance.

Despite significant disease-related strategies and approaches (e.g. Council Recommendation on cancer screening) set up by the European Commission to promote the exchange of best practices among European Union (EU) member states, health stakeholders have noted a lack of disease-specific action on topics other than cancer. Access to early diagnosis, which is a central component of secondary prevention, can vary significantly from one country to another, challenging the EU's goal of giving people equal access to high-quality health care.

Despite important medical advances over the past few decades, the progression of chronic diseases continues to be the leading cause of death in the European Union (EU). For instance, cardiovascular diseases remain a leading cause of death globally and the number one cause of death in the EU.

A greater focus on early detection and a significant investment in different, effective strategies of managing chronic conditions, would not only improve patients' health but also reduce the financial burden on Europe's healthcare systems that results from late diagnosis and more complex, longer and expensive treatments. Two examples: stronger integration of care across healthcare settings by leveraging the use of digital solutions for better care, and using large-scale health data for population risk analysis.

This Insight Report, picking up on previous work of HFE (HFE, 2018), examines five representative disease areas, namely breast cancer, type 2 diabetes, HAIs and antimicrobial resistance (AMR), heart failure, new-born and severe combined immune deficiency (SCID). These five case studies provide a detailed explanation of each disease and related burden on healthcare systems, describe the lessons learned from concrete examples, and end with concrete policy recommendations to improve patients' outcomes while contributing to the sustainability of European healthcare systems.

Since its inception in 2004, Health First Europe and its member organisations have worked to improve healthcare delivery and healthcare systems in Europe, in part by encouraging health stakeholders and policy makers to invest in early diagnosis, screening and other secondary prevention programmes. This report collects the latest evidence for a stronger focus on screening and secondary prevention programmes in Europe and illustrates the public health benefits that such an approach offers.

Although healthcare is a national competence, this should not stop EU policy makers from working toward better coordination and mutual learning that will lead to more targeted, effective opportunities for prevention, treatment and care at the national level.

BREAST CANCER

THE DEFINITION

An increase in life expectancy globally has been accompanied by an increase in cancer, a burden that affects not only individual patients but entire health systems and society as a whole. The World Health Organisation (WHO) recently estimated that in 2018, there were approximately 18.1 million new cases of cancer and 10 million deaths from cancer worldwide (WHO, 2020). It predicts that this global burden will double to about 29 million–37 million new cancer cases by 2040. Cancer is also the first or second leading cause of premature death in 134 of 183 countries in the world. These deaths occur unequally, as countries with lower incomes generally have significantly worse health outcomes at the population level (WHO, 2020).

WHO prediction

The World Health Organisation predicts that this global burden will double to about 29 million–37 million new cancer cases by 2040.

Scholars and scientists disagree on the definition of cancer. Some have focused on clinical aspects (Merkle, 20211; Eggert, Cancer basics, 2010) while others have focused more on the genetics of cancer including on the molecular definition of the disease (Eggert & Kasse, 2010). The European Parliament decided to propose a broad definition, describing cancer as "a disease of unwanted growth, where cells of an individual's body grow and proliferate in an uncontrolled manner (European Parliament, 2020, p. 13)". This latter process is called metastasising and is a major cause of death from cancer. We will use this broader definition to understand the term 'cancer' in this Insight Report, especially because cancer is the common name for a large group of diseases all characterised by uncontrolled growth and the spread of abnormal cells. (Olsen & LeFebvre, 2019; WHO, 2020).

Cancer cells are very similar to cells of the organism from which they originated and have similar (but not identical) DNA and RNA. In fact, cancer cells are formed from normal cells due to a modification or mutation of DNA or RNA (or both) (WHO, 2020). Cancer will then develop if the immune system is not functioning properly, or the number of cells produced is too great for the immune system to eliminate. This process occurs in most cancers, including breast cancer.

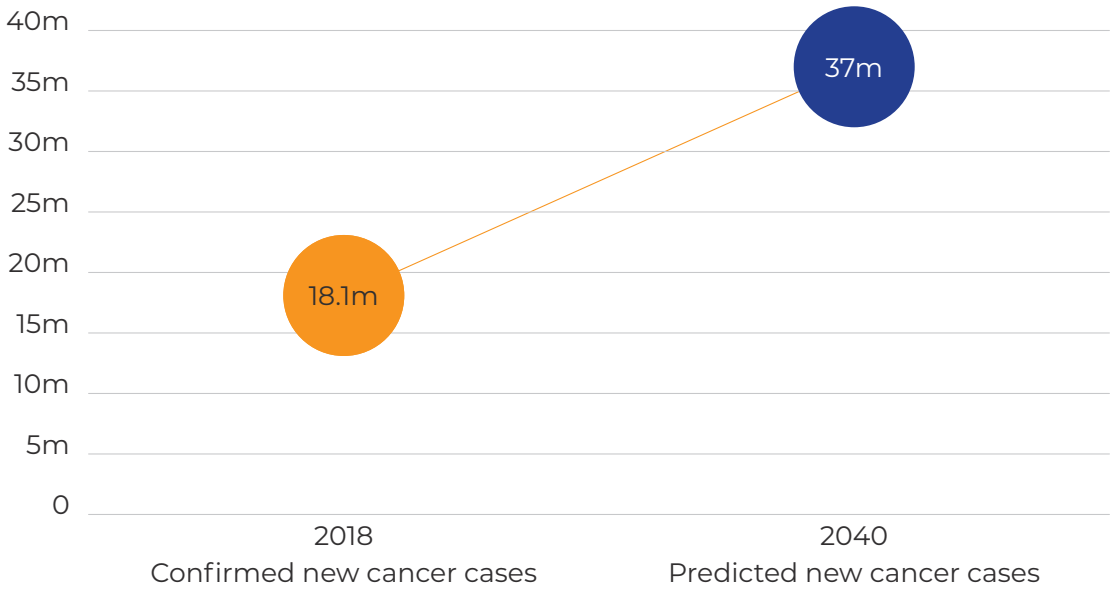
Building on previous Health First Europe work, this Insight Report will focus on breast cancer, the most common form of cancer in women, accounting for around 12% of new cases of cancer. One in nine women globally is likely to have breast cancer during their lifetime. It is also the second cause of cancer death in women around the globe.

One in nine women globally is likely to have breast cancer during their lifetime

Breast cancer usually begins either in the cells of the lobules (the milk-producing glands) or in the ducts that drain mothers' milk from the lobules to the nipple. Less commonly, breast cancer can begin in the stromal tissues, which include the fatty and fibrous connective tissues of the breast. There are various types of breast cancer with each one referring to the type of cell where the abnormal growth comes from. This includes ductal carcinoma (from the milk ducts), lobular carcinoma (from the Lobules), and others (European Institute of Women's Health, 2017).

Breast cancer also tends to be divided into various stages using the tumour, node, and metastasis (TNM) categorisation, a coding system for cancer staging. Stages describe the size of the cancer and whether or not it has spread to other parts of the body (Cancer Research UK, 2021). The most advanced stage of breast cancer is metastatic breast cancer (mBC), which occurs when the cancer spreads to other parts of the body. About 5-10% of new breast cancer diagnoses are metastatic, and patients diagnosed with it tend to live only two to four years after their diagnosis (Cardoso & al., 2012). On average, only one in five women with mBC will survive longer than five years. Unfortunately, there is no known cure (European Institute of Women's Health, 2017).

NEW CANCER CASES



THE SCALE OF THE CHALLENGE IN EUROPE

Recently the Joint Research Centre of the European Commission, in collaboration with the International Agency for Research on Cancer (IARC), launched new estimates of the burden of cancer in each of the EU member states in 2020. They unveiled the fact that a total of 2.7 million new cases of cancer (excluding non-melanoma skin cancers) and 1.3 million cancer-related deaths are estimated for 2020. Breast cancer is still the most commonly diagnosed cancer type in Europe, and it claims the lives of more European women than any other cancer (Ferlay, et al., 2020).

According to the Global Cancer Observatory, there were more than 530,000 breast cancer incidents across the continent of Europe with more than 140,000 people dying from it (Ferlay, et al., 2020). There are more incidents in Western Europe, yet more deaths in Eastern Europe, especially in Poland.

"It is expected that 1 in 11 women in the EU-27 will develop breast cancer before the age of 74

Overall, it is expected that 1 in 11 women in the EU-27 will develop breast cancer before the age of 74 (European Commission, 2020). The highest breast cancer incidence is in women between the ages for 50-64 (35%). Women younger than 50 can also develop breast cancer, comprising 21% of all cases.

The burden that breast cancer puts on our society is not solely in terms of the patients themselves; healthcare systems and healthcare workers are also severely impacted. At 15 billion Euros, breast cancer is estimated to have the highest healthcare costs in Europe, accounting for around 12% of the total cancer healthcare costs in the EU (ESMO, 2012; Luengo-Fernandez, Leal, Gray, & Sullivan, 2013). This is due to the highly effective but expensive treatment that is needed after detection. Breast cancer treatment often consists of a combination of surgery, radiation therapy and medication to treat the microscopic cancer that has spread from the breast tumour through the blood (WHO, 2021).

"Studies have found that that more than 70% of breast cancer deaths were among the 20% of people who did not participate in screening

Although breast cancer treatment can be highly effective, especially when the disease is identified early, the best scenario for both patients and health systems is early diagnosis and treatment. This can only be achieved with screening. Indeed, studies have found that that more than 70% of breast cancer deaths were among the 20% of people who did not participate in screening (Lauby-Secretan, et al., 2014).

THE VALUE OF SCREENING AND LESSONS LEARNED

Screening has the ability to decrease both cancer incidence, through detection and tackling precursor lesions before they are capable of developing into an invasive cancer, and cancer stage at diagnosis (WHO, 2007; European Parliament, 2020). Indeed, screening allows for the identification of cases before the onset of symptoms and for an ensuing referral to a cancer specialist, consequently decreasing mortality. Screening also allows for a reduction of the economic costs imposed by cancer, a phenomenon which has already been observed in several EU Member States.

In Europe, mammographic screening has been widely accepted as a primary tool for the early detection of breast cancer (European Commission, 2018) as a breast ultrasound or breast MRI can also be used for diagnosis. Using these techniques, breast cancer screening programmes began to be carried out across the continent in the late 1980s, the first ones occurring in Sweden and Finland (European Parliament, 2014; European Commission, 2018). Although all European countries offer some form of breast cancer screening, as of 2021, 25 EU Member States had introduced population-based screening programmes for breast cancer in their National Cancer Control Plans (NCCPs) (European Commission, 2020b, p. 14). These population-based screening programmes offer testing to an entire target age group in order to detect breast cancer at an early stage (European Institute of Women's Health, 2017). The number of screening programmes have increased in the last decades, but different levels of maturation exist currently across the EU-27, ranging from 3 to 20 years from implementation. This is due to some extent to the Council Recommendations of 2003 on cancer screening, which recommended EU countries implement mammographic screening programmes in women aged 50-69 (European Council, 2003). The current inequalities exist in terms of the stage of implementation of the programmes, the degree to which such programmes are organised, invitation coverage, coexistence with opportunistic screening activity and screening attendance (Basu, et al., 2018; Zielonke, et al., 2021). The lack of cohesion develops from the fact that it is up to each EU Member State to develop such plans, and to extend or shorten the screening age (European Commission, 2018). For instance, Bulgaria and Romania are the last member states that still have not put breast cancer screening as part of their NCCPs (European Commission, 2018; Peintinger, 2019).

10 million
deaths from cancer worldwide

Among the many inequalities in screening for breast cancer is the socioeconomic background of women. Studies have found that women with higher socioeconomic status show significantly higher breast cancer incidence, which may be explained by reproductive factors, mammography screening, hormone replacement therapy and lifestyle factors, while women with lower socioeconomic status are not as present in the data due to lower screening attendance (Lundqvist, Andersson, Ahlberg, Nilbert, & Gerdtham, 2016).

Yet we see a reduction of mortality rate wherever a such a screening programme is implemented. For instance, Ireland established its Breast Cancer Screening Programme, Breast Check, as a pilot in 2000. The programme has since been extended nationwide, utilising both designated hospital and mobile units (women between the ages of 50 and 69 are invited for a free mammogram every two years). Due to such efforts, there has been a constant increase in breast cancer screening uptake in the country. From 2013 to 2014, the uptake rate in the target population increased from 70.2% to 76.5%, surpassing the 70% programme target. The programme now provides more than 168,000 women with testing and detecting around 1,200 cancers. (Altobelli & Lattanzi, 2014; BreastCheck , 2020). To a large extent due to such programmes, over the last decades, Ireland has witnessed a reduction in breast cancer mortality of roughly 40% (European Institute of Women's Health, 2017).

Nevertheless, we need to acknowledge that there might be some areas that need to be observed when conducting screening programmes for breast cancer. Patients might be subject to overdiagnosis, overtreatment, false-positive and false-negative findings, as well as anxiety, radiation exposure and pain. Some studies have also shown that mammography may not be sufficient to detect cancers in women of 40 to 49 years of age and could even be inadequate for women younger than 40 or older than 69 years of age (Lauby-Secretan, et al., 2014). Yet even with such areas of concern, evidence is clear that the benefits substantially outweigh any risk of radiation-induced cancer, or overdiagnosis (Lauby-Secretan, et al., 2015).

Unfortunately, we have seen an overall decrease of cancer screenings, testing, and diagnosis due to the COVID-19 pandemic. The Netherlands Cancer Registry reported declining cancer incidence rates of up to 40% at the peak of the pandemic, while Slovenia saw its three national cancer screening programmes, including breast cancer screening, come to a complete stop (The IQVIA Institute, 2021, pp. 4-5). This pause in cancer screening programmes will delay diagnosis and impact follow up treatment for breast cancer patients.

POLICY RECOMMENDATIONS

The European Union has taken many actions over the past decades to tackle the rise of breast cancer in Europe. From the passage of the 2003 and 2006 European Parliament resolutions on breast cancer and the 2010 and 2015 European Parliament written declarations on the fight against breast cancer in the EU, Europe has been at the forefront of this fight, most recently with the European Beating Cancer Plan and with the draft INI report by MEP Trillet-Lenoir [EC, COM(2021) 44 final; EP BECA 2020/2267(INI)].

We applaud the EU's efforts in this area, yet further actions are needed, especially as Europe evidences disparities in access to cancer care and significant social inequalities between and within European countries. These factors deeply impact cancer incidence, survival, and mortality. We call on European and national policy makers to follow the evidence and:

- Integrate primary and secondary preventive strategies through comprehensive approaches to support the implementation of best practices and to minimise the current inequalities in breast cancer control;
- Ensure that care is multidisciplinary, and that delivery is timely in specialist cancer units to empower patients with care options while guaranteeing quality;
- Provide patients and healthcare providers with clear, objective and independent guidance on breast cancer screening and diagnosis;
- Promote adequate health information systems linked to the screening programs with existing cancer and mortality registries;
- Keep on investing in training for highly qualified specialists, critical to the quality-of-care screening and care.

TYPE 2 DIABETES

THE DEFINITION

Diabetes is a global epidemic. Around 9.3% of adults aged 20–79 years – a staggering 463 million people – are living with diabetes. A further 1.1 million children and adolescents under the age of 20 live with type 1 diabetes. The International Diabetes Federation (IDF) expects that 578 million adults will live with diabetes by 2030, and 700 million by 2045 (International Diabetes Federation, 2019). This will impact every country, age group and economy.

Approximately 9.3% of adults aged 20-79 are living with diabetes

The WHO defines diabetes mellitus as 'a group of metabolic disorders characterised (WHO, 2020, p. 9). Yet, this definition doesn't refer to the defects in insulin that lead to such hyperglycaemia, and which is so crucial for the health of people living with diabetes. Thus, for this report, we have decided to adopt another definition which also has been widely used, namely that of the IDF, which (International Diabetes Federation, 2019, p. 12).

Assigning a type of diabetes to an individual often depends on the circumstances and symptoms present at the time of diagnosis. Many people living with diabetes do not easily fit into a single class and will require additional tests for their type of diabetes to be defined. As the definition notes, diabetes is a group of diseases, but for the purposes of this article, we will mostly focus on Type 2 Diabetes (T2D).

First, Type 1 Diabetes (T1D), accounts for 5–10% of diabetes globally (American Diabetes Association, 2015, p. 10). It is caused by an autoimmune reaction in which the body's immune system attacks the insulin-producing beta cells of the pancreas. As a result, the body produces very little or no insulin. The causes of this destructive process are not fully understood but a likely explanation is that the combination of genetic susceptibility (conferred by a large number of genes) and an environmental trigger, such as a viral infection, initiate the autoimmune reaction. Among its most common symptoms are an increased thirst, frequent urination, hunger, fatigue, and blurred vision. People living with T1D need daily administration of insulin to regulate the amount of glucose in their blood. They cannot survive without access to insulin.

Type 2 Diabetes "encompasses individuals who have insulin resistance and usually relative insulin deficiency" (American Diabetes Association, 2015; WHO, 2016). The vast majority of people with diabetes around the world live with this type of diabetes. Symptoms of T2D may be similar to those of T1D but may be less marked or absent for many years. This means people living with the disease can remain undiagnosed for several years, until complications have already arisen. For many years, type 2 diabetes was seen only in adults, but it is now also observed in children, although this remains infrequent (WHO, 2016).

Some authors have suggested that that T1D and T2D should not be regarded as distinct disorders, and that instead, they "are the same disorder of insulin resistance set against different genetic backgrounds with their differences being the evolution of the disease" (Wilkin, 2007; Kharroubi & Darwish, 2015). Yet, this classification is widely accepted and has clear impacts on treatment strategies.

THE SCALE OF THE CHALLENGE IN EUROPE

It is hard to estimate the current numbers of people with diabetes across the continent. The latest data from Eurostat (through 2016) recorded more than 114,000 deaths across the EU from diabetes, or 2% of all deaths (Eurostat, 2019). The standardised death rate from diabetes stood at 22 deaths per 100,000 people in the EU. More recently, IDF estimated a much higher figure, projecting that almost 465,900 deaths in adults aged 20–79 years are attributable to diabetes and its complications in 2019 (8.5% of all-cause mortality) (International Diabetes Federation, 2019, p. 67). Yet, just finding out the numbers of deaths in the EU due to diabetes does not provide the whole picture, instead, we need to look at cases. The latest data from the IDF Diabetes Atlas of the International Diabetes Federation tells us that an estimated 59 million adults (20-79 years) were living with diabetes in Europe in 2019. This is expected to grow to more than 68 million people by 2045 (International Diabetes Federation, 2021).

We know that T2D is far more common than T1D, and that the prevalence of diabetes is increasing among all ages in European, reflecting unhealthy diets, lack of physical activity and sedentary lifestyles (WHO Europe, 2021; WHO, 2016), not to mention socio-economic determinants of health. Another major issue is that almost half the people living with diabetes are unaware of it and frequently remain undiagnosed until complications appear. Prolonged lack of diagnosis can have negative effects, such as a higher risk of diabetes related complications, and increased healthcare use and related costs. (IDF Diabetes Atlas 9th edition – page 49).

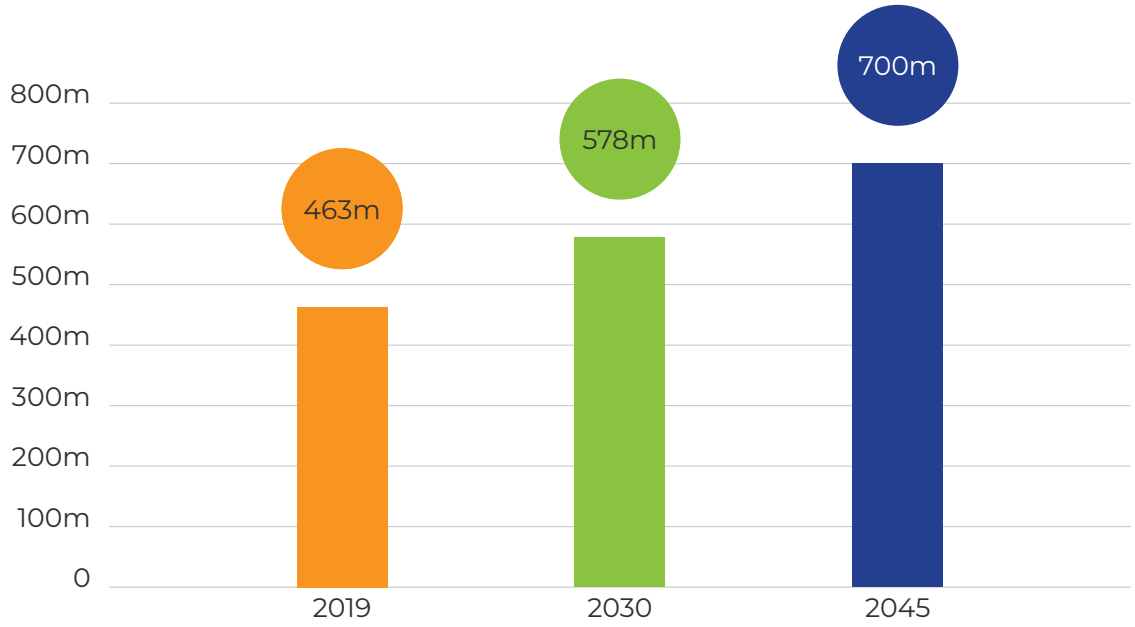
On average, diabetes reduces life expectancy in people aged 40-60 by 4-10 years and independently increases the risk of death from cardiovascular disease, renal disease and cancer. In 2019, close to one third of diabetes-related deaths were in people under the age of 60 and diabetes and its complications accounted for 8.5% of all-cause mortality (Blueprint for action on diabetes in the EU by 2030).

"On average, diabetes reduces life expectancy in people aged 40-60 by 4-10 years

Diabetes also puts a heavy financial burden on healthcare systems. In 2019, the total diabetes-related cost to healthcare systems in the EU was around €100 billion. This makes up an estimated 9% of total health expenditure (Blueprint for action on diabetes in the EU by 2030). Diabetes complications, as frequent causes of disability, premature mortality and absence from work due to sickness, are important drivers of indirect costs (IDF Atlas 9th edition). A study from Catalonia, Spain showed that the estimated higher costs for people living with T2D compared with the general population was more that 72%. These steep costs were due mainly to hospitalisations and medications required (Mata-Cases, et al., 2016).

It is therefore clear that premature diabetes-related mortality, the negative impact on quality of life and the high costs associated with the condition and its treatment would all greatly benefit from improved prevention and screening.

PEOPLE LIVING WITH DIABETES WORLDWIDE



THE VALUE OF SCREENING AND LESSONS LEARNED

More than 38% of people living with diabetes are undiagnosed across the Union (MEPs Mobilising for Diabetes, 2021, p. 17). By the time that they discover they have the disease; many have already developed one or more complications. Given the silent and progressive nature of T2D, early detection and prompt diagnosis are vital to avoiding further complications such as retinopathy, kidney and cardiovascular disease. These complications are devastating from a personal viewpoint and add costs to our already stretched health systems.

Screening programmes have shown their effectiveness in reducing the risk of people developing, and treating early, conditions such as T2D (WHO, 2020) time and time again. Evidence suggests that early detection helps to prevent and/or delay the onset of diabetes-related complications thanks to early action and treatment. While the investment in up-front screening and risk-reduction campaigns might be significant, the case for the cost-effectiveness of prevention has been clearly demonstrated (International Diabetes Federation, 2016).

A successful example is an initiative in Flanders, Belgium by HALT2Diabetes. This initiative was set up to understand the feasibility of an integrated strategy to identify people at high risk of type 2 diabetes as well as cardiovascular disease and direct them towards a healthier lifestyle (Lampaert, Buyse, Pottelbergh, Verstraete, & Muylle, 2018). They used an internationally recognised two-step screening procedure with the FINDRISC (Finnish Diabetes Risk Score) as a first step in people older than 45 years old with a least one type 2 diabetes modifiable risk factor. Those who showed a high FINDRISC score (≥ 12) were sent to a doctor to identify the cardiometabolic risk via a standardised protocol. It was clear from the initiative and the study that this two-step screening allowed for the efficient identification of people at risk.

The results showed that 81% of the screened people had a high FINDRISC score and overall, 91% had a high cardiometabolic risk. The study also confirmed the role of the GP screening, and their guidance towards a healthier life (Lampaert, Buyse, Pottelbergh, Verstraete, & Muylle, 2018).

Yet it is not enough to detect people with T2D or at risk of developing the condition. Individuals living with T2D should also be screened regularly for diabetes related complications, such as diabetes retinopathy, diabetes foot, CVD etc. (WHO, 2020).

Of course, how screening programmes to identify undiagnosed people living with T2D, and/or those at risk, should be developed is a matter of debate. One of the key factors to consider is how to reach the targeted population. There is evidence that different methods of screening reach people from different social and economic backgrounds. A Swedish study, for instance, suggested that people in Stockholm that were born in Africa and Asia were better reached through community screening rather than facility-based screening, while people born in Sweden and other European countries were easily reached by facility-based screening (Timm, et al., 2020). This is a factor that needs to be considered when developing such screening programmes.

Bearing in mind such considerations, screening programmes are needed for the overall benefit of patients and European health systems. Not only will they save lives, improve the quality of life of patients with diabetes and reduce costs, but they will also provide better overall care to citizens around the Union and improve the resilience of healthcare systems. T2D, because of its slow progression and permanent complications, needs to be put at the top of the list of 'to-dos' of screening programmes around the Union.

POLICY RECOMMENDATIONS

Flattening the curve of type 2 diabetes, preventing and/or delaying the onset of diabetes-related complications and improving the lives of those who live with diabetes is feasible. With the right care and education, someone who lives with diabetes can lead a long and prosperous life, fully realising their personal ambitions. We already know what we need to do, yet many of the measures taken are too limited in scope or face too many barriers to implementation. Bearing this in mind, we recommend the following actions to help prevent and/or delay the onset of type 2 diabetes:

- Develop an EU-wide strategy for diabetes prevention and screening;
- Support early action via improved national screening.
- Support the development and implementation of a National Diabetes Plan in all EU Member States, which includes a risk reduction and screening component;
- Encourage the use of a common screening tool across Europe to promote data and best practice exchanges;
- Promote the exchange of best practices across Member States and encourage the implementation of incentive programmes at primary care level to support systematic screening;
- Encourage the digitalisation of health services in Member StatesS and the adoption of new tools and technologies allowing for more effective monitoring and action to reduce the risk of diabetes-related complications and improve quality of life;
- Develop pan-European screening programmes to identify people living with T2D or at risk of developing the condition;
- Encourage member states to periodically update their national policies for screening for T2D based on the most recent scientific evidence.

HEALTHCARE-ASSOCIATED INFECTIONS / ANTIMICROBIAL RESISTANCE

THE DEFINITION

Since Alexander Fleming discovered penicillin in 1928, the management of bacteria-associated diseases has been considered a success, and bacterial infections no longer represent the threat that they were in the past. Yet since then, the massive use of antibiotics has led bacteria to adapt and increase the range of ways they can survive an antibiotic attack, leading to global and continuous growth of antimicrobial resistance (AMR) in many important human and animal pathogens. Growing AMR is a key cause of healthcare-associated infections (HAIs). These infections, which first occur in the hospital or clinic, and are often caused by multidrug-resistant organisms, take a heavy toll on patients and their families by causing illness, prolonged hospital stay, potential disability, excess costs and even death.

There is an overall consensus on the definition of both threats; HAIs can be defined as 'infections that occur while receiving health care, developed in a hospital or other health care facility that first appear 48 hours or more after hospital admission, or within 30 days after having received health care' (Haque, Sartelli, McKimm, & Bakar, 2018) and AMR is defined as 'the ability of a microorganism (e.g., a bacterium, a virus, or a parasite, such as the malaria parasite) to resist the action of an antimicrobial agent (ECDC).

33,000
deaths every year in EU countries from AMR bacteria

Among the most common HAIs are healthcare-associated pneumonia (HAP), healthcare-associated urinary tract infection (HA UTI), surgical site infections (SSIs), healthcare-associated Clostridium difficile infection (HA CDI), healthcare-associated neonatal sepsis, and healthcare-associated primary bloodstream infection (HA primary BSI). Many of these complications are preventable and are caused by methicillin-resistant staphylococcus aureus (MRSA), a bacteria which creates several difficult-to-treat infections in patients.

As both of these threats are interlinked, they need to be tackled at the same time.

2/3 of the 671,689 infections with antibiotic resistant bacteria in Europe are HAIs

THE SCALE OF THE CHALLENGE IN EUROPE

The latest European Centre for Disease Control and Prevention (ECDC) data on AMR in 2019 demonstrates that AMR remains one of the biggest threats to public health today and a challenge for Europe (ECDC, 2020). At the same time, HAIs are a global threat impairing the clinical outcome of 15% of all hospitalised patients in the world (Allegranzi, et al., 2011). Hundreds of millions of patients are affected by HAIs worldwide each year, leading to significant mortality and financial losses for health systems.

HAIs are a global threat impairing the clinical outcome of

15%

of all hospitalised patients in the world

A total of 8.9 million healthcare-associated infections were estimated to occur each year in European hospitals and long-term care facilities (ECDC, 2018). The ECDC estimates that the number of patients with an HAI on any given day in European hospitals is just under 100,000. And more than 90,000 people die each year in EU countries, as well as in Iceland, Norway and the United Kingdom, due to the six most common infections in health care settings (Cassini, et al., 2016). Of these cases, about 1 in 3 HAIs was associated with bacteria resistant to antibiotics. And indeed, it is similar on the AMR front as well. About two thirds of the 671,689 infections with antibiotic resistant bacteria in Europe are HAIs (HFE, 2020, p. 6).

Across EU countries, patients in medical specialty areas (including cardiology, oncology and neurology) accounted for 40% of all infection cases in 2016-17 (OECD, 2018, p. 166). Patients in surgical specialty areas represented another 33% of cases, while intensive care patients accounted for 13% of infections. For such patients, the most common types of HAIs were pneumonia (26% of all cases), urinary tract infections (19%), surgical site infections (18%), bloodstream infections (11%) and gastrointestinal infections (9%) (OECD, 2018, p. 166).

Although some HAIs can be treated easily, others may affect a patient's health more seriously, increasing their stay in the hospital and leading to additional hospital costs. Studies show that HAIs are the single most deadly and costly adverse event, representing up to 6% of public hospital budgets (Slawomirski, Auraaen, & Nicolaas S. Klazinga, 2017). These costs are especially high in cases where the bacteria is resistant to antibiotics. It is estimated that a single HAI which resists treatment can cost about EUR 8,500 to 34,000 more than a non-resistant infection, due to additional hospital days and additional treatment costs (OECD, 2017). These vary across the continent as the OECD estimates that the share of antibiotic-resistant infections ranges from about 5% in Finland to over 60% of all HAI cases in Romania and Cyprus (OECD, 2020). It is clear then that there are disparities on the treatment of patients across the Union.

Thus, HAIs as well as AMR are of considerable concern to patients, healthcare professionals and policy makers alike. Initiatives to prevent and control HAIs are resource intensive, and it is not always clear which interventions are economically sound. However, it is clear that Europe badly needs a preventive approach that tackles HAIs before they become an even greater concern. Increasing screening capabilities a proven way of doing this.

THE VALUE OF SCREENING AND LESSONS LEARNED

Due to the severe outcomes that HAIs can lead to, one of the best approaches is to prevent or at least reduce the risk of such infections from occurring in the first place. Screening, for instance, can provide information on the number of positive carriers of a resistant microorganism, including subjects not suffering from an infection (Anderson, Cecchini, & Mossialos, 2019). This has led to the development of ideas that attempt to reduce the prevalence of HAIs and antibiotic-resistant bacteria in hospitals.

One of the places where antibiotic-bacteria are most commonly found is within hospitals. This is highly dependent on the pathogen, setting, and country (Harris, Nemoy, Johnson, & al., 2004). However, comprehensive, systematic screening policies for admissions are uncommon, except in the case of patients being transferred to another hospital or undergoing a high-risk procedure. This is due to the historically high costs and resources needed to perform such tests. As a result, clinicians have to make their own decisions regarding the potential existence of bacteria, such as MRSA, in patients (Gould & van der Meer, 2005, p. 288). However, these same clinicians agree that screening patients for bacteria such as MRSA is a useful procedure, as they cannot control and thus reduce the risk of HAIs if they do not have reliable information about it.

> *"Screening can provide information on the number of positive carriers of a resistant microorganism, including subjects not suffering from an infection*

The implementation of controls on the admission of high-risk patients is one strategy that works. Targeted screening of other specific classes of patients has also proved to be an effective strategy (Gould & van der Meer, 2005, p. 289). Such programmes have led to a decrease, or at least a halt, of the incidences of MRSA, and thus HAIs, across the continent. In France, a national hospital infection control programme has developed for more than 16 years, resulting in a 30% reduction of surgical site infections and a 20% decrease in MRSA rates from blood cultures (Carlet, et al., 2009). In Belgium, a decrease of HAIs related to MRSA was recorded between 2004 and 2008 due to a decrease in the mean proportion of MRSA of S. aureus (30–25%) and a decrease in the median incidence of nosocomial MRSA (3.2 to 1.6 per 100 admissions) (Köck, et al., 2010, p. 5).

Even as we continue to develop new and effective antibiotics, appropriate antimicrobial stewardship of existing antibiotics as well as regular diagnostic testing remains highly important. Stewardship programmes can contribute to reducing healthcare-associated infections by 71% and overall healthcare

expenditures by 80%. Moreover, well known preventive measures in health care including behavioural compliance in hand hygiene, checklists and safety protocols as well as the implementation of digital technologies remain crucial to prevent and control infections.

The COVID-19 pandemic has underlined the need to understand the complex connections between bacterial and viral infections (JPIAMR, 2020). AMR may increase through the heavy use of antibiotics in COVID-19 patient treatment. Hence, the importance of diagnosing, encouraging more responsible behaviour and promoting the optimal prescription and sustainable use of antibiotics. The result would be stronger preparedness for our healthcare systems and more timely responses to this public health challenge.

POLICY RECOMMENDATIONS

- Increase awareness and understanding of AMR and HAIs and stimulate debate on both public health challenges through effective communication, education, and training at all levels. This will be key to promoting behavioural change among veterinary and health personnel that will lead to further compliance with evidence-based guidelines;
- Establish and promote clear governance arrangements at the local, national and European levels to ensure leadership, engagement, accountability and coordination of actions to combat AMR and HAIs;
- Improve infection prevention and control measures across human health and animal care settings to help prevent infections and the spread of AMR;
- Relentlessly advocate to put in place and monitor national targets for the surveillance of antibiotic use in human and animal health, as well as infection surveillance standards at European level;
- Implement antibiotic stewardship programmes in primary and secondary care settings with active engagement of patients as well as communicate infection risk, and preventative measures in a transparent manner;
- Invest in and promote the use of existing health technology solutions (e.g., antiseptic sutures and implants, wound care solutions, air and environment control, diagnostics etc.). in preventing AMR and HAIs, leading to better patient outcomes and generating cost savings for hospitals, health systems and society at large;
- Encourage the implementation of active screening programmes through rapid diagnostic technologies.

HEART FAILURE

THE DEFINITION

Cardiovascular diseases (CVDs) are the number one cause of death globally. An estimated 17.9 million people die from such diseases every year, accounting for an estimated 32% of total deaths around the globe. CVD-related deaths have been increasing since the 1990s and are expected to rise to 23.6 million by 2030 (Roth & al., 2020; Alissa & Ferns, 2011). More than four out of five CVD deaths are due to heart attacks and strokes, and one third of these deaths occur prematurely (in people under the age of 70). The number of people living with CVDs is growing, nearly doubling from 271 to 523 million between 1990 and 2019. These high numbers highlight the urgency of the issue, a life-or-death situation that health policymakers face on a constant basis.

23.6 million
CVD related deaths expected by 2030

This challenge might be easier to address if CVDs consisted of only one disease. Yet as the definition from the WHO states, CVDs are "a group of diseases of the heart muscle, valves, conduction system and blood vessels" (WHO, 2021a, p. 4). They include coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, deep vein thrombosis, and heart failure (RAND Europe, 2007).

There are many factors that increase the risk of developing CVDs. The key behavioural risk factors of heart disease are an unhealthy diet, tobacco use, alcohol consumption and physical inactivity (WHO, 2021b). In fact, physical inactivity can explain close to 75% of the new CVD diagnoses in high-income countries since the 1970s (Beaglehole, Saracci, & Panico, 2001). These behavioural risks factors have now expanded to other parts of the world, and not only to high-income countries (Yusuf, et al., 2020). Without such risk factors, CVDs are rare as a cause of death (Stampfer, Hu, Manson, Rimm, & Willett, 2000). These lifestyle factors may lead to high blood pressure (hypertension) and blood glucose, among others. These "intermediate risk factors" can be assessed in primary care facilities and indicate an increased risk of heart attack, stroke, heart failure and other complications.

> *"Physical inactivity can explain close to 75% of the new cardiovascular disease diagnoses in high-income countries*

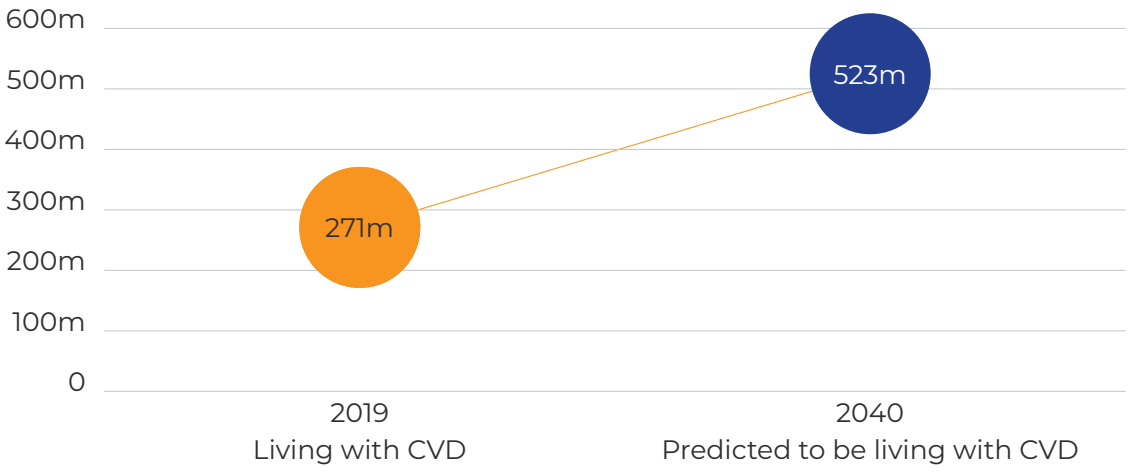
Though such risks and intermediate developments might be similar on most types of CVDs, each are prevalent in some and not others. Building on previous work from Health First Europe, and the variety of CVDs noted previously, this Insight Report focuses on one particular form of CVDs: heart failure (HF).

"Globally, one in five people can expect to be diagnosed with heart failure at some point in their lives

There are many definitions of HF. However, it has been defined as "not a single pathological diagnosis, but a clinical syndrome consisting of cardinal symptoms that may be accompanied by signs [...] due to a structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise" (McDonagh, et al., 2021, p. 14). This is normally caused by a reduced left ventricular myocardial function, however, dysfunction of the pericardium, myocardium, endocardium, heart valves, or great vessels, alone or in combination, might also cause HF (Inamdar & Inamdar, 2016).

People with HF experience various physical and psychological symptoms such as shortness of breath, extreme fatigue, sleeping difficulties, chest pain and depression (Heart Failure Policy Network, 2021). Many describe their diagnosis as a life-changing moment – symptoms can be severe and can limit routine aspects of everyday tasks, including climbing stairs, showering, shopping, and cooking (Roth & al., 2020). HF then places a considerable burden on patients, and as a result, on healthcare systems and whole economies.

NUMBER OF PEOPLE LIVING WITH CVDS



THE SCALE OF THE CHALLENGE IN EUROPE

Globally, one in five people can expect to be diagnosed with HF at some point in their lives (Heart Failure Policy Network, 2021). An estimated 26 million people are living with the syndrome globally, with higher prevalence rates in North America and Europe (Seferović, et al., 2020). The total global cost of HF was estimated at $108 billion in 2012, with direct and indirect costs accounting for approximately $65 billion and $43 billion respectively (Cook, Cole, Asaria, Jabbour, & Francis, 2014; Seferović, et al., 2020). Such high costs are due to the high levels of hospitalisations and inpatient care, which account for up to 87% of spending associated with HF (Giles, Freeman, Field, & al., 2020). Unfortunately, patterns of population ageing, and lifestyle and behavioural risk factors suggest that the number of people living with HF will rise.

In Europe, about 15 million people live with HF

The situation is similar in Europe, where about 2% of the population or 15 million people live with HF. Estimates have suggested that HF costs healthcare systems around €15 billion (Cook, Cole, Asaria, Jabbour, & Francis, 2014). These costs are expected to rise as the age group at highest risk of developing HF (population aged 65 and over) is projected to grow by almost 50% in the next 30 years (Heart Failure Policy Network, 2020). As hospital admissions are projected to rise by 50% by 2035, policymakers should also see tackling HF as key to reducing preventable admissions (Cowie, Anker, Cleland, & al., 2014; NICE, 2015). The OECD identified HF as the leading cause of preventable hospitalisations in Europe with almost 250,000 avoidable hospitalisations coming from HF, which leads to higher costs and patient suffering (Heart Failure Policy Network, 2021, p. 7; OECD, 2018). All such factors are underlined by the fact that despite improvements in treatment options, mortality from HF remains high in Europe and, in some countries, survival rates are worse than for several types of cancer (Heart Failure Policy Network, 2020). For example, a national registry in Sweden reported that every year around 126,000 premature life-years are lost due to HF, compared with close to 120,000 due to cancer (Savarese & Lund, 2017).

As noted before, HF has also an indisputably adverse impact on patients' quality of life. This includes their mental well-being, and many patients perform physical and social activities or engage in fulfilling relationships after having HF (Mbakwem, Aina, & Amadi, 2016). All such factors are exacerbated when health inequalities come into play. People at a socioeconomic disadvantage may experience higher risk of HF and HF-related hospitalisation or have higher mortality and poorer outcomes overall (Heart Failure Policy Network, 2020, p. 15).

This trend seems certain to be accelerated by the COVID-19 pandemic (The British Heart Foundation, 2021). Heart damage arising from COVID-19 infection is predicted to increase the number of HF cases. The pandemic has also caused widespread disruption to existing HF services, stalling crucial efforts to prevent HF or delay its progression (Heart Failure Policy Network, 2020).

Unfortunately, HF touches many other aspects of health in Europe than just in patients. HF generates a strong burden as well to our healthcare systems. Direct health-related expenditure in Heart Failure is high. In Germany, for instance, it is 2.9 billion euros per year (Lesyuk, Kriza, & Kolominsky-Rabas, 2018). Ireland, on the other hand, is estimated to incur 158 million euros of direct medical costs linked to HF with the costs of informal care estimated to be twice as high (IACO, 2017; The Heartbeat Trust; Irish Heart Foundation; NUI Galway; et al., 2015; MedTech Europe, 2020). It is estimated that patient care for people with HF can cost from €14,297 to €19,762, depending on the frequency and length of hospital stays (Lesyuk, Kriza, & Kolominsky-Rabas, 2018). Comorbidities such as diabetes add to such costs (Heart Failure Policy Network, 2021).

17.9 million

deaths from cardiovascular diseases (CVDs) every year - 32% of total deaths around the globe

Many of such issues result from the late diagnosis of HF as well as limited access to best-practice care (Heart Failure Policy Network, 2018). Severe damage to the heart reduces recovery prospects, and increases mortality and increases healthcare costs. Screening is a proven tool to increase early diagnosis.

THE VALUE OF SCREENING AND LESSONS LEARNED

Symptoms of HF are vague and non-specific, making it difficult to distinguish the syndrome from other conditions such as stress or respiratory disease. A recent UK study showed that around three quarters (74.8%) of patients surveyed had their initial HF diagnosis following their initial hospital admission – with nearly half (48.3%) of those diagnoses taking place in emergency care. Unfortunately, a hospital stay doesn't ensure an accurate – nor quick – diagnosis. More than a third (34%) of the patients surveyed in the research had gone to cardiology as an outpatient in the last six months yet had not been diagnosed (Pumping Marvellous, 2020). Still, delaying hospital treatment for as little as 4-6 hours after the acute onset of HF symptoms can increase a patient's risk of death. Screening and timely diagnosis has thoroughly demonstrated that it may help to avoid hospitalisation and achieve optimal outcomes for patients (Heart Failure Policy Network, 2020, p. 31).

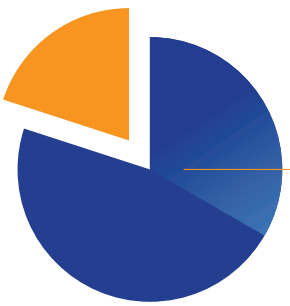
As mentioned above, diagnosing HF can be challenging, even for trained professionals, due to the similar risk factors that contribute to HF and other CVDs. Not all patients with HF have the typical symptoms, and the same symptoms can be experienced by patients who do not have HF (Ponikowski, et al., 2014).

Making an accurate diagnosis requires a range of diagnostic tools and information in conjunction with clinical judgement and expert knowledge. Natriuretic peptide (NP) testing, for instance, has been shown to be cost-effective in supporting timely diagnosis of HF, primarily by safely ruling out patients for echocardiography (Lobos Bejarano, Horrillo Garcia, Gonzalez-Gonzalez, & al., 2012; Barrios, Llisterri, Escobar, & al., 2011). The Irish Cardiac Society estimated that NP testing could reduce demand on specialist diagnostic services by 30% (Irish Cardiac Society, 2016). Unfortunately, these specialist diagnostic services currently have long waiting lists due to demand and pandemic-related backlogs.

74.8%
of patients surveyed had their initial HF diagnosis following their initial hospital

More recent studies have implemented newer methods to detect and diagnose HF early with biomarkers such as NP (Cannone & al., 2021). A landmark study in Ireland, for instance, has shown techniques that can be applied to HF and screen high-risk populations (Ledwidge, et al., 2013). This study investigated the efficacy of B-type natriuretic peptide (BNP) based screening in combination with collaborative care between primary care physicians and cardiovascular specialists in the prevention of HF and left ventricular dysfunction. The results from the study showed that a clinical approach focused on a BNP-based screening and cooperative care reduced the risk of developing left ventricular dysfunction and HF (Ledwidge, et al., 2013). This has led to uptake of biomarkers in the diagnostic process for HF across Europe. Recently, a pilot in Germany showed that the use of the diagnostic information provided by NT-pro B-type Natriuretic Peptide, for instance, led to a reduction of hospitalisation and an increase in life expectancy (MedTech Europe, 2020).

Much could also be done to reduce progression to HF among high-risk groups (Ponikowski, Voors, Anker, & al., 2016). This requires intensive therapy and active management of risk factors of HF, such as high blood pressure, high cholesterol, and type 2 diabetes. Studies have shown that intensive treatment of high blood pressure could reduce progression to HF by as much as 40% (Wright, Williamson, Whelton, & al, 2015).



4/5 CVD related deaths due to heart attacks or strokes

1/3 of these deaths in people under the age of 70

However, one challenge in Europe is that governments tend not to have specific or coordinated plans on HF, and if they do, these tend to be outdated, lack funding, or have even stalled. Such lack of plans and screening is due to the low recognition of HF by the wider public as well as policymakers. There is also a lack of integrated HF care pathways and information technology (IT) systems and telemedicine platforms, and disease management models and key diagnostics are often unavailable. Such issues need to be addressed to not only raise awareness of the problems caused by HF but also boost the resilience of our healthcare systems and decrease costs for treating HF.

POLICY RECOMMENDATIONS

Governments have been slow to recognise the significance of HF, and existing CVD policy initiatives commonly neglect HF, despite it falling within their scope. Years of underinvestment in HF have left Europe unprepared for future pressures to the European health workforce and European health systems. Bearing this in mind, we recommend that European and national policymakers:

- Promote public awareness programmes to help people recognise signs and symptoms of heart failure and understand the importance of seeking early diagnosis and care;
- Encourage the development and use of heart failure education programmes for appropriate healthcare professionals;
- Set up a strong information system to ensure information sharing between providers and across levels of care;
- Ensure patients have timely access to diagnostic services and treatment of heart failure, through appropriate reimbursement procedures in all relevant settings.

NEWBORN AND SEVERE COMBINED IMMUNE DEFICIENCY (SCID)

THE DEFINITION

The first stories of fatal congenital deficiency of lymphocytes date back to the 1950s in Switzerland. The subsequent term "Swiss-type agammaglobulinemia" was then used to distinguish infants with fungal infections, lymphopenia, and early death from the less severely impacted children who came to medical attention somewhat later in life with disorders such as isolated agammaglobulinemia. This term, however, was a source of confusion (Puck, 2013). This label was applied to families in which Severe Combined Immunodeficiency (SCID) was inherited as an X-linked recessive genetic trait. In the following decades, SCID designations became more accurate due to enhanced immunological tools to describe immune defects and to the identification of immunodeficiency genes.

"Although this is a life-threatening disease, it can be treated successfully if recognised early in life

A constant feature in all SCID is the defective production of T cells. In most SCID, B cells are also defective, but even normal B cells cannot produce antibodies without T cell help. Sometimes, natural killer (NK) cells are also affected and compromised (Kwan, et al., 2014). As a result, SCID can be defined as "an inherited primary immunodeficiency, which is characterised by the absence or dysfunction of T lymphocytes affecting both cellular and humoral adaptive immunity" (Notarangelo, 2010; Burg & Gennery, The expanding clinical and immunological spectrum of severe combined immunodeficiency, 2011). Such syndromes are noted as 'severe' as they lead to early death due to overwhelming infection, with this occurring typically in the first year of life, especially when children are around 4-6 months old (Meehan, et al., 2018). As a consequence, infants with SCID are susceptible to life-threatening infections as they have little or no immune system and are therefore highly susceptible to bacterial, viral, fungal and opportunistic infections.

The true frequency of SCID is not known, though estimates put the incidence at approximately 1:50,000 – 1:100,000 live births

Although this is a life-threatening disease, it can be treated successfully if recognised early in life. Sadly, the early recognition needed to optimise treatment is not available to all children in Europe.

THE SCALE OF THE CHALLENGE IN EUROPE

The true frequency of SCID is not known, though estimates put the incidence at approximately 1:50,000–1:100,000 live births. Most likely this is an underestimate as children die from severe infection without an underlying diagnosis being made throughout the world (Gaspar, et al., 2017, p. 6). The prevalence of SCID also varies according to the populations studied and may vary from one country to another.

There is strong evidence that the outlook for the firstborn child of families with multiple cases of SCID is significantly worse than that for any subsequent children. This is because the identification of SCID in the second and subsequent children may be anticipated, allowing treatment to be initiated before the start of a first, severe infection (Gaspar, et al., 2017, p. 5).

Failure to recognise immunodeficiency despite recurrent diarrhoea, septicaemia, fungal infections, and pneumonia is clear in many family stories. Many of the patients with SCID, both in the past and present, have erroneously been diagnosed with dietary intolerances due to diarrhoea, poor weight gain or pulmonary infections. Some have received the diagnosis of scarlet fever while others have been diagnosed with diphtheria as these conditions share features with the clinical presentation of SCID.

There are many ways that SCID can be identified. Other than the clinical presentation described above one of the easiest ways to diagnose SCID is to measure the peripheral (or cord) blood lymphocytes. Infants usually have around 4,000 lymphocytes/mm3 of blood in the first year of life, 70% of which are T cells. While infants with SCID have very low levels of T cells, their global lymphocyte count can be normal in certain types of SCID, so it is necessary to perform a lymphocyte subset count. Low T cell readings should prompt referral to a clinical centre with expertise in managing infants with PID (International Patient Organisation for Primary Immunodeficiencies, 2019). Another method is to check immunoglobulin levels as they tend to be low in patients with SCID. This, though, is not error-proof as levels might be normal in the blood of newborns affected by SCID. This is due to the presence of maternal IgG that are passively transferred through the placenta prior to birth, contrasting with very low to absent IgA (which can be normal in healthy newborns) and IgM.

> *“Regardless of how SCID is identified, the crucial step is actually identifying the disease*

Regardless of how SCID is identified, the crucial step is actually identifying the disease. Without early diagnosis and treatment, infants will not survive and there is a 100% lethality within the first year of life in undiagnosed patients. Universal Newborn Screening is the only robust way to detect SCID in asymptomatic babies prior to the development of a severe infection.

THE VALUE OF SCREENING AND LESSONS LEARNED

The aim of newborn screening (NBS) is the early detection of conditions for which rapid treatment can mitigate mortality or irreversible damage. In most cases, whole population-based screening is the only means to detect SCID before the onset of infection as more than 80% of cases lack a clear family history (Kwan, et al., 2014, p. 730).

Recent technological developments using the recognition of T cell receptor excision circles (TRECs), as a biomarker for T lymphopenia have allowed the identification of SCID cases by analysis of dried blood spot samples collected during newborn screening. This has been implemented in seven countries as a routine service so far and six others are running pilot projects or regional programmes. The Netherlands began national SCID screening in January 2021 and Ireland will likely start at the end of 2021. Italy is also considering adding conditions to its SCID regulatory programme (Loeber, et al., 2021, p. 14).

Survival following transplant in SCID patients diagnosed at birth and transplanted in the first month of life is around

92%

Once SCID has been diagnosed, it needs to be confirmed with laboratory testing. These tests assess the immune system of the patient, including the lymphocyte count with subset analysis of naïve and memory T cells, B and NK cells and lymphocyte proliferation studies (Meehan, et al., 2018). When the diagnosis is suspected or confirmed, the patient can then be protected while waiting for curative treatment.

The diagnosis needs to occur before effective management (including avoiding harmful vaccinations such as the BCG) and curative treatment are able to follow. The early diagnosis of SCID also allows for the limitation of contact with other relatives and risks associated with unprotected social contact while permitting additional measures to protect a child within the home.

Most importantly, screening allows treatment before infections make it less successful. Among treatments for patients with SCID, haematopoietic stem cell transplantation (HSCT) is extremely effective (Gaspar, et al., 2017, p. 9). Data is available to show that survival following transplant in SCID patients diagnosed at birth and transplanted in the first month of life is around 92%. This result is irrespective of donor status, and the sort of conditioning regimen used (Brown, Xu-Bayford, Allwood, & al, 2011; Myers, Patel, Puck, & Buckley, 2002). We still need to acknowledge that the survival following transplant is significantly influenced by the type of donor available, and by the presence of active respiratory infection at time of HSCT. Still, if screening does not occur at birth, transplantation becomes more difficult and less successful. Another method is via chemotherapy conditioning regimens, which also results in patients leading normal lives after treatment (Gaspar, et al., 2017). We must note that these treatments are relatively inexpensive compared with interventions that are delayed and which can result in avoidable complications and costs.

New developments in screening such as newer methodologies, logistics, and improved algorithms within the screening pathway can also improve the effectiveness of screening by reducing the false positive rate, which causes distress to families. Next generation sequencing, for instance, may help improve the specificity of screening. This technology has been implemented in Norway, where it has been used to detect SCID as a second-tier test (Tangeraas, et al., 2020). It is likely that this technology will claim its place in screening, yet its growth in Europe still needs to be evaluated (Loeber, et al., 2021, p. 15).

There can be little doubt that newborn screening for SCID saves lives. For example, a multi-site study conducted by the Primary Immune Deficiency Treatment Consortium in the United States found that infants not tested until symptoms manifested themselves had a 58% survival rate, compared to 85% survival for infants tested at birth. In Europe, another study showed that due to earlier detection, the number of deaths due to SCID reduced from 0.57 to 0.23 per 100,000 children and a number of 11.7 quality adjusted life-years (QALYs) gained was also expected (Van der Ploeg, Blom, Bredius, & al, 2019). This study showed that the cost-utility ratio was €33,400 per QALY gained, suggesting that newborn screening is a highly cost-effective intervention.

“There can be little doubt that newborn screening for SCID saves lives

In conclusion, the evidence shows that newborn screening for SCID can improve both the survival and the quality of life for children in a cost-effective way, shortening the diagnostic odyssey significantly and ensuring a better treatment outcome. Therefore, all developed countries with an integrated healthcare system should give its introduction serious consideration.

POLICY RECOMMENDATIONS

We call on European and national policymakers to follow the evidence and implement the following policy recommendations:

- Universal newborn screening for SCID needs to be carefully considered by all member states within the EU to ensure equity of access for children at risk;
- Including and performing systematic screening programmes at birth for SCID;
- Raise awareness at EU and national level by means of educational campaigns and materials to ensure SCID and other PID patients can be diagnosed and treated;
- There should be an update to the guidelines and recommendations from the European Commission as a follow-up to the 2008 recommendations for the detection of rare diseases;
- An EU coordinating action aimed at facilitating exchange of expertise, the results of national pilots/evaluations, data and information including those on outcomes is key.

CONCLUSIONS

The case studies in this Insight Report are intended to encourage key health stakeholders and policymakers to better plan and invest in early diagnosis and screening and other secondary prevention programmes as critical financial investments in patient safety and public health.

> *Screening and early diagnosis play a critical role in detecting a disease in its earliest stages before any symptoms become noticeable*

Screening and early diagnosis play a critical role in detecting a disease in its earliest stages before any symptoms become noticeable. Secondary prevention is key to curbing disease progression and maximising quality outcomes for patients while reducing healthcare costs. Also, screening programmes and systemic health checks for noncommunicable diseases are still not routine in most European countries.

In line with Health First Europe's experience and previous policy recommendations, we call on the EU and national policy makers to better implement and harmonise screening and early diagnosis programmes across Europe as key investments in saving and improving citizens' lives while ensuring the sustainability of our healthcare systems in the face of growing public health threats.

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ABOUT HEALTH FIRST EUROPE

Health First Europe is a non-profit, non-commercial alliance of patients, healthcare workers, academics, healthcare experts and the medical technology industry. We are joining forces to transform health care through innovative solutions. Since we believe that every European citizen should benefit from the best medical treatments available, we aim to ensure that equitable access to modern, innovative and reliable health care solutions is seen as a vital investment in the future of Europe. Our alliance was born in 2004 thanks to commitment of our co-Patrons and our members to build truly patient-centred healthcare systems in Europe.

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