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Executive Summary

i. Introduction

Substantial economic resources are devoted to healthcare across Europe, but there is evidence that a large proportion of these resources do not benefit patients or society. Around 10% of European Gross Domestic Product (GDP) is spent on healthcare (OECD, 2018) and estimates suggest that as much as one-fifth of this amount (2% of GDP) is spent on interventions that make no meaningful contribution to health outcomes (OECD, 2017b)**.** In economic terms, these resources are used inefficiently.

Improving the efficiency of European healthcare is in the interest of many stakeholders, including governments, payers, providers, patients, and the life sciences industry. Identifying and reallocating inefficient spending would allow for better care, greater access to innovative treatments, and superior outcomes within existing budgets. However, identifying specific inefficiencies is challenging, in part because it is usually difficult to know the 'counterfactual': what the costs and outcomes of an alternative strategy would have been. This challenge is magnified by the diversity of populations and health systems in Europe, from universal public systems to social or private health insurers, which makes direct cross-country comparisons difficult.

To help address the challenge of improving efficiency in European healthcare, EFPIA commissioned the Office of Health Economics (OHE) and the Swedish Institute for Health Economics (IHE) to:

- Develop a comprehensive conceptual framework to define heath care inefficiencies;
- Generate actionable insights for policymakers by identifying clear examples of inefficiency;
- Estimate the scale of the potential savings and health gains that could be realised by addressing specific inefficiencies.

ii. Conceptualising and categorising efficiency

In economic terms, **efficiency** describes how well inputs (i.e. physical or financial resources) are converted into valuable outputs. If one process generates a greater amount of outputs with the same amount of inputs than an alternative process, it is **more efficient**. A process can also be more efficient if it produces the same amount of outputs with fewer inputs than an alternative process. Conversely, a process that requires more inputs than an alternative process to produce the same amount of resources is described as **less efficient** or **inefficient**. The relationship between relative inputs, outputs and efficiency is shown in Table 1.

In healthcare, inputs are financial or medical resources, whilst outputs are positive health outcomes. Healthcare is efficient if it minimises ("avoids") unnecessary expenditure, morbidity or mortality. In the context of

Table 1, avoiding unnecessary expenditure can be seen as reducing inputs, whilst avoiding unnecessary morbidity and mortality can be seen as increasing positive health outcomes.

TABLE 1: THE RELATIONSHIP BETWEEN INPUTS, OUTPUTS AND EFFICIENCY

		Outputs/outcomes		
		Lower	**Same**	**Higher**
Inputs	**Lower**	Ambiguous	More efficient	Much more efficient
	Same	Less efficient	Efficiency unchanged	More efficient
	Higher	Much less efficient	Less efficient	Ambiguous

This project adapted a framework from the Organisation for Economic Cooperation and Development (OECD, 2017b) to illustrate and categorise different types of healthcare inefficiency, their drivers and the relevant actors (see Figure 1). The categories of inefficiency it describes include governance related waste, operational waste and wasteful clinical care, and stem from drivers ranging from poor decision making to deliberate fraud or deception. This framework was used to inform the identification of priority areas for the efficiency case studies.

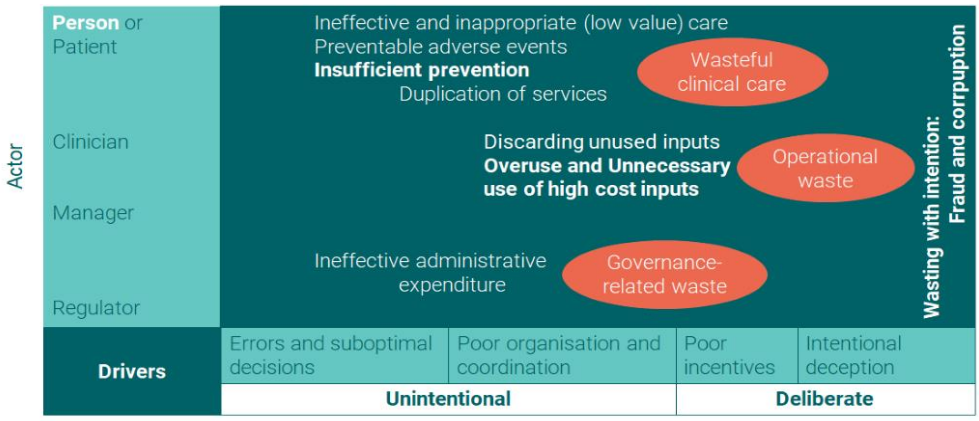

FIGURE 1: REVISED CONCEPTUAL FRAMEWORK OF WASTE AND INEFFICIENCY
Adapted from OECD 2017; revisions shown in bold white.

iii. Case studies

The core of the project was the development of case studies in **four priority areas** (screening, coordination of care, rational use of medicine, and healthcare associated infections). The case studies were intended to highlight best practice by contrasting more successful and less successful examples of efficient healthcare delivery. The priority areas and case studies were selected by an external Steering Group and EFPIA. These case studies are briefly outlined in the following sections and summarised in Table 2 of the main report.

Priority area 1: Colorectal cancer screening

Early diagnosis and prompt initiation of appropriate treatments have been shown to reduce the number of preventable deaths in many diseases, including cancer (World Health Organization, 2017). Conversely, delays in diagnosis are associated with a greater number of preventable deaths and, by definition, greater inefficiency. In general, there are two approaches to population screening (Miles et al., 2004):

- Organised systems: invitations to screening are issued using registered and centralised data.
- Opportunistic systems: invitations are conditional on an individual's decision or on visits to healthcare providers.

Compared with opportunistic systems, organised screening for early detection of colorectal cancer shows better results in improving screening participation (Eisinger et al., 2008; Senore et al., 2015), reducing disparities in screening uptake (Eisinger et al., 2008) and minimising harms such as over-screening, low quality screening, and screening-related complications (Levin et al., 2011).

The screening cases relate to organised screening programmes for colorectal cancer (CRC). CRC is the second most frequent cause of cancer mortality in Europe, associated with 16% of total cancer deaths (Ferlay et al., 2013). Many of these deaths, though, are preventable with early detection. The case studies contrast organised screening programmes in the Basque Country of Spain and Paris, France. The Basque experience has been effective in screening high-risk populations and has resulted in overall cost-savings and system efficiencies, whilst the Parisian experience has been less successful in terms of coverage and cost-savings.

Case study lessons

Key lessons from contrasting the Basque and Parisian examples include:

- **Make participation as simple as possible.** The Basque programme, like programmes in The Netherlands and Flanders (Belgium), included the Faecal Immunochemical Test kit with the invitations and made it as easy as possible for recipients to return a sample. The Parisian programme, in contrast, required individuals to collect the kit from their GP. This extra step is likely to have discouraged participation. Paris has already decided to include the kit with the invitation, but only for those individuals considered at greater risk of not participating. This includes: 1) individuals who did not participate in the first invitation; and 2) individuals who have previously participated in CRC screening.

- **Build on networks that are already in place, such as regular neighbourhood meetings, or working with existing associations.** From interviews conducted as part of the case study, we know that efforts are already being made in Paris to involve more primary care professionals, allowing them to provide as much information as possible to individuals in the target demographics who may be visiting primary care facilities for other reasons. Expert interviews highlighted the importance of educating and involving stakeholders such as patients' organisations, primary care professionals, journalists, politicians and other community leaders. Information campaigns could be of greater impact if using celebrities or other well-known individuals. The use of social media to promote screening was also suggested.

- **Other suggestions** generated from expert interviews referred to ways to maximise avenues of communication, or to the importance of the use of past information regarding specific aspects that have generated a delay to diagnosis. For example, ensuring appropriate targeting strategies could reduce demand for tests that are less likely to be beneficial. If those services are expensive services, that might also substantially reduce healthcare utilisation costs.

Another suggestion was qualitative research with non-participants to understand their reasons for not participating, which could be used to improve information campaigns.

Priority areas 2A & 2B: Disease management and standardised patient pathways

The direct and indirect costs of chronic diseases are substantial. The direct healthcare costs associated with chronic conditions account for 70-80% of total EU26+UK healthcare expenditure (Economist Intelligence Unit, 2012), or more than €1 trillion in 2017, and indirect costs of lost productivity associated with chronic conditions can represent up to 7% of GDP for some countries (Suhrcke et al., 2006). Much of this cost stems from inadequate management of cardiovascular diseases, chronic obstructive pulmonary disease (COPD), cancer and diabetes, which require long-term monitoring and ongoing adherence to treatment. Failures in monitoring and adherence impose avoidable costs on healthcare systems in the form of unplanned outpatient visits and hospital admissions. Effective disease management and treatment coordination can avoid these events, reducing costs and improving patient outcomes.

Disease management programmes (DMPs) are a means to help patients with chronic diseases maintain treatment adherence and thus avoid costly outpatient visits and hospital admissions, increasing overall healthcare efficiency. Standardised patient pathways (SPPs) are a means to improve the structure and consistency of the patient's route through the system by clearly defining all necessary steps to be taken in diagnosis and treatment.

2A. Disease Management Programmes for Chronic Obstructive Pulmonary Disease

Chronic Obstructive Pulmonary Disease (COPD) is a chronic disease with an estimated prevalence rate of around 12 percent in people aged 40 years and older across Europe (Blanco et al., 2017). Poor treatment adherence is a common cause of hospitalisation and a leading cause of death, and as such, it is associated with a substantial economic burden.

Two case studies of DMPs for COPD are considered: Bourbeau et al. (2019) evaluate the outcomes of a trial of a home-based COPD disease management intervention in France, Germany, Italy, and Spain for severe COPD patients led by nurses, and Achelrod et al. (2016) evaluate the outcomes of a disease management programme for COPD run by primary care physicians that has been running in Germany since 2005.

Case study lessons

The COMET trial of a home-based DMP for COPD indicated gains in overall efficiency in France and Spain, with improved patient outcomes including gains in Quality Adjusted Life Years (QALYs) and reduced mortality, with no increase in total costs. Both German examples are less clear regarding efficiency. In both the trial and real-world experience, German DMPs were associated with improved outcomes but also an increase in overall costs among DMP participants. This likely reflects better case management and treatment adherence, but it is not an unambiguous improvement in efficiency.

In general, it is difficult to conclude best practice from a comparison of the two cases. Germany was included in both cases and saw a similar result in each: an increase in costs as well as outcomes, leading to an ambiguous effect on efficiency. However, comparison of the features and outcomes of the COPD management programmes described in the case studies suggests some general conclusions about the features of an efficient DMP:

- **Patients need to be equipped with the right knowledge on self-management of their disease**. Patient education is important for adopting healthier lifestyles (most importantly smoking cessation) and increasing medication adherence. Patient education in the COMET-trial was based on the "Living Well with COPD" programme, whereas the DMPs in Germany are supposed to adhere to up-to-date evidence-based clinical guidelines.

- **Regular reminders and encouragement for patients are key for successful condition management.** A single initial training session is not likely to be enough to change behaviour. The DMPs in Germany try to achieve change through agreement on personal therapy goals. In the COMET-trial, patients were motivated through regular phone calls with their case manager, and they self-monitored their condition through symptom reporting.

- **The design of a DMP must take cultural factors into consideration**. In countries where primary healthcare is centred around the primary care physician (as in Germany), a greater role for nurses in patient management might be initially met with scepticism by patients and result in lower adherence to advice from nurses.

2B. Patients' pathways in cancer care

Cancer represents a substantial share of the total disease burden in Europe: more than one in four deaths are due to cancer, making it the second most common cause of death after cardiovascular diseases (Jönsson et al., 2016a). The economic burden of cancer is also significant with direct healthcare costs of €83.2 billion in the EU27+UK in 2014, and the indirect costs of lost productivity due to premature mortality and morbidity, together with informal care costs thought to be a similar amount (Jönsson et al., 2016b).

Standardised patient pathways (SPPs) in cancer care lay out the essential steps from suspicion of cancer to recommended diagnostic procedures and treatments. They are intended to enhance the coordination of care to enable timely access to diagnostics and treatment, with the primary aim of increasing patient survival.

Two case studies of programmes intended to improve coordination of cancer care are considered. Probst, Hussain and Andersen (2012) and (Jensen et al., 2015; Jensen, Tørring and Vedsted, 2017) provide an evaluation of a Danish SPP whilst the National Board of Health and Welfare (2019c) evaluates a Swedish SPP modelled on the Danish programme.

Case study lessons

In both cases, the implementation of the SPPs reduced waiting times and regional variability but had no statistically significant effect on survival rates compared to patients treated outside the SPP. If the process of care is an important outcome for a health system, then improvements in this process represent gains to the health system – although the additional costs of achieving these through SPPs mean that the impact on efficiency is ambiguous. However, the introduction of SPPs may also have had negative impacts on the care received by non-cancer patients, which should be better understood before conclusions about the effects of SPPs can be reached.

Despite these ambiguous results, a comparison of the features of the SPPs in Denmark and Sweden provide some insights for the implementation of efficient care pathways:

- **Careful consideration must be given to the ultimate aim of SPPs.** In Denmark, the aim of the SPPs was to reduce waiting times, improve health outcomes of patients with cancer, and increase patients' satisfaction by ensuring treatment as quickly as possible. In Sweden, the aim of the SPPs was to reduce waiting times and regional variability in cancer care. Both SPPs achieved some of the objectives, but there is little evidence that the SPPs improved

survival outcomes or overall system efficiency. This highlights the importance of understanding the objective of such initiatives: ensuring a positive patient experience or maximising health outcomes.

- **Attention should be paid to not 'crowd out' patients in other disease areas**. In both Denmark and Sweden, the increased focus on cancer patients appears to have led to longer waiting times for patients with other diseases. This suggests that the resources allocated to implement the SPPs were insufficient to avoid the 'crowding out' of patients in other disease areas.

- **There should be clear referral tracks from primary care to hospital care.** Denmark has developed a clear strategy on how to refer patients from the GP to hospital care based on the severity of patient symptoms. No such strategy was implemented in Sweden. It was not possible to assess the impact of this difference, but it is likely to lead to inconsistent referral and possibly differences in outcomes.

Priority area 3: Rational use of medicines

The rational use of medicines covers many problems including over-prescription, inappropriate use of medicines (e.g. antibiotics), and poor adherence to prescribed treatment, all of which can lead to suboptimal outcomes and adverse events. Polypharmacy is a more complex example which lacks a standard definition but is commonly described as the concurrent use of five or more medicines (Masnoon et al., 2017; World Health Organisation, 2019).

Polypharmacy is common in the elderly due to the prevalence of multimorbidity (i.e. two or more chronic conditions) in this population which has been increasing in recent decades (Wastesson et al., 2018).

Polypharmacy in the elderly population can be associated with poor outcomes as the possibilities of adverse drug-drug and drug-disease interactions increase (Maher, Hanlon and Hajjar, 2014; Wastesson et al., 2018). If these interactions are not recognised and are incorrectly diagnosed as new illnesses, additional medicines may be prescribed, potentially leading to further unintended interactions in what has been called a "prescription cascade". Adverse effects associated with polypharmacy can lead directly or indirectly to an increased number of outpatient visits and hospitalisations whilst physical and cognitive functioning, as well as quality of life, deteriorate and the risk of mortality increases. Medication non-adherence also increases with the number of medicines taken (Zelko, KlemencKetis and TusekBunc, 2016), contributing to the risk of suboptimal health outcomes.

The cost of mismanaged polypharmacy has been estimated to be 0.3 percent of all global health expenditure – US$18 billion worldwide – much of which could be avoided through improved polypharmacy management (Aitken and Gorokhovich, 2012).

Two programmes aimed at improving the management of polypharmacy in elderly people are considered: an evaluation of medication reviews in Scotland (UK) by the Scottish Government Polypharmacy Model of Care Group (2018), and a medication review programme in Lower Saxony, Germany, evaluated by McIntosh, Alonso and Codina (2016) as part of the SIMPATHY Project and by Seidling et al. (2017).

Case study lessons

The Scottish experience indicates potential improvements in health system efficiency. Reviews were associated with estimated cost savings ranging from €9 to €232 per patient per year and a reduced proportion of patients on potentially harmful combinations of medicines. Long-term patient outcomes such as mortality, morbidity, and quality of life were not assessed, but are likely

to be positive. The German experience was less successful and identified challenges in the design and implementation of medication reviews, particularly related to the incentivisation of pharmacists and information sharing with physicians.

Contrasting the Scottish and German experience highlights some key lessons:

- A successful medication review programme requires involvement of all relevant stakeholders – especially pharmacists and primary care physicians. The Scottish polypharmacy guidelines were a joint effort by geriatricians, pharmacists, and General Practitioners (GPs). Medication reviews are performed by both pharmacists and GPs. In contrast, the ATHINA programme in Lower Saxony was independently developed by the Chamber of Pharmacists, with no involvement of GPs. A situation in which GPs perceive pharmacists as trying to challenge their competence in prescribing medications needs to be avoided.

- **Widespread participation of healthcare providers and low patient fees are critical for patient access.** The Scottish government was successful in having all local NHS Boards follow the polypharmacy guidelines on conducting medication reviews. In Lower Saxony, participation of pharmacists in the ATHINA programme was voluntary and led to low participation. Furthermore, patients in Lower Saxony had to pay out-of-pocket for voluntary medication reviews, whereas in Scotland medication reviews were embedded in standard working practices and free for patients.

- **Appropriate financial incentives are necessary.** In Scotland, pharmacists and physicians perform the medication reviews as part of their general service and are paid for the reviews. In Lower Saxony, pharmacists initially received no remuneration for the time spent on medication reviews from the sickness funds, forcing some of them to conduct the reviews in their spare time.

- **The recommendations from medication reviews need to be implemented.** In Scotland, physician participation in the reviews facilitates changes in medications. This is not necessarily the case in Lower Saxony, where patients may choose not to share the pharmacist's recommendations with their prescribing physician.

Priority area 4: Healthcare-associated infections

Healthcare-associated infections (HCAIs) have a substantial impact on health system efficiency as they are associated with significant costs from the hospital perspective (Roberts et al., 2003; Perencevich et al., 2003), and are detrimental to patients' quality-of-life and survival. The World Health Organisation estimates that each year there are 4 million HCAIs in acute care hospitals in Europe, resulting in 37,000 deaths and €13–24 billion in avoidable costs (World Health Organization, 2009). Of these costs, €7 billion are direct costs to the healthcare system (World Health Organisation, 2013). In Europe, it is estimated that HCAIs occur in 7.1% of all hospital admissions (Danasekaran et al., 2014) and represent 16 million avoidable hospitalisation days (Manoukian et al., 2018).

The risk of HCAIs is associated with a lack of standardisation of procedures, and the absence of local and national guidelines and policies, as well as a lack of training and information with respect to the prevention and management of HCAI. Staff education and accountability are essential for making healthcare providers and patients aware of risks and consequences of HCAIs and for promoting prevention strategies.

One approach to prevent HCAIs is through the use of clinical surveillance, but the implementation of such surveillance is challenging as there is a lack of consensus on the best approaches and best indicators of care quality. Two case studies are presented with different approaches to surveillance: a Lean Six Sigma (LSS) clinical surveillance programme in Italy (Improta et al., 2018), and a surveillance programme of health professionals in the hospital setting in Germany (Hagel et al., 2019).

Case study lessons

The implementation of the LSS in Italy was associated with substantial improvements in clinical outcomes, almost halving the number of HCAIs across the Federico II University Hospital. Moreover, given that this reduction in infections translated to a decrease in the mean number of hospital days associated with HCAIs from 45 to 36 per patient, it is likely that the programme also generated cost savings – and therefore unambiguous efficiency improvements. The clinical surveillance programme implemented in the Jena Hospital in Germany, however, neither decreased HCAIs nor generated substantial improvements in compliance with best hygiene practices. There are several differences between the approaches to clinical surveillance used in Italy and Germany which are likely to have contributed to these contrasting effects, and which can be extrapolated to generate broader lessons:

- **Data should be used to tailor interventions to context.** In the German case, interventions were implemented to deal with the most common sources of HCAIs, based on external evidence and international best practice, but it is unclear that these were sufficient to address the causes of HCAIs in the Jena Hospital. Moreover, the interventions implemented may not have been appropriate within the operational structures of the hospital. Indeed, although Arefian et al. (2019) speculate that lack of time and high workload may have contributed to low compliance observed over the course of the study, these factors do not appear to have been recognised or corrected at the time. In contrast, in Italy data were used to identify the specific deviations from good practices which were contributing to HCAIs in the Federico II University Hospital.

- **Engagement of staff is critical, during design and implementation.** The interventions designed in the Italian case were not only hospital-specific, but also validated by staff in order to ensure their appropriateness – thereby avoiding some of the challenges which have been speculated to have occurred in the German case. The poor compliance with interventions identified in the German case additionally indicates that, if staff are not engaged in interventions through measures such as training or consultation, the possibility of reducing HCAIs is likely to be severely constrained.

- **Improvement should be a continuous process.** In the Italian case, ongoing monitoring allowed insight into the success of the interventions, and how they might be refined. Had a similar approach been utilised in the German case, this could have alerted the hospital to the lack of progress and provided an opportunity to improve.

iv. Quantification of benefits

Quantitative estimates were estimated for the potential efficiency gains associated with the cases previously discussed. These estimates are based upon the findings from the more successful case studies and extrapolated for each of the 27 EU Member States and the UK as well as to the aggregate European level (EU27+UK). These quantifications provide an indicative estimate of the scale of potential efficiency gains that could be realised, but they must be interpreted with some caution. Many of the cases were based on small trials (e.g. the Lean Sigma Six clinical surveillance programme in Italy), whilst, in other cases, the results are based on

models rather than observed outcomes (e.g. colorectal cancer screening in the Basque Country, Spain). Finally, many of the health benefits and cost savings associated with these interventions will only be realised in the future (e.g. the full cost and survival benefits of colorectal cancer screening will accrue over a 30-year period).

Quantification 1: Efficiency gains from colorectal cancer screening

The CRC screening extrapolation was based on simulating life expectancies for a hypothetical cohort accounting for national demographic characteristics, including health status. These simulated cohort outcomes were combined to produce aggregate measures of costs and health outcomes. Each scenario combines information on the intervention, including costs, eligibility, participation rates and expected efficacy to estimate expected outcomes. These outcomes include changes in incidence, mortality, length of stay, resource utilisation (for example, follow-up procedures, treatments), direct health care costs, life expectancy, and quality-adjusted life-years (QALYs).[1]

If all EU27+UK countries could achieve the midpoint between the minimum rate recommended by European guidelines (Segnan et al., 2010) and the Basque screening participation levels, aggregate annual direct savings would reach €405 million (0.027% of the aggregate health expenditure), ranging between €274.3 and €535.4 million (0.018% to 0.035% of aggregate health expenditure). This participation rate would also reduce CRC deaths by between 10,000 and 20,000 and be associated with an additional 171,000 to 331,000 QALYs per year through morbidity and premature mortality avoided. Using a willingness-to-pay of €30,000 per QALY, this implies an additional indirect efficiency gain of between €5.1 and €9.9 billion.

Quantification 2: Efficiency gains from disease management programmes for chronic obstructive pulmonary disease

DMPs for COPD have the potential to reduce COPD-related hospitalisations and mortality, contributing to substantial gains in efficiency. To estimate the baseline cost of COPD admissions in the EU27+UK, information on COPD prevalence, the annual rate of hospital admission, and the mean length of hospital stays along with estimates of the cost per inpatient bed day were combined. We tested 75% and 50% compliance rates with the DMP, and lower and upper COPD hospitalisation rates of 12% and 38% for the sensitivity analysis. The case study has shown that the DMP for COPD also improved mortality rates, suggesting a relative 87% reduction in mortality (1.9% vs. 14.2%). This reduction was assumed to be constant across the EU27+UK and was factored into the calculations.

Given the uncertainty in cost-reductions associated with reduced COPD mortality, we do not include these in our estimates of aggregate cost savings associated with a DMP. Estimates of aggregate savings are based on length of stay-related efficiency gains only.

For the EU27+UK, 50% compliance with a DMP for COPD was associated with up to 12,000 COPD-related deaths avoided and mid-point cost savings of €426.4 million per year (0.028% of aggregate health expenditure), ranging between €204.3 and €648.5 million (0.01% to 0.04%

[1] *The Quality-Adjusted Life Year (QALY) is used to measure how well a medical treatment improves and lengthens patients' lives and is often used by health economists and health care decision makers to estimate the benefits of treatments for cost-effectiveness analysis.*

of aggregate health expenditure). In a 75% DMP compliance scenario, up to 17,000 COPD-related deaths are avoided and mid-point cost savings are €1.4 billion (0.092% of aggregate health expenditure), ranging between €689.1 million and €2.1 billion (0.05% to 0.14% of aggregate health expenditure).

Quantification 3: Efficiency gains from rational use of medicines

Addressing inappropriate polypharmacy through medication review has the potential for substantial efficiency gains by improving disease management, avoiding adverse outcomes, and potentially reducing prescribing costs. To illustrate the scale of potential efficiency gains associated with a systematic prescription review programme, a simulation analysis based on the outcomes observed in the Scottish case study was performed.

For the purposes of the analysis, polypharmacy was defined as the use of 10 or more medications daily. On the basis of nationally representative UK micro-data, the prevalence of polypharmacy was estimated to be 2.7% in the UK.[2] The potential cost savings associated with different levels of population uptake and the net effects of reviews, including the rationalisation of medicines and a lower risk of hospitalisation due to adverse interactions, were estimated. Medicine rationalisation represents the net change in the number of medicines per individual and can include additional medicines for some patients and reductions for others. For sensitivity analyses, a population uptake over a range of 10-100% and average net medication reductions of 20-60% were adopted.

FOR THE EU27+UK, THE AGGREGATE EXPECTED SAVINGS OF A MEDICATION REVIEW PROGRAMME AIMING AT A RATIONAL USE OF MEDICINES WOULD BE OF €1.2 BILLION (0.081% OF THE AGGREGATE EU27+UK HEALTH EXPENDITURE) RANGING FROM €150 MILLION IN THE LESS OPTIMISTIC SCENARIO (0.01% OF THE AGGREGATE HEALTH EXPENDITURE) TO €2.3 BILLION IN THE MORE OPTIMISTIC SCENARIO (0.153% OF THE AGGREGATE HEALTH EXPENDITURE). IT COULD ALSO AVOID BETWEEN 500 AND 5,000 PREMATURE DEATHS ANNUALLY.

Quantification 4: Efficiency gains from reducing healthcare-associated infections

The size of the potential efficiency gains associated with clinical surveillance programmes to reduce HCAIs was estimated using the results of the evaluation of the more successful case (thus generating a 'best case' estimate), the Lean Sigma Six clinical surveillance intervention in Italy. Improta et al. (2018) estimate a 43% to 49% reduction in the incidence of HCAI and an EU27+UK incidence of HCAI in 7.1% of all patient admissions was assumed. This represents approximately 7 million patients in the EU27+UK each year.

FOR THE EU27+UK, EXPECTED AGGREGATE COST SAVINGS ASSOCIATED WITH A REDUCTION IN THE INCIDENCE OF HCAIS WOULD BE €8.1 BILLION ON AVERAGE (0.53% OF AGGREGATE HEALTH EXPENDITURE), RANGING FROM €7.6 TO €8.5 BILLION (0.50% TO 0.56% OF AGGREGATE HEALTH EXPENDITURE). IT WOULD ALSO AVOID 15,000 TO 18,000 PREMATURE DEATHS.

v. Discussion and conclusions

[2] *https://www.understandingsociety.ac.uk/documentation/health-assessment*

The case studies described in section 3 highlight the potential for efficiency gains across a range of priority areas as well as key challenges in achieving these gains. These have generated the following high-level insights, in addition to more specific lessons which are elaborated in section 3:

- Interventions that rely on patient participation should make participation as easy as possible;
- Implementers of interventions that require health actors to take on new roles should be aware of, and take steps to mitigate potential resistance due to cultural norms or existing incentive structures, for example to avoid participants booking extra appointments with their general practitioner to confirm advice given by a nurse;
- Local data might be needed to tailor existing interventions to address the specific drivers of inefficiencies in a given context. Ongoing data collection allows for refinement of these interventions;
- The operational constraints of the broader health system should be considered when designing interventions.

The absolute scale of efficiency gains in different healthcare systems will depend on the relative efficiency of each system. There is greater scope for efficiency gains in relatively less efficient systems, whilst the potential gains are smaller in relatively more efficient systems. Each healthcare system, therefore, must consider the relative efficiency and inefficiency of its different components when prioritising between efficiency initiatives such as those described above.

As the more successful cases show, meaningful efficiency gains are possible in every healthcare system. However, many of the less successful examples show that innovations cannot necessarily be directly applied between different systems without accounting for local organisational and cultural differences. The insights described above may be helpful in addressing this challenge but are not necessarily easy to implement. For example, ongoing data collection to understand and refine initiatives is challenging given the continuous, urgent demands on many healthcare systems. However, innovative approaches can potentially produce substantial efficiency gains across a range of therapeutic areas, improving health outcomes and freeing up resources that can be re-allocated to improve outcomes in other areas.

1 Introduction

Substantial economic resources are devoted to healthcare across the 27 countries of the European Union (EU) and the United Kingdom (UK),[3] but there is evidence that a large proportion of these resources do not benefit patients or society. In economic terms, these resources are used inefficiently. Around 10% of European Gross Domestic Product (GDP) is spent on healthcare (OECD, 2018) and estimates suggest that as much as one-fifth of this amount (2% of GDP) is spent on interventions that make no meaningful contribution to health outcomes (OECD, 2017b). At a national level, studies have estimated a similar scale of inefficiency in the Netherlands (OECD, 2017a) and the United States (Berwick and Hackbarth, 2012; Shrank, Rogstad and Parekh, 2019), whilst estimates from Australia suggest that as much as one-third of health expenditures could be inefficient (OECD, 2017a).

Spending is inefficient when an equivalent outcome could have been achieved with fewer resources, or when better outcomes could have been achieved with the same resources. Sources of inefficiency can include the use of more expensive branded medicines when a generic could have achieved the same outcome or admitting people to hospital when they could have been treated in the community. Inefficiency can also stem from unnecessary or inappropriate use of medications, diagnostic testing or therapeutic procedures. There is evidence to suggest that this type of inefficiency has been growing over time (Brownlee et al., 2017).

Some specific examples of inefficiencies include:

- In England, the proportion of patients experiencing a delayed discharge increased significantly over the period 2011-2016, generating 2.25 million excess bed days in 2016 (NHS England, 2018).
- The use of generic medicines in Europe is mixed. Average generic market share by volume across Europe in 2016 was 40%, but this ranged from 10% in Luxemburg to 85% in the UK (OECD, 2018).
- More than a quarter of total knee replacements in Spain and more than a third in the US are considered to be inappropriate (Cobos et al., 2010; Riddle, Jiranek and Hayes, 2014).
- More than 10% of hospital expenditure in OECD countries is spent correcting preventable medical errors or treating hospital acquired infections (OECD, 2017a).

Improving the efficiency of European healthcare is in the interest of many stakeholders, including governments, payers, providers, patients, and the life sciences industry. Identifying and reallocating inefficient spending allows for better care, greater access to innovative treatments, and superior outcomes within existing budgets. However, identifying specific inefficiencies is challenging, in part because it is usually difficult to know the 'counterfactual': what the costs and outcomes of an alternative strategy would have been. This challenge is magnified by the diversity of populations and health systems in Europe, from universal public systems to social or private health insurers, which makes direct cross-country comparisons more difficult.

To help address the challenge of improving efficiency in European healthcare, EFPIA commissioned the Office of Health Economics (OHE) and the Swedish Institute for Health Economics (IHE) to:

[3] *In this report, we refer to an aggregation of the EU and the UK as the EU27+UK.*

- Develop a comprehensive conceptual framework to define heath care inefficiencies;
- Generate actionable insights for policymakers by identifying clear examples of inefficiency;
- Estimate the scale of the potential savings and health gains that could be realised by addressing specific inefficiencies.

1.1 Overview of methods

This work was completed in sequential stages, as detailed in Figure 1.

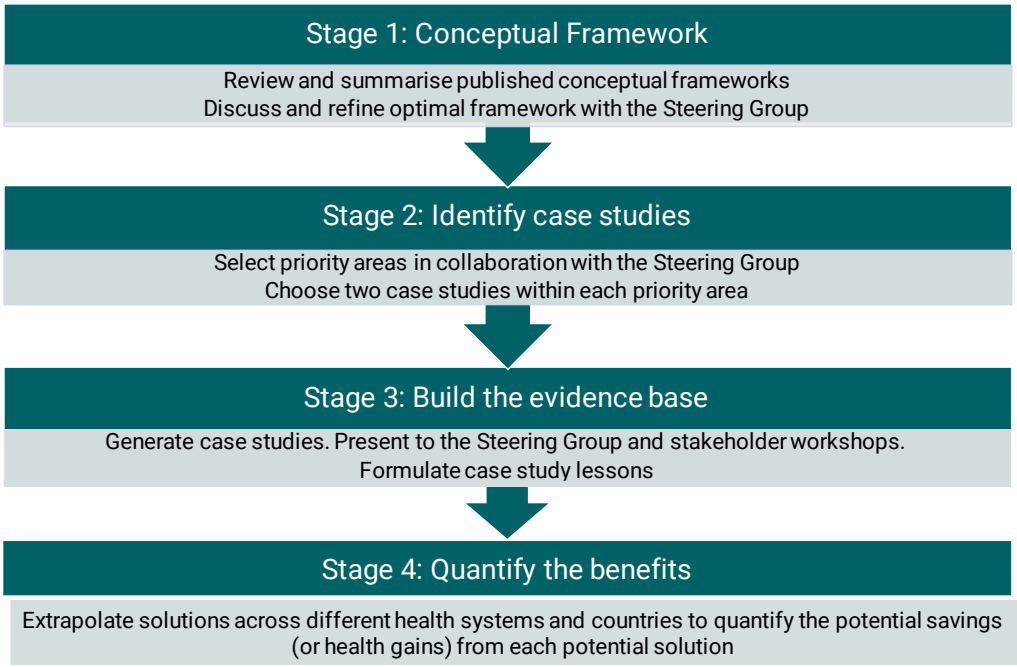

FIGURE 1: OVERVIEW OF METHODS

At each stage, key decisions were reviewed and approved by an external Steering Group of stakeholders. The Steering Group was a multi-national and multi-disciplinary group comprised of two representatives of patient organisations, one provider representative, one health management representative, two clinical representatives, and two industry representatives (one EFPIA representative and one member of the EFPIA Healthcare Systems Working Group). Members were identified in collaboration with EFPIA.

The review of conceptual frameworks was conducted via a literature search and presented to the Steering Group. The Steering Group then refined the frameworks to develop a comprehensive conceptual framework to define heath care inefficiencies. As part of stage 2, the Steering Group used the conceptual framework to generate a list of types of inefficiencies and areas in which inefficiencies can arise. From the full list, each Steering Group member was asked to vote for their top three priorities to explore further via case studies. The three areas which received the most votes were prioritised, and EFPIA (in collaboration with EFPIA Healthcare Systems Working Group) selected one additional topic.

Within each of the four priority areas, two case studies were identified by the Steering Group to highlight best practice by contrasting more successful and less successful examples of attempts

to improve the efficiency of healthcare delivery. Where the group were not aware of any case studies, the examples were identified via a targeted literature search. Each case study is based on published and grey literature relating to the study, plus interviews with a small number of key stakeholders involved in the organisation or implementation of the case study where possible. The two case studies in each area were designed to highlight more successful and less successful examples to enable key lessons to be identified. However, it should be noted that due to the heterogenous nature of the case studies, some are based on ongoing programmes, whilst others are historical, and the conditions under which each operates (including different populations and health systems) and their duration are very different, and therefore the more and less successful examples should not be considered to be directly comparable. Further, it is acknowledged that this process was not thoroughly systematic but was designed as a pragmatic process to suit the objectives of the project.

The case studies were supplemented by stakeholder workshops in Spain, Poland, the Netherlands, Germany, and Sweden, chosen to provide a broad overview of European experiences. Within the workshops, stakeholders from different backgrounds provided different perspectives. Clinicians provided information on incidence and prevalence, morbidity and mortality, and relevant data sources; policy makers provided feedback on the feasibility of specific case study recommendations based on their own policy experiences; patient representatives recounted their experiences (positive or negative) with different healthcare services. The workshops therefore fed directly into the case studies and the recommendations and results are not presented separately.

Stage 4 involved developing quantitative estimates of the potential efficiency gains associated with the cases previously discussed. The estimates were based upon the findings from the more successful case studies and extrapolated for each of the 27 EU Member States and the UK as well as to the aggregate European level (EU27+UK). These quantifications provide an indicative estimate of the scale of potential efficiency gains that could be realised, but they must be interpreted with some caution. Many of the cases were based on small trials (e.g. the Lean Sigma Six clinical surveillance programme in Italy), whilst in other cases the results are based on models rather than observed outcomes (e.g. colorectal cancer screening in the Basque Country, Spain). Finally, many of the health benefits and cost savings associated with these interventions will only be realised in the future (e.g. the full cost and survival benefits of colorectal cancer screening will accrue over a 30-year period). Further detail on the methods is provided in Chapter 4.

1.2 This report

In section 2 we describe in more detail the concepts of efficiency and inefficiency, particularly in the context of healthcare, and describe the development of a conceptual framework for considering inefficiencies in healthcare and the identification of priority areas with high potential for efficiency gains. In section 3, the methods and results of a series of case studies is presented, contrasting alternative approaches to specific healthcare challenges in the identified priority areas and highlighting lessons for improving efficiency in these areas. In section 4, we present estimates of the potential cost savings and/or health gains, by country and Europe-wide, that could be realised by adopting the best practices identified by the case studies. Finally, in section 5, we present specific policy recommendations and conclusions around promoting efficiency in European healthcare.

2 Considering efficiency in healthcare

2.1 Conceptualising efficiency

In economic terms, **efficiency** describes how well inputs (i.e. physical or financial resources) are converted into valuable outputs. If one process generates a greater amount of outputs with the same amount of inputs than an alternative process, it is **more efficient**. A process can also be more efficient if it produces the same amount of outputs with fewer inputs than an alternative process. Conversely, a process that requires more inputs than an alternative process to produce the same amount of resources is described as **less efficient** or **inefficient**. The relationship between relative inputs, outputs and efficiency is shown in Table 1.

TABLE 1: THE RELATIONSHIP BETWEEN INPUTS, OUTPUTS AND EFFICIENCY

		Outputs/outcomes		
		Lower	**Same**	**Higher**
Inputs	**Lower**	Ambiguous	More efficient	Much more efficient
	Same	Less efficient	Efficiency unchanged	More efficient
	Higher	Much less efficient	Less efficient	Ambiguous

Efficiency improves when inputs decline or outputs increase, holding the other constant. The change in efficiency is ambiguous when inputs and outputs increase or decrease together.

In healthcare, inputs are financial or medical resources, whilst outputs are positive health outcomes. Healthcare is efficient if it minimises ("avoids") unnecessary expenditure, morbidity or mortality. In the context of Table 1, avoiding unnecessary expenditure can be seen reducing inputs, whilst avoiding unnecessary morbidity and mortality can be seen as increasing positive health outcomes.

The focus on "avoidable" events in healthcare dates back to at least the early 20th century in the UK, when efforts were made to identify medical errors that led to preventable maternal deaths (Holland, 2009). The notion of avoidable was refined by Rutstein et al. (1976) in distinguishing between "amenable deaths" and "preventable deaths". A death is "amenable" if it could have been avoided with optimal healthcare. "Preventable death" is broader and includes deaths which could have been avoided with public health interventions that address behaviour and lifestyle factors, socioeconomic status, or environmental factors. Consideration of efficiency in healthcare tends to focus on "amenable" factors and has been extended to include indicators such as adverse outcomes and excess healthcare utilisation or expenditure, in addition to mortality.

A recent development in the consideration of efficiency in healthcare has been the notion of "low-value care". Such care is not associated with conventional avoidable morbidity or mortality, but rather is defined as "*an intervention where evidence suggests it confers no or very little benefit on patients, or risk of harm exceeds likely benefit, or, more broadly, the added costs of the intervention do not provide proportional added benefits.*" (Scott and Duckett, 2015). In efficiency terms, it represents expenditure with very little resulting output. Low-value care can be a controversial

concept, as few clinical interventions are of absolutely *no* value, and efforts to label interventions as being so will be met with professional resistance. If a certain intervention has stood the test of time, and conferred benefit on some patients with no safety concerns, abolishing such an intervention might be difficult in clinical practice (Scott and Duckett, 2015).

To encourage the provision of the highest-value care, the American Board of Internal Medicine (ABIM) has launched the 'Choosing Wisely initiative'[4]. As of September 2019, this initiative lists over 600 recommendations on services that can be characterised as low-value care.

The European Commission (2010) has defined efficiency in healthcare in terms of how resource inputs such as labour (physicians, nurses, and other health staff), capital (hospitals, health centres) or equipment (e.g. MRI units) relate to outputs (e.g. number of patients treated/discharged, waiting time for specific interventions) and final health outcomes (e.g. changes in health status of the population that can be attributed to public spending on health). It notes that efficiency in healthcare "*corresponds to the economic notion of cost-effectiveness and the popular notion of value for money*" (European Commission, 2010).

2.2 Categorising inefficiency

The Organisation for Economic Cooperation and Development (OECD) developed the framework depicted in Figure 2 (OECD, 2017b) to illustrate different types of healthcare inefficiency, their drivers and the relevant actors. The categories of inefficiency it describes include governance related waste, operational waste and wasteful clinical care, and stem from drivers ranging from poor decision making to deliberate fraud or deception.

FIGURE 2:TACKLING WASTEFUL SPENDING ON HEALTH: A CONCEPTUAL FRAMEWORK
Source: Adapted from OECD (2017b)

> ***Wasteful clinical care*** *(or low-value care) occurs when patients receive ineffective and/or inappropriate care. This includes preventable clinical adverse events and unnecessary duplication of services driven by errors, suboptimal decisions and organisational factors, particularly poor co-ordination across providers and poor incentives.*
>
> ***Operational waste*** *occurs when care could be produced using fewer resources within the system while maintaining the benefits. Examples include situations where lower prices*

[4] https://www.choosingwisely.org/

could be obtained for the inputs purchased, where costly inputs are used instead of less expensive ones with no benefit to the patient, or where inputs are discarded without being used. This type of waste mostly involves managers and reflects poor organisation and co-ordination.

***Governance-related waste** pertains to use of resources that do not directly contribute to patient care, either because they support the administration and management of the healthcare system or because they are diverted from their intended purpose through fraud, abuse and corruption. Administrative waste can take place from the micro (manager) to the macro (regulator) level and is driven primarily by poor system organisation and co-ordination. Fraud, abuse and corruption can involve any of the actors and is distinguished from other types of waste by an intention to deceive.* (OECD, 2017b)

The PricewaterhouseCoopers' Health Research Institute (2008) propose three similar "baskets" of healthcare waste or inefficiency:

1. **Behavioural**, including obesity, smoking, non-adherence, and alcohol abuse;

2. **Clinical**, including defensive medicine, preventable hospital readmissions, poorly managed diabetes, medical errors, unnecessary Emergency Room (ER) visits, treatment variations, hospital acquired infections, over-prescribing antibiotics; and

3. **Operational**, including claims processing, ineffective use of IT, staffing turnover, paper prescriptions.

They estimate that these three baskets represent about half of all U.S. healthcare spending and are largely avoidable. They also note, however, that factors such as culture, politics, funding and incentives, and a lack of a coordinated focus represent formidable barriers to eliminating this spending.

Finally, Berwick and Hackbarth (2012) propose six categories of waste: overtreatment, failures of care coordination, failures in execution of care processes, administrative complexity, pricing failures, and fraud and abuse. They estimate that spending in these categories exceeds 20% of total healthcare expenditures in the U.S. in 2011.

An expert interview undertaken for this study[5] provides useful insight on distinguishing between economic concepts of efficiency and the more pragmatic notions of waste described in the conceptual framework above. In the interviewee's view, efficiency expresses the relationship between inputs and outputs of a particular programme. The idea of "waste", on the other hand, describes instances where healthcare resources are allocated to services and processes that are harmful or do not deliver benefits. In this sense, 'efficiency' can be seen as a relative concept whereas 'waste' is more absolute. In the expert's view, the notion of "waste" (which embeds a negative value judgement) may be a more effective term for bringing inefficiencies to the attention of policymakers.

2.3 Refinement of the conceptual framework

The Steering Group discussed the conceptual frameworks and agreed the OECD framework was the most comprehensive and the most relevant to this project. However, they recommended

[5] Federico Pratellesi (DG Health and Food Safety) was speaking on personal behalf and not on behalf of the European Commission. Interviews were undertaken as part of the case studies (see Chapter 3).

some refinements to make it more specific and actionable. Their suggested amendments included:

- Extending the definition of unintentional inefficiency to include insufficient prevention, so as to capture the impact of suboptimal immunisation and other preventative initiatives.
- Extending the actors to include all persons, not just patients, to account for suboptimal primary prevention activities.
- Combining "Paying an excessive price" and "Overusing high-cost inputs" into a single concept of "Overuse and Unnecessary use of high-cost inputs"

The adapted conceptual framework is shown in Figure 3 below and was used to inform the identification of priority areas for the case studies, presented in the next section.

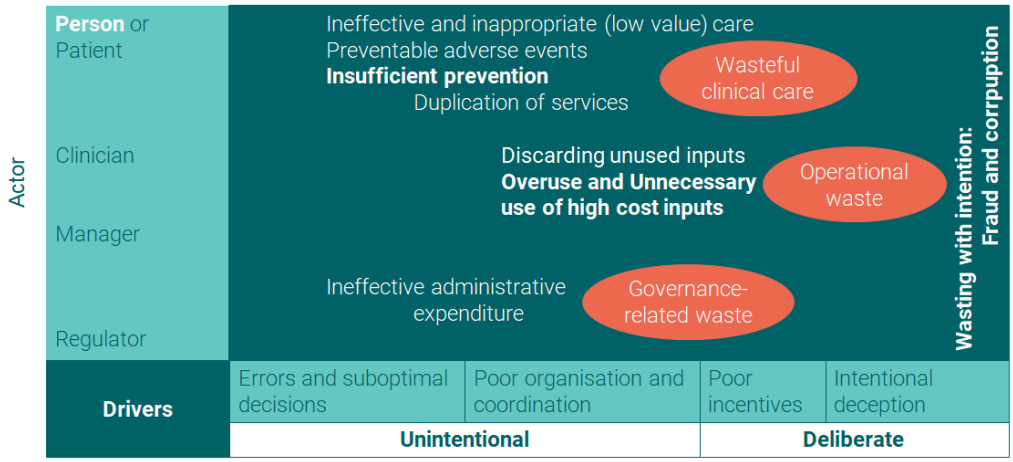

FIGURE 3: REVISED CONCEPTUAL FRAMEWORK OF WASTE AND INEFFICIENCY.
Adapted from OECD 2017; revisions shown in bold white.

3 Case studies

Screening, coordination of care and healthcare associated infections were chosen as priority areas by the Steering Group, whilst EFPIA selected rational use of medicines as an additional topic to ensure there was sufficient focus on areas in which industry can play a key role in reducing healthcare inefficiencies.

1. **Screening**: Early diagnosis and treatment of diseases, especially cancer, is a priority worldwide. Already in 2003, the Council of the European Union had issued recommendations to Member States setting out best practice in the early detection of cancer. More recently, the new European Commissioner for Health Stella Kyriakides was tasked in her mission letter with the development of Europe's Beating Cancer Plan to support Member States to improve both cancer prevention and care. Within early diagnosis, screening for the early detection of colorectal cancer was selected as a case study because it is one of the most prevalent types of cancer, and leading causes of cancer deaths, across European countries (Portillo et al., 2018). Indeed, low participation in screening may lead to preventable colorectal cancer-related costs and deaths. A screening programme implemented in the Basque Country in Spain is presented as a successful example of increasing increased efficiency in screening, whilst a programme in Paris, France is presented as a less successful example.

   The literature review has been complemented by interviews with two local experts: Maria Isabel Portillo, for the Basque Country Colorectal Cancer Programme, and Marc Bardou, for the Colorectal Cancer Parisian Programme[6].

2. **Coordination of care**: The cost of non-communicable diseases, including cardiovascular diseases, cancers, respiratory diseases and diabetes, is substantial, accounting for up to €115 billion, or 0.8% of EU27+UK GDP (OECD/EU, 2016). Much of these costs stem from inadequate disease management. Better care coordination can avoid failures in monitoring and long-term treatment adherence that impose avoidable costs and morbidity or mortality. Two coordination of care cases, capturing the two types of non-communicable diseases (chronic and not chronic) are considered:

   i. In the first case, two **disease management programmes (DMPs)** in chronic obstructive pulmonary disease (COPD) are contrasted, with an emphasis on healthcare utilisation and patient mortality. COPD is a common cause of hospitalization and a leading cause of death (Bourbeau et al., 2019). As an example of effective practice, we consider a DMP for COPD trialled in France, Germany, Italy, and Spain; a real-world DMP for COPD in Germany provides a study of a less successful programme.

   ii. In the second case, two **standardised patient pathways (SPPs)** intended to improve consistency and access to cancer care in Denmark and Sweden are contrasted. Both countries had regional variability in access to cancer care and

[6] *Mrs. Portillo, is the Manager of the Colorectal Cancer Screening Programme in the Basque Health Service (Osakidetza). Mr. Bardou, is the Medical Coordinator at CIC1432, and Staff Member of the Gastroenterology and Liver Department at the CHU Dijon Bourgogne.*

the SPPs are intended to reduce regional inequities as well as to improve survival and patient satisfaction with their care.

3. **Rational use of medicines**: Polypharmacy, often defined as the concurrent use of 5 or more medicines (Masnoon et al., 2017; World Health Organisation, 2019), is prevalent amongst the elderly. Promoting the rational use of medicines through medication review provides an opportunity to both reduce unnecessary costs and reduce the risk of unintended adverse drug interactions. We contrast medication review programmes in Scotland, UK, and Lower Saxony, Germany, as examples of more and less successful interventions.

4. **Healthcare-associated infections**: Healthcare-associated infections (HCAIs) are associated with nearly 50,000 preventable deaths in Europe each year and can add between €5,000 and €11,000 to the cost of a hospital admission. We contrast two approaches to reducing the incidence of HCAIs. The Lean Six Sigma Programme in Naples, Italy, provides an example of best practice, whilst a surveillance programme amongst healthcare professionals in Germany provides a less successful case.

   The Italian case study is complemented by interviews with local experts Giovanni Improta and Alfonso Ponsiglione.[7]

Table 2 below provides an overview of the case studies, while the full cases are presented in the following sections. The estimations of potential efficiency gains for each case are presented in section 4.

[7] *Giovani Improta is a Researcher in Biomedical Engineering at the Department of Public Health of the School of Medicine and Surgery of the University of Naples Federico II. Alfonso Ponsiglione is Ph D in "Industrial Product and Process Engineering" at the University of Naples Federico II.*

TABLE 2: SUMMARY OF THE CASE STUDIES

Priority area	Source of inefficiency	Country [study date]	Key features	Key actors	Impact on efficiency	Sources of information
1. Screening						
Colorectal cancer screening	Low participation in CRC screening, leading to preventable CRC-related costs and deaths.	Spain (Basque Country) [2009]	People aged 50-69 years and without a previous diagnosis of CRC, terminal illness, or a history of colonoscopy in the past five years, identified biennially and mailed a faecal immunological test (FIT) kit.	Primary care physicians; oncology specialists; coordinating office staff; patients.	• Average **participation rate** (**72% of the invited population)** following initiation of organised screening. • High **adherence to colonoscopy** after positive FIT (**more than 92%** compared to 70% in other programmes). • Projected **reduction of colorectal cancer incidence by 16% and mortality by 26.1%** (over a 30-year time horizon) and **increase in survival rates** (90% if diagnosed at stage 1 versus 10% survival if diagnosed at stage 4). • Projected **net savings of €93 million** (over a 30-year time horizon) associated with better health outcomes and lower utilisation of healthcare resources. • **Strong, positive impact on efficiency, with improved health outcomes and reduced costs.**	Arrospide et al. (2018); Idigoras et al. (2018); Portillo et al. (2018); Interview with Maria Isabel Portillo
		France (Paris) [2016]	People aged 50-74 years identified biennially and invited to collect a FIT kit from their physician.	Primary care physicians; oncology specialists; social workers; coordinating office staff; patients.	• Average **participation rate of 32% of the invited population** following initiation of organised screening: no significant increase on past rates, and well below minimum target participation levels according to European Guidelines. • High **adherence to colonoscopy** after positive FIT (**over 80%**). **Costs increased** following introduction of the programme, primarily due to contacting large numbers of persons who ultimately did not participate in screening. • **Overall, negative impact on efficiency as costs increased with no effects on outcomes.**	Pellat et al. (2018); Moutel et al. (2019); Lejeune et al. (2014); Interview with Marc Bardou

2. Coordination of care						
A. Patient management programme in COPD	Poor management of COPD leads to avoidable hospitalisations and mortality	France, Germany, Italy, Spain [2010–2015]	Patients with COPD enrolled on home-based disease management programme with support from coaches (nurses).	Patient, coaches (nurses).	• **23% reduction in all-cause hospital days** in treatment arm compared to control arm. • **87% reduction in mortality** in treatment arm compared to control arm. • **Statistically insignificant cost increase of €37 per patient** in treatment arm compared to control arm, ranging from €319 to €806. • **Overall, improved efficiency as health outcomes improved with no significant increase in costs.**	Kessler et al. (2018); Bourbeau et al. (2019)
		Germany [2005]	Patients with COPD enrolled on GP-coordinated disease management programme following evidence-based clinical guidelines.	Primary care physicians, sickness funds, Federal Joint Committee (G-BA).	• **7% increase in all-cause hospital admissions** in treatment arm compared to control arm. • **11% reduction in mortality** in treatment arm compared to control arm. • **Mixed results on morbidity**: decrease in depressive episodes but increase in medication-induced osteoporosis and non-invasive ventilation. • **Additional costs of €553 per patient** per year due to higher healthcare utilisation. • **Ambiguous overall effect on efficiency as costs and positive health outcomes increased.**	Achelrod et al. (2016)
B. Standardised Patient Pathways in Cancer	Variability in wait times and treatment leading to sub-optimal outcomes for cancer patients.	Denmark [2007–2008]	Standardised patient pathways (SPPs) spanning the whole care pathway (diagnostics, treatment and clinical control).	Patient organisations, healthcare providers, healthcare professionals, government, health authorities.	• **35% decrease in waiting times** from GP referral to start of treatment after introduction of SPPs. • **Lower one-year excess mortality**, but **no significant change in 1-year or 3-year survival** following introduction of SPPs. • **Additional initial costs of around €31 per capita** (across entire Danish population). • Suggestion that focus on cancer waiting times **'crowded out'** diagnosis/treatment of other diseases. • **Ambiguous impact on efficiency as costs and waiting times both improved; no impact on survival rates.**	Probst, Hussain and Andersen, (2012) ; Jensen et al., 2015; Jensen, Tørring and Vedsted, 2017

		Sweden [2015– 2018]	SPPs spanning from diagnostics to first treatment.	Healthcare providers, healthcare professionals, government, health authorities, patient organisations.	• **Some reduction in waiting times** after introduction of SPPs (for example a 17% reduction in time to treatment for prostate cancer) but reductions did not achieve targets. • **Effect on survival not evaluated**. • **Additional initial costs of around €19 per capita** and **subsequent costs of around €2 per capita** per year (across entire Swedish population). • As in Danish case, suggestion that focus on cancer waiting times **'crowded out'** diagnosis/treatment of other diseases. • **Negative impact on efficiency as there was an increase in costs with no corresponding improvement in wait times; no evidence around improvements in outcomes.**	National Board of Health and Welfare (Socialstyrelsen), 2019a, 2019b, 2019c
3. Rational use of medicines						
Review of polypharmacy in the elderly	Polypharmacy increases possibility of adverse drug-drug and drug-disease interactions and may involve treatment with unnecessary drugs.	Scotland (UK) [2012]	Guidelines on medication review in patients with polypharmacy for use by pharmacists or physicians in the community, care homes and primary care.	Community pharmacists and physicians.	• **Reduced proportion of patients on harmful combinations of medicines** and net reduction in average medicines per person after introduction of guidelines (although no studies of effectives on morbidity and mortality to date). • **Reduction in adverse drug reaction related hospitalisations** leading to an estimated **saving of €1.24 million per year** on treating patients with polypharmacy. • Estimated **net cost savings of €9 to €232 per polypharmacy patient** per year following introduction of guidelines. • **Strongly positive impact on efficiency as intervention was associated with improved health outcomes and net cost savings.**	Scottish Government Polypharmacy Model of Care Group (2018); Mair, Wilson and Dreischulte, 2019
		Lower Saxony (Germany) [2013]	Medication review in patients with polypharmacy.	Community pharmacists.	• **Low uptake** due to undervaluation of pharmacist time and out-of-pocket costs to the general population: there were 2000 reviews over 4 years in a region of 35 million people. • **No meaningful impact on efficiency.**	McIntosh, Alonso and Codina (2016); Seidling et al. (2017)
4. Healthcare-associated infections						

Reduction of hospital-acquired methicillin-resistant Staphylococcus Aureus (MRSA) infections	Avoidable infections increase patients' length of stay and require additional treatment.	Italy [2011]	Clinical surveillance programme to reduce Health Care Associated Infections (HCAIs) in hospital using Lean Six Sigma methodology.	Healthcare professionals; patients; policy makers; engineers; members of the Hospital Infection Committee.	• **>40% reduction in the number of patients contracting HCAIs** after introduction of programme. • **20% reduction in the mean length of hospital stays** after introduction of programme • Cost estimates not available for this study, but similar approaches in comparable settings have been associated with a **43% decrease in costs** (Iannettoni et al., 2011). • **No cost estimates available, but a reduction in negative health outcomes would be associated with an improvement in efficiency even with no reduction in costs. Any cost savings would strengthen the efficiency gains.**	Bender et al. (2015); Gijo and Antony (2014); Improta et al. (2018); Iannettoni et al. (2011); Mason, Nicolay and Darzi (2015); Montella et al. (2017); Hudson et al., (2013); Interview with Alfonso Ponsiglione and Giovanni Improta
		Germany [2009]	Clinical surveillance programme to reduce Health Care Associated Infections (HCAIs) in hospital using international evidence-based guidelines.	Healthcare professionals and administrators.	• **Slight increase in the number of patients contracting HCAIs** after programme • **Additional costs** attributable to healthcare–associated infections in Germany have been estimated in **€5,823-€11,840 per infected patient** • **Negative impact on efficiency as outcome worsened following the intervention.**	Arefian et al. (2019), Arefian (2016); Schönfeld et al. (2018)

Abbreviations: CRC, colorectal cancer; FIT, faecal immunological test; COPD, chronic obstructive pulmonary disease; SPPs, standardised patient pathways; HCAI, Health Care Associated Infection.

3.1 Priority area 1: Colorectal cancer screening

Early diagnosis and prompt initiation of appropriate treatments have been shown to reduce the number of preventable deaths in many diseases, including cancer (World Health Organization, 2017). Conversely, delays in diagnosis are associated with a greater number of preventable deaths and, by definition, greater inefficiency. Figure 4 illustrates how delays in the diagnosis of colorectal cancer (CRC) can result in more advanced disease at diagnosis and a greater number of preventable deaths. This pathway illustrates an important source of inefficiency in healthcare (Hiom, 2015).

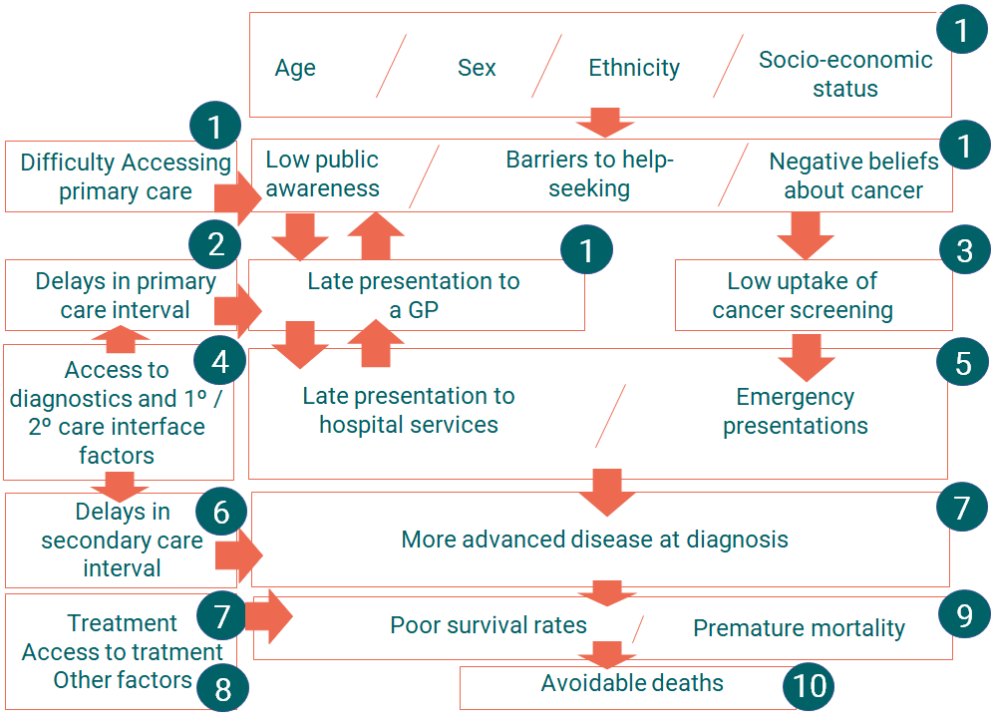

FIGURE 4: DIAGRAM OF THE LINK BETWEEN DELAYED DIAGNOSIS AND AVOIDABLE DEATHS
Source: Adapted from Hiom et al. (2015)

In general, there are two approaches to population screening (Miles et al., 2004):

- *Organised systems*: invitations to screening are issued using registered and centralised data.
- *Opportunistic systems*: invitations are conditional on an individual's decision or on visits to healthcare providers.

Compared with opportunistic systems, organised screening for early detection of colorectal cancer shows better results in improving screening participation (Eisinger et al., 2008; Senore et al., 2015), reducing disparities in screening uptake (Eisinger et al., 2008) and minimising harms such as over-screening, low quality screening, and screening-related complications (Levin et al., 2011). A recent study in the context of human papillomavirus screening showed that an organised programme was less costly and more effective in terms of coverage than an opportunistic cytology screening programme (Diaz et al., 2018). Indeed, the opportunistic programme was characterised by over-screening of low-risk populations and very low rates of screening among higher risk groups.

The following cases relate to organised screening programmes for colorectal cancer (CRC). CRC is the second most frequent cause of cancer mortality in Europe, associated with 16% of total cancer deaths (Ferlay et al., 2013). Many of these deaths, though, are preventable with early detection. The case studies contrast organised screening programmes in the Basque Country of Spain and Paris, France. The Basque experience has been effective in screening high-risk populations and has resulted in overall cost-savings and system efficiencies, whilst the French experience has been less successful in terms of coverage and cost-savings. As noted previously, the context in which these two programmes operated were different, and as such they are not directly comparable.

3.1.1 More successful case: Colorectal cancer screening in the Basque Country, Spain

Prior to the introduction of an organised screening programme, colorectal cancer was a problem in the Basque Country, with high incidence and mortality rates. In 2008, the year before the programme started, there were 642 cases and 286 deaths among women and 1,227 cases and 504 deaths among men (Izarzugaza et al., 2010).

The Basque Country introduced an organised screening programme in 2009 based on European Surveillance Guidelines (Council of the European Union, 2003), targeting individuals aged between 50 and 70 years of age. Only 10% of CRC cases are diagnosed before age 55 (Kolligs, 2016; Center, Jemal and Ward, 2009). The programme uses faecal immunochemical testing (FIT) to detect microscopic bleeding from adenomas, or preclinical CRC, followed by confirmatory colonoscopy tests where indicated. The FIT kit is posted to eligible persons aged 50 to 69 years old, at no cost to them. The healthcare system covers all the associated costs of the programme, including the kit, the colonoscopies, and the treatment for those who are diagnosed with CRC.

The design of the programme took into account the expected incidence in the different health areas of the Basque Country and the colonoscopy capacity of local hospitals in these areas. This ensured that hospitals would be able to manage the daily demand for colonoscopies. If demand exceeds the capacity to deliver, the implementation of screening programmes will be difficult (Arrospide et al., 2018). A coordinating office, which included epidemiologists and statisticians, planned, organised and evaluated the programme. To ensure appropriate targeting of the population to be screened, individuals between the ages of 50 and 70 were identified by their coordinating office and their records linked to the Basque population cancer database and medical procedure registries. This made it possible to exclude individuals previously diagnosed with CRC, terminal illnesses, or those who reported having a colonoscopy in the past five years. The same coordinating office also registered all negative FIT tests in each call for screenings to invite these individuals to participate in the next call in two years (Idigoras et al., 2018).

Programme results and impact on efficiency

In total 924,416 people were invited between 2009 and 2013, reaching almost all of the target population by the beginning of 2014 (Idigoras et al., 2018), with participation rates increasing from 58.1% to 70.3% and 95.8% across the first, second and third invitations.

An evaluation of the screening programme in 2013 (Portillo et al., 2013) reported the following outcomes:

- An average participation rate of 72% of the population invited to participate;
- Average wait times for a colonoscopy of 30 days or less;
- Follow-up with colonoscopy after positive FIT was more than 92% in all years of the study (compared to 70% in other programmes);

- Detection rates for advanced adenoma and CRC of 23.9% and 3.4%, respectively.

Costs associated with the Basque CRC screening programme were estimated based on the MISCAN-Colon simulation model (Arrospide et al., 2018) over a time horizon of 30 years. The model simulated the remaining life expectancy of the invited screening population, applying observed rates of incidence and mortality and variation in health outcomes, and estimated expected costs with and without an organised CRC screening programme.

Over a 30-year time horizon, the total costs for screening, diagnostic follow-up, surveillance and treatment were estimated to be €2.1 billion. However, screening was associated with a reduction in CRC incidence and treatment costs, resulting in net cost savings of €93.1 million compared to a no-screening scenario (Arrospide et al., 2018). Thus, the organised screening programme was dominant (less costly and more effective) relative to no screening at an expected cost per invitation of €6.06. Sensitivity analyses, summarised in Table 3, show that this dominance holds up to a cost of €20.00 per invitation, more than three times the baseline cost per invitation.

TABLE 3: COST-EFFECTIVENESS SENSITIVITY ANALYSIS OF THE IMPLEMENTATION OF CRC SCREENING IN THE BASQUE COUNTRY DURING 2009-2014
Source: Arrospide et al. (2018)

		Screened population costs		Incremental costs		QALYs gained	ICER
Cost per invitation	**Adenoma prevalence**	**Treatment cost**	**Total costs**	**Treatment cost**	**Total costs**		
€6.06 per invitation	Base case						
	Men	1,199.90	1,317	-179.1	-81.7	37,132.50	Dominant
	Women	664.2	740.2	-77.1	-11.4	19,532.30	Dominant
	Total	1,864.10	2,057.20	-256.3	-93.1	56,664.80	Dominant
	Prevalence Bibliography						
	Men	1,227.50	1,318.90	-168.6	-97.2	36,616.90	Dominant
	Women	661	726.9	-77.6	-21.8	20,438.50	Dominant
	Total	1,888.50	2,045.70	-246.2	-119	57,055.40	Dominant
€15.00 per invitation	Base case -Total	1,864.10	2,103.20	-256.3	-41.1	56,664.80	Dominant
€20.00 per invitation	Base case - Total	1,864.10	2,128.90	-256.3	-21.4	56,664.80	Dominant
€25.00 per invitation	Base case - Total	1,864.10	2,154.60	-256.3	4.2	56,664.80	74.1
€30.00 per invitation	Base case - Total	1,864.10	2,180.30	-256.3	30	56,664.80	529.4
€40.00 per invitation	Base case - Total	1,864.10	2,231.80	-256.3	81.5	56,664.80	1,438.30
€50.00 per invitation	Base case - Total	1,864.10	2,283.20	-256.3	132.9	56,664.80	2,345.40

ICER incremental cost effectiveness ratio

The authors note that savings due to reduced CRC incidence take time to materialise, so in the early years of the programme the costs of screening exceed savings due to cases avoided. They estimate a 10-year lag between the implementation of organised screening and realisation of savings. However, once a 'steady state' is achieved, the MISCAN-colon simulation model predicted the following outcomes:

1. A reduction in incidence of 16.3% (17.2% for men, and 14.7% for women);

2. A reduction in CRC-related mortality of 26.1% (28.1% for men, and 22.4% for women);

3. A reduction in years of life lost due to CRC of 21% (22.6% for men and 18.4% for women).

The model predicts stable net savings of €73.4 million from 2023 onwards, and an average of 18,843 colonoscopies per year from 2029 to 2038. This number of colonoscopies is within the existing capacity of the Basque Health Service, so no delays in diagnosis are expected.

In the stakeholder interviews, Dr. Portillo suggested that efficiencies from organised screening could be measured by the increase in participation rates and the consequent reduction of the incidence and mortality for this type of cancer. It is, though, too early to evaluate these outcomes (note that the 30-year benefits presented here are modelled rather than actual).

3.1.2 Less successful case: Colorectal cancer screening in Paris, France

Colorectal cancer is the third most common cancer in France, with more than 40,000 new cases in 2012 (Ferlay et al., 2013), and the second most common cause of cancer mortality. According to Marc Bardou, CRC is a public health problem that affects everyone; it can have extremely bad consequences for the patient and high costs due to the use of healthcare resources and productivity losses.

France has had a nationwide organised CRC screening programme since 2009 with the aim of identifying individuals with advanced adenomas and/or early cancer. Before 2009, screening for CRC was opportunistic. Initially, each department managed its own programme but now it is managed by regions. Variabilities remain, but since 2015 the programme has been implemented in a more consistent and centralised manner.

The redesigned CRC screening programme in the Paris region is the focus of this case study. The target population for the Parisian screening programme was asymptomatic adults aged 50 to 74 years-old, enrolled in the Parisian health insurance scheme and not participating in an opportunistic CRC screening programme. This included 620,227 individuals (around 28% of the population in 2014). Under the programme, targeted individuals were contacted and invited to collect a faecal immunological test (FIT) kit from their physician.

Programme results and impact on efficiency

Since the 2015 redesign of the Parisian screening programme, the participation rate has been in the range of 30-35%, substantially below the 65% that European Guidelines define as desirable as well as below the 45% that is considered as a minimally acceptable rate (Segnan et al., 2010). Despite efforts, no significant improvements in participation rates have been seen since 2014 and the current programme has had no substantive impact on participation.

Detection rates for adenomas, advanced adenomas and CRC were 4.3, 8.3 and 2.3 per 1,000 persons, respectively, which were substantially lower than the detection rates observed in the Basque Country. It is difficult to accurately estimate the rate of colonoscopies being performed under opportunistic screening, but the best estimate is around 10% (source: expert interview). For FIT positives, participation rate in colonoscopies was above 70% but the mean time to colonoscopy was 74.5 days, compared to a recommended time of 31 days.

Screening 100,000 individuals aged 50–74 years using immunochemical tests, every two years for 20 years, is estimated to cost around €75 million (Moutel et al., 2019). The fixed costs of producing and distributing the test kits make up 6% of the total cost (Lejeune et al., 2014). If the participation is low, the impact on mortality is also low and the cost per life saved is high. Greater participation spreads the fixed costs over a larger population and improves outcomes and overall efficiency.

3.1.3 Case study lessons: Colorectal cancer screening

The Basque screening programme achieved higher rates of participation and detection rates, and these detection rates translated into cost savings of €93 million and a decrease in CRC mortality, improving system efficiency. The Parisian programme achieved much lower participation and detection rates.

A key difference between the programmes was that the Basque invitation included the FIT kit (Zubero et al., 2014), whereas the Parisian invitations asked recipients to visit their GP to collect the kit. This additional burden disincentivizes participation. A key lesson is that participation in the screening programme should be made as simple as possible.

The main challenge for both programmes is increasing participation of the most vulnerable groups. This encompasses difficulties in changing cultural, lifestyle, and socio-economic factors, fears of negative results, and a feeling of being healthy despite early-stage CRC (Chapple et al., 2008). A lack of awareness of increasing age-related risk (Institut de Veille Sanitaire (InVS), 2019) and mortality (Gimeno García, 2012; Institut National du Cancer, 2016) also contributes to lower participation rates. Low socioeconomic status is generally correlated with lower participation in screening programmes (Whynes et al., 2003; Molina-Barceló et al., 2011), but this does not seem to be a key driver in France as stakeholder interviews suggest similarly low participation rates in more and less wealthy areas (source: interview with Marc Bardou).

It is important to note that although screening can reduce avoidable deaths and improve healthcare efficiency, screening itself can be associated with inefficiencies if the screened population is too broad or too low-risk, resulting in a high number of false-positive tests than can overwhelm treatment pathways. Low uptake by patients can also lead to inefficiencies if it means the resources invested in identifying and contacting at-risk individuals are essentially wasted. There is a limit, therefore, to how broadly a screening programme should be targeted. The Basque programme provides an example of how linking of patient data can prevent resources from being wasted on patients whose medical history makes screening inappropriate.

The key lessons that can be drawn from contrasting the Basque and Parisian organised screening programmes are detailed below:

- Make participation as simple as possible. The Basque programme, like programmes in The Netherlands and Flanders (Belgium), included the FIT kit with the invitations and made it as easy as possible for recipients to return a sample. The Parisian programme, in contrast, required individuals to collect the kit from their GP. This extra step is likely to have discouraged participation. Paris has already decided to include the kit with the invitation, but only for those individuals considered at greater risk of not participating. This includes: 1) individuals who did not participate in the first invitation; and 2) individuals who have previously participated in CRC screening.

- Build on networks that are already in place, such as regular neighbourhood meetings, or working with existing associations. From interviews conducted as part of the case study, we know that efforts are already being made in Paris to involve more primary care professionals, allowing them to provide as much information as possible to individuals in the target demographics who may be visiting primary care facilities for other reasons. Expert interviews highlighted the importance of educating and involving stakeholders such as patients' organisations, primary care professionals, journalists, politicians and other community leaders.

- Maximise avenues of communications. Information campaigns could be of greater impact if using celebrities or other well-known individuals. The use of social media to promote screening was also suggested. Another aspect to consider is qualitative research with non-participants to understand their reasons for not participating. This understanding could be used to improve

information campaigns. For example, ensuring appropriate targeting strategies could help prevent obstruction due to an excessive demand of some services. If these are expensive services, this might also substantially reduce healthcare utilisation costs.

3.2 Priority area 2A & 2B: Disease management and patients' pathways

The direct and indirect costs of chronic diseases are substantial. The direct healthcare costs associated with chronic conditions account for 70-80% of total EU26+UK healthcare expenditure (Economist Intelligence Unit, 2012), or more than €1 trillion in 2017, and indirect costs of lost productivity associated with chronic conditions can represent up to 7% of GDP for some countries (Suhrcke et al., 2006). Much of these costs stem from inadequate management of chronic diseases such as cardiovascular diseases, chronic obstructive pulmonary disease (COPD), cancer and diabetes, which require long-term monitoring and ongoing adherence to treatment. Failures in monitoring and adherence impose avoidable costs on healthcare systems in the form of unplanned outpatient visits and hospital admissions. Effective disease management and treatment coordination can avoid these events, reducing costs and improving patient outcomes.

Disease management programmes (DMPs) are a means to help patients with chronic diseases maintain treatment and thus avoid costly outpatient visits and hospital admissions, increasing overall healthcare efficiency, whilst standardised patient pathways (SPPs) are a means to improve the structure and consistency of the patient pathway by clearly defining all necessary steps to be taken in diagnosis and treatment.

Poor coordination of cancer care is a prime example of inefficiency in healthcare systems. There are many different steps involved in the initial examination and treatment of cancer (diagnostic testing, surgery, radiation therapy, chemotherapy, adjuvant care) and these steps might be repeated or occur in different sequence for different patients. The diagnosis and treatment of cancer can also involve a range of healthcare professionals, including primary care physicians, surgeons, radiologists, oncologists, and pathologists, who may work in different units or locations. Poor coordination of care can lead to long waiting times, missed examinations, and unnecessary or duplicated tests and treatments, all of which may increase costs and reduce the likelihood of a positive survival outcome.

In the next sections we contrast DMPs for COPD and SPPs for cancer. The DMP cases describe: 1) a trial involving patients in France, Germany, Italy, and Spain, and 2) real-world practice in Germany. The first case shows the introduction of a DMP is associated with improved health system efficiency in the form of improved health outcomes and a small reduction of costs, whilst the second case is more ambiguous in terms of efficiency, with improved outcomes and increased costs. The SPP cases contrast cancer diagnosis pathways as implemented in Denmark and Sweden. As before, we note that the two case studies are not directly comparable due to the different contexts in which they operated.

Disease Management Programmes for Chronic Obstructive Pulmonary Disease

Chronic Obstructive Pulmonary Disease (COPD) is a chronic disease with an estimated prevalence rate of around 12 percent in people aged 40 years and older in Europe (Blanco et al., 2017). It is a common cause of hospitalisation and a leading cause of death, and as such, it is associated with a substantial economic burden. The estimated direct healthcare costs (covering inpatient and outpatient care, primary care, and medicine costs) amounted to €23.3 billion in the EU27+UK in 2011, and the indirect costs (lost production due to absence from work and early retirement) to €25.1 billion (European Respiratory Society, 2019).

We considered the following two case studies of DMPs for COPD:

1. Bourbeau et al. (2019) evaluate the outcomes of the results of the COMET-trial. This trial, conducted in France, Germany, Italy, and Spain, investigated a home-based COPD disease management intervention for severe COPD patients run by nurses.

2. Achelrod et al. (2016) evaluate the outcomes of a disease management programme for COPD run by primary care physicians. It was implemented in Germany in 2005 and is still in place today.

3.2.1 More successful case: The COMET trial of a disease management programme for Chronic Obstructive Pulmonary Disease in France, Germany, Italy, and Spain

The COPD Patient Management European Trial (COMET) investigated the outcomes of a home-based disease management intervention for patients with severe COPD. This randomised controlled trial included 345 patients and was conducted in 33 centres across four countries, France (12 centres), Germany (eight), Italy (six), and Spain (seven) between September 2010 and March 2015.

Patients in the treatment group received self-management education from a nurse (called a case manager) during four individual home sessions throughout a run-in period, which lasted for three to five weeks. During a 12-month follow-up period, patients in the treatment group continued to receive monthly group or individual telephone sessions about self-management. The disease management intervention was received in addition to routine care and follow-up. Patients in the control group received the usual COPD care, which varied by centre and country. Usual COPD care could also include educational interventions (e.g. educational booklets, educational sessions, exercise programmes).

The DMP had several key elements (Bourbeau et al., 2019):

- Patient self-management education and coaching by a nurse in order to help patients to adopt sustainable self-management skills and behaviours. The self-management programme was based on the "Living Well with COPD" programme developed at the Montreal Chest Institute of the McGill University Health Centre, Montreal, Canada (www.livingwellwithcopd.com). Prior to the trial, nurses received a standardised 4-day training course with specific focus on motivational communication. During the trial, nurses had continuous access to "reference guides" describing the objectives, interventions, suggested questions, expected results, and available resources.

- Home telemonitoring of patients for early detection of symptom worsening through an e-health platform. This consisted of the transmission of health status information by patients using a telephone-based questionnaire at least once per week, and any day they experienced worsening symptoms. An e-health telephone/web platform allowed timely patient follow-up by nurses for early detection of potential exacerbations and symptom worsening.

- Healthcare coordination to reduce treatment delays and improve chronic disease management. This was done by a hospital physician based on the information transmitted via the web platform. Physicians made all decisions regarding medication to reduce the risk of inappropriate medication.

Programme results and impact on efficiency

The results of the trial showed that the DMP was associated with improvements in patient outcomes (Kessler et al., 2018). Specifically, the DMP was associated with a 23% relative reduction in all-cause hospitalisation days (17.4 all-cause inpatient days with the DMP vs. 22.6 under usual management),

an 87% lower relative mortality rate with the DMP (1.9% vs 14.2%), and improved patient symptoms based on an index composed of body mass index, airflow obstruction, dyspnoea and exercise. The frequency of exacerbations was also reduced, although these reductions were not statistically significant.

Bourbeau et al. (2019) further analysed the cost-effectiveness of the DMP from the COMET trial. The analysis was conducted separately for each country, although Italy was excluded from the analysis due to a small sample size. A pooled analysis of the change in costs and QALYs in France, Germany, and Spain was also conducted. The results are shown in Figure 5 below. They found differences in costs and outcomes varied by country. The DMP was associated with direct and indirect cost savings of €806 per patient per year in France and €51 in Spain, and a cost increase of €391 in Germany. In all three countries, these differences were not statistically significantly different from zero. In terms of outcomes, a greater number of QALYs was recorded in all countries as well as fewer deaths.

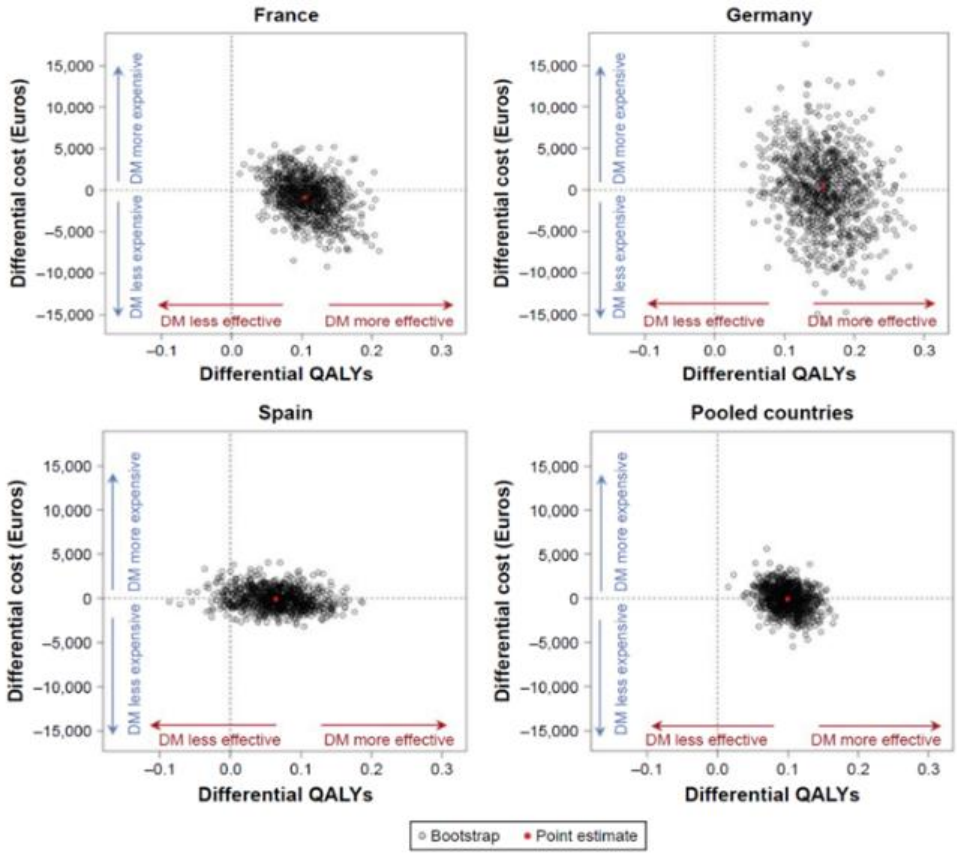

FIGURE 5: COMPARISON OF COSTS AND OUTCOMES (QALYS) PER PATIENT BETWEEN THE PATIENT MANAGEMENT PROGRAMME (DM) AND USUAL CARE
Source: Bourbeau et al. (2019)

Kessler et al. (2018) note that a potential explanation for the heterogenous findings across countries was that patient profiles and hospitalisation practices varied substantially. Thus, even though the design of the patient management programme was the same in all countries, the comparator in each country differed in important respects, leading to different relative changes in costs and outcomes. The results must therefore be interpreted with caution.

3.2.2 Less successful case: A real-world disease management programme for Chronic Obstructive Pulmonary Disease in Germany

Germany has experience with DMPs for COPD as part of national practice, outside of the COMET trial. Since January 2005, sickness funds have been allowed to develop and introduce DMPs for COPD based on evidence-based clinical guidelines (Gemeinsamer Bundesausschuss, 2019).

The Federal Joint Committee (Gemeinsamer Bundesausschuss, 2019) defined the aims of DMPs for COPD as including the:

- Avoidance and/or reduction of:
  - Acute and chronic impairments of the disease (e.g. symptoms, exacerbations, co-morbidities)
  - Impairments of physical and social activities in daily life due to the disease
  - A quick progression of the disease, while aiming to maximise the lung function and minimise unwanted side effects
- Reduction of COPD-related mortality
- Adequate treatment of co-morbidities

Different sickness funds offer different DMPs, although because each DMP must be approved by the Federal Insurance Office (Bundesversicherungsamt), they all have strong similarities. Primary care physicians manage the DMPs. They also decide whether to enrol a patient. Both patient enrolment and physician participation is voluntary. The key features of a DMP for COPD are:

- Training of physicians in the management of COPD
- Training and courses for patients consisting of:
  - Guidance to stop smoking / participation in a tobacco cessation programme
  - Recommendation for physical training
  - Comprehensive information about the disease and how to manage it (self-management)
- Agreement of personal therapy goals to increase patient motivation
- Regular discussions with the physician and medical check-ups
- Regular examinations and continuous care
- Coordination of care between the primary care physician and other specialists
- Treatment with effective medications
- Structured drug management in patients requiring the permanent prescription of five or more medicines due to co-morbidities.

Programme results and impact on efficiency

Achelrod et al. (2016) evaluated the patient outcomes and the costs of DMPs for COPD, based on administrative data from Barmer GEK, a nationwide operating sickness fund that covers more than 10% of the German population. Specifically, they examined: (i) direct medical costs (outpatient and inpatient care, pharmaceuticals, medical appliances and rehabilitation, and administrative expenses for the DMP), (ii) mortality and morbidity (prevalence of co-morbidities), (iii) healthcare utilisation (outpatient visits, inpatient stays/days, pharmaceutical prescriptions, exacerbations), and (iv) process quality (share of patients receiving COPD-specific medications and vaccination against influenza in line with clinical guidelines) associated with the DMP.

The results showed that the DMP cohort was associated with an 11% reduction in all-cause mortality (9.99% compared to 11.2% mortality rate) as well as a reduction in depressive episodes, although the incidence of medication-induced osteoporosis and non-invasive ventilation increased. Adherence to COPD-specific medications and vaccination against influenza was significantly higher in the DMP group.

The DMP cohort had greater healthcare utilisation than the control group (COPD patients receiving usual management). The number of outpatient physician visits and the number of all-cause and COPD-related hospitalisations were significantly greater in the DMP group than in the control group, although the average length of a hospital admission due to COPD was lower for hospitalised patients in the DMP group. The proportion of patients visiting a physician due to a COPD exacerbation was also higher in the DMP cohort, and DMP cohort also received significantly more prescriptions per year, although both could reflect better disease awareness and patient management that could lead to better health outcomes and net savings in the longer term.

In terms of direct medical costs, the DMP cohort was associated with a statistically significant increase in the annual cost per patient of €553, made up of a combination of higher costs associated with inpatient admissions (€109), outpatient care (€128), pharmaceuticals (€236), medical appliances and rehabilitation (€31), and the administrative expenses for the DMP (€48).

Overall, the effect of the real-world COPD DMPs on health system efficiency in Germany is ambiguous as they are associated with improvements in mortality and treatment adherence but also an increase in overall costs.

3.2.3 Case study lessons: Disease management programmes

The COMET trial of a home-based DMP for COPD indicated gains in overall efficiency in France and Spain, with improved patient outcomes including gains in QALYs and reduced mortality, and no increase in total costs. The German cases are less clear regarding efficiency. In both the trial and real-world experience, German DMPs were associated with improved outcomes but also an increase in overall costs among DMP participants. This likely reflects better case management and treatment adherence, but it is not an unambiguous improvement in efficiency.

As a caveat, conclusions drawn from these cases need to consider the heterogenous patient populations across the case studies and the fact that the patient populations in both cases were not necessarily representative of the general COPD population. In the first case study, the DMP was trialled in patients with severe COPD. In the second case study, the results may have been influenced by participant self-selection as DMPs in Germany are voluntary. Patients who enrol in DMPs are likely to be more motivated to seek care than the control patients who were not interested in enrolling. Indeed, Achelrod et al. (2016) note that only around 10% of all German COPD patients are enrolled in DMPs. More broadly, the potential gains associated with the introduction of a DMP will be related to the quality of care currently provided by a healthcare system. The more effective the current care at

managing chronic disease, the smaller the gains likely to be associated with the introduction of a patient-level DMP.

In general, it is difficult to draw any conclusions around best practice from a comparison of the two cases. Germany was included in both cases and saw a similar result in each: an increase in costs as well as outcomes, leading to an ambiguous effect on efficiency. However, comparison of the features and outcomes of the COPD management programmes described in the case studies suggests some general conclusions about the features of an efficient DMP:

- **Patients need to be equipped with the right knowledge on self-management of their disease**. Patient education is important for adopting healthier lifestyles (most importantly smoking cessation) and increasing medication adherence. Patient education in the COMET-trial was based on the "Living Well with COPD" programme, whereas the DMPs in Germany are supposed to adhere to up-to-date evidence-based clinical guidelines.

- **Patients need to be motivated and reminded to continuously manage their condition.** A single initial training session is not likely to be enough to change behaviour. The DMPs in Germany try to achieve change through agreement on personal therapy goals. In the COMET-trial, patients were motivated through regular phone calls with their case manager, and they self-monitored their condition through symptom reporting.

- **The design of a DMP must take cultural factors into consideration**. In countries where primary healthcare is centred around the primary care physician (as in Germany), a greater role for nurses in patient management might be initially met with scepticism by patients and result in lower adherence to advice from nurses.

Patients' pathways in cancer care

Cancer represents a substantial share of the total disease burden in Europe: more than one in four deaths are due to cancer, making it the second most common cause of death after cardiovascular diseases (Jönsson et al., 2016a). The economic burden of cancer in Europe is also high: direct healthcare costs amounted to €83.2 billion in the EU27+UK in 2014, and the indirect costs of lost productivity due to premature mortality and morbidity, together with informal care costs, are likely to be a similar amount (Jönsson et al., 2016b).

There is no single approach to treating cancer, as each of the more than one hundred types of cancer has a specific treatment pathway. In addition, patients are managed by different units and different healthcare professionals during the care process. Patients who live in more rural areas might even be managed by different hospitals over the course of their care. Effective coordination of care is imperative for the patient to receive timely access to appropriate treatments and to reduce waiting times over the entire treatment pathway. Different treatment pathways exist within and between different types of cancer, and thus exploring case studies of different pathways may serve to highlight particular pathways (or elements of pathways) that promote efficiency.

Standardised patient pathways (SPPs) in cancer care lay out the essential steps from suspicion of cancer to recommended diagnostic procedures and treatments. They are intended to enhance the coordination of care to enable timely access to diagnostics and treatment, with the primary aim of increasing patient survival.

We considered the following two case studies of programmes to improve coordination of cancer care:

1. The introduction of standardised patient pathways in Denmark in 2007–2008 (still in place today). Probst, Hussain and Andersen (2012) and (Jensen et al., 2015; Jensen, Tørring and Vedsted, 2017) provide an evaluation of the outcomes of the SPPs.

2. The introduction of standardised patient pathways in Sweden in 2015 (still in place today). The National Board of Health and Welfare (2019c) provides an evaluation of the outcomes of the SPPs.

3.2.4 More successful case: Patients' pathways in cancer care in Denmark

Before the introduction of SPPs for cancer patients in 2007, long waiting times between referrals by general practitioners (GPs) and a diagnosis from a cancer specialist care were common. Patient organisations as well as healthcare professionals perceived long waiting times as a major problem and the latter group also pointed out that these waits might be partly responsible for Denmark's poor survival rates in comparison with other similar countries (Probst, Hussain and Andersen, 2012).

In a joint effort by relevant stakeholders, SPPs (called "kræftpakker" or "pakkeforløb for kræft") for 32 cancer types were established and implemented between 2007–2008. The Danish Health Authority[8] states that "*(t)he aim of the SPPs is to increase and ensure the quality throughout the patient pathway, including that patients quickly receive the diagnosis and avoid unnecessary waiting times. The SPPs have been prepared for a number of selected cancer types and must ensure that all patients receive uniformly high-quality treatment regardless of where in the country they live.*" It is noteworthy that this aim focuses on wait times and the quality of treatment but does not define improved cancer outcomes or efficiency as an explicit aim of the initiative, although this can be a consequence of an improved quality of care.

The SPPs define the medical procedures, the necessary organisation (primary care, outpatient and inpatient care in hospitals), the responsible health professional or department in all phases, the procedures for referral, and the exact timeframes between each step. They also define the information to be given to patients and stipulate the use of multidisciplinary teams in decision making regarding diagnosis and treatment (Probst, Hussain and Andersen, 2012).

Together with the introduction of the SPPs, clearly defined referral pathways from the GP to specialist care were gradually established. Indeed, for patients with symptoms of cancer, GPs are the first point of contact within the healthcare system; this did not change following the SPPs' introduction. There are now three different tracks for a GP to refer patients for further analysis based on patients' symptoms (Vedsted and Olesen, 2015).

1. **PATIENTS WITH PREDEFINED SYMPTOMS SUGGESTIVE OF A HIGH RISK OF A SPECIFIC CANCER CAN BE DIRECTLY REFERRED TO HOSPITAL THROUGH AN URGENT REFERRAL PATHWAY.**
2. Patients with non-specific but serious symptoms first undergo fast-tracked diagnostic tests with their GP, followed by a referral to a hospital-based diagnostic centre if the initial tests are inconclusive.
3. Patients with vague or low-risk symptoms are managed entirely by their GP. The GP has access to fast investigations in "Yes-No-Clinics" in hospitals that perform the necessary diagnostic test without needing to admit the patient to the hospital.

[8] https://www.sst.dk/da/viden/kraeft/kraeftpakker *(accessed September 4, 2019)*

Programme results and impact on efficiency

The government invested DKK 225 million (€5.50 per capita across the Danish population) in 2007 and DKK 175 million (€4.30 per capita) in 2008 to support the implementation of the SPPs (Probst, Hussain and Andersen, 2012). A further DKK 850 million (€21 per capita) was earmarked for general medical and technical investment, such as the acquisition of scanners. There were also organisational changes, including the organisation of multidisciplinary team conferences and the establishment of pathway coordinators, which led to increased costs.

Following the establishment of SPPs, median waiting times (defined as the time from GP referral to the start of treatment) decreased for many – but not all – cancer types between 2006 and 2010. Jensen et al. (2015) investigated changes in the diagnostic interval (defined as the time from patient's first presentation of symptoms in the healthcare system until diagnosis) associated with SPPs. They found that the overall median diagnostic interval decreased by 35% from 49 days before the implementation of the SPPs to 32 days after their establishment. For patients with vague symptoms who did not receive an "urgent referral", the decrease was 16% (from 49 to 41 days).

Jensen, Tørring and Vedsted (2017) found that combined 1-year and 3-year survival for seven cancer types improved from 61% and 45% before the introduction of the SPPs (2004–2005) to 69% and 54%, respectively, following the introduction of SPPs. When comparing SPP against non-SPP referred patients (i.e. those without an "urgent referral") in 2010, there was a lower one-year excess mortality among the SPP referred patients but no statistically significant differences in 1-year or 3-year survival, although it is important to note that the characteristics of two cohorts were different. Further reservations stem from the conclusion of researchers that the SPP "unquestionably also caused delays for other groups of patients" (Probst, Hussain and Andersen, 2012).

Overall, the effect of SPPs on cancer care efficiency in Denmark is ambiguous. Although cancer survival rates improved following their introduction, it is difficult to separate the effect of the SPPs from secular improvements in survival rates over time. The decline in the waiting times from GP referral to the start of cancer treatment associated with the SPPs may have had a positive effect on survival at the margin. The SPPs appear to have had an important effect on reducing patients' dissatisfaction with waiting times (from being seen by a health professional to diagnosis) – which represents a gain in the sense that the *process* by which an outcome is achieved is more satisfactory to patients. Finally, it appears that efforts to provide faster cancer referral from the GP to the hospital caused delays for other patient groups, which may have had unmeasured but offsetting effects in other disease areas. Ultimately, it is unclear whether the costs associated with introducing the SPPs resulted in increased efficiency in terms of cancer patients' outcomes and experience of the treatment process, and what the trade-offs for other patient groups may have been.

3.2.5 Less successful case: Patients' pathways in cancer care in Sweden

As in Denmark, access to care and waiting times in cancer care have been a concern in the Swedish healthcare system. In response, in 2015, Sweden introduced SPPs in cancer care modelled on SPPs in Denmark discussed above (Schmidt et al., 2018; Wilkens et al., 2016). The programme started with pilots for five selected cancer types and by 2019 more than 30 cancer types were covered.

The SPPs had three main aims (National Board of Health and Welfare (Socialstyrelsen), 2019a):

- Shortened waiting times among patients with suspected cancer
- Provision of more equal care, i.e. reduced regional variation
- Increased patient satisfaction

As in Denmark, there was no explicit aim of improving cancer outcomes.

Programme results and impact on efficiency

The Swedish National Board of Health and Welfare published an evaluation of the SPPs in 2019 based on data from the four-year implementation phase (2015–2018). The government provided SEK 500 million (€4.70 per capita) per year from 2015 to 2018 to support the implementation. In addition, interviews by the National Board of Health and Welfare with county councils indicated that annual costs for SPP-related work would be in the range of SEK 170–244 million (€1.60–2.30 per capita) if scaled up to the national level. However, the county councils also noted that SPPs might reduce costs in areas such as primary care and some outpatient cancer clinics (National Board of Health and Welfare (Socialstyrelsen), 2019b).

The SPPs have led to shorter waiting times overall, especially for SPPs covering more common cancers, but these have not met the maximum waiting times set by the SPPs in any cancer type. A prominent example is prostate cancer where waiting times to receive radiation therapy decreased from 203 days in 2015 to 169 days in 2017, whereas the maximum waiting time defined by the SPP for prostate cancer was 68 days. In some cancer types with SPPs, such as pancreas and brain, waiting times have increased. Lack of healthcare human resources (such as nurses and specialists in pulmonary medicine and urology) and lack of care places have been cited as reasons for the slow progress (National Board of Health and Welfare (Socialstyrelsen), 2019c).

Variation in waiting times has decreased across several (but not all) cancer types and across county councils. Changes in patient satisfaction over time could not be evaluated due to changes in the questionnaire used to survey patients (National Board of Health and Welfare (Socialstyrelsen), 2019c). No analyses of health outcomes such as survival and mortality have been conducted to date, and as noted, were not an explicit objective of the initiative.

As in Denmark, a negative consequence of the SPPs was a crowding out effect where patients with other diseases experienced lower priority and a corresponding increase in their waiting times (Delilovic et al., 2019; Schmidt et al., 2018; Wilkens et al., 2016). This was particularly the case for computer tomography examinations carried out for the investigation of cancers of the bladder and urinary tract which crowded out other patients due to capacity shortages in pathology and imaging and functional medicine.

Overall, cancer care SPPs in Sweden have reduced waiting times and the variability in treatment between regions, although they have not fully met most of the waiting time targets. Some of the challenges seen in the Swedish case have been related to: a) a lack of capacity and skills in some counties and regions (e.g. radiologists, pathologists and urologists related to prostate cancer), and b) a disconnect between project leaders and management, with insufficient support for or understanding of cancer SPPs (Schmidt et al., 2018).

3.2.6 Case study lessons: Patients' pathways in cancer care

It is difficult to identify clear evidence of improvements in efficiency in either Denmark or Sweden as a result of the SPPs. In both cases, the implementation of the SPPs reduced waiting times and regional variability, but had no significant effect on survival rates compared to patients treated outside of the SPP.

Denmark saw improvements in 1-year and 3-year survival following the introduction of the SPPs, but it is difficult to distinguish an effect of the SPP from overall secular improvements in survival over the same period. This is illustrated in Figure 6 below, which compares overall 5-year survival rates in cancer in the Nordic countries over the period 1982–2016. It is difficult to identify a meaningful change in trends in cancer survival in Denmark following the introduction of SPPs in 2007. SPPs were first introduced in Sweden in 2015 and cannot be assessed in these figures.

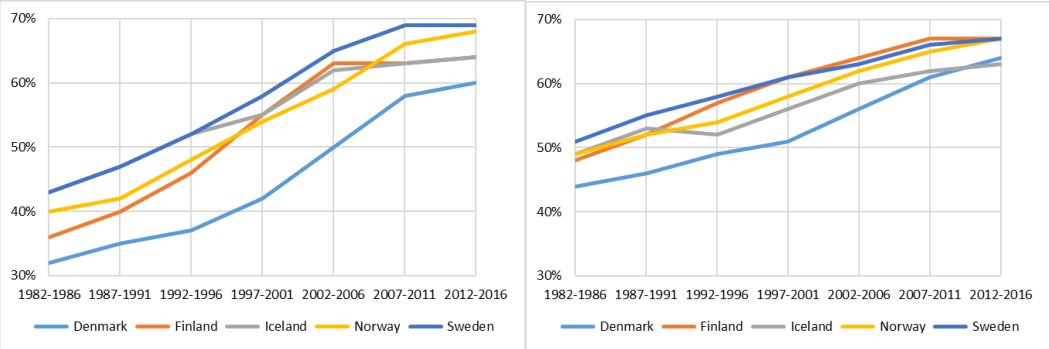

FIGURE 6: 5-YEAR AGE-STANDARDISED RELATIVE SURVIVAL IN MEN (LEFT) AND WOMEN (RIGHT) FOR ALL CANCERS BUT NON-MELANOMA SKIN CANCER BY TIME PERIOD OF DIAGNOSI
Source: Danckert et al. (2019)[9]

If improving the process of care is an important goal of a health system, then improvements in this process represent gains to the health system – although the additional costs of achieving these through SPPs mean that the impact on *efficiency* is ambiguous. However, the introduction of SPPs may also have had negative impacts on the care received for non-cancer patients, which should be better understood before conclusions about the effects of SPPs can be reached.

Despite these ambiguous results, a comparison of the features of the SPPs in Denmark and Sweden do suggest some lesson for the implementation of efficient care pathways.

- **Careful consideration must be given to the ultimate aim of SPPs.** In Denmark the aim of the SPPs was to reduce waiting times and improve the care of patients with cancer, and to increase patients' satisfaction by ensuring treatment as fast as possible. In Sweden, the aim of the SPPs was to reduce wait times and regional variability in cancer care. Both SPPs achieved some of the objectives around improving patient experience, but there is little evidence that the SPPs improved survival outcomes or overall system efficiency. This highlights that efficiency – particularly in terms of cost savings or improved health outcomes – is not an inevitable result of improvements in patient satisfaction, and if efficiency is the ultimate aim (which was not the case in the case studies), this should be specifically targeted in the development of the SPP.

- **Attention should be paid to not 'crowd out' patients in other disease areas**. In both Denmark and Sweden, the increased focus on cancer patients appears to have led to longer waiting times for patients with other diseases. This suggests that the resources allocated to implement the SPPs were not sufficient to avoid 'crowding out' patients in other disease areas.

- **There should be clear referral tracks from primary care to hospital care.** Denmark has developed a clear strategy on how to refer patients from the GP to hospital care based on severity of patient symptoms. No such strategy was implemented in Sweden. It was not possible to assess the impact of this difference, but it is likely to lead to inconsistent referral and possibly differences in outcomes.

3.3 Priority area 3: Rational use of medicines

[9] *Age at diagnosis 0-89.*

Over-prescription, inappropriate use of medicines (e.g. antibiotics), and poor adherence to prescribed treatment, can lead to sub-optimal outcomes and adverse events. Efficiency can also be improved by avoiding the prescribing and reimbursement of medicines that lack scientific evidence of benefit, including homeopathic products. Effective competition in the off-patent market also provides an opportunity for improving efficiency without limiting outcomes.

A more complex area is polypharmacy. Polypharmacy lacks a standard definition, but it is commonly described as the concurrent use of 5 or more medicines (Masnoon et al., 2017; World Health Organisation, 2019). It is common in the elderly due to the prevalence of multimorbidity (i.e. two or more chronic conditions) in this population. As an illustration, Figure 7 shows how the use of multiple medications increases throughout the lifetime in Scotland. The incidence of polypharmacy is 50 percent in 65–69-year olds and 75 percent in 80–84-year olds. Although polypharmacy is not necessarily an indicator of ineffective or inefficient use of medicines in itself, as the number of medicines increases, so does the risk of adverse drug interactions.

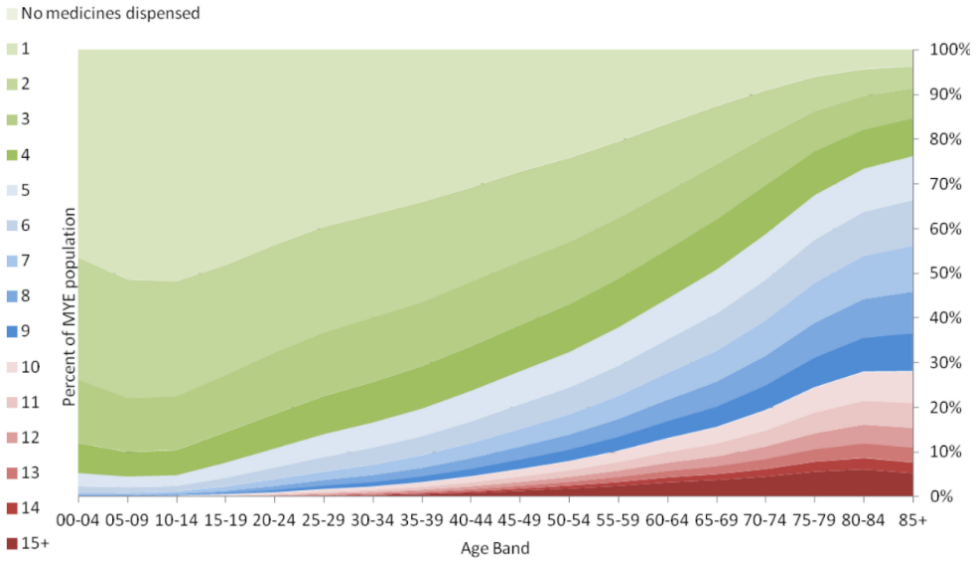

FIGURE 7: NUMBER OF DISTINCT MEDICINES DISPENSED IN SCOTLAND BY FIVE-YEAR AGE GROUPS, JANUARY–JUNE 2017
Source: Stewart et al. (2018)

The observed prevalence of polypharmacy has been increasing in recent decades (Wastesson et al., 2018). Several factors have contributed to this increase, including increasing life expectancy and the resultant growth in the prevalence of multimorbidity, the availability of effective drug treatments for more conditions, and prescribing guidelines that recommend the use of more than one drug in the prevention and management of specific health conditions (Cadogan, Ryan and Hughes, 2016).

Polypharmacy in the elderly population can be associated with poor outcomes as the possibilities of adverse drug-drug and drug-disease interactions increase (Maher, Hanlon and Hajjar, 2014; Wastesson et al., 2018). If these interactions are not recognised and are incorrectly diagnosed as new illnesses, additional medicines may be prescribed, potentially leading to further unintended interactions in what has been called a "prescription cascade". Adverse effects associated with polypharmacy can lead directly or indirectly to an increased number of outpatient visits and hospitalisations whilst physical and cognitive functioning, as well as quality of life, deteriorate and the risk of mortality increases. Medication non-adherence also increases with the number of medicines taken (Zelko, KlemencKetis and TusekBunc, 2016), contributing to the risk of sub-optimal health outcomes. A large Swedish study (The Swedish National Institute of Public Health, 2007) found that the percentage of hospital admissions caused by adverse reactions to medicines varies from

approximately 4% in the younger population up to 16% and over among older persons and ranks between the fourth and the sixth cause of death in hospitalized patients.

The cost of mismanaged polypharmacy has been estimated to be 0.3 percent of all global health expenditure – US$18 billion worldwide – much of which could be avoided through improved polypharmacy management (Aitken and Gorokhovich, 2012).

Appropriate management of polypharmacy in elderly people can improve the efficiency of healthcare systems. Medication reviews are one means of addressing inappropriate polypharmacy. Healthcare costs may be reduced by avoiding the prescribing of potentially inappropriate medicines, as well as through reductions in avoidable outpatient visits and hospitalisations. Several European countries have launched programmes to address inappropriate polypharmacy in elderly people, but their design, and therefore their efficiency, varies.

We considered the following two programmes aimed at improving the management of polypharmacy in elderly people:

- Guidelines on medication review in Scotland (UK), introduced in 2012. An evaluation has been conducted by the Scottish Government Polypharmacy Model of Care Group (2018).
- Medication review in Lower Saxony (Germany), introduced in 2013. Evaluations have been conducted by McIntosh, Alonso and Codina (2016) as part of the SIMPATHY Project and by Seidling et al. (2017).

3.3.1 More successful case: Guidelines on medication review in patients with polypharmacy in Scotland

Early guidance on polypharmacy in Scotland was produced by the National Health Service (NHS) Highland in 2010 (The Pharmaceutical Journal, 2012). On this basis, the Scottish Government installed a working group that developed a model of care for polypharmacy, which was published in 2012 (Scottish Government, 2012). The guidelines on polypharmacy have been updated twice, in 2015 and in 2018.

The aim of the polypharmacy guidelines is to systematically address inappropriate polypharmacy and improve adherence across Scotland in order to minimise harm, optimise benefits, and reduce hospitalisations and medication waste (McIntosh et al., 2018).

The core of the Scottish polypharmacy guidelines consists of a 7-step process for medication review:

1. (Aims) What matters to the patient (i.e. aims and objectives of drug therapy)
2. (Need) Identify essential drug therapy
3. (Need) Does the patient take unnecessary drug therapy?
4. (Effectiveness) Are therapeutic objectives being achieved?
5. (Safety) Is the patient at risk of adverse drug reactions (ADRs) or suffers actual ADRs?
6. (Efficiency) Is drug therapy cost-effective?
7. (Adherence/Patient-centredness) Is the patient willing and able to take drug therapy as intended?

All Scottish NHS Boards have adopted these guidelines and developed plans to identify priority patients with potentially inappropriate polypharmacy. The medication reviews are now embedded in

standard working practices (McIntosh, Alonso and Codina, 2016). The Scottish polypharmacy guidelines consist of a seven-step process which includes an assessment of the prescribed indication, the relative effectiveness of the prescribed medicine, adverse side effects and contra-indications, and a holistic discussion with the patient about their medications (Mair, Fernandez-Llimos and SIMPATHY Consortium, 2017).[10] The review takes about 15 to 30 minutes and is typically conducted by a pharmacist or a physician in the community, general practice, or nursing home, but healthcare professionals from hospitals (physicians and pharmacists) may also undertake work in the community (Mair, Fernandez-Llimos and SIMPATHY Consortium, 2017). During the review, the pharmacist/physician suggests changes to the patient's medicines as needed and the patient is informed about potential benefits. Modifications can include switching to a new or different version of a medicine, changing the dose, changing the time of day the medicine is taken, or stopping a medicine entirely.

The recommended target group for the medication review has broadened over time (Scottish Government, 2012; Scottish Government Polypharmacy Model of Care Group, 2018). It currently includes persons: (1) aged 50+ and resident in a care home, regardless of the number of medicines prescribed, (2) approaching the end of their lives, (3) prescribed with ten or more medicines, (4) on high-risk medication, regardless of the number of medicines taken (Scottish Government, 2012; Scottish Government Polypharmacy Model of Care Group, 2018).

Programme results and impact on efficiency

The impact of the medication reviews has been assessed by the Scottish Government Polypharmacy Model of Care Group (2018). The evaluation took a top-down approach and included estimated costs of the medication reviews, the average cost of medicines, and costs of hospital admissions (in terms of bed days) related to adverse drug reactions (ADRs).

The medication reviews were estimated to range from £24.36 to £67.01 (€28–78) per review and the net number of medicines was estimated to decrease by between 4.9 and 18.2 items per patient per year. Lower and upper estimates of the cost per item (£10.17 and £10.90; €11–12) are calculated based on BNF prices[11]. These resulted in net savings ranging from £50 to £198 (€58–231) per patient per year. Total savings from the reduction in ADR-related hospital admissions was estimated to be £1.07 million (€1.24 million) per year in the target population[12]. Sensitivity analyses showed health system savings across the range of scenarios from £0.33 million (€0.38 million) to £8.53 million (€9.93 million) per year (€9–232 per patient per year).

With regard to outcomes, Mair, Wilson and Dreischulte (2019) provide evidence on a continuously declining share of Scottish patients aged 65+ on harmful combinations of medicines since the publication of the first guidelines in 2012. However, no evaluations to date have analysed direct measures of mortality, morbidity, or quality of life.

Overall, the Scottish medication reviews appear to be associated with decreased costs and a lower incidence of potentially harmful drug combinations, suggesting a clear improvement in health system efficiency.

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[10] *The SIMPATHY project is being delivered by a consortium of 10 institutions from eight European countries. Additional partners in the SIMPATHY consortium undertaking review of appropriate polypharmacy in the hospital setting include Sweden, Naples, Catalonia and Northern Ireland.*

[11] *BNF prices are calculated from the net cost used in pricing NHS prescriptions and generally reflect whole dispensing packs. BNF prices are not suitable for quoting to patients seeking private prescriptions or contemplating over-the-counter purchases because they do not take into account VAT, professional fees, and other overheads (see BNF 2017 report: https://vnras.com/wp-content/uploads/2017/06/BNF-73-2017.pdf)*

[12] *The target population was defined as patients aged 75+ on 1st May 2017 with a SPARRA (Scottish Patients at Risk of Readmission and Admission) score of 40-60% who were dispensed items from 10 or more BNF sections.*

3.3.2 Less successful case: Medication review in patients with polypharmacy in Lower Saxony, Germany

ATHINA ("ArzneimittelTHerapiesicherheit IN Apotheken") is a medication review programme organised by the Lower Saxony Chamber of Pharmacists in Lower Saxony, Germany. The programme involves community pharmacists who perform medication reviews for patients with polypharmacy and was launched in December 2013 (Lübke, 2015). They provide advice to patients by analysing their medications, identifying issues, and suggesting improvements (McIntosh et al., 2016).

Before 2012, pharmacists in Germany were only allowed to supply medications; only licensed physicians were permitted to prescribe and review medications. Since 2012, pharmacists have been permitted to perform medication reviews. In response, the North Rhine Chamber of Pharmacists developed ATHINA in 2012 (McIntosh, Alonso and Codina, 2016). The two aims of the ATHINA programme are:

- To benefit patients by making them aware of inappropriate polypharmacy and the consequences of non-adherence to prescribed medications
- To expand the role of pharmacists from merely providing medicines to influencing therapeutic actions in partnership with physicians

ATHINA is a voluntary training programme enabling previously trained community pharmacists to undertake medication reviews. It consists of a 16-hour seminar plus the presentation of four medication reviews evaluated by a pharmacist tutor. Medication reviews can only be performed at the discretion of the patients.

The medication review is recommended for patients on 5 or more medications who are 60 years or older. It consists of two separate patient visits to the pharmacist. The medication review is based on a "brown bag review", which has been used in the US for many years. During the first visit, the patient brings all of their (prescribed and non-prescribed) medications and dietary supplements to the pharmacy, followed by a short interview. Afterwards, the pharmacist inspects the medications and checks: (1) expiration dates, (2) duplications, (3) dosages, (4) actual use and adherence, and (5) drug-drug interactions. The second visit consists of a consultation between the pharmacist and the patient during which the results of the review are discussed. The patient receives advice on how to optimise their use of medications to increase adherence and to avoid unwanted side effects. The review is documented, and the patient receives a medication plan that they should take to their physician for further consultation (Fabricius and Holthaus, 2019).

Until mid-2017, around 10–15% of all pharmacies in Lower Saxony had at least one pharmacist (around 500 in total) who had participated in ATHINA (Behrendt et al., 2018). Approximately 2,000 medication reviews had been performed in the five (of seventeen) Chamber of Pharmacists districts (including Lower Saxony) in Germany that adopted ATHINA by mid-2017 (Behrendt et al., 2018).

Patients pay out-of-pocket for medication reviews and pharmacists decide freely on the price of the reviews. The Chamber of Pharmacists has recommended a price of about €69 (Lübke, 2015), but some pharmacists charge only around €15 to €25 (Klein, 2016).

Programme results and impact on efficiency

Evaluations by McIntosh, Alonso and Codina (2016) and Seidling *et al.* (2017) provide information on the effectiveness of the ATHINA programme and highlight a number of challenges and shortcomings:

1. **Low participation by patients**. Only around 2,000 reviews had been performed in the first four years of the programme in an area that covers around 35 million people. One reason for this may be that patients have to pay out-of-pocket for the medication reviews. In addition, some patients feel that having a pharmacist check their prescribed medications undermines the relationship with their physician (McIntosh, Alonso and Codina, 2016).

2. **Low participation and remuneration of pharmacists**. Community pharmacists are not reimbursed by the sickness funds for the time spent on medication reviews, and pharmacists feel the patient fee is not sufficient compensation. Pharmacists also felt that medication reviews interfere with the regular pharmacy workflow and as a result some pharmacists were forced to conduct the reviews in their spare time (McIntosh, Alonso and Codina, 2016).[13]

3. **Patient reluctance**. Pharmacists discuss the recommendations with the patient but it is up to the patient to choose to share the recommendations with their physicians. Many patients are reluctant to do so, out of concern that this might undermine the doctor-patient relationship. This means that many reviews do not change prescribing (McIntosh, Alonso and Codina, 2016).

4. **Inefficient and inadequate sharing of patient data**. The ATHINA programme is not interoperable with the software used by pharmacists, and thus requires inefficient double entry of patient information. Legal restrictions prevent sharing of patient information, limiting accuracy and scope of the reviews and recommendations (McIntosh, Alonso and Codina, 2016).

5. **Poor support from physicians and policy makers**. Although the Chamber of Pharmacists sees the polypharmacy management initiative as an opportunity to bolster the position of pharmacists in the care process, physicians have been suspicious and the Chamber feels health policy makers have not considered the full role pharmacists could play in the management of polypharmacy (McIntosh, Alonso and Codina, 2016).

Seidling et al. (2017) concluded that the medication reviews were effective in identifying issues, but low uptake among pharmacists and the public meant that the overall impact of the programme was minimal.

3.3.3 Case study lessons: Medication review

The Scottish experience indicates potential improvements in health system efficiency. Reviews were associated with estimated cost savings ranging from €9 to €232 per patient per year and a reduced proportion of patients on potentially harmful combinations of medicines. Long-term patient outcomes such as mortality, morbidity, and quality of life were not assessed but are likely to have been improved. The German experience was less successful and identified challenges in the design and implementation of medication reviews, particularly related to the incentivisation of pharmacists and information sharing with physicians.

Contrasting the Scottish and German experience highlights some key lessons:

- A successful medication review programme requires involvement of all relevant stakeholders – especially pharmacists and primary care physicians. The Scottish polypharmacy guidelines were

[13] *Since March 2017, one local sickness fund in Lower Saxony (AOK Niedersachsen) has started to reimburse primary care physicians with €60 per medication review. Physicians may choose to refer a patient to a pharmacist to conduct the review in which case both the physician and the pharmacist receive €60 (Behrendt et al., 2018). Thus, pharmacists are currently still not remunerated if they recruit patients for reviews directly.*

a joint effort by geriatricians, pharmacists, and GPs. Medication reviews are performed by both pharmacists and GPs. By contrast, the ATHINA programme in Lower Saxony was independently developed by the Chamber of Pharmacists, with no involvement of GPs. A situation in which GPs perceive pharmacists as trying to challenge their competence in prescribing medications needs to be avoided.

- Widespread participation of healthcare providers and low patient fees are critical for patient access. The Scottish government was successful in having all local NHS Boards follow the polypharmacy guidelines on conducting medication reviews. In Lower Saxony, participation of pharmacists in the ATHINA programme was voluntary and led to low participation. Furthermore, patients in Lower Saxony had to pay out-of-pocket for voluntary medication reviews, whereas in Scotland medication reviews were embedded in standard working practices and free for patients.

- Appropriate financial incentives are necessary. In Scotland, pharmacists and physicians perform the medication reviews as part of their general service to the NHS and are paid for the reviews. In Lower Saxony, pharmacists received initially no remuneration for the time spent on medication reviews from the sickness funds, forcing some of them to conduct the reviews in their spare time.

- The recommendations from medication reviews need to be implemented. In Scotland, physician participation in the reviews facilitates changes in medications. This is not necessarily the case in Lower Saxony, where patients may choose not to share the pharmacist's recommendations with their prescribing physician.

- Inter-connected electronic systems to facilitate sharing of patient records need to be established. The medication review in Scotland is currently not linked to electronic health records, which makes it more difficult to deliver reviews consistently (Mair, Wilson and Dreischulte, 2019). The situation is similar in Lower Saxony, where pharmacists could not connect information from their usual prescribing system to the system used for medication reviews. The World Health Organisation acknowledges the potential of systems that share information between outpatient and inpatient facilities and pharmacies as well as patients to improve polypharmacy management. However, even the best IT systems are reliant on the information entered. Over-the-counter-medicines, which are often recommended but not prescribed by GPs, and herbal and dietary supplements are difficult to record.

3.4 Priority area 4: Healthcare-associated infections

Healthcare-associated infections (HCAIs) have a substantial impact on health system efficiency as they are associated with significant costs from the hospital perspective (Roberts et al., 2003; Perencevich et al., 2003), and are detrimental to patients' quality-of-life and survival. The World Health Organisation estimates that each year there are 4 million HCAIs in acute care hospitals in Europe, resulting in 37,000 deaths and €13–24 billion in avoidable costs (World Health Organization, 2009). Of these costs, €7 billion are direct costs to the healthcare system (World Health Organisation, 2013). In Europe, it is estimated that HCAIs occur in 7.1% of all hospital admissions (Danasekaran et al., 2014) and represent 16 million avoidable hospitalisation days (Manoukian et al., 2018).

The risk of HCAIs is associated with a lack of standardisation of procedures and the absence of local and national guidelines and policies, as well as a lack of training and information with respect to the prevention and management of HCAI. Staff education and accountability are essential for making healthcare providers and patients aware of risks and consequences of HCAIs and for promoting prevention strategies.

One approach to prevent HCAIs is through the use of clinical surveillance which allows: 1) an analysis of trends; 2) evaluation of the effects of interventions being implemented; 3) implementation of

effective infection prevention and control measures. However, the implementation of surveillance programmes is challenging as there is a lack of consensus on the best approaches and best indicators of care quality. Two case studies are presented with different approaches to surveillance:

- A Lean Six Sigma clinical surveillance programme aimed at eliminating inefficiencies and reducing HCAIs in a University Hospital in Naples, Italy (Improta et al., 2018).
- A methicillin-resistant Staphylococcus aureus (MRSA) surveillance programme of health professionals in the hospital setting in Germany aimed at supporting local health authorities in their mandate to prevent and control HCAIs (Hagel et al., 2019).

3.4.1 More successful case: The Lean Six Sigma programme in Italy

Between January 2011 and December 2016, a Lean Six Sigma (LSS) programme was undertaken at Federico II University Hospital in Naples (Italy). The first phase of the programme (from January 2011 to December 2014) aimed to reduce the number of patients acquiring HCAIs in surgicaldepartments, and the second phase (January 2015 to December 2016) rolled the programme out to all departments (Improta et al. 2018). Both phases were compared to analyse effects of the project. The LSS approach attempts to reduce deviations from the ideal processes in a system by identifying and addressing their root causes through a process of continuous monitoring and improvement; it is an approach which has been validated in other surgical settings (Sunder, 2013; Mason, Nicolay and Darzi, 2015). In this approach, all healthcare professionals (physicians, technicians, physician assistants, nurses, clinical officers, and operating department practitioners) are expected to contribute to the identification of problems and their solutions, regardless of their specific area of expertise (Improta et al., 2018).

Causes of infections were identified through analysis of data collected on the source of HCAIs, and validated through consultation with hospital representatives; the deviations from ideal processes included contamination of surgical instruments, a lack of hygiene of health professionals, and missing hygiene protocols. In line with the LSS methodology, the interventions introduced to address these deviations were again designed with the participation of hospital staff and continuously refined through ongoing data collection and evaluation. Staff also participated in education and efforts were made to increase accountability (Improta et al., 2018).

Programme results and impact on efficiency

The LSS programme was associated with a more than 40% reduction in infected patients, from 0.37% to 0.21% in the first phase of the study in the surgical setting, and to 0.19% in the second phase in the broader hospital setting (Improta et al., 2018). The programme also reduced the mean number of hospital days associated with HCAIs by 20% from 45 (standard deviation 30.78) to 36 (standard deviation 5.68).

A systematic review of LSS methodologies in surgical settings (Mason, Nicolay and Darzi, 2015) reported reductions in colonised patients of 45% to 60%, and another study found a 43% reduction in the costs associated with HCAIs (Iannettoni et al., 2011).

The Italian experience suggests the potential of substantial improvement in healthcare efficiency, with a 50% reduction in the incidence of colonised patients and the mean number of hospital days associated with HCAIs. However, the cost of implementing the LSS programme was not reported.

3.4.2 Less successful case: Hand hygiene promotion in Germany

Jena University Hospital, a tertiary care medical centre in Germany, implemented a multifaceted intervention programme for hospital-wide infection control (ICP) as part of the ALERTS quasi-experimental study. The primary aim of this study was to examine the effectiveness of a hospital-

wide ICP for reducing the overall burden of HAIs without targeting specific pathogens, types of HCAIs or hospital wards (Hagel et al., 2019).

Prior to the study, infection control efforts at the hospital focused primarily on non-patient centred hospital hygiene. The intervention consisted of promoting of hand hygiene in combination with 'bundles' for the prevention of HCAIs. The bundles combined interventions recommended by evidence-based best practice guidelines at the time of study initiation, but it is noted that the majority of the recommendations with the bundles were already in place as part of current practice. The hand hygiene promotion programme was based on the recommendations of the World Health Organisation Multimodal Hand Hygiene Improvement Strategy (Hagel et al., 2019). The intervention was supported by previous studies that had demonstrated a reduction of HCAIs through improved hand hygiene behaviour (Sickbert-Bennett et al., 2016; Pittet et al., 2000).

Programme results and impact on efficiency

The overall incidence of HCAIs was not reduced over the period of the study. Indeed, the incidence of HCAIs increased from 4.3 per 100 admissions prior to the intervention to 4.9 afterwards (Hagel et al., 2019). There was some evidence of a reduction in the incidence of HCAIs in intensive care units (ICUs), but as there were a number of changes made to infection protocols in the ICU over the period, it is not possible to conclude that the change was associated with the hand hygiene intervention. Overall, the intervention generated only a small increase in hand hygiene compliance, from 41% to 51%, and authors are unable to provide an explanation for the low post-intervention levels of compliance compared to other hospital-wide hand hygiene interventions (Hagel et al., 2019; Arefian et al., 2019).

3.4.3 Case study lessons: Healthcare-associated infections

The implementation of the LSS in Italy was associated with substantial improvements in clinical outcomes, almost halving the number of HCAIs across the Federico II University Hospital. Moreover, given that this reduction in infections translated to a decrease in the mean number of hospital days associated with HCAIs from 45 to 36 per patient, it is likely that the programme also led to cost reductions – and therefore unambiguous efficiency improvements. The clinical surveillance programme implemented in the Jena Hospital in Germany, however, did not decrease HCAIs or generate substantial improvements in compliance with best hygiene practices. There are several differences between the approaches to clinical surveillance used in Italy and Germany which are likely to have contributed to these contrasting effects[14], and which can be extrapolated to broader lessons:

- Data should be used to tailor interventions to context. In the German case, interventions were implemented to deal with the most common sources of HCAIs, based on external evidence and international best practice, but it is unclear that these were sufficient to address the causes of HCAIs in the Jena Hospital. Moreover, the interventions implemented may not have been appropriate within the operational structures of the hospital. Indeed, although Arefian et al. (2019) speculate that high activity level, lack of time and high workload may have contributed to low compliance observed over the course of the study, these factors do not appear to have been recognised or corrected at the time. In contrast, in Italy data were used to identify the specific deviations from good practices which were contributing to HCAIs in the Federico II University Hospital.

[14] Note also the difference in context, including the initial infection rate which was substantially higher in the German case.

- Engagement of staff is critical, during design and implementation. The interventions designed in the Italian case were not only hospital-specific, but also validated by staff in order to ensure their appropriateness.

- Improvement should be a continuous process. In the Italian case, ongoing monitoring was used to track the success of the interventions, and how they might be refined. Had a similar approach been utilised in the German case, this could have alerted the hospital to the lack of progress and provided an opportunity to improve.

4 Quantifying potential efficiency gains

This chapter describes the methods, data sources and key assumptions used to derive estimates of potential efficiency gains at national and European levels.

4.1 Quantification 1: Efficiency gains from colorectal cancer screening

4.1.1 Methodology, inputs and key assumptions

The CRC screening extrapolation was based on simulating life expectancies for a hypothetical cohort accounting for national demographic characteristics, including health status. These simulated cohort outcomes were combined to produce aggregate measures of costs and health outcomes. Each scenario combines information on the intervention, including costs, eligibility and participation rates, and expected impacts. These impacts include changes in incidence, mortality, length of stay, resource utilisation (for example, follow-up procedures, treatments), direct health care costs, life expectancy, and quality-adjusted life-years (QALYs).[15]

The most important factor in estimating the potential efficiency gains for each country is the current screening participation rate. We estimate the range of efficiency gains associated with each country achieving: a) the participation rate observed in the more successful case study (upper bound, 72%); and b) the minimally acceptable rate as per European Guidelines (lower bound, 45%) (Segnan et al., 2010). Current CRC screening participation rates for the EU27+UK are shown in Figure 8 below.

[15] *The Quality-Adjusted Life Year (QALY) is the gold standard for measuring how well a medical treatment improves and lengthens patients' lives and is often used by health economists and health care decision makers to estimate the benefits of treatments for cost-effectiveness analysis.*

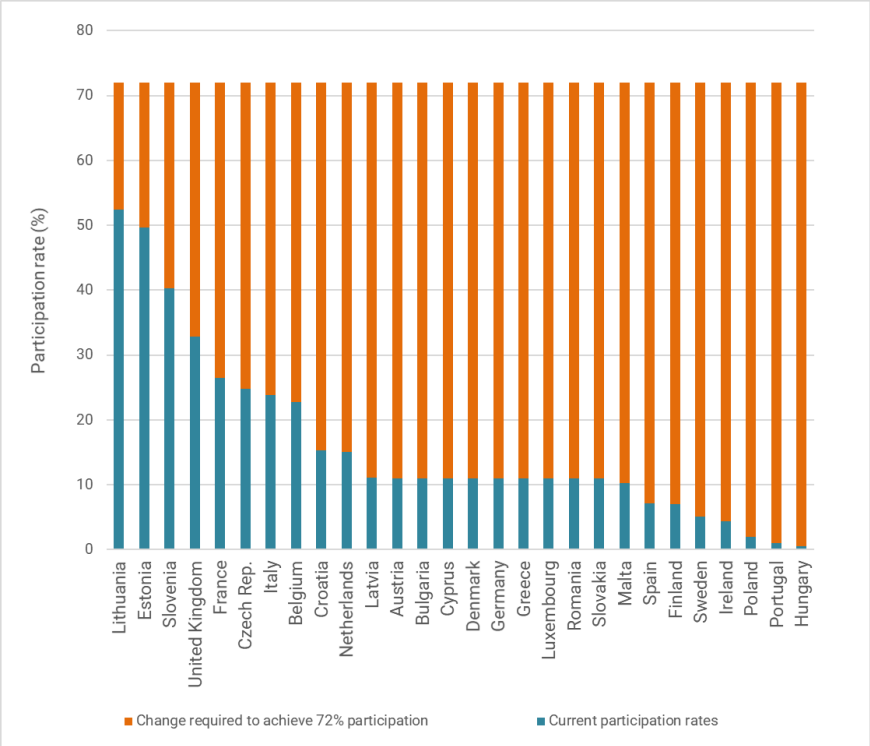

FIGURE 8: CURRENT CRC SCREENING PARTICIPATION RATES (BLUE) AND ABSOLUTE CHANGE IN PARTICIPATION REQUIRED TO ACHIEVE BEST-CASE RATE OF 72% (ORANGE)

The impact on CRC mortality in each country was estimated as a function of the change in screening participation rates. Prior to the Basque programme, the average Spanish CRC screening rate was 7% (Ponti A et al., 2017), and the 72% rate observed in the case study implies an absolute 65% improvement in screening rates. On the basis of the 25% average mortality reduction estimated by the evaluation of the Basque case study (a 28.1% reduction in men, 22.4% in women (Arrospide et al., 2018)), we assume that an absolute 65% increase in screening participation is associated with a 25% reduction in population CRC mortality. This mortality reduction was scaled by the change in each country's participation rate implied by moves to 45% and 72%, relative to the Basque experience. To illustrate, if a screening rate of 45% implied an *absolute* improvement of 32% in a country's screening participation, this would represent a 50% *relative* improvement compared to the Basque experience. Therefore, we scaled the Basque mortality reduction by the country-specific relative improvement to estimate the country-specific CRC mortality reduction, i.e. (32%/65%) x 25% = 12% reduction. This reduction in mortality was applied to the total number of deaths in each country associated with malignant neoplasm of colon, rectosigmoid junction, rectum, anus and anal canal (Eurostat).

Per-country QALY gains were estimated by extrapolating results from the Spanish case study (Arrospide et al., 2018), which reported a per-screened patient QALY gain of 0.034 for men and 0.017 for women. Aggregate QALY gains were estimated by multiplying the expected number of patients screened under the high and low scenarios and converted to monetary efficiency gains by weighting by an assumed willingness-to-pay of €30,000 per QALY.

We note that some countries (Lithuania, Estonia) already have rates of screening participation greater than the lower bound of our sensitivity analysis (the minimum acceptable rate of the European Guidelines. For these countries, there would be no efficiency gains associated with meeting the (lower) minimally acceptable participation (45%) and therefore we only consider the gains associated with screening rates greater than their current baseline.

The case study results estimated cumulative cost and health outcomes over a 30-year cohort life expectancy. To facilitate comparison with the other case study quantifications, we have converted cumulative savings to an annual net present value by dividing by discounted life expectancy using a 3% discount rate.

4.1.2 Quantitative estimates of efficiency gains

Figure 9 below presents the potential cost savings (on the right-hand axis) and change in mortality (on the left-hand axis) associated with the introduction of organised CRC screening for 50 to 69-year olds across the EU27+UK, expressed as a percentage of national health expenditure. The upper and lower bounds represent the Basque best-case participation rate (72%) and the minimally acceptable participation rate (45%).

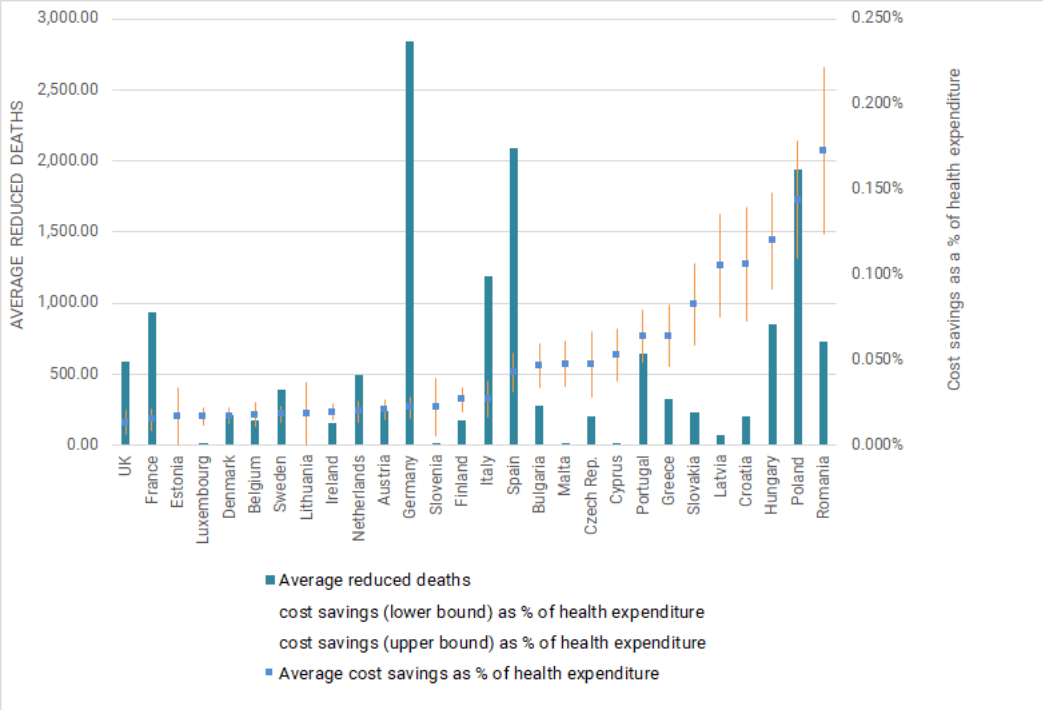

FIGURE 9: RANGE OF POTENTIAL SAVINGS AS A PERCENTAGE OF TOTAL HEALTH EXPENDITURE AND AVERAGE REDUCED DEATHS FROM INCREASES IN RATES OF PARTICIPATION (FROM BASELINE TO 45% AND 72%) IN CRC SCREENING BY EU COUNTRIES AND THE UK.

The potential savings in healthcare expenditure associated with a CRC screening programme reflect foregone treatment costs after accounting for the costs of screening. The costs of screening are based on costs reported in the CRC screening case study in the Basque Country (Arrospide et al., 2018). Potential efficiency gains in each country are a function of their baseline screening rates and the current level of health care expenditure.

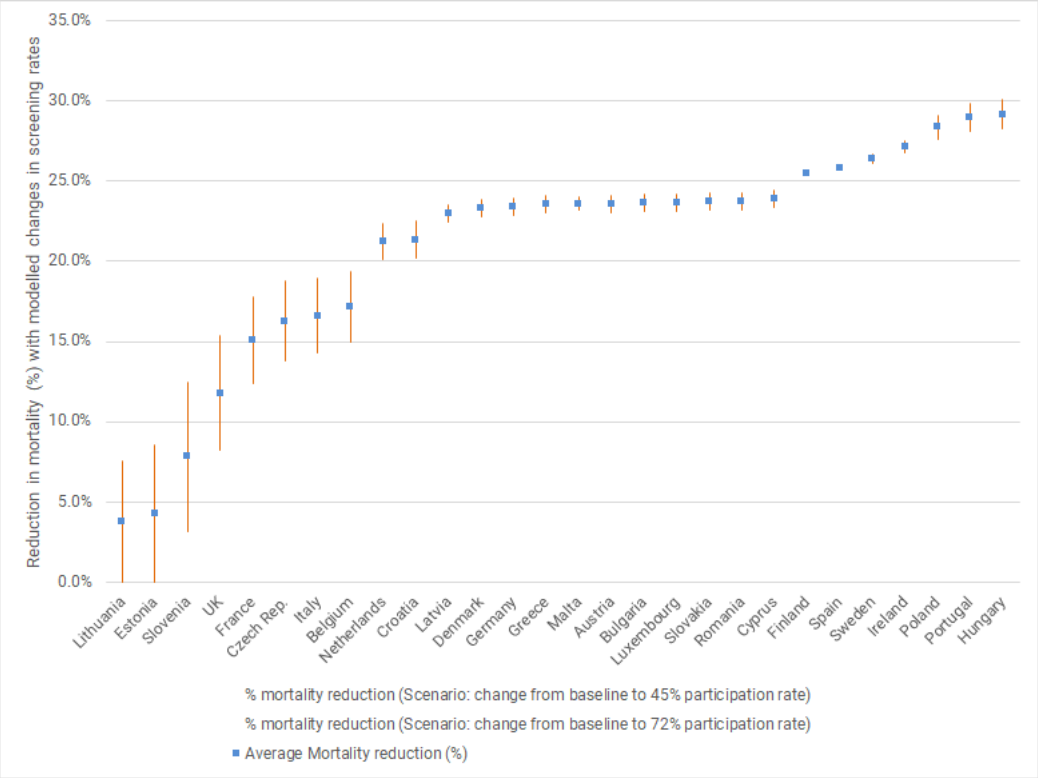

FIGURE 10: REDUCTION IN CRC DEATHS (%) WITH MODELLED CHANGES IN SCREENING PARTICIPATION RATE.

If all EU27+UK countries could achieve the midpoint between the minimum European guideline rate and the Basque screening participation levels, aggregate annual direct savings would reach €405 million (0.027% of the aggregate health expenditure), ranging between €274.3 and €535.4 million (0.018% to 0.035% of aggregate health expenditure). These participation rates would also reduce CRC deaths by between 10,000 and 20,000 and be associated with an additional 171,000 to 331,000 QALYs per year through morbidity and premature mortality avoided. Using a willingness-to-pay of €30,000 per QALY, this implies an additional indirect efficiency gain of between €5.1 and €9.9 billion.

4.2 Quantification 2: Efficiency gains from disease management programmes for chronic obstructive pulmonary disease

4.2.1 Methodology, inputs and key assumptions

As illustrated by the more successful case study in section 3.2.1, DMPs for COPD have the potential to reduce COPD-related length-of-stay (LOS) as well as mortality, contributing to substantial gains in efficiency.

To estimate the baseline cost of COPD admissions in the EU27+UK, we combined information on COPD prevalence, the annual rate of hospital admission, and the mean length of hospital stays:

- In 2017, the prevalence of COPD in the EU27+UK among men and women aged 50 years or older was 18.9% and 16.7%, respectively (source: Global Burden of Disease (GBD), data for 2017). This translates to 17.9 million men and 18.5 million women with COPD in the EU27+ UK.

- In the case study, the reported baseline admission rates were 12% to 38% across the different countries in the trial (Kessler et al., 2018). This range was tested in the sensitivity analysis.

- Average all-cause length-of-stay was derived from Eurostat for the EU27+UK. As per the Eurostat definition, we used the International Classification of Diseases, ICD-10 codes16.

- The cost per inpatient hospitalisation bed day, was derived from Eurostat, as the ratio of total health expenditure and total hospitalisation days multiplied by the number of COPD hospitalised patients (which we calculate using prevalence data from the Global Burden of Diseases database17, multiplied by the hospitalisation rate). All hospitalisation causes have been considered.

- We test 75% and 50% compliance rates with the DMP, and lower and upper COPD hospitalisation rates of 12% and 38% for the sensitivity analysis.

The case study observed that the DMP for COPD also reduced mortality rates, suggesting a 87% relative reduction in mortality (1.9% with DMP vs. 14.2% with usual management). This reduction was assumed to be constant across the EU27+UK and was factored into our calculations. We also assume the LOS reduction observed in the more successful case study (23% reduction in LOS) for two different DMP compliance scenarios (75% compliance and 50% compliance), with upper and lower sensitivity analyses within each scenario based on COPD hospitalisation rates between 12% and 38%. We report efficiency gains from the reduction in LOS separately from those associated with mortality reductions.

4.2.2 Quantitative estimates of efficiency gains

REDUCTIONS IN COPD-RELATED LENGTH-OF-STAY (LOS) ASSOCIATED WITH A 50% DMP COMPLIANCE SCENARIO WERE ESTIMATED TO RESULT IN AGGREGATE EU27+UK SAVINGS OF BETWEEN €204.6 AND €647.9 MILLION (0.01% TO 0.04% OF AGGREGATE HEALTH EXPENDITURE), WITH MID-POINT SAVINGS OF €426.3 MILLION (0.028% OF AGGREGATE HEALTH EXPENDITURE). IN THE 75% DMP COMPLIANCE SCENARIO, SAVINGS WOULD BE BETWEEN €690.6 MILLION AND €2.186 BILLION (0.046% TO 0.144% OF AGGREGATE HEALTH EXPENDITURE), WITH A MID-POINT OF €1.438 BILLION (0.09% OF AGGREGATE HEALTH EXPENDITURE).

Figure 12 and Figure 11 below illustrate potential LOS-related cost savings by country, expressed as a proportion of national health expenditure.

[16] *Eurostat ICD-10 classification A00-Z99, excluding V00-Y98 and Z38, is provided.*
[17] *Global Burden of Disease Study 2017. Global Burden of Disease Study 2017 (GBD 2017) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2018. Available from http://vizhub.healthdata.org/gbd-compare/*

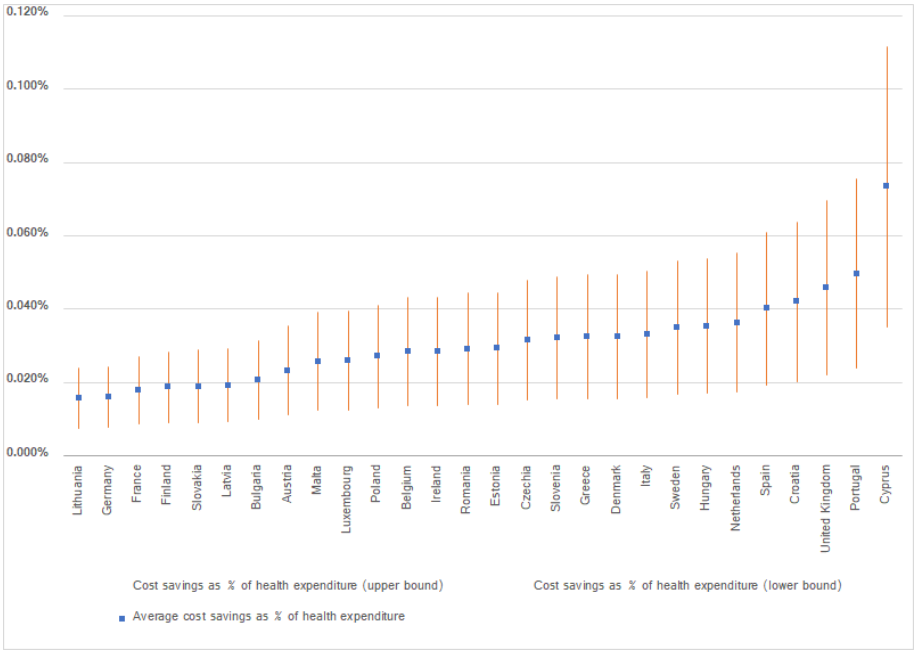

FIGURE 11: COST SAVINGS AS A PERCENTAGE OF THE HEALTH EXPENDITURE ASSOCIATED WITH A REDUCTION IN ALL-CAUSE LOS, 50% DMP COMPLIANCE SCENARIO.
Note: Orange vertical lines represent savings across upper and lower hospitalisation rates (12-38%); blue points represent the mid-point expected value.

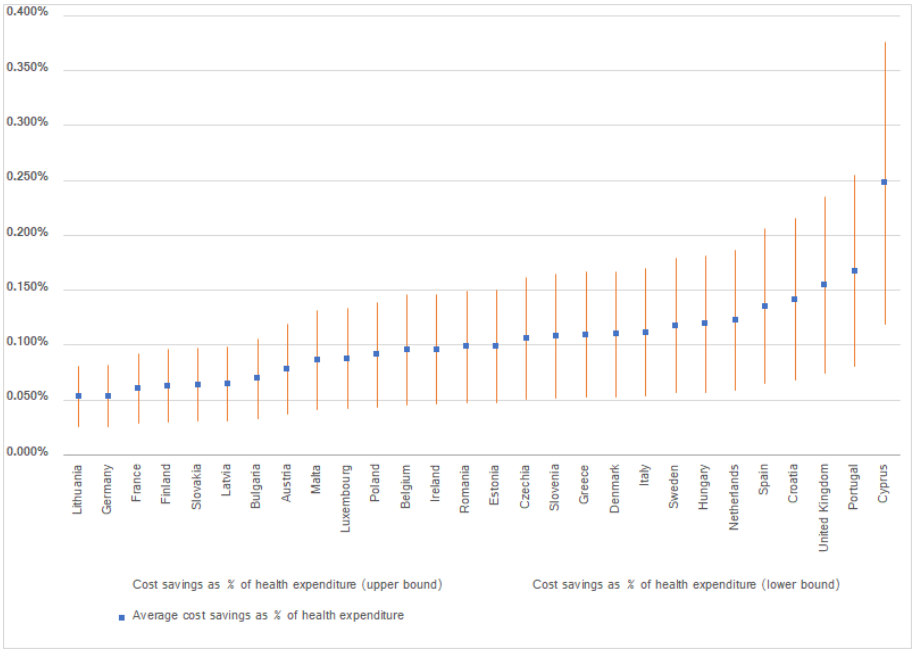

FIGURE 12: COST SAVINGS AS A PERCENTAGE OF THE HEALTH EXPENDITURE ASSOCIATED WITH A REDUCTION IN ALL-CAUSE LOS, 75% DMP COMPLIANCE SCENARIO.

Note: Orange vertical lines represent savings across upper and lower hospitalisation rates (12-38%); blue points represent the mid-point expected value.

Mortality reductions associated with the DMP were estimated to avoid between 12,000 and 17,000 premature deaths annually across the EU27+UK for the 50% and 75% participation scenarios, respectively. The range of net cost savings associated with a reduction in mortality crosses zero, as the case study showed that the DMP was cost-saving in some countries but cost-increasing in others (i.e. Germany). Estimates of the net impact on mortality and cost are illustrated in Figure 13 and Figure 14 below. These illustrate the non-significance of the net cost savings but also highlight the potential number of COPD deaths avoided across the EU27+UK.

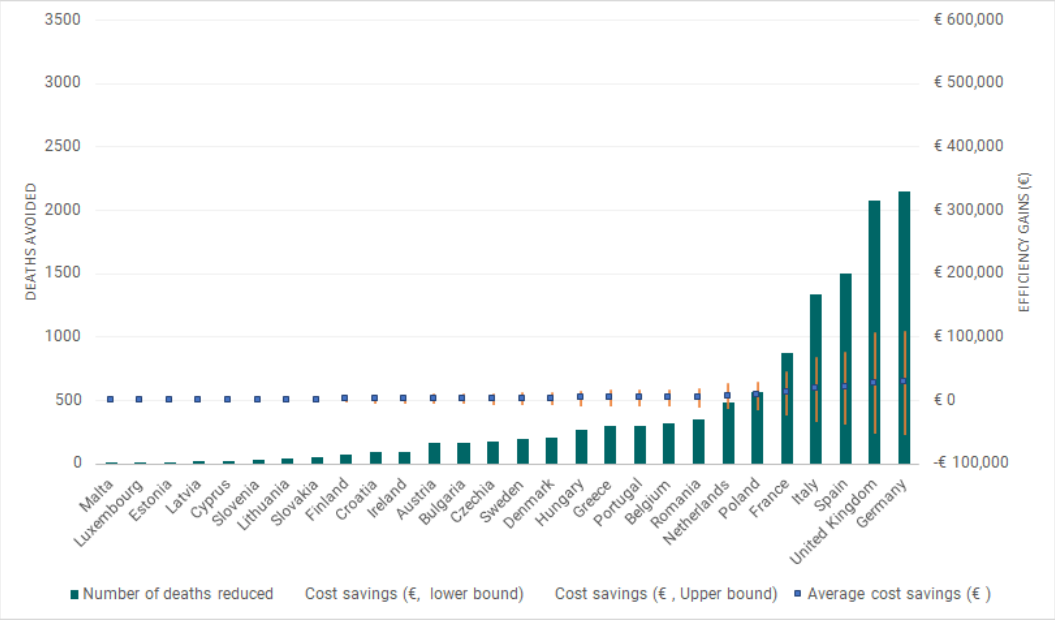

FIGURE 13: ABSOLUTE MORTALITY REDUCTION (GREEN BARS) AND ASSOCIATED COST SAVINGS (ORANGE BARS) BY COUNTRY; 50% DMP COMPLIANCE SCENARIO

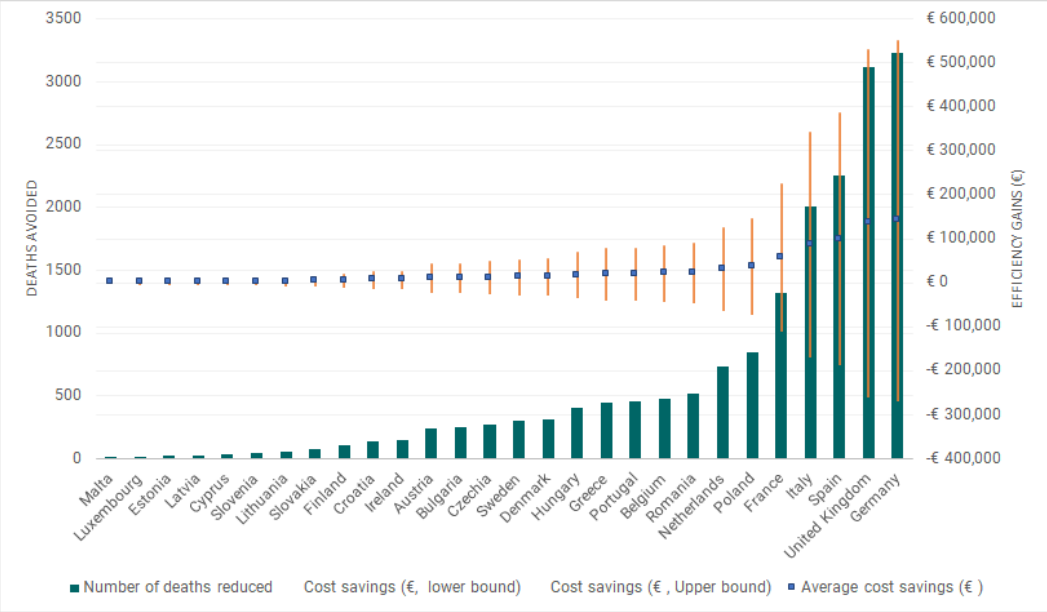

FIGURE 14: ABSOLUTE MORTALITY REDUCTION (GREEN BARS) AND ASSOCIATED COST SAVINGS (ORANGE BARS) BY COUNTRY; 75% DMP COMPLIANCE SCENARIO.

Given the uncertainty in net cost-savings associated with reduced COPD mortality, we do not include these in our estimates of aggregate cost savings associated with a DMP. Estimates of aggregate savings are based on LOS-related efficiency gains only.

For the EU27+UK, 50% compliance with a DMP for COPD was associated with up to 12,000 COPD-related deaths avoided and mid-point cost savings of €426.4 million per year (0.028% of aggregate health expenditure), ranging between €204.3 and €648.5 million (0.01% to 0.04% of aggregate health expenditure). In a 75% DMP compliance scenario, up to 17,000 COPD-related deaths are avoided and mid-point cost savings are €1.4 billion (0.092% of aggregate health expenditure), ranging between €689.1 million and €2.1 billion (0.05% to 0.14% of aggregate health expenditure).

4.3 Quantification 3: Efficiency gains from rational use of medicines

4.3.1 Methodology, inputs and key assumptions

Addressing inappropriate polypharmacy through medication review has the potential for substantial efficiency gains by improving disease management, avoiding adverse outcomes, and potentially reducing prescribing costs.

To illustrate the scale of potential efficiency gains associated with a systematic prescription review programme, we performed an analysis based on the outcomes observed in the Scottish case study discussed in section 3.3.1. For the purposes of the analysis, polypharmacy was defined as the use of ten or more medications daily. On the basis of nationally representative UK micro-data, the prevalence of polypharmacy was estimated to be 2.7% in the UK.[18] The potential cost savings associated with different levels of population uptake and the net effects of reviews, including the

[18] https://www.understandingsociety.ac.uk/documentation/health-assessment

rationalisation of medicines and a lower risk of hospitalisation due to adverse interactions, were estimated. Medicine rationalisation represents the net change in the number of medicines per individual and can include additional medicines for some patients and reductions for others. For sensitivity analyses, we tested population uptake over a range of 10-100% and average net medication reductions of 20-60%.

Outcomes in the Scottish case were expressed in terms of net medicine rationalisation, but we expanded our consideration of efficiency to include health gains and cost savings associated with avoiding hospitalisation admissions due to adverse interactions. The SIMPATHY study (Mair, Fernandez-Llimos and SIMPATHY Consortium, 2017) reported that up to 11% of all unplanned hospital admissions are attributable to medicines related harm and 16% of hospitalisations in the elderly are the result of inappropriate use of medication. Therefore, for our sensitivity analyses, we assumed that 11% to 16% of total expenditure on hospital admissions could be avoided through medication review, scaled by the proportion of the population participating in these reviews. This will be a slight overestimate of the costs avoided as we were not able to distinguish 'planned' and 'unplanned' hospital admissions and therefore used the cost of all hospital admissions, including planned and unplanned admissions as a baseline.

The average cost of per medicine in each country was based on UK prices adjusted for cross-country differences in the purchasing power. This adjustment is a simplification and does not account for differences in the actual price paid in each country. However, to the extent that other countries may have higher prices than in the UK, these figures will underestimate potential cost savings associated with rational use and therefore can be seen as a conservative estimate of potential efficiency gains.

4.3.2 Quantitative estimates of efficiency gains

Figure 15 and Figure 16 present estimates of the country-level efficiency gains associated with addressing inappropriate polypharmacy, including the rational use of medicines and adverse drug-interactions avoided. There are expressed in absolute monetary terms and as a percentage of health expenditure of the countries, respectively.

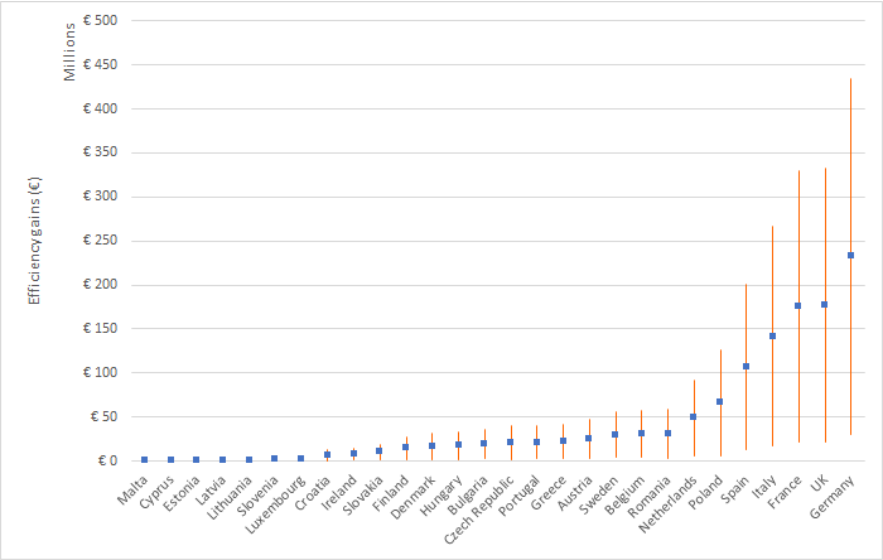

FIGURE 15: POTENTIAL EFFICIENCY GAINS ASSOCIATED WITH ADDRESSING INAPPROPRIATE POLYPHARMACY, EXPRESSED AS MONETARY VALUES. THE VERTICAL LINES REPRESENT THE

RANGE OF THE SENSITIVITY ANALYSES AND THE BLUE BOX REPRESENTS THE MID-POINT EXPECTED VALUE.

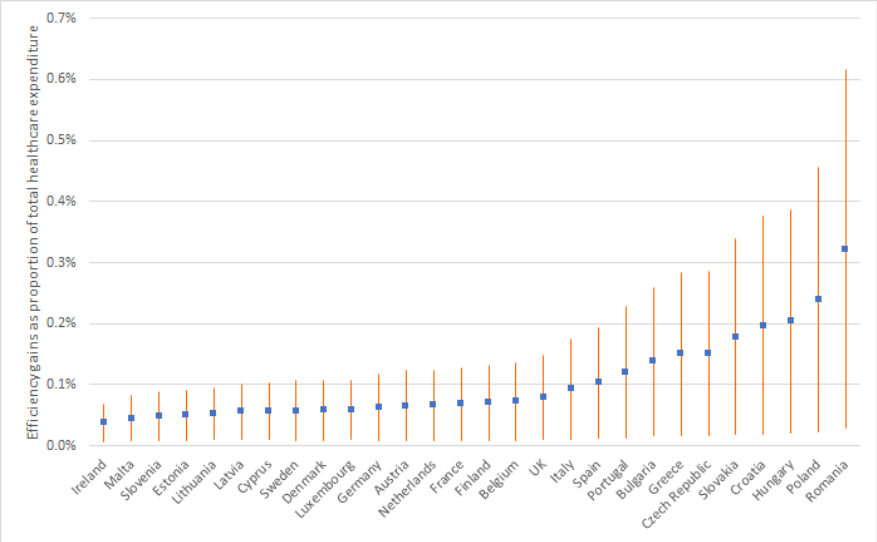

FIGURE 16: POTENTIAL EFFICIENCY GAINS ASSOCIATED WITH ADDRESSING INAPPROPRIATE POLYPHARMACY, EXPRESSED AS A PROPORTION OF TOTAL HEALTHCARE SPENDING.
Note: The vertical line represents the range of the sensitivity analyses and the blue box represents the mid-point expected value.

For the EU27+UK, a medication review programme to promote rational use of medicines could be associated with aggregate expected savings of €1.2 billion (0.081% of the aggregate EU27+UK health expenditure), ranging from €150 million in a less optimistic scenario (0.01% of the total health expenditure of the EU27+UK) to €2.3 billion in a more optimistic scenario (0.153% of the total health expenditure). Between 500 and 5,000 premature deaths could also be prevented.

4.4 Quantification 4: Efficiency gains from reducing healthcare-associated infections

4.4.1 Methodology, inputs and key assumptions

Healthcare-associated infections (HCAIs) have a substantial impact on health system efficiency. They are detrimental to patients' quality-of-life and survival and associated with significant costs (Roberts et al., 2003; Perencevich et al., 2003).

We estimate the size of the potential efficiency gains associated with clinical surveillance programmes to reduce HCAIs using the results of the evaluation of the more successful case, the Lean Sigma Six clinical surveillance intervention in Italy (outlined in section 3.4.1). As the evaluation (Improta et al., 2018) did not report the direct effects of the reduced incidence of HCAI on morbidity or mortality, we extrapolated this impact on the basis of the following inputs and assumptions:

- Following the results of the evaluation of the Italian case published by Improta et al. (2018), we estimate the impact on efficiency of a 43% to 49% reduction in the incidence of HCAI (with a 46% midpoint).

- The average prevalence of HCAIs in the EU27+UK is 7.1%.[19] This represents approximately 4 million patients each year.
- A case of HCAI is associated with an average excess of hospital length of stay of 8.5 days (95% confidence interval: 5.72 to 11.28 days) (Manoukian et al., 2018).
- HCAIs account for 37,000 deaths in Europe each year (Danasekaran et al., 2014). This translates to a mortality rate of 0.9% per colonised patient.
- Country-specific cost per bed day was derived from Eurostat 2017 data, as total hospital expenditure divided by total bed days. This ranged from €142 per day in Romania to €1,484 per day in Luxembourg and €2,752 in Sweden.

4.4.2 Quantitative estimates of efficiency gains

The quantification of benefits suggests that effective infection control measures can have a substantial impact on efficiency. Figure 17 shows potential cost savings across the EU27+UK, with aggregate savings from a reduced incidence of HCAI in the range of €7.6-8.5 billion.

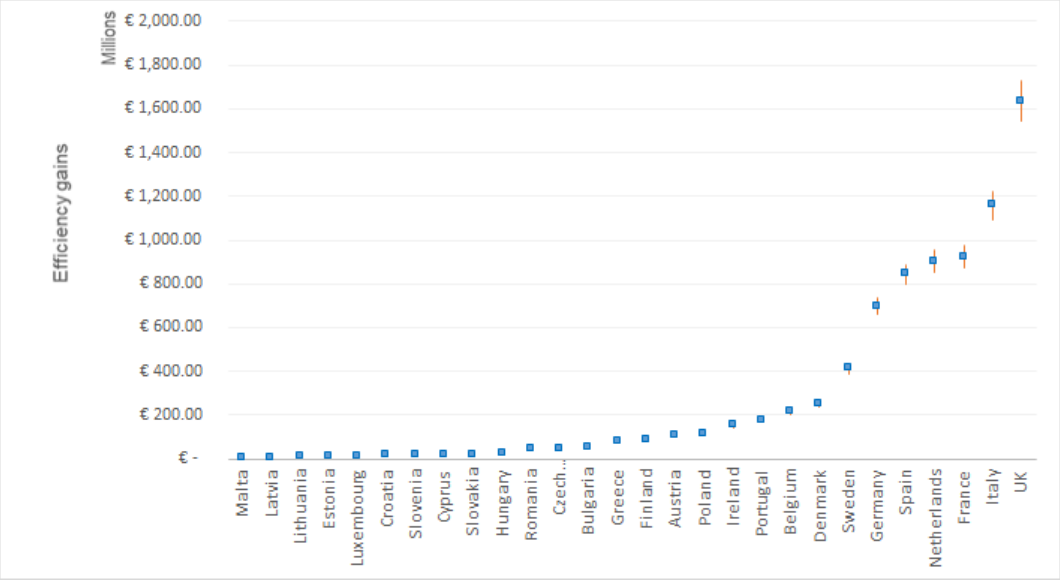

FIGURE 17: POTENTIAL EFFICIENCY GAINS ASSOCIATED WITH A REDUCTION IN THE INCIDENCE OF HCAIS BETWEEN 43% AND 49%

Figure 18 presents the same information as a proportion of total healthcare expenditure in each country and suggests that foregone costs would be between 0.53% and 0.56% of aggregate health expenditure in the EU27+UK.

[19] *Health care-associated infections fact sheet:* https://www.who.int/gpsc/country_work/gpsc_ccisc_fact_sheet_en.pdf

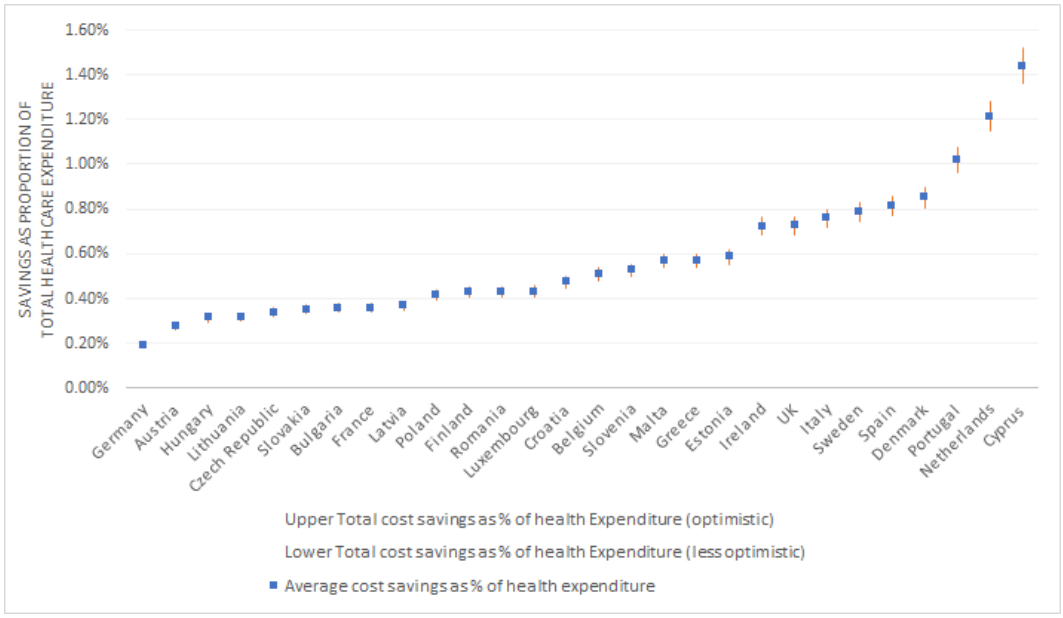

FIGURE 18: POTENTIAL EFFICIENCY GAINS AS A PERCENTAGE OF HEALTH EXPENDITURE OF THE COUNTRY.

Finally, Figure 19: HCAI-related deaths avoided shows the number of HCAI-related deaths avoided across the EU27+UK. More effective HCAI prevention could prevent between 15,000 to 18,000 deaths.

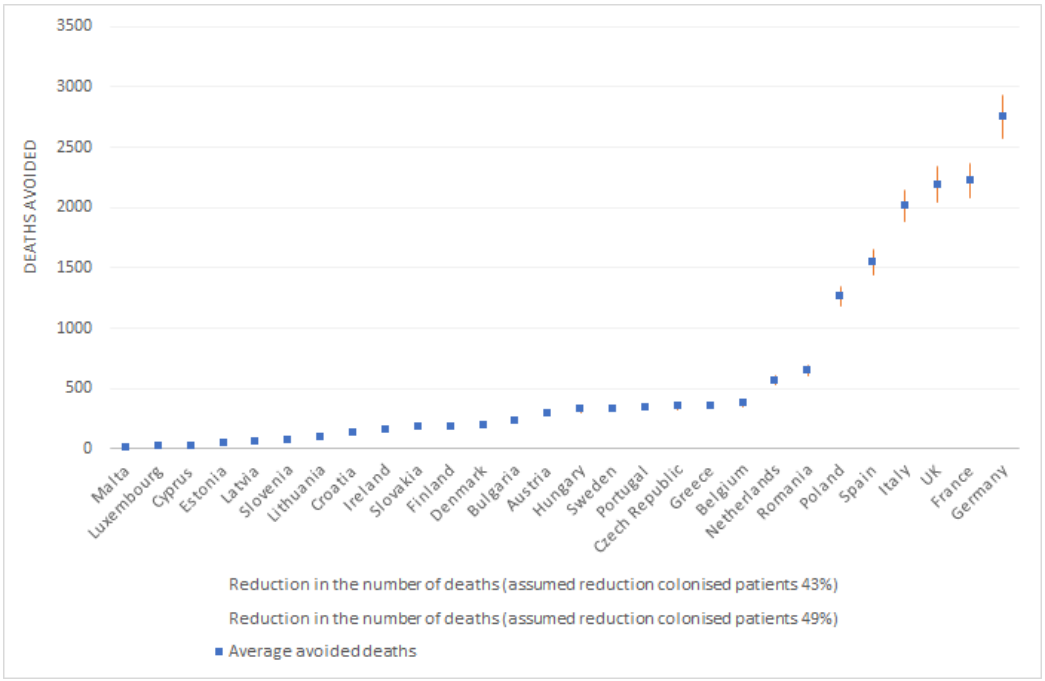

FIGURE 19: HCAI-RELATED DEATHS AVOIDED

For the EU27+UK, a reduction in the incidence of HCAIs would be associated with expected aggregate cost savings of €8.1 billion on average (0.53% of aggregate health expenditure), ranging from €7.6 to €8.5 billion (0.50% to 0.56% of aggregate health expenditure), and could prevent 15,000 to 18,000 premature deaths.

5 Discussion and conclusions

Improving the efficiency of European healthcare is in the interest of many stakeholders, including governments, payers, providers, patients, and the life sciences industry. Identifying and reallocating inefficient spending allows for better quality care, greater access to innovative treatments, and superior outcomes within existing budgets. However, identifying specific inefficiencies is often challenging, in part because it is difficult to know the 'counterfactual', or what the costs and outcomes of an alternative strategy would have been.

To gain an understanding of the counterfactual in selected priority areas, this study utilised a modified conceptual framework to frame and identify a series of case studies across four priority areas. The case studies contrast successful and less successful examples of interventions that have the potential to improve health system efficiency through a combination of cost savings and improved health outcomes. The case studies were chosen to reflect a range of priority areas, including preventative screening, standardised disease management and care pathways, rational use of medicines, and controlling healthcare-related infections. These cases should not, however, be seen as the only, or even necessarily the most important, sources of inefficiency in European healthcare systems, but rather those that were prioritised by the Steering Group and EFPIA.

The case studies highlight the potential for efficiency gains across a range of priority areas as well as key challenges in achieving these gains. These have generated the following high-level insights, in addition to more specific lessons which are set-out in section 3:

- Interventions that rely on patient participation should make participation as easy as possible:
  - An organised cancer screening programme in the Basque Country of Spain focused on making it as easy as possible for individuals to participate and achieved significant mortality improvements and long-term cost savings. In contrast, a similar programme in Paris, France, failed to achieve its objectives of improving screening rates, in part because participants were required to visit their GP to collect test kits rather than having them mailed directly to participants as in the Basque Country.

- Interventions that require health actors to take on new roles should be aware of, and take steps to mitigate potential resistance due to cultural norms or existing incentive structures:
  - A trial of a home-based disease management programme (DMP) for COPD led to improved health gains with no statistically significant increase in costs. This represents an efficiency gain by achieving more with the same resources. A real-world Germany DMP produced a more ambiguous result, as it was associated with health gains but also an increase in costs. The increase in costs appears to have been driven in part by patients visiting their GPs to verify advice given by nurses as part of the DMP, highlighting how cultural aspects can impact the outcomes of an intervention.
  - A medication review programme in Scotland, supported by national guidelines, ensured that patients with multi-morbidity were treated as effectively as possible whilst minimising the risk of adverse drug-drug and drug-disease interactions. The initiative produced strong efficiency gains as the upfront cost of the reviews was offset by cost savings from a net reduction in medicine use and a reduction in hospitalisations associated with adverse drug interactions. A pharmacist-led review programme in Germany was much less effective, in large part because the programme was voluntary, and pharmacists were not adequately

compensated for their time. This led to limited participation among pharmacists and minimal overall impact.

  - A clinical surveillance programme in Germany that relied primarily on the top-down promotion of hand hygiene protocols failed to promote hygiene compliance and the overall incidence of HCAI increased. One of the reasons for the comparatively greater success of the clinical surveillance programme in Italy may have been the involvement of staff in the design of interventions, and the provision of education and training on accountability.

- Local data might be needed to tailor existing interventions to address the specific drivers of inefficiencies in a given context. Ongoing data collection allows for refinement of these interventions.

  - An Italian initiative adopted a 'Lean Six Sigma' approach to reducing inefficiencies associated with healthcare-associated infections (HCAIs) in a hospital. This approach included using data and feedback from hospital staff to identify the root causes of HCAIs, design appropriate interventions, and continually refine them. An alternative approach was adopted in Germany that relied primarily on the top-down promotion of existing hand hygiene protocols. The intervention failed to promote hygiene compliance and the overall incidence of HCAI increased.

- The operational constraints of the broader health system should be considered when designing interventions.

  - A Danish initiative to define Standardised Patient Pathways (SPPs) in cancer reduced waiting times, improved patient satisfaction, and reduced costs in some areas, but had a limited impact on survival rates in different cancers and increased overall net costs. A similar initiative in Sweden, modelled on the Danish SPPs, performed less well. However, in both cases, there was evidence that a focus on waiting times in cancer may have 'crowded out' other disease areas.

  - One of the reasons identified by pharmacists as problematic in the medication review programme in Germany was that the programme interfered with regular pharmacy workflow.

  - An organised screening for CRC in the Basque country was able to avoid obstruction due to unmanageable increases in demand for colonoscopies – which has previously been observed in similar programmes – by estimating the expected incidence and colonoscopy capacity across the region prior to the introduction of the intervention.

The absolute scale of efficiency gains in different healthcare systems will depend on the relative efficiency of each system. There is greater scope for efficiency gains in relatively less efficient systems, whilst the potential gains are smaller in relatively more efficient systems. Each healthcare system, therefore, must consider the relative efficiency and inefficiency of its different components when prioritising between efficiency initiatives such as those described above.

As the more successful cases show, meaningful efficiency gains are possible in every healthcare system. However, many of the less successful examples show that innovations cannot necessarily be directly applied between different systems without accounting for local organisational and cultural differences. The insights described above may be helpful in addressing this challenge but are not necessarily easy to implement. For example, ongoing data collection to understand and refine initiatives is challenging given the continuous, urgent demands on many healthcare systems.

However, innovative approaches can produce substantial efficiency gains across a range of therapeutic areas, improving health outcomes and freeing up resources that can be re-allocated to improve outcomes in other areas.

6 References

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Founded in 1962 by the Association of the British Pharmaceutical Society, the Office of Health Economics (OHE) is not only the world's oldest health economics research group, but also one of the most prestigious and influential.

OHE provides market-leading insights and in-depth analyses into health economics & health policy. Our pioneering work informs health care and pharmaceutical decision-making across the globe, enabling clients to think differently and to find alternative solutions to the industry's most complex problems.

Our mission is to guide and inform the healthcare industry through today's era of unprecedented change and evolution. We are dedicated to helping policy makers and the pharmaceutical industry make better decisions that ultimately benefit patients, the industry and society as a whole.

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Areas of expertise

- Evaluation of health care policy
- The economics of health care systems
- Health technology assessment (HTA) methodology and approaches
- HTA's impact on decision making, health care spending and the delivery of care
- Pricing and reimbursement for biologics and pharmaceuticals, including value-based pricing, risk sharing and biosimilars market competition
- The costs of treating, or failing to treat, specific diseases and conditions
- Drivers of, and incentives for, the uptake of pharmaceuticals and prescription medicines
- Competition and incentives for improving the quality and efficiency of health care
- Incentives, disincentives, regulation and the costs of R&D for pharmaceuticals and innovation in medicine
- Capturing preferences using patient-reported outcomes measures (PROMs) and time trade-off (TTO) methodology
- Roles of the private and charity sectors in health care and research
- Health and health care statistics

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