Investing in European health R&D
A pathway to sustained innovation and stronger economies

Janssen Pharmaceutica N.V.
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Based on research delivered by
the Deloitte Health Economics group

Commissioned by
Janssen Pharmaceutica N.V.
The collaborative research efforts of academia and the pharmaceutical industry in developing new treatments have resulted in the most spectacular increase in life expectancy and quality of life in the history of mankind. It has been estimated that around 40% of the increase in life expectancy in the last decades is because of the introduction of innovative new drugs. Yet, for the first time in recent years, there is a stagnation in health R&D funding, both by public and by private organisations, as you can read in this report. This is extremely worrying if we consider that for the last decade the cost of conducting clinical research has increased by 10% on average per year.

It is even more worrying in the context of the increasing burden of disease and an ageing population in Europe, and the millions of people whose health cannot be improved without new therapeutic approaches. The development of new pharmaceuticals is crucial to meeting these challenges, and while pharmaceuticals in general only represent around 17% of healthcare budgets, their innovative value has a much greater impact, helping to reduce overall treatment costs significantly across many areas of care.

Pharmaceutical R&D expenditure is typically generated from company revenue, rather than from public funding. At Janssen R&D investments represent 21% of our sales, and as our business grew, so did our R&D investments, reaching more than $5.3 billion last year. Pharmaceutical research is primarily encouraged by offering the appropriate price to innovative new drugs. Very few industries incur the same financial risks as the innovative pharmaceutical industry, and with on average only 4% to 6% of early development (phase I) compounds ever reaching the market, it is critical that a fair reward system is in place for those molecules that actually become medicines.

Today, with effective treatments being available for many diseases, we are moving into an era of transformational innovation, trying to tackle diseases of very high complexity, where breakthrough science is needed to deliver value to patients. All this comes at a price, but the initial cost of innovation to society is small compared to the long term economic benefits of having new treatments.

Because of this high risk environment, and because of the increasing specialisation of research technology, collaboration is the key word. Janssen has set the tone by creating a number of initiatives to increase our collaboration with external private and academic partners. Last year we created Janssen Healthcare Innovation, which is looking at new business models, partnership structures and novel concepts of healthcare delivery. This year we created the Johnson & Johnson Innovation Centers, with a European office in London, to develop research partnerships. Additionally, we created Transcelerate Biopharma with 15 other pharmaceutical companies to simplify and accelerate the drug development process; we participate in various projects of the Innovative Medicines Initiative, with the European Medical Information Framework as its latest creation. Next to that we also created or contribute to disease specific programmes, such as the Global CEO Initiative on Alzheimer’s Disease,
the Bill & Melinda Gates Foundation Initiative on Neglected Diseases, collaboration with the Global TB Alliance and the International Partnership for Microbicides, to name but a few.

Finally, this year, we are creating the Janssen Health Policy Centre where we are engaging in conversation and debates with healthcare providers, policy makers and patients to be more efficient in delivering healthcare, with a holistic approach to healthcare systems and diseases of major impact to society such as diabetes, schizophrenia, hepatitis C, tuberculosis, cancers and Alzheimer’s disease.

There is a growing agreement among industry players, the academic world and public health organisations that we need to collaborate more broadly and efficiently to obtain substantial results for patients. At Janssen, we are a strong proponent of this approach.

This report sets the scene for a comprehensive and open discussion on what Europe can do to encourage research and development even more. We just cannot afford not to innovate.

Jane Griffiths
Company Group Chairman
Janssen Pharmaceutical Companies of Johnson & Johnson
Europe, Middle East & Africa
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CAGR Compound Annual Growth Rate
EFPIA European Federation of Pharmaceutical Industries and Associations
EMA European Medicines Agency
EU European Union
FP7 Seventh Framework Programme
GBAORD Government Budget and Appropriations or Outlays for Research and Development
GDP Gross Domestic Product
GERD Gross Expenditures on Research and Development
Health R&D Research and Development investments in healthcare and life sciences technologies
HTA Health Technology Assessment
IMI Innovative Medicines Initiative
OECD Organisation for Economic Co-operation and Development
PPP Purchasing Power Parity
R&D Research and Development
Vfa Verband Forschender Arzneimittelhersteller
WBSO Wet vermindering afdracht loonbelasting en premie voor de volksverzekeringen – Speur & Ontwikkelingsactiviteiten (Incentive for Research and Development Cost in the Netherlands)
Europe as a whole has historically lagged behind the US in terms of investment in research and development (R&D) in healthcare and life sciences technologies. Since the start of the economic crisis in 2007/8, R&D investments in Europe – from both public and private sources – have been under further pressure. Janssen commissioned this study from Deloitte’s European Center on Health Economics and Outcomes Research to draw together the relevant data and information into one document and to evaluate this issue in detail. The aim was to present a thorough analysis of the potential consequences of current trends and, based on the evidence, to explore possible scenarios for the future with relevant stakeholders.

R&D investments in health have generated substantial and positive outcomes for us today. The most self-evident direct benefit of investing in health R&D is the subsequent improvement in health outcomes and longevity. There are numerous examples over recent decades of how new medical interventions have greatly improved population health and wellbeing. In addition, there are also several other benefits of health R&D, such as improving the efficiency of healthcare provision, gains in productivity as a result of the improved health status of the working age population, and the positive contributions of health R&D to overall economic growth and to the knowledge economy in Europe. Each of these benefits has been documented and demonstrated to be crucial by various commentators, academics, clinicians, health policy experts and patients alike.

In this paper, we aim to present these benefits in detail and set them within the context of the continued growth in healthcare expenditure. Taking a broad look at the trends and increasing demand for healthcare services, we argue that further increases in the budget allocated to healthcare in Europe can be expected in the coming decades. Spending on healthcare is projected to increase to 12%-15% of Europe’s GDP by 2030. From an economic perspective, healthcare will be the largest R&D driven sector in the global economy. This makes the consequences of health R&D even more important. As healthcare spending continues to increase, each efficiency or productivity gain made possible by technological improvements from health R&D will free up resources, for example to invest in even healthier lives.

In this context, recent trends in attitudes towards investment in health R&D are alarming. Austerity measures are generating constrictions in the mechanisms that reward technological advancements in healthcare, leading to lower rates of return from investment in new technologies. This raises doubts about whether current healthcare financing policies will generate sufficient incentives to allow Europe to improve its expertise in the field of healthcare innovation. The many uncertainties around the level of investment in health R&D and the future financing of new technologies may jeopardise the capability of Europe to sustain its technological position in the global economy. It is these issues that this paper seeks to bring to public attention.

In this paper we argue that policymakers need to prioritise approaches that will enhance health R&D investments. Strategies are needed that both address public investment in health R&D and produce incentives for private enterprises so that the current decline in private sector investment is halted.
A large number of factors point to an unavoidable rise in healthcare expenditure of an estimated 5 percentage points to 12%-15% of Europe’s GDP by 2030, even with policy interventions and/or budget caps that aim to counterbalance these pressures. Trends that pushed up healthcare expenditure in the past will become even more intense in the coming decades. (See chapter 1)

• First, there is an expansion of demand for healthcare services mainly due to: an ageing and more obese population; better informed patients; and an increase in the societal and individual willingness to pay for healthcare as a result of higher income levels.
• Second, supply is accelerating thanks to the biomedical revolution of recent medical advancements, such as personalised medicine, and the convergence of different technologies.
• And third, the nature of healthcare provision, and specifically its heavy reliance on trained labour to deliver healthcare services, makes it difficult to achieve significant productivity gains, unlike some sectors such as the computing and automotive industries. Over time, healthcare therefore inevitably claims an increasing share of a country’s economy.

This growth in healthcare costs need not be undesirable, as is frequently stated. This is especially so when higher spending on healthcare leads to improved healthcare quality and life expectancy. With this in mind, the challenge is not so much “how do we reverse the growth of healthcare costs?” but more about “how can we best deploy the increasing resources spent on healthcare to create optimal benefits for the European population?”

Health R&D is the key to being able to respond to this dilemma. Increased investment in R&D has a fundamental role to play in economic growth in Europe as there are direct and indirect links between increasing R&D spend on healthcare, improved healthcare services, and the consequent wider benefits to the overall economy. This is even more the case in a context of growing healthcare expenditure. (See chapter 2)

• First, there is the direct impact of innovative technologies on the quality of healthcare provision, leading to improved health outcomes and extended years of life.
• Second, shifting healthcare budgets from delivery of care to newer technologies leads to higher efficiency gains on the long term, as the price of new technologies tends to decrease over time for both medicines (through the loss of patent exclusivity) and medical devices (due to decreasing prices, e.g. for bare metal stents). This creates further budgetary room for better care and newer and better technologies – which, in turn, have their own positive impact on population health gains.
• Third, improved health leads to better productivity among the working population and may even increase the maximum working age from its current level.
• And fourth, R&D investments, if appropriately rewarded, have the potential to provide high economic yields both in terms of return on investment and also by creating a knowledge economy and deploying a highly educated workforce with technical skills. This has a widespread positive impact on society and not only on a section of society (i.e. the patients).

These last two points lead to improved levels of GDP, benefiting the whole population, and, with GDP being a main driver for the willingness to pay for health, this also benefits patients.

However, the outlook for Europe is not as positive as it could be. Over recent years
there has been a stagnation in European private and public investment in R&D, while at the same time most cost components driving the total expenditure on health R&D have steadily increased in price. (See chapter 3)

- **Private biopharmaceutical investments in health R&D**, which are double the size of total public health R&D, have been slowing down since the start of the economic crisis in 2007/8. Biopharmaceutical companies have faced increased difficulties in marketing innovative products in the European markets, as well as reduced financial returns as a result of increasingly limiting reward mechanisms for innovative technologies. At the same time, the price of most cost components driving total expenditure on health R&D have increased significantly over the last decade. The combination of this pressure on both revenues and costs has had a negative effect on the private resources made available to R&D. Uncertainty around future market conditions is casting a shadow over opportunities to reverse recent developments, and is likely to have a negative influence on current private investment decisions. Publicly-funded R&D is unlikely to make up for this situation.

- **Public R&D investments** in Europe are only one-third the level of public investments made by the US. At country level, they declined or stagnated in most European countries, fell for the first time in total absolute numbers in 2011 and will be further under pressure in the near future due to public budget deficits. Investments at the European Union level account for only 2% of total public and private R&D and the current Horizon 2020 budget could lead to a stagnation in EU level funding for seven years.

These developments will have a negative impact on future health gains as well as future efficiency, productivity and economic benefits. Imagine if Europe and pharmaceutical companies had taken the decision 20 to 30 years ago to cut health R&D; would we be willing to live with the consequences today for our health and economies?

The potential of R&D investment to increase the health of European populations and positively impact Europe’s economies makes it crucial that governments adopt policies that will encourage the growth and success of health R&D. First, these policies should adequately reward new technologies. Second, the future willingness to pay for innovation should be reflected in transparent and predictable policy decisions now, in order to promote future positive decisions on private long-term investment. And third, governments should prioritise their direct investment in public health R&D and create explicit incentives for private health R&D. (See chapter 4)

The following chapters outline the arguments and underlying facts in support of increased investment in health R&D in Europe. The paper first looks at current and future trends in healthcare expenditure (chapter 1). It then substantiates the argument that increased R&D will have a positive impact on the health of populations and European economies (chapter 2). Further analysis investigates the recent trends in R&D investment on healthcare innovation in Europe (chapter 3). Finally, it looks at the policy options available to European and national institutions and governments to promote health-related R&D (chapter 4).
people may know what we do. Sometimes patients who are waiting, to bring them help and the sometimes very complex problems we have torn down against incurable diseases. We seek solutions, the founder of one medical companies: we want nothing to hide. Unable to measure our actual gain in dollars or in lives saved, one of the reasons is one of the reasons so.
Background: an unavoidable rise in healthcare expenditure in the decades to come

Recent developments in healthcare spending

Healthcare spending in Europe has increased substantially over the past three decades. In 1980, European countries on average allocated US$518 PPP\(^1\) per citizen. By 2011 this had more than quadrupled to US$2,937. A large part of this increase can be attributed to the ability to pay. About 90% of the observed cross-national variation in health spending across the OECD countries in 2001 can be explained simply by differences in GDP per capita.\(^1\)

However, healthcare expenditure in European countries has risen faster than economic growth, gradually committing a far higher share of their annual GDP to healthcare (see Figure 1). For example, in the 1980s France, Germany and the Netherlands each spent almost 8% of GDP on healthcare, but by 2011 this had risen to 11%. Similarly, the UK’s healthcare spending increased from as low as 5.6% of GDP to 9.6% over the same period. Europe is not alone in this trend; the most striking example has been in the United States, where healthcare expenditure as a percentage of the total economy increased from 9% in 1980 (US$1,100 per capita) to 17.0% (US$8,175 per capita) in 2011. It should be noted that more than half of the expenditure in the US is private, compared to typically a quarter in Europe. Nevertheless, even public expenditure as a percentage of GDP more than doubled from 1980 to 2011 in the US, from 3.7% to 8.5%.\(^2\)

There has been widespread debate in recent years as policymakers and academics sought to understand the underlying causes of the increased expenditure.

One straightforward, but only partial, explanation is population dynamics. In 1950, the proportion of people in Europe aged 60 and older was 15%, whereas by 2010 this had increased to 26%.\(^3\) Given that the health of individuals

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\(^1\) Purchasing power parity

![Figure 1: Annual healthcare expenditure (% GDP; 1980-2010)](Source: OECD 2012)
typically deteriorates with increasing age, a growing proportion of older people has been one contributing factor behind increased healthcare spending. Contrary to widely held perceptions, the effect of population ageing only explains one-third or less of this increase and non-demographic factors have a bigger part in explaining the reasons behind the rise in healthcare spend.

A majority of health economists agree that some of the most important factors underlying the persistent increase in healthcare costs have been technical advancements and medical innovation. Macroeconomic studies have found that technological change and new care pathways have accounted for up to two-thirds of the total growth in healthcare expenditure since the mid-20th century. The willingness to pay for these medical innovations and better care is high as they have the potential to improve quality of life and increase life expectancy.

The greater use of new and improved health technologies has been powered by rising levels of national income. There is a direct correlation between the wealth of nations and the share of their overall spending on health. Several studies have found that income elasticity of health spending is greater or very close to one, indicating that health-related expenditure rises faster than income. Health is therefore, in economic terms, a “luxury good” reflecting a willingness of developed economies to pay increasing shares of income for advanced medical technologies and medications. Indeed, healthcare expenditure growth has been 1.7 times higher than GDP growth in Europe over the last two to three decades.

Developments in technology have also changed the way we communicate and acquire knowledge in many areas – and healthcare is no exception. Patients are taking a more proactive role in the medical decision-making process and are exercising more control and choice. Over the past decade, healthcare information has become widely available through the internet, empowering patients and encouraging them to contribute to the clinical process.

One typical example is the proliferation of online patient networks like PatientsLikeMe.com (US), Medinfo.de (Germany), EntrePatients.fr (France), HealthUnlocked.com (UK) and Somospacientes.com (Spain), where people with medical conditions share information about symptoms, treatments and outcomes, allowing users with the same condition to learn from the personal experiences of others, and to obtain advice on how to improve their day-to-day lives. This higher level of awareness of the existence of alternative treatment options can fuel demand from patients for new treatments.

Jointly, these trends have underpinned the consistent growth over the past 30 years in healthcare spend, both in absolute terms and as a share of GDP. The current economic climate may lead to a temporary pause or slowdown in the rate of this growth but, as the next section outlines, healthcare spending is expected to continue to rise over the long-term.

**Future trends in healthcare spending**

There are several drivers for further growth in healthcare expenditure as a share of countries’ economies.

The four historic trends mentioned earlier in the text will, arguably, become more intense in the coming decades. The impact of the ageing population will be more evident, leading to a bigger proportion of the population living with
multiple long-term chronic conditions and pushing up the demand for healthcare (see Box 1). While it took two decades for the proportion of people in Europe aged 60 and over to increase from 20% in 1990 to 26% in 2010, that figure will jump to 34% in the 20 years to 2030.16 Within the older population, the number of ‘very old’ will rise at an even steeper rate over the same period, with the proportion of people aged 80 and over increasing from 1 in 100 to an estimated 1 in 25 by 2050.16 This ageing of the population will have a significant impact on healthcare systems. Recent research has confirmed that it is specifically the share of the population aged 85 and older that drives healthcare spending.6

The conversion of different technologies (mobile communications, IT, personalised medicine, DNA sequencing, gene therapy, etc) has the potential to create a step-change in technological advancements, which are also likely to be costly both to develop and to provide to a wider population. The increasing demand for healthcare services and (in the long term) overall economic growth will also remain as drivers of healthcare spend.

Box 1  The clinical and economic burden of four chronic diseases

Most of the burden of illness and mortality arises from non-communicable, often chronic, diseases (NCDs). Worldwide, NCDs lead to 63% of deaths17 and in Europe an estimated 70% of total healthcare costs relate to chronic diseases.18

Four major chronic diseases are described here to illustrate current trends in morbidity and the future impact on healthcare systems. These four examples have been selected based on WHO prevalence data for Europe and disease-specific healthcare spending in a number of countries. The increasing clinical burden of these diseases, for which the incidence or prevalence is growing on average by 1% per year, will be reflected directly in healthcare expenditure. In order to avoid a deterioration of care to these patients, healthcare budgets have to increase by 1% per year just to cover the growth in patient numbers (see Figure 2) and hence by 23% by 2030. This is before taking into account any of the other drivers of healthcare spend outlined in this chapter.

Clinical burden

The Survey of Health, Ageing and Retirement in Europe (SHARE) found that, in the European Union, 40% of people aged 50 and over were suffering from at least two chronic conditions; at the age of 65, two-thirds of those surveyed fell into this category, and an on-going longitudinal study at the UK’s University of Newcastle of the over-85 population – the fastest-growing demographic group in Europe – found that on average participants had four chronic conditions. The growth in the prevalence of these conditions is often linked to increased longevity, but lifestyle-related factors, such as obesity and alcohol consumption, are also playing a role.19,20

All other factors aside, healthcare budget for these four chronic diseases should increase by 1% per year just to cover the growth in patient numbers.
A review of the data on the four selected chronic conditions shows that:

- **Dementia** is found in 7.2% of the 60+ population, but this proportion rises sharply with age and up to 41% of those aged 90 and over are affected by the condition. Based on the growth and ageing of the population, by 2030 the number of people in Western Europe with dementia is projected to increase by 48% to around 10 million, equivalent to 2.4% of the population.\(^i\)\(^2\)

- As estimated by the International Diabetes Federation, **diabetes** will see a relatively modest growth in prevalence in the EU-27, rising from 6.9% to 8.1% between 2010 and 2030. This implies that the number of people with diabetes will rise from approximately 33 million to 38 million over this period.\(^2\)

- **Cancer** will remain one of the major causes of death. According to the International Agency for Research on Cancer’s GLOBOCAN database, the number of new cases a year will increase in the EU-27 from 2.6 million to 3.2 million between 2015 and 2030.\(^3\)

- **Cardio-vascular diseases** (diseases involving the heart or blood vessels) currently cause nearly half of all deaths in the WHO European region. Between 2010 and 2030 the prevalence of cardio-vascular diseases in the US is projected to increase from 36.9% to 40.5%.\(^\)\(^4\) Similar data are currently unavailable for Europe as morbidity from cardio-vascular diseases is more difficult to obtain compared to mortality.\(^5\)

### Economic burden

The increasing clinical burden of these four chronic conditions will have a direct impact on the costs of meeting the demand for healthcare. These costs not only include direct medical costs, but also other health-related services and capital investments.

- For **dementia**, the WHO estimates an annual cost per patient in Western Europe of $30,122. With a projected 48% increase in patients in Europe, these total costs will increase from €105 billion in 2010 to €158 billion by 2030. In Western Europe, this means the annual cost of dementia per head of population will rise from €923 in 2010 to €1,294 by 2030, based on demographic changes alone.\(^6\)

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\(^i\) Western Europe as “Global Burden of Disease” region of WHO, which includes 421 million inhabitants from countries such as France, Germany, Italy and UK but also Norway, Greece, Switzerland, Spain, Portugal, Sweden, Belgium, Austria amongst others.
In addition to the continued or increased impact of these historic trends, there are other economic reasons for significant increases in healthcare expenditure in the coming decades. First, one of the most prominent factors which is predicted to drive significant increases in healthcare costs is related to the difficulty of achieving large scale efficiency gains in the healthcare sector. Several policy initiatives may cap or reduce the growth of healthcare costs in the short term. These measures can be efficient, such as coordinating primary care with secondary care, rational use of interventions, chronic disease management, improved patient diagnosis and prevention. However, arbitrary cuts to essential services may destabilise the health system if they erode financial protection to patients, equitable access to care and the quality of care provided, and this can lead to increasing health and other costs in the longer term. In the extreme case of Greece, for example, health trends have been affected negatively by the financial crisis. For example HIV infections rose...
“Some approaches for dealing with health care costs can make spending more efficient, but will not address some of the key underlying pressures fuelling long-term cost growth [...] they are not likely to bring health care spending growth to down to the level of GDP growth.”


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Figure 3: Future annual healthcare expenditure (% of GDP, 2010-2030)
(Source: OECD)
GDP growth. An extrapolation of historic trends alone (using real GDP growth of 2%) shows an average increase in healthcare expenditure as a proportion of GDP of 5 percentage points by 2030 across the European Union. Even a conservative estimate (using real GDP growth of 1%) shows an average increase of almost 2 percentage points (see Figure 3). The acceleration of a number of trends (as mentioned above) is not included in this historic extrapolation, hence the final expenditure is likely to be closer to a 5 percentage points increase than to the 2 percentage point increase. Projections for individual countries are similar. This is confirmed also by individual estimates from different countries. For example, taking an even longer perspective, in the UK health expenditure is expected to grow to approximately 18% of GDP by 2050.

In summary, there is an increasing demand for healthcare services due to population dynamics; supply of healthcare is growing as a result of technological advancements and technology conversions; and the potential for productivity gains is limited due to the nature of the healthcare sector. Unless societies will deny care to, for example, diabetes, dementia and cancer patients, all these factors point to rising healthcare budgets in the years to come. With a wide range of new state-of-the-art technologies to anticipate, it appears that an increasing share of most countries’ economies will continue to be spent on healthcare services, regardless of policy interventions or budget caps that attempt to reverse this trend. Yet this is not a bleak picture as some commentators keep indicating. It is true that from one perspective this expenditure growth presents a tremendous budgetary challenge to governments. But there is an increasing willingness to pay for healthcare thanks to higher incomes. It can also be seen as an opportunity to improve the health of populations. As will be further argued in the following pages, the growth in healthcare spending can also generate economic growth if it is coupled with increased investment in the knowledge economy and healthcare related innovation. In the next chapter we argue that investing in health R&D has an important role to play in this regard.

The problem to be tackled should not so much be “how to curb the growth of healthcare expenditures” but rather the focus should be on finding the best methods to allocate the increasing healthcare expenditure so that higher health related and economic returns can be accomplished.
In this chapter, the benefits of medical innovations will be assessed by examining the impact of R&D outcomes on health; these include efficiency and productivity gains on the one hand and the impact of investments in R&D on Europe’s economy on the other.

Research innovation improves the health and longevity of the population

The level of every individual’s health is of primary concern to themselves and to their family. The statement that “the greatest wealth is health” stands as valid now as when it was written 2,000 years ago – and is perhaps even more so at a time when other threats to life have lessened. In this context, the value of harnessing the outcome of scientific developments (research) by converting them to applicable technologies (development) cannot be overstated. R&D in any area has the potential to bring improvements to human life. R&D in the area of healthcare has the potential to render a particularly valuable outcome as it improves life expectancy and the quality of life drastically. The achievements of modern healthcare and medications over the past century have been remarkable. In Western Europe, life expectancy at birth has increased from 67 years in the 1950s, to 74 in the 1980s, and reached 80 in 2010. This means that every five years, one extra life year is being added.

Effective technological innovations from biopharmaceutical R&D have made a huge contribution to this improved level of health and longevity, with the launch of newly discovered drug therapies increasing the probability of survival from diseases by one-third compared to older medications. The introduction of new medicines is estimated to have accounted for 40% of the increase in life expectancy between 1986 and 2000 alone and almost three-quarters of the 1.74 years increase in life expectancy at birth between 2000 and 2009. For example, vaccines, one of the greatest medical advances of all time, have almost eradicated viral diseases such as polio, for which incidence rates in the developed countries have dropped by more than 90%. Comparable successes have been witnessed in common childhood diseases such as measles, tetanus and pertussis (whooping cough). Antiretroviral therapy has benefited a large number of HIV-infected patients in high-income countries, decreasing the mortality rate and potential life years lost. These benefits led to an increase of 13.3 years in the life expectancy of patients at age 20 between 1999 and 2005 in Europe and US. In the area of oncology there have also been wide-ranging gains. For example, it has been estimated that the increase in the stock of cancer drugs led to an increase of 0.4 years in the life expectancy of the whole US population and accounted for 10.7% of the overall increase in the life expectancy at birth over this period.

“As a result of innovation in healthcare and medical technologies, modern medicine can now tackle disease in a way unthinkable 100 years ago. Death rates from coronary heart disease – one of the world’s biggest killers – have dropped; cancer survival rates have been transformed; and the devastating effects of modern diseases such as HIV/AIDS, have been alleviated”

– Dr. Frank Lichtenberg
The introduction to healthcare markets of these and an array of biopharmaceuticals in other therapy areas represents one of the most crucial factors behind the historical gains in health of populations over the past 40 to 50 years.

**Efficiency and cost saving health technologies create budgetary room for further investment in healthcare**

A second impact of implementing the outcomes of health R&D can be efficiency and cost savings. In the context of growing healthcare expenditure, this creates budgetary room for the provision of further health improving technologies, creating a ‘vicious circle’ of investment.

Medicines can support a more efficient use of resources by avoiding or postponing major health events. For instance, drugs such as aspirin, beta blockers, statins and angiotensin receptor blockers are used in preventing cardiac events, thereby avoiding the utilisation of more expensive surgical procedures such as bypass surgery and angioplasty. This results in more efficient use of resources. Another example is the introduction of new formulations such as ‘once daily’ tablets and long acting injections, which increases compliance and/or reduces length of hospital stay. From a cost perspective, this shift from expensive interventions and care, to effective biopharmaceutical innovations, will over the long term release resources that can be made available for further investments in health. Currently, the major contributor (59%) to the cost of providing healthcare is the provision of health in expensive settings, such as in-patient care (mostly in hospitals) and institutionalised long-term care (residential and nursing homes for older people). These are labour-intensive settings where productivity gains are hard to achieve (see chapter 1). Indeed, recent research has confirmed that incremental innovation in both drugs and devices has a reducing effect on healthcare expenditure.

It might be expected that shifting these costs towards effective biopharmaceutical innovations would lead to an increase in the proportion of total healthcare expenditure that is accounted for by biopharmaceuticals and other medical products. On the contrary, shares of biopharmaceuticals and other medical products related to healthcare expenditure have remained constant at 17% and 4% respectively over the last decade. Savings through a wider use of biopharmaceuticals (e.g. through the worldwide cost reduction of $21 billion in 2013 due to drug patent expirations) and other medical products (e.g. through the reduction in the price of bare-metal coronary stents), create budgetary room for new technologies in the mid to long term. Any such analysis needs to look at the long term impact of new technologies. For example, the introduction of statins might have increased costs initially, but they became substantially cost saving once they went off-patent (see Box 2).

Another example can be found in the area of stroke. New research on the cost-effectiveness of stroke care found that new stroke care provision (such as the use of multi-disciplinary specialists and specialised facilities for stroke patients) saved money as well as improving outcomes over a 10-year period in the UK. The results showed a higher proportion of healthier patients (with mild disability), for whom long term care costs were lower than patients with severe disability.
Also for our economy, we need healthy people who can work longer

Improved health outcomes as a result of innovative technologies also have an impact on economic productivity rates. Better health has a direct impact on the population’s productivity in the workforce. A recent study calculated that permanent illness reduces the “number of hours worked” for the population over a year by 6.9% for men and by 4.5% for women in the US.59 Similarly a study from Ireland found that for people with chronic diseases or disabilities which affected their daily lives, the probability of participating in the economically active population was 61% lower for men and 52% lower for women, compared to people without chronic conditions.60

Health innovations can play an important role in enabling individuals to be economically active for a longer period of time. This is particularly relevant as several European countries have increased, or are considering raising, the state retirement age. In Germany for example, the retirement age increased from 65 to 67 in 2007, and may rise to 69 in the future.61 In the UK, the government has proposed increasing the state pension age to 67 between 2026 and 2028.62 This trend is also driven by the European Commission, which issued a white paper arguing for member states to link retirement age with life expectancy.63

Effective biopharmaceutical intervention can also help avoid the heavy costs of early retirement due to ill health. In a number of countries such as Finland, Norway Ireland and UK, up to 20% of older employees stopped working before retirement due to disability.64 Or as Ulf Smith, President of the Alliance for Biomedical Research in Europe, stated in an interview: “Also for our economies, we need healthy people who can work longer.”

The economic value to Europe of R&D investments continues to rise

The three arguments discussed so far in this chapter concern the impact of health-related R&D outcomes on healthcare. From an industrial and economic policy perspective, it is crucial for Europe’s economy that the actual R&D on new medical technologies is performed in Europe. As discussed in chapter 1, healthcare expenditure in Europe is growing, and will consume an estimated 12%
to 15% of GDP by 2030, of which around 21% will be spent on pharmaceuticals and medical goods. Even in the short term, the biopharmaceutical market is an expanding market worldwide with an estimated growth of 3% - 6% per year until 2016. With Europe’s historic strength in this industry, investing in health R&D will provide significant benefits and opportunities for the European economy.

Private R&D investments are supporting Europe’s knowledge economy in several ways. The net trade balance of pharmaceutical and medicinal products shows a consistently upwards trend, tripling in value over the period 2000-2012 (Figure 4 Trade balance for the EU-27 in pharmaceutical and medicinal products). Of all large high technology sectors, the biopharmaceutical industry accounts for the highest net trade balance. Seven out of the top 20 R&D investors in Europe are pharmaceutical and biotechnology companies and seven out of the top 20 high-performing companies are from this sector.

The European Commission estimates that of all industries, pharmaceuticals is the most R&D intensive (R&D investments as percentage of turnover) and the second largest R&D sector in Europe (see Figure 5). It is therefore one of the key contributors to a knowledge based economy operating in a global growing market.

For public investments, R&D produces above average overall rates of return. Investment in biomedical research yields economic returns both through improved health gains and as a result of commercial exploitation of research outputs. Estimating the return on investment of public R&D is difficult as there is little available macro-level data

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iv Large is defined as all sectors that together account for more than 80% of total high technology exports.
on public R&D investments per therapy area. The best estimate comes from a UK study demonstrating that the health and GDP gains resulting from the country’s public and charitable investments in biomedical research are equivalent to an annual rate of return of about 39% for cardiovascular disease research and 37% for mental health research. These figures combine an annual rate of return of 30% in GDP gains from R&D investments with another 9% (for cardiovascular) and 7% (for mental health) in health gains from new preventive and therapeutic interventions. Similarly, another study in the US found that every $1 spent by the National Institutes of Health (NIH) typically generated $2.21 in additional economic output within a year. These trends are unlikely to change in the near future as most of the direct cost of dementia is driven by social care costs, where wages are expected to increase and productivity gains are hard to achieve.

Dementia is an example of how the four benefits from health R&D described in this chapter apply. First, if the outcome of research on dementia can postpone the onset of the disease by 5 years, the prevalence of dementia would reduce by 42% by 2025 and the number of deaths from the disease would be halved. Second, direct healthcare costs account for only 16% of total expenditure on the disease; within this figure, just 0.5% of total expenditure is spent on drugs. The potential savings in social care and informal costs are therefore extensive. Third, improved population health leads to higher economic productivity, directly for the patients and in this case by shifting the scarce talent of healthcare workers to other jobs and improving the productivity of informal carers. And fourth, with Europe’s ageing populations making it quite literally the “old” continent, Europe is well placed to drive international research on dementia.

Dementia is also an example of a condition where any evaluation of new health technologies should include its total societal impact including, for example, the productivity losses of informal care providers.

In summary, in the context of a world that is facing long-term growth in healthcare expenditure, the pathways from health R&D to health gains in the population are both direct and indirect. First, there is the direct impact of health improving technologies, extending years of life and improving quality of life. Second, efficiency improvements and the long-term price decline of any technology create budgetary room for more health improving technologies – which, in turn, does even more to secure population health gains. Third, this improved health leads to higher productivity among the working population. And fourth, R&D investments have a high overall return on investment. These last two effects lead to higher GDP and, as discussed in chapter 1, a higher GDP leads to proportionally even greater potential to invest in health improving technologies. All factors considered, increased investment in health R&D has a core role in economic growth – but as the next chapter demonstrates, governments cannot take for granted continuing growth in this investment.

Box 3  The potential impact of research on dementia

As stated in Box 1, the total European expenditure on dementia care is projected to increase from €105 billion in 2010 to €158 billion by 2030 due to the rise in the prevalence of the disease. Yet even this figure is very likely to be an underestimate, as the cost of care per patient may also continue to increase as it has in the past: expenditure on dementia in Europe grew at a rate of 11% per year from 2004 to 2010, of which 6.8 percentage points was due to inflation and higher service costs per patient. These trends are unlikely to change in the near future as most of the direct cost of dementia is driven by social care costs, where wages are expected to increase and productivity gains are hard to achieve.

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Dementia is also an example of a condition where any evaluation of new health technologies should include its total societal impact including, for example, the productivity losses of informal care providers.
As demonstrated in Chapter 2, as well as helping us directly or indirectly to live longer and healthier lives, health R&D also has a large positive impact on Europe’s knowledge economy. In this context, the recent stagnation in public and private investments in health R&D in European countries is an area of concern. This chapter looks at the main sources of health R&D investment and the reasons behind its changing profile.

Before looking in-depth at the sources of investment in health R&D, it should be noted that total European health R&D investments are dwarfed by total healthcare expenditures. Only 3% or €47 billion of total expenditure on health is on health R&D, while the remaining 97% or €1.4 trillion is spent on healthcare (Figure 6). European health R&D investments are also lower than US investments, both for public and private health R&D (see Figure 8).

### Three sources of investment in health R&D

We have reviewed three main sources of investments in health R&D: private R&D from the biopharmaceutical industry; public health R&D at country level; and the European Framework Programmes. In absolute terms, total health R&D spending in Europe is mainly driven by private sector funds: at a total of €29 billion, investments from pharmaceutical companies accounted for almost two thirds of total R&D investments in 2011 (Figure 6). The other one-third is primarily funded through public R&D at the national level, plus a relatively small contribution at European level, most recently through the EU’s Seventh Framework Programme for Research and Technological Development (FP7).

Looking at the level of total R&D investments per country, four countries (UK, France, Germany and Switzerland) stand out (see Figure 7). Relative to the size of the countries, there are nations with high private R&D activity, such as Switzerland and Belgium, and those with a greater emphasis on public R&D, such as the Netherlands. These are discussed in the sections below.
Private and public health-related R&D in Europe is stagnating

Looking at the sources of investment in Europe over time, both public and national private health R&D investments have contributed historically to an increase in health R&D investment. However, since 2008, the growth in investment has slowed down, with even an absolute decline in public health R&D for the first time in 2011. The 2011 GBAORD data indicate a stagnation in 2010 and a decline of 1% in 2011 for public health R&D. At the same time, the growth in private health R&D investments has slowed down since 2008, although there were signs of an improvement in 2011 (see Figure 8 and the Annex).

There remains a significant gap between total spending on health R&D in Europe and the US (Figure 8). At the height of the recent financial crisis, the US actually increased its public health R&D budgets by $10.4 billion over the period 2009-2010 through the American Recovery and Reinvestment Act (ARRA), a stimulus package designed to counteract the economic crisis.

The following sections look at the details of, and the reasons for this stagnation and the contrast with the increasing costs of clinical research.

Figure 7: Private and public R&D per country (Source: EFPIA; Eurostat GERD; European Commission; Local Sources for UK and France (Public R&D))
Private R&D investments from the biopharmaceutical industry are stagnating while costs are increasing

The previous section demonstrated how growth in EU private investments has stagnated since the start of the financial crisis, although there were signs of an improvement in 2011 in privately-funded health R&D. This becomes clearer at a global level when looking at these investments as a percentage of GDP (see Figure 9).

More than 85% of private health R&D investment in Europe is concentrated in the EU-5 countries (France, Germany, Italy, UK and Spain), Switzerland, Belgium and Denmark. In line with the trends illustrated above, most of these countries, except for Switzerland, are investing at similar or lower levels than at the start of the financial crisis (see Figure 10).

Alongside this stagnation has been a reduction in the R&D workforce. In Europe, while the growth rate in the number of researchers employed in health was still 17% in 2000, it declined to a growth of just 0.4% in 2010; final figures for 2011 are expected to show a 1% fall in the number of researchers. Further reductions in the R&D workforce have been announced by Sanofi and AstraZeneca. Following efforts since 2009 to refocus its research activities, Sanofi will eliminate 900 jobs in France by 2015 as part of an ongoing R&D restructuring programme; meanwhile AstraZeneca plans to cut a total of 7,300 jobs by the end of 2014, of which 2,200 are researchers.

Figure 8: Total health-related R&D 2004-2011 (€ billion) \(^7\)
(Source: EFPIA; Eurostat GERD; GBAORD; European Commission, Research America)

Figure 9: Europe, US and Japan private health-related R&D as a percentage of GDP
(Source: EFPIA: Private R&D investments; Eurostat: GDP)

$v\text{ There is no consistent long term data on public R&D expenditure in health. Therefore, GBAORD, GERD and local data have been used. Detailed information on this calculation can be found in the Annex.}$
Various potential causes of the slowdown in R&D spend can be identified. Biopharmaceutical companies have been facing an increasing number of obstacles in getting innovative products to the European markets, as well as reduced financial returns as a result of diminishing rewards for innovative technologies. For example, recent austerity measures throughout Europe, such as price cuts, clawback systems, rebates and delays in market entry for new therapies, are causing a decline in the financial returns from innovative biopharmaceutical products:

- According to EFPIA, in five European countries alone (Greece, Ireland, Italy, Portugal and Spain), discounting and price cuts, contributed to over €7 billion in savings for the countries in 2011. For example, in Portugal a payback system was introduced, whereby pharmaceutical industry will pay the amount of overspend, if spend on prescription drugs exceeds the target of 1.25% of GDP. There were additional mandatory price cuts in 2012 such as the in the agreement between the Irish Pharmaceutical Healthcare Association (IPHA), the Department of Health and the Health Service Executive in October 2012.

- International reference pricing systems (e.g. benchmarking prices with other European and non-European countries) disregard the fundamentals of rewarding innovation and focus only on price reduction.

- The introduction of additional pricing and reimbursement hurdles to limit the use of premium-priced or branded drugs through the implementation of market access or prescribing restrictions, for example the Act on Reform of the Market for Medicinal Products (Gesetz zur Neuordnung des Arzneimittelmarktes – AMNOG) introduced in Germany on 1 January, 2011.

- This situation is exacerbated by other factors such as difficulties, and in some instances failure, of Governments to pay their drug bills. At the end of 2011, EFPIA estimated that the pharmaceutical industry was owed over €12.5 billion by Greece, Italy, Portugal and Spain, with the majority of debt owed by hospitals and local governments.

Regulatory and market access problems effectively lead to a reduction in a drug’s market exclusivity period and hence the volumes of sales while under patent protection. This has an important impact on the expected return on investment in health R&D. In the US and Japan, market access automatically follows the granting of market authorisation for a biopharmaceutical product. In Europe this is the case only in Germany. All other
countries have processes that postpone market access after approval by the European Medicines Agency, and it can take several years for healthcare systems to deploy a new drug for the treatment of patients in the majority of European countries. Policies which hinder a straightforward transition between European Medicines Agency (EMA) approval for drugs and market access — for instance through delays in the reimbursement decision process — effectively curb demand for such products. Local experts confirm that countries are postponing approval decisions for new innovative molecules, for example by responding within the set 180 days (according to the EU directive) with a negative response and questions (but without asking for new data). This leads to another period of 180 days for a response to the adapted reimbursement application. Professor Koen Debackere, Managing Director of Leuven University (Belgium), gave as an example a reimbursement application that has already been pending for four years. Additional controls and restrictions (e.g. linked to patient age or disease severity) on the population groups that are allowed to access new biopharmaceutical and medical technology products also have a negative impact on demand. Public payers in Europe are also increasing the demands for more detailed evidence of biopharmaceutical products, not only on efficacy in clinical trials, but also on effectiveness in practice. This is pushing up development costs and extending approval timelines. In the past, this increased cost could be covered by increasing sales, but as stated above, this might not be the case in the future.

At the same time, most cost components driving the total expenditure on health R&D have steadily increased in price. The financial return on R&D is influenced by the costs of bringing a new drug to the market; this is estimated to have increased on average to US$1,506 million in 2011 compared to US$1,031 in 2003. Some research has even suggested an estimated average of $4.2 billion in research dollars spent for every drug that is approved, taking into account the cost of drug failures. The drivers of this trend are diverse:

• Higher than inflation rises in input costs such as wages, equipment and facilities.
• Higher complexity of clinical trials such as smaller number of patients per site and increase in the effort required by investigators due to the complexity of study protocols.
• Reduced R&D productivity for the sector. (That said, a recent study by Deloitte indicated that the strategies implemented by industry leaders over recent years are starting to have a positive effect on R&D productivity.)

Recent research estimated that clinical trial costs grew on average 9.45% annually during the last decade (1999–2011), compared to a growth of 3.98% in the years before (1989–1999). If the cost of R&D continues to rise, the current stagnation of R&D investments by the industry might have a direct negative impact on R&D output.

The combination of this pressure on both revenues and costs creates a lack of confidence in the future return on investment in health R&D. That, in turn, has a detrimental effect on decisions about future R&D investment: it is one thing that prices will be less, but another if the industry does not know what the willingness to pay will be. In economic theory (and practice), investment rates are directly correlated with confidence. With R&D only offering returns over the long term, uncertainty around the potential prices governments are willing to pay for new medicines, combined with shifting regulatory requirements, serve.

“Stricter market access leads to lower returns on development, so other decisions are made” — Prof. Koen Debackere, Managing Director, Leuven University, Belgium
to undermine companies’ willingness to invest. As one industry specialist stated: “It is not the price decrease now that influences investments, it is the uncertainty around the price level in the future that is fatal.” Specifically in the biopharmaceutical industry, where the top 20 companies account for almost 80% of total worldwide investments in private biopharmaceutical R&D, any policy change on investment decisions by one company has an immediate and strong effect on total R&D investments in Europe.

Public R&D is in decline

Public health-related R&D is funded from different sources. The majority (94%) of resources comes from national funding organisations, the rest (6%) is from the EU through the Framework programmes and the European Research Council (ERC). Other investments come from other European level health research funding framework programmes, such as the Competitiveness and Innovation Framework (CIP), (€18 million in 2011) and the Innovative Medicines Initiative (IMI) public-private partnership, which is funded by the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA) with a budget of €2 billion (€1 billion coming from the FP7 and €1 billion in ‘in kind’ contributions from EFPIA) over a 10-year period 2008-2017.

At national level, there are significant differences between European countries in their levels of health R&D spending. Overall, the EU-5 plus the Netherlands account for more than 70% of total expenditures (Figure 11).

Overall, average 2010 European national health-related R&D spending at 0.14% of GDP was considerably lower than the US’s 0.44%. As a percentage of GDP, the Nordics, Netherlands and Austria are the countries with the highest investment. Most Eastern European countries, but also countries like UK and Italy are investing proportionally less in public health R&D than the EU average (Figure 12).

National EU public health R&D has grown significantly over the last decade, but as illustrated, overall it fell for the first time in 2011 (see Figure 8). Except for Germany, Ireland and Czech Republic, public R&D investments declined or stagnated in all European countries (see Figure 13 and the Annex).

vi. Calculations based on Eurostat GERD and European FP7
vii. Calculations based on Eurostat GERD; OECD: GDP and Research America for US data
Within the current context, it is expected that in the near future national budgets for health-related R&D are set to decrease or, at best, stay the same. For example, in Germany the Federal Ministry of Education and Research has a total budget for 2013 of €13,740 million, of which €252 million will go to health research – this represents a 3.5% decrease in the health research budget compared with 2012.

Public investments in health R&D at European level are not likely to make up for the contraction at national level. Firstly, European investments in absolute terms account for only 3% of total health R&D in Europe (see Figure 6). Secondly, within the European framework programmes, less than 15% of expenditure is being spent on health R&D, compared to 20%-35% at national level. Thirdly, although health R&D spend within the FP7 framework has grown on average by 7.4% per year to €1 billion in 2013, the expenditure between 2014 and 2020 through Horizon 2020 looks less promising. In the initial budget of almost €80 billion proposed by the European Commission, only €8 billion (10%) was designated for “Health, demographic change and wellbeing”. Additionally, the €80 billion budget may be further reduced by the European Council to €69 billion. If the share of health R&D then remains the same as in the initial proposal, this would mean a budget of €7 billion, equivalent to an annual expenditure of only €1 billion, for the next 7 years. This represents stagnation in European-level investment in public R&D and is a concern, according to Ulf Smith, President of the Alliance for Biomedical Research in Europe, since “it will not cover increases in costs and will not enable additional efforts in R&D.”

It should also be noted that European public budget decisions have an impact on national public budgets. For example, in Italy national R&D resource funds partially mirror the organisation of Horizon 2020.

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"There are significant differences in the relative shares of funds allocated to the different R&D performing sectors between the European states. While in the UK, the largest share of the funds went to the university sector, in France, for example, governmental research organisations like Inserm (Institut national de la santé et de la recherche médicale) or CNRS (Centre National de la Recherche Scientifique) can be identified as key players in the national research landscape. In Germany, the governmental sector, with institutions like Fraunhofer or the Max Planck Society, as well as the industry and university sectors were allocated roughly equal funding amounts.” (Source: ESF-EMRC – A Stronger Biomedical Research for a Better European Future.)
The interaction between public and private R&D

In addition to the separate public and private health R&D investments, it is essential for both sectors to be interlinked, as the interaction between public and private stakeholders fuels innovation. For example, a strong knowledge base from basic research in universities and the capability of hospitals to perform clinical trials attracts private R&D investments. On the subject, Professor Koen Debackere, Managing Director of Leuven University, Belgium, stated: “R&D follows the ‘production’ (i.e. hospitals). If you have good clinical centres, private R&D investments will follow. Therefore, a good framework for clinical trials is essential to attract R&D.”

The link between universities and the industry has been investigated in a study by Owen-Smith et al (2002). The authors’ comparison of the systems in the US and EU demonstrates clearly that Europe has fallen behind its peers in this area. The paper suggests that the heterogeneity of the system in the US based on close ties between basic sciences and clinical development has worked to its advantage. The existence of numerous small firms and public research organisations across various therapeutic areas and in different stages of development process coupled with strong ties between such organisations is a major factor in their superior success compared to EU institutions. The authors suggest that Europe, on the other hand has regional centres of expertise “with a less diverse group of public research organisations working in a smaller number of therapeutic areas”.

The EU Commission also published a report on how The European Union could generate such initiatives. The report prepared by a group of experts suggested that

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Figure 13: National level public health-related R&D spending trends (2010) ix
(Source: Eurostat GERD (2000-2010) and GBAORD (2011))
bridging the gap between risk capital and R&D spending for smaller, innovative but financially constrained firms could be a policy option to adopt. This is because private sector R&D investment levels, including projects by larger firms that are outsourced to smaller firms to solve bottlenecks, are critically dependent on a well-functioning risk capital market. The authors suggest that public funding would be more cost-effective if it would be targeted at the beginning of the risk capital investment cycle. Even though they estimate that this would generate significant returns they acknowledge that there would be a lag in realising returns. The policy side suggestions that were attached to the estimates made in the report included items such as the need for better networking between universities and funds in Europe.

One of the most recent advances towards building a robust public private partnership to support technology growth in bio-pharmaceuticals has been the launch of the Innovative Medicines Initiative (IMI), a joint venture of DG Research of the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA) set up with a budget of €2 billion. IMI, aiming to address the bottlenecks in drug development process in Europe, was expanded recently to generate growth in the biopharmaceuticals sector by creating a single innovation market and will help spread the benefits of innovation across the EU and beyond. The outline of the initiative establishes that “Europe’s future economic growth and jobs will increasingly depend on our ability to drive innovation in products, services and business models.”

Recently there have been some successful ventures where the cycle of R&D was initiated by not-for-profit organisations and at a later stage brought to a successful completion by large pharmaceuticals. One example is the case of a drug developed to treat castration-resistant prostate cancer. The scientists of the Institute of Cancer Research were funded by a not-for-profit organisation, Cancer Research UK, and the research was then taken over by the industry at the development stage. The drug initially faced challenges over reimbursement and, after an evaluation by NICE, was initially rejected for reimbursement by the NHS. However, a recent agreement between the authorities and the manufacturer has enabled the drug to be reimbursed in the UK.

In short there is a potential to improve the integration between the public and private initiatives in Europe to bring life sciences technologies successfully to the market and to patients.

The poor outlook for health R&D has wider implications

To summarise, current conditions in Europe appear to have had a detrimental effect on private investments in R&D in Europe and doubts on future market conditions are likely to influence current investment decisions negatively. Public R&D is not likely to make up for this loss as it is roughly only half the size of private R&D, is recently in decline and has little scope for growth in the near future due to public budget deficits. Current public R&D is only one-third of the public R&D investments in the US and the gap is also widening for private R&D. Given the role of health R&D on our health and our economies (see chapter 2), it is crucial for governments to adopt policies that will encourage its growth and success.

“If you have good clinical centres, private R&D investments will follow”
– Prof. Koen Debackere, Managing Director, Leuven University, Belgium
Chapter 2 discussed how medical advances have made a crucial contribution to the significant increases in life expectancy and quality of life that have been achieved over the past century, and how the outcome of health R&D also contributes to efficiency gains, to productivity and to our economy. The European Union also recognises the importance of innovation and R&D in healthcare. The European Commission’s Directorate-General for Enterprise and Industry (DG Enterprise) states:

“To set the conditions right for a creative and innovative Europe is a must in order to preserve our standard of living as well as to cope with the challenges of the future. The ramifications of ageing societies, the emergence of new public health challenges and the internationalisation of the value chain for healthcare products are just a few examples of issues the EU has to face.”

There is therefore no doubt that it would be to the long term benefit of society that public health policies throughout Europe reflect these challenges and ensure that the momentum and growth in medical innovation is sustained and encouraged over the coming years. This can only be ensured by:

- rewarding innovative technologies adequately by setting up appropriate reimbursement and market access processes;
- allowing innovative technologies to access the market rapidly and reach a large share of the population;
- removing the uncertainties created by shifting regulatory requirements and changing pricing structures, all of which erodes confidence in decisions about future private investment in health R&D, and;
- directly promoting and enhancing public and private investment in healthcare R&D.

Policies rewarding innovation are necessary to incentivise private R&D spend

Despite evidence of inexorable pressures for the long-term increase in healthcare expenditure (see chapter 1), short term policy is currently targeted on cost containment. In the context of this budgetary imperative to “slow the growth of healthcare spending”, it is important to realise that focusing primarily on cutting costs will have serious negative consequences both for patients and for biopharmaceutical R&D. This paper has shown that private R&D is the largest health R&D driver in Europe and that 15% of pharmaceuticals sales is reinvested in health R&D. The indirect investment in health R&D by national public health budget through reimbursement of pharmaceuticals is greater than the direct investment through public R&D budgets. It is important that stakeholders responsible for public health, such as the national ministries of health, realise their role in contributing to healthcare research by rewarding innovation.

It is impossible to create an environment where innovative solutions are discovered unless those new technologies are properly utilised by national healthcare systems and adequately rewarded by the healthcare financing structures.
In this context, DG Enterprise has identified the current issues around reimbursement as a problem; it comments that the limits of willingness and ability to pay for biopharmaceutical products have been reached, and that there is now a need for joint efforts in order to secure the financing of new medical technologies.

Instead, policies that focus only on curbing rising costs have acted to discourage further private R&D investment (see chapter 3). Against this background, policymakers in Europe will have to find new ways to incentivise the outcomes of public and private R&D. One of the biggest steps in this direction would be to create clear policies to reward innovative technologies. This is especially needed when ad-hoc pricing agreements are being replaced by value based pricing methodologies, with the aim of public institutions being to reduce reimbursement prices of medical technologies as much as possible.

Pricing systems that recognise high investment costs, and thus encourage the development of healthcare technologies, lead to significant improvements in the speed of technology developments and as a result save lives. This is illustrated by the high rate of innovation in therapy areas such as oncology, where the average financial rewards are high, and in chronic diseases, where this is also the case due to the long term need for treatment. In contrast, innovation is limited in therapy areas such as antibiotics, because of low prices, and HIV, where low cost comparators lead to a low willingness to pay for incremental innovation.

Another area where policy development is needed is in the parameters of the analysis that lies behind the economic case for a drug. At the moment, most health technology assessment (HTAs) compare a new treatment with the current standard of practice, using current costs and current treatment differences. This disregards the dynamics of incremental innovation and does not take into account that after an “investment period” by payers during 8-10 years of reimbursement, payers will experience cost reductions when the patent expires. It is crucial for any national HTA system to introduce more sophisticated analytic methods to determine the fair price for a technology.

Prices should also reflect the relative value of a medicine to a particular society. International reference pricing leads to price convergence, which in its turn leads to affordability and market access issues in poorer countries. As suggested by Richard Torbett, Chief Economist at EFPIA, “the goal of a proper pricing mechanism should be to achieve a convergence of market access rather than a convergence towards low prices” which, in the end, has a negative impact on R&D investment.105

Approved technologies should be rapidly available to the market

A fair pricing framework is a key element of rewarding innovation, but other aspects of the market are also crucial. The demand side policies that some governments have put in effect (see chapter 3) have curbed utilisation of biopharmaceutical goods and hence reduced the returns on R&D investment. Allowing new treatments to reach a wider population more rapidly would create the desired effect, and focusing health targets on specific therapy areas can play an important role in this respect (such as the European focus on cardio/cerebrovascular diseases over the past 10 years).

One way to speed the time to market would be an improved collaboration between regulatory approval
processes and pricing/reimbursement decisions in each European country. This would have a positive impact on the utilisation of new technologies and thereby indirectly contribute to the increased investment in R&D. An example of such a policy can be found in Australia where pricing and reimbursement can run parallel with the approval process.\textsuperscript{106}

Other hurdles for faster market access are the differences in the ways data are interpreted on surrogate end points, patient choice and comparator technologies by European health technology assessment (HTA) agencies. This can lead to different recommendations when assessing the same products. By understanding these differences and learning from assessments that have either succeeded or failed in achieving positive recommendations, a system can be established whereby both manufacturers and HTA agencies can improve the quality of the evidence generation and evaluation processes. This would help ensure that the incremental health and technological benefits provided by new medicines find their way to patients more quickly. For example, it would be constructive for evidence requirements and evaluation methods to be made more explicit by HTA agencies, and for manufacturers to pursue available opportunities to gather input on research designs early in the drug development process.\textsuperscript{107}

The number of “orphan drugs” with market authorisation is an example of the impact of policy incentives. Since 2000, companies in Europe have been able to apply for orphan drug status for pharmaceuticals that are being developed to treat rare diseases affecting no more than 5 in 10,000 EU citizens. Drugs applying for this status are given a number of advantages during registration process such as fee reductions during the application process to the European Medicines Agency, free scientific consulting (protocol assistance) during the development phase and exclusive marketing rights for a maximum of ten years. Before the introduction of the Orphan Drugs Legislation, on average not more than one orphan drug was receiving marketing authorisation every year in Europe. Since 2000 this number has increased dramatically (see Figure 14) and currently a total of 87 orphan drugs have marketing authorisation in the EU.\textsuperscript{108}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure14.png}
\caption{Marketing authorisations for orphan drugs in the EU}
\end{figure}

\textbf{Lack of market confidence will undermine the future of private health R&D}

When cost and demand-cutting policies lead to uncertainty in the healthcare field, as is currently the case, it becomes much harder for researchers, investors and industry companies to make the mid to long-term plans necessary to ensure success in the decades-long course of developing new treatments.
It is therefore crucial for governments to create an environment in which innovator companies can be confident that innovation will be rewarded. This is particularly the case for the medical technology and biopharmaceutical sectors, as drug development has the highest R&D intensity of any sector. Investors are already enduring a high risk in order to develop new medical solutions \(^{109}\), even before any further market access related uncertainties.

One important step to create clarity would be for national health systems openly to share their definitions of innovation, coupled with policies to reward innovative technologies as discussed above. Overall, the solution for building confidence is for countries to work towards a clear policy framework and clarify what will be rewarded. A good example of this could be the stroke care provision policies established in the UK about 10 years ago. At the beginning of the millennium, provision of care to stroke patients in the UK had lagged greatly behind other European countries. The provision of innovative and effective medical technologies (such as recombinant tissue plasminogen activator (rTPA) used to thrombolyse ischaemic stroke patients within 3-6 hour window following the occurrence of the acute stroke event) was much lower than their utilisation in other European countries such as Germany and France. The issue was first identified in 2005 as an area requiring the attention of the government. In 2007, the Department of Health launched a programme to improve stroke services, the National Stroke Strategy. \(^{110}\) Early evaluation of this policy in 2010 already demonstrated significant healthcare gains both in terms of preventing disabilities and also extending the lives of stroke sufferers. \(^{111}\) Very recent research into the cost-effectiveness of these innovative stroke care services demonstrates improved outcomes in addition to cost savings over a 10-year period in the UK. \(^{58}\)

**Public and private investment in healthcare R&D can also be promoted directly**

There are a number of cross-border programmes in Europe with the objective of addressing the need for continued health R&D expansion. For example, as mentioned earlier, Research and Development Framework Programmes, the Innovative Medicines Initiative and the launch of the European Drug Discovery Consortium all aim to foster innovation and allow the provision of better and safer medicines to the public. National governments also have their own research funding programmes. However, as chapter 3 demonstrated, the overall European public commitment to health R&D is only one-third of the commitment in the US and the gap has widened recently. The European Union and individual national governments could make use of various policies and funding mechanisms to catalyse R&D investment.

European governments can increase public spending on R&D at a national level, for example by increasing the funds allocated to research centres and academic institutions, and at European level, for example as the European Medical Research Councils stated by “substantially increasing the total amount of European investments in biomedical and health research […] so as to reach at least the same level as generated by the national or regional funding agencies (25-35%).”\(^{94}\) Ideally, public organisations play an elevated role on the research side of R&D, while life sciences technology firms focus on developing new technologies so that they can rapidly be used in the wider population. In part this depends on whether governmental research institutes and academic institutions, which operate free from market pressures, can move effectively and speedily to translate their research into utilisable technologies. In this context, government

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policies to encourage universities and research institutes to collaborate more closely with industry could have a positive impact. A related policy development has been to allow academic researchers to create commercial ventures for themselves. Incentivising the formation of spin-off companies by public institutes, supported by public finances, could further increase the footprint of the life sciences industry in Europe.

Promotion should not only be reflected in R&D budgets, but also in creating public awareness of the importance of health R&D investments and in sharing success stories of public-private partnerships (PPP). Frameworks and PPP initiatives like the Innovative Medicines Initiative (IMI) maybe successful when measured by R&D input and output metrics, but according to Professor Chataway of RAND Europe “they often fail to focus adequately on issues relating to public awareness and opinion. The inclusion and design of this aspect of public/private collaborations can be crucial to the public’s recognition of the biopharmaceutical industry as a positive driver of health, employment and research.”

Governments can also incentivise private R&D. An indirect method for augmenting innovative processes is through the introduction of incentives in national tax policies. A combination of input incentives (e.g. R&D payroll tax exemptions and R&D tax credits) and output incentives (e.g. tax deductions of income from patent) can be implemented. This enables the creation of tax frameworks that will encourage biopharmaceutical firms to invest in R&D. Belgium is a prominent example of how such policies can successfully boost R&D investment. Meanwhile, Switzerland is currently exploring the introduction of more R&D input and output incentives.

**Summary of policies to secure the future of health R&D**

In order to reap the benefits from health R&D (as explained in chapter 2) and to curb the reduced investment in health R&D (as described in chapter 3), governments have two main levers that should be employed simultaneously.

First, governments need to reward new technologies adequately and transparently. Recent austerity measures both on the pricing side (tougher price regulation, international reference pricing) and on demand side (lengthier reimbursement procedures and demand restrictions) are reducing the willingness of industry to invest in new compounds. Governments should set up appropriate reimbursement systems that reward innovative technologies, cooperate to align reimbursement (and health technology assessment) requirements, and allow for fast and broad market access in line with European approval processes. In addition, the future willingness to pay for innovation should already be reflected in transparent and predictable policy decisions, to allow for long-term investment decisions.

Second, governments can have a direct impact by investing in public health R&D (such as through the European Framework Programmes) or by creating explicit incentives for private health R&D (such as tax incentives).

Combined, these two approaches can secure the future of health-related R&D, and all its consequent wider societal and economic benefits.
Private R&D spending
(Source: European Federation of Pharmaceutical Industries and Associations (EFPIA))
The data on private health-related R&D were extracted from information held by the European Federation of Pharmaceutical Industries and Associations, the body that represents the pharmaceutical industry in Europe. The data were collected by EFPIA’s 33 national member associations and relate to the R&D carried out by pharmaceutical companies in each country.

Public R&D spending (Source: Eurostat)

Gross Domestic Expenditure on R&D (GERD)
GERD statistics contain the R&D spending by country as reported by different sectors. It is divided into four sectors of activity (Business Enterprise, Government, Higher Education and Private non-profit institutes) and by field of science. This source was mainly used to calculate the growth of public health-related R&D (medical sciences) spending, therefore only the Government and Higher Education sectors’ data were used.

Government Budget Appropriations or Outlays on R&D (GBAORD)
The GBAORD is classified using the Nomenclature for the Analysis and Comparison of Scientific Programmes and Budgets (NABS). This classification includes the funding allocated to health which comes from different funders: Government, General University Funds (GUF) and other sources. The government contributes directly through R&D contracts and specific grants. GUF include own funds from universities such as income from endowments, shareholdings and property, as well as receipts from the sale of non-R&D services such as fees from students, subscriptions to journals and other sources of income. GUF can also include general grants received from the Ministry of Health or from provincial or local authorities. Finally, ‘other sources’ represent all other funding streams apart from the government and university funds. It is important to mention that, although the classification sounds straightforward, the way funds are allocated and categorised depends on the individual methodologies employed in each country.

Differences between GBAORD and GERD
According to the Frascati Manual, GBAORD and GERD differ mainly in three aspects.
1. The reporting unit of GERD is formed by R&D performers, whereas GBAORD reporting unit is formed by funders.
2. GERD covers only R&D performed on national territory, whilst GBAORD includes payments to foreign performers, including international organisations.
3. Government-financed GERD include R&D financed by central (or federal), provincial (or state) and local government, whereas GBAORD excludes local government and sometimes provincial government.

Public R&D sources used in this report:
The main source for Public Health-related R&D spending in this report is the Eurostat GERD complemented with Local sources for France (DREES) and UK (BIS) due to missing observations for these countries. The main drivers to use GERD instead of GBAORD is that it (1) includes R&D financed by federal, provincial and local government, whereas GBAORD only includes federal investments, and (2) includes investments from the higher education sector with a higher degree of completeness than GBAORD. In Sweden, for instance, the GERD totalled €860 million in 2009, whereas GBAORD only accounted for €25 million in the same year. The total amount of both sources is comparable: 2010 GERD and local data for France and UK sum up to €18 billion; the total from GBAORD is €15 billion, but misses about €2.1 billion of investments from Austria, Belgium, Denmark, Poland, Sweden and Switzerland. On the other hand, GERD data experience a lag of minimum two years thus, expenditures since 2011 are unavailable for this source. Therefore, a growth rate (see notes for figure 13) for 2011 was calculated using GBAORD and applied to the previous GERD absolute numbers.
The Nomenclature for the Analysis and Comparison of Scientific Programmes and Budgets (NABS) is mainly used for government budget appropriations or outlays on R&D (GBAORD) and R&D statistics at a national and international level. This classification, developed and maintained by Eurostat and linked to the Frascati Manual (OECD), breaks down annual spending according to socio-economic objectives. In its last revision (2007), Eurostat improved and updated chapters according to user requirements, improved data availability at the country level and aligned its content with the Revised Field of Science and Technology Classification (FOS), the Classification of the Functions of Government (COFOG), Essential Public Health Functions (EPHF) and the Statistical Classification of Economic Activities in the European Community (NACE).

The Frascati Manual

The Frascati Manual, developed by the OECD, sets the international methodology for definitions of basic concepts, collection guidelines, and classification for compiling R&D statistics. It is considered as the standard for R&D surveys, having become essential for statistical systems, not only for OECD members but for other countries as well.

Figure 8

The absolute public health-related R&D spending over time is based on the calculated growth rates as described in the notes for Figure 13. These growth rates were applied on GERD absolute numbers of 2009. This was selected as baseline value since it represents the most complete data (containing data from 28 European countries).

Figure 13


For country specific growth some countries were excluded since the growth trend could not be calculated due to the lack of data in GERD data and inconsistencies in the GBAORD data for 2011. These countries are: Austria, Belgium, Denmark, Netherlands, Norway, Poland, Sweden and Switzerland.
### Table 1: Private Health-related R&D per country (€ million; 2005-2011)

Source: EFPIA

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**Notes**

10. Sensitivity of elasticity estimates for OECD health care spending: analysis of a dynamic heterogeneous data field
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