R&D spillovers: do they exist, and if so, does medical research expenditure in the UK generate them?

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Abstract

It is extremely important to consider wider economic gains as well as health gains when assessing the economic benefits of medical research. Investment in medical research by one organisation may benefit not only that organisation but also other organisations in the medical sector, in other sectors, and also in other countries: i.e. spillovers.

We review and present the findings of the research spillovers literature in general and as applied to medical research. The literature clearly suggests that R&D investment generates a direct return, usually captured by the original investor, but also some indirect benefits 'spilling over' to third parties. There is evidence that R&D spending, both private and public: produces new knowledge, which can be accessed and exploited by other organisations for new technology development; contributes to the formation of a more skilled labour force; and more generally facilitates knowledge dissemination and technology transfer. The evidence shows that innovative activity tends to cluster more in industries where knowledge spillovers play a decisive role, and that new firm start-ups' decisions to locate are influenced by the opportunity to access knowledge generated by universities.

The literature is more ambiguous about the quantification of spillovers than about the mechanisms through which they travel. The literature estimating the size of the spillovers for medical research is scarce. There is some evidence for pharmaceutical R&D. This suggests that R&D spillovers are important, and that publicly funded research and private pharmaceutical R&D investment are complements rather than substitutes.

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1. Introduction

The main organisation responsible for publicly funded medical research in the UK, the Medical Research Council (MRC), along with the largest UK medical research charity, the Wellcome Trust, and the Academy of Medical Sciences want to understand more about the economic value of the research they fund. They have commissioned Brunel University, OHE and RandEurope to investigate this in a one year research project.

In this paper we *only* focus on the non-health benefits of medical research and development (R&D). It is extremely important to consider non-health as well as health gains. Returns to investment in medical research by one organisation may benefit not only that organisation but also other organisations in the medical sector, in other sectors, and also in other countries: that is, there are spillovers. In this paper, we present the findings of our review of the research spillovers literature in general and as applied to medical research.

The structure of this paper is as follows. In Section 2 we describe the concepts of knowledge and information and go on to discuss the differences between private and social rates of return to R&D, to introduce the concept of spillovers.. Section 3 defines spillovers and discusses the main transmission mechanisms identified. In this section we also touch upon the literature on the economics of the geography of innovation, highlighting how spillovers have helped develop this strand of work. Section 4 reflects on the literature analysing the sources of spillovers. We focus here on university research, private R&D and social networks. In Section 5 we discuss the relationship between public and private R&D, and the question: are they complements or substitutes? Section 6 offers some tentative conclusions.

2. Measuring Rates of Return from R&D

Our starting point is defining the basic characteristics of 'knowledge'.

2.1 Knowledge: basic characteristics

Arrow (1962) suggests that knowledge is inherently a public good. He also argues knowledge differs from the typical factors of production (labour, capital) in two ways. First, it is non-excludable, non-rivalrous or non-exhaustible. Thus, knowledge developed for any particular application can easily spill over and have economic value in very different applications, but it also incites what has become known as the appropriability problem for any firm generating that new information. This problem may diminish firms' incentives to invest in R&D. Second, knowledge has greater degree of uncertainty, higher extent of asymmetries and greater cost of transacting new ideas.

It is also useful to distinguish between tacit and codified knowledge. Tacit knowledge can be difficult to write down in such a way that is meaningful and readily understood. It needs face-to-face and even nonverbal communication as well as reciprocity, all of which may be ineffective or infeasible over longer distances. It has also been referred to as 'sticky knowledge' (von Hipple, 1984). Codified knowledge, on the other hand, can be written down – it is more akin to information than to tacit knowledge. It is better structured and less ambiguous. The cost of transfer of information (or codifiable knowledge) is lower than for tacit knowledge and is not bounded by close proximity of the source of knowledge. This distinction is critical in giving rise to the concept of 'localised knowledge spillovers', as discussed later.

2.2 Private versus social rate of return from R&D

Three main methodological approaches have been used to assess the value and benefits from research: econometric studies, surveys and case studies. The first method relies on the analysis of large databases – pointing also to the importance of spillovers from research. Surveys have been conducted of R&D managers, while case studies attempt to trace all the antecedents to an innovation. Each method has its own advantages and disadvantages. In this paper we draw upon the evidence generated by all three methods.

At the more general level, it is possible to distinguish between:

- private or direct return to investment, which includes the economic benefits generated by a specific R&D project and accrued by the organisation originally involved through royalties and/or sales of a new product or process; and
- social or indirect return to investment, which includes economic and non-economic benefits spilling over for third parties to exploit, e.g. new knowledge and economic conditions that stimulate and enhance innovation and technical progress.

The difference between social and the private rate of return represents R&D spillovers arising from innovative initiatives or projects undertaken by a public or private organisation and not directly internalised by the originator.

Early attempts to identify the link between national R&D spending and economic performance employ macroeconomic models of growth which integrate R&D stock into the traditional production function as an input (treated as a residual factor accounting for growth in earlier works (Solow, 1957) and as a source of endogenous growth in more recent models (Romer, 1986; Lucas, 1988)).

Empirical estimation of the impact of R&D stock on economic performance has proved to be problematic due to difficulties in:

- measuring R&D stock and economic output;
- developing reliable econometric models using aggregate data which do not allow for variations across sectors and firms.

In general, the main limitation of these models is that they work as a ‘black box’ producing financial measures of social return to R&D investment, unable to explain how R&D spending and innovation generate economic development.

Empirical evidence suggests that social rate of return is substantially higher than the private return. Table 1 summarises main findings available in the literature.

Table 1: Estimates of private and social rate of return to private R&D spending

Study	Private rate of return	Social rate of return
Minnasian (1962)	25%	NA
Terleckyj (1974)	27%	48-78%
Mansfield (1977)	25%	56%
Sveikauskas (1981)	10-23%	50%
Scherer (1982-1984)	29-43%	64-147%
Mohnen&Lepine (1988)	56%	28%
Bernstein & Nadiri (1988)	9-27%	10-160%
Goto&Suzuky(1989)	26%	80%
Bernstein & Nadiri (1991)	14-28%	20-110%
Nadiri (1993)	20-30%	50%

Source: Salter et al. 2000, Griliches, 1995

As Table 1 shows, private R&D is associated with a large return to society, with most estimates exceeding 50%. The variability of these figures is partly due to the lack of a widely accepted theoretical model explaining accurately the complexity of the innovative process and to a paucity of reliable data providing robust support to the research question. In particular, some studies measure benefits induced by R&D spending in terms of production of new products and process, not taking into account that investment on R&D also contribute significantly to building absorptive capacity and accumulate capability to solve complex problems (see later). With regard to the available data, one of the main limitations is related to a high degree of aggregation not accounting for inter-industry or inter-firm differences.

The literature also provides estimates related to specific sectors. In particular, a series of studies focus on technological innovations in the agricultural sector, particularly on the social return to public investment in agricultural research. Table 2 summarises main findings.

Most of the works estimate that the rate of return to publicly funded research in the agricultural sector is in the range of 20-50%. Main limitations of these studies are that they may be biased towards those government R&D programmes that proved successful and the preponderance of US data which may not translate directly to the situation of the (smaller) national economies of Europe.

Table 2: Estimates of rate of return to public R&D in the agricultural sector

Study	**Rate of return**
Griliches (1958)	20-40%
Peterson (1967)	21-25%
Schmitz-Seckler (1970)	37-46%
Griliches (1968)	35-40%
Evenson (1968)	28-47%
Davis (1979)	37%
Evenson (1979)	45%
David & Peterson (1981)	37%
Huffman &Evenson (1991)	43-67%

Source: Griliches (1991), Salter et al. (2000)

More recent contributions on the issue of measuring the rate of return of publicly funded R&D include the studies conducted by Mansfield, which focus on the contribution of basic research conducted by academic centres on innovation delivered by commercial sectors. Mansfield (1991, 1998) bases the analysis on a survey of R&D executives from a sample of manufacturing firms operating in the US, including drug and medical products. The 1991 study considers data from 1975-1985 and indicates that over 10% of new products and processes marketed by surveyed firms could have not been developed (without substantial delay) in the absence of academic research. The time lag between relevant academic results and the commercialisation of the new products or processes is estimated to be seven years. The results of the 1998 study are similar with respect to the impact of academic research on commercial innovation but show, on average, a lower lag for market introduction (from 7 to 6 years). Note that the proportion of new products attributable to academic research and mean time lag for academic results implementation are both highest in the pharmaceutical sector (27-31% and 8.5-8.8 years, respectively).

Mansfield (1991) also provides an estimate of the social rate of return on academic research (28%) – but this analysis is not replicated in the 1998 study.

3. Mechanisms Transmitting Spillovers

Our interest lies on spillovers generated by R&D. Given the link between R&D and knowledge, we do not in this paper distinguish between R&D spillovers and knowledge spillovers but refer to both. Note that whenever we refer to 'spillovers' generically, we are referring to R&D/knowledge spillovers.

The literature defines spillovers in different ways. For our purpose, we define spillovers as occurring when at least some of the benefits from research accrue to other parties than the organisation that undertook the original research. The literature is unambiguous in accepting that R&D/knowledge spillovers exist and are important. However, the literature is less clear in setting up and understanding the actual mechanisms by which spillovers are transmitted. Krugman (1991) argues that knowledge flows are invisible, as they leave no paper trail – making spillovers difficult to measure. Jaffe et al. (1993) argue the contrary to the assertion that knowledge flows are invisible: there is a paper tail in the form of patented inventions and new product introductions.

Probably, most researchers involved in this area will agree with the assertion about the difficulty of measuring spillovers. There have been several attempts. Before going into the details of how spillovers are measured (section 3.1), we briefly discuss some of the mechanisms identified in the literature as facilitating spillovers' transmission.

First, there are the mechanisms facilitated by universities, which include their pool of talented graduates, the ideas generated by faculty, their high quality libraries and other facilities of research universities and their publications. Networking and social interactions are also deemed to be important mechanisms – and these include both the informal and formal ways of interaction. Formal ways of interaction include technology transfer programmes, such as licensing from universities to firms. Both means of interaction seem to be relatively important for the pharmaceutical and biotech market. We pick up later on networks when discussing sources of spillovers.

The third mechanism discussed in the literature relates to the possibility of 'absorptive capacity', which refers to the ability of economic agents to recognise, assimilate and apply new scientific knowledge – and then to appropriate some of the returns accruing to investments in new knowledge made externally (Cohen and Levinthal, 1989). Indeed, as these authors argue, the conventional wisdom was that R&D generated only one product: new information. They argue, however, that R&D also enhances the firm's ability to assimilate and exploit existing information – the firm's 'learning' or 'absorptive' capacity. This second 'face' of R&D is very important, as it represents an important element of a firm's ability to create new knowledge. Griffith at al. (2004a) find strong evidence that R&D has this second face: industries lagging behind the productivity frontier catch up particularly fast if they invest heavily in R&D. They identify human capital as having a role in stimulating innovation and absorptive capacity. Entrepreneurship has been also identified as an important mechanism, in that knowledge spillovers are the source of knowledge creating the entrepreneurial opportunities for new firms.

International trade is usually deemed to be one of the most important mechanisms by which spillovers are transmitted across countries, but international spillovers are outside the scope of this paper. The interested reader is referred to Coe and Helpman (1995), Keller (1998, 2002a, 2002b and 2004) and Griffith et al. (2004b).

3.1 Measuring spillovers – the rise of the economics of geography of innovation

Griliches' (1979) seminal paper offered for the first time the tool to measure spillovers, by suggesting the production function approach to the estimation of the return to R&D. He argued the level of productivity achieved by one firm or industry depends not only on its own research efforts but also on the level of the pool of general knowledge accessible to it. Moreover, the productivity of own research may be affected by the size of the pool or pools it can draw upon. A simple model of such within-industry spillover effect is given by:

$$Y_i = B\ X_i^{1-\gamma}\ K_i^{\gamma}\ Ka^{\mu}$$

where Yi = output of *ith* firm, which depends on an index of conventional inputs, Xi, its specific knowledge capital, Ki, and on the state of aggregate knowledge in this industry, Ka. He assumed the aggregate level of knowledge capital was the sum of all specific firm R&D capital levels. Aggregating the individual production functions, the coefficient of aggregate knowledge capital ($\gamma + \mu$) is higher than at the micro level (γ), since the aggregate level reflects not only the private but also the social returns to R&D.

This production function approach is aspatial or insensitive to issues involving location and geography. As argued by Audretsch (1998), there is considerable empirical evidence supporting the model of the knowledge production function. The empirical link between knowledge inputs and innovative output becomes stronger when the unit of observation becomes increasingly aggregated e.g. when the unit of observation is the country or the industry. However, these authors argue that at the level of the firm, the link between knowledge inputs and innovative output becomes tenuous and only weakly positive in some studies, and even non-existent or negative in others. They also assert that this is probably not surprising, as formal R&D is concentrated among the largest corporations and small firms account disproportionably more to new product innovations. Several economists (see references below) modified the model of the production function to include an explicit specification for both spatial and product dimensions. The modified knowledge production function becomes:

$$I_{si} = IRD^{\beta_1} * (UR_{si})^{\beta_2} * [UR_{si} * (GC_{si})^{\beta_3}] * \varepsilon_{si}$$

where I = innovative output; IRD is private corporate expenditures on R&D; UR is research expenditures undertaken by universities, and GC measures geographic coincidence between university and corporate research. This co-location variable was added later. The unit of observation is at the spatial level, *s*, a state, and industry level, *i*.

The estimation of the equation above shifts the model of knowledge production function from the unit of observation of a firm to that of a geographic unit – be it a state, region or metropolitan area. This work has sometimes led to the phrase ‘localised knowledge spillovers’. The breakthrough paper on the topic is probably that by Jaffe (1989), who argued that transport mechanisms for spillovers at the time were still not understood. As a first approach to analyse these issues, he examined (for the US) production of patents assigned to corporations by state over time, and related this to industry R&D and university research. The author interprets the influence of university research on these patens at the state level (after controlling for industry R&D) as evidence of existence of geographically mediated spillovers. Several papers have followed a similar methodology (see for instance, Feldman (1993), Acs et al. (1994a), Feldman (1994), Audretsch and Feldman (1996), Audretsch (1998), Feldman and Audretsch (1999), Feldman (2000), Arundel and Geuna (2001), Audretsch et al. (2003), Baum and Sorenson (2003), Audretsch and Feldman (2004), Audretsch and Lehmann (2006)). The authors of these papers, to a greater or lesser extent, argue that the empirical evidence presented therein suggests location and proximity clearly matter in exploiting knowledge spillovers. They argue one of greatest developments in the literature of economics of innovation is that geography, the spatial context, matters.

This strand of the literature has gone one step further to analyse the different ‘elasticities’ according to firm size. Empirical results from the US suggest small firms are the recipients of R&D spillovers from knowledge generated in the R&D centres of their larger counterparts and in universities (Acs et al. (1994b)). Such spillovers are apparently more decisive in promoting the innovative activity of small firms than of large corporations. Audretsch and Vivarelli (1996) replicated the analysis for 20 Italian regions over nine years – and found similar results in that while firm R&D expenditures contribute to the generation of innovative output for all firms, the spillovers from university research are apparently more important for small-firm innovation.

Jaffe et al. (1993) provide an alternative analysis for looking at the importance of geography. They show, based on US data, that patent citations are highly localised. These authors also argue that it is probable that knowledge spillovers are not confined to closely related regions of technology space – in their study, approximately 40% of citations do not come from the same primary patent class. This is consistent with Jaffe (1986) who found that a significant fraction of the total flow of spillovers affecting firms' own research productivity comes from firms outside the receiving firm's immediate technological neighbourhood.

Partly due the emergence of this literature, the so-called Knowledge Spillover Theory of Entrepreneurship (KSTE) has been developed. It identifies one source of entrepreneurial opportunity: new ideas and knowledge. Under this theory, the implementation of new knowledge and new ideas, by starting a new firm, created in one source but left uncommercialised or not fully pursued generates entrepreneurial opportunities, involves knowledge spillovers. Thus, the creation of a new firm in a localised context is an important mechanism by which knowledge spills over. By serving as a conduit for knowledge spillovers, entrepreneurship is the missing link between investments in new knowledge and economic growth (Audretsch et al., 2006b).

Botazzi and Peri (2003) use total number of patents granted to inventors residing in a European region as a measure of that region's innovative output to investigate R&D externalities (identified as the effect of R&D intensity in one region on the innovative output of another region). These authors find evidence supporting that spillovers are important. However, they find the effects of R&D in generating innovation quite localised – most of the benefits accrue to the region that employs the R&D resources and small positive externalities accrue to regions within 300 km from it. Quantitatively, they find that doubling R&D in a region would increase by 2-3% the patenting activity in another region within 300km of distance. Closer to its border (within first 100km) and for regions of the same country the effect could be as large as 5-6%. They offer a tentative explanation for the small size and the short range: spillovers are the result of diffusion of non-codified knowledge between people who have frequent (weekly or monthly) interactions. In Europe, the authors argue, people probably commute and interact much more within countries than across borders.

Summarising this literature, the above mentioned papers argue that geographic concentrations of knowledge are likely to create higher levels of innovation than would otherwise be achieved. Product innovations exhibit a tendency to cluster in regions that contain concentrations of innovative inputs and innovative activity tends to cluster more in industries where knowledge spillovers play a decisive role. The propensity for innovative activity to cluster is more attributable to the role of knowledge spillovers and not merely the geographic concentration of production. However, it is argued that spillovers are geographically bounded: innovative activity is more likely to occur within close geographic proximity to the source of that knowledge – 'localised knowledge spillovers'.

Several observers have criticised this literature (Breschi and Lissoni, 2001a, 2001b). They recognise there is hardly any doubt that innovation networks are often localised. However, the rationale for co-localisation may have less to do with knowledge spillovers mediated by physical proximity, than with the need to access a pool of skilled workers and to establish transaction-intensive relationships with suppliers and customers. Thus, in their critique, they argue the notion of localised knowledge spillovers has been largely abused, generating great conceptual confusion. Again, these authors do not deny that knowledge flows may be an extremely important agglomeration force; but they question the strategy of putting all of these flows under the common heading of localised knowledge spillovers.

4. Sources of Spillovers

We have grouped under three general headings the potential sources of knowledge/R&D spillovers: universities; firms; and social networks.

4.1 The role of universities as sources of spillovers

There is wide agreement about the importance of universities in generating economic growth. As argued by Nelson (1986), universities are a recognised repository of public knowledge. Also, centres of commercial innovation and entrepreneurship are linked to proximity to universities. Hughes (2006) identifies four kinds of interactions that work at the university-industry interface: (1) basic university role of educating people, including providing suitably qualified human capital for the business sector; (2) research activity and the role it plays in increasing the stock of codified knowledge which may have useful or commercial elements; (3) problem-solving in relation to specifically articulated business needs; (4) "public space" functions. The last of these includes a wide range of interaction mechanisms between university staff and the business community: informal social interactions, specially convened meetings, conferences, specified convened centres to promote entrepreneurship and entrepreneurship activities, and the exchange of personnel including the role of internships. These may lead to the transfer of both codified and tacit knowledge and the establishment of relationships which may feed back into the other three roles.

Martin and Tang (2007) refer to many studies which, they aregue, suggest that the recruitment of skilled graduates represents the most important mechanism through which firms derive economic benefits from basic research.

The literature has identified three potential effects of university research spillovers on: (1) innovation (patents/new product innovations); (2) location of firms / new firm start-ups; (3) performance / growth of firms.

For the first effect, Jaffe (1989) uses a modified 'knowledge production function' (see above), where the dependent variable is state-level (US) corporate patents (proxy for useful knowledge). The two inputs are private R&D and university research. Jaffe also models simultaneously industry R&D and university research. The results provide some evidence of the importance of geographically mediated commercial spillovers from university research, which turns out to be strongest for the subsegment classified as 'drugs'. The overall elasticity of corporate patents with respect to university R&D is around 0.1. However, what is significant is that the indirect or inducement effect, via increasing private R&D, is even larger. Given the elasticity of industry R&D with respect to total university research (0.704) and the elasticity of corporate patents with respect to corporate research (0.814), the implied elasticity of induced corporate patents with respect to university research is almost 0.6 (0.704*0.814). This author also finds evidence, albeit weak, of the impact of co-location of universities and research labs. Acs et al. (1992) replicate this analysis using actual product innovations from the US, and find even higher elasticities and stronger support for co-location. Based on a survey of companies, Nelson (1986) also supports these results, as he claims university research is positively and significantly related to R&D intensity of the industry in question.

Arundel and Geuna (2001) use the PACE survey of Europe's largest industrial firms to test, among other things, the importance of proximity in the transfer of knowledge from publicly funded research organisations (PROs), which includes universities, to firms. Their descriptive results show that PROs are the most important external source of knowledge for firms' innovation. Also, results show firms use a variety of methods to acquire different types of knowledge from PROs, including some that provide access to codified knowledge (e.g. reading publications or attending conferences), and methods that provide the opportunity to access non-codified knowledge, such as informal personal contacts, joint research, and hiring trained scientists and engineers.

In terms of the effect of university research on firm location and firm start-ups, Audretsch and Lehmann (2004) and Audretsch et al. (2003) show, based on German data, that university spillovers play an important role and have a strong influence in shaping strategic locational decisions of firms. Two main results can be highlighted from this work. First, the number of entrepreneurial startups is greater in those regions with a greater presence of knowledge inputs. Second, the ‘type’ of knowledge generated and the mechanism by which the knowledge is transmitted are important. The authors make a distinction at two levels – between research carried out in the social sciences and natural sciences areas, and between human capital and publications – which relates back to whether the knowledge is tacit or codifiable. For those university outputs and spillover mechanisms that are more tacit in nature (social sciences and human capital), geographic proximity plays a greater role in accessing and absorbing university spillovers. As a conclusion, the authors argue that new firm start-ups decisions to locate are influenced by traditional regional characteristics as well as by the opportunity to access knowledge generated by universities. But the impact of university output on new firm location depends on both the type of knowledge and mechanism used to access that knowledge.

Mansfield (1995) distinguishes between basic and applied research. He argues firms tend to trade off faculty quality for geographical proximity, particularly in the case of applied research. For basic research, firms seem to pay less attention to location in choosing universities to work with and support, perhaps because in many kinds of applied R&D it is very useful for academics and firm personnel to interact and work together face-to-face, whereas in basic research ties may be weaker and more sporadic. This relates back to the distinction between tacit and codified knowledge – the former being probably more akin to applied research and the latter to basic research.

Martin and Tang (2007) reinforce the previous results in that researchers and students can spin out from universities to exploit new ideas and technologies, by establishing start-up companies. This in turn transfers skills, tacit knowledge and the other benefits of university know-how mentioned above into the commercial environment. These authors cite three examples illustrating how universities can stimulate regional and firm growth: Route 128 in Boston (MIT), Silicon Valley in California (Stanford), and the development of new ‘high technology’ firms around Cambridge University in the UK. The references found therein again reinforce the relation between new firms and their interactions with universities – with a particular focus on the biotech sector.

According to a UK report by the then Minister of Science (Biotechnology clusters, 1999), the biotech sector in the UK (broadly defined as the sector focusing on new technologies, including pharmaceuticals) offers an example of the development of clusters and factors encouraging them. The UK has a strong research base spread across a number of regions supported by the presence of world leading research institutes such as the Sanger Centre and Roslin Institute. To these areas of research strength correspond areas of concentration of biotechnology companies in East Anglia (Cambridge), South East England (Oxfordshire and Surrey) and Central Scotland.

For the impact on firms performance and growth, and based on the German dataset used in Audretsch and Lehmann (2004a) and Audretsch et al. (2003), the empirical evidence in Audretsch et al. (2003), Audretsch and Lehmann (2006) and Audretsch and Lehmann (2004b) suggests geographic proximity and university spillovers are complementary determinants of firm performance. A combination of both factors (but not alone) results in significantly higher stock market performance. This effect, as with the decisions to locate and start a new firm, also depends on university output. If the spillover involves knowledge in the natural sciences, geographic proximity is less important; if in the social sciences, geographic proximity is seen to be a necessary condition for generating abnormal profits. Moreover, the closer the distance from the nearest university and the higher the number of academic papers published, the higher the growth rate of firms.

4.2 The role of private R&D as a source of spillovers

We have identified three potential effects of private R&D spillovers: (1) productivity of other firms' R&D; (2) entry decision of potential competitors; (3) reduction of production costs.

For the first effect, Jaffe (1989b) carries out an analysis of firms' patents over patent classes. He defines classes or technological groups, and measures a pool of spillovers. This pool is the sum of all other firms' R&D, weighted by technological proximities. He finds that a firm's R&D productivity is increased by the R&D of technological neighbours, though neighbours' R&D lowers profits and market value of low R&D intensity firms. Moreover, if everyone increased their R&D by 10%, total patents would increase by 20%, with more than half the increase coming from the spillover effect; and if everyone increased their R&D by 10%, the aggregate profits would increase by about 3%, with about one third of the net increase coming from the spillovers.

Frantzen (2000) performs a cointegration analysis on annual panel data with respect to a set of manufacturing industries in a series of OECD countries over the period 1972-1991. Results show that not only own R&D capital, but also domestic and international R&D knowledge spillovers, as well as human capital, play an important role in helping to explain the evolution of manufacturing productivity in OECD countries. The spillover effects were shown to be both intersectoral and intrasectoral in nature and there was evidence that they are especially strong in research intensive industries. Similar results, based on the same data, are obtained in Frantzen (2002a, 2002b).

Guellac and de la Potterie (2001) investigate the long-term effects of various types of R&D on multifactor productivity growth (MFP), which, as argued by the authors, is the spillover effect of R&D. Econometric estimates are conducted on a panel of 16 OECD countries, over the period 1980-98. These authors argue business R&D has a positive and significant impact on MFP, indicating there are substantial spillovers from business R&D – the return to the economy as a whole is larger than the private return. Also, the impact of business R&D on MFP is larger in countries where R&D intensity is higher, and the effect of government and university performed research on productivity is positive and significant.

Park (2004), based on a pooled time-series data of 14 OECD economies and three East Asian Economics for the period 1980–1995, allows for simultaneous presence of international and intersectoral (manufacturing to non-manufacturing) R&D spillovers. He finds an asymmetry in intersectoral R&D spillovers; while manufacturing R&D has a strong intersectoral R&D spillover effect on non-manufacturing TFP, the reverse is not true. Pard argues that the manufacturing sector provides relatively more technology-embodied intermediate goods for the non-manufacturing sector.

Cassiman and Veugelers (2002), based on Belgian data in the 1993 Community Innovation Survey (CIS) survey, show that incoming spillovers have a positive and significant effect on the probability of firms cooperating. Cooperating firms, because of the improved technological competence of the partners, better tap the existing base of know-how. Firms with better appropriability have a higher probability of cooperating in R&D. Moreover, firms that find the publicly available pool of knowledge more important for their innovation process are more likely to benefit from cooperative agreements with other research institutes

A number of articles analyse the spillover effects specifically in pharmaceutical R&D. Cockburn and Henderson (1994) use detailed data on R&D investments and outcomes at the level of individual research programmes conducted within 10 pharmaceutical firms over a period of 17 years. They find that competitors' research appears to be a complementary activity to own R&D: rivals' R&D results are positively correlated with own research productivity. The authors interpret this as evidence of significant spillovers of knowledge across firms, rather than the depletion externality implied by "winner takes all" models. Henderson and Cockburn (1996) focus on the 'knowledge production function'. Knowledge is measured as grants of "important" patents, and the explanatory variables include two measures of "spillovers": (1) count of competitors' output in the same narrow research area; (2) count of competitors' output in all the other programmes in the wider therapeutic class. Results, based again on programme-level data, show that a programme whose competitors' programmes are in the same and in related fields that are roughly 10% more productive, will be approximately 2% more productive itself.

Henderson and Cockburn (1996) argue that the pharmaceutical industry is characterised by high rates of publication in the open scientific literature. They carried out an extensive interview programme with scientists and researchers. They note that many of the scientists interviewed stressed the importance of keeping in touch with the science conducted both within the public sector and by their competitors. Nearly all of the interviewees, according to the authors, had a quite accurate idea of the nature of the research currently being conducted by competitors, and they often described ways in which their rivals' discoveries had been instrumental in shaping their own research.

Moreover, these authors believe that there may have been a concomitant change in the role of spillovers in shaping research productivity in the pharmaceutical industry in particular. Some decades ago, when research in the pharmaceutical industry was done via screening compounds, there was little to be learned from others unless they found a particularly promising molecule. Now, however, pharmaceutical companies actively invest in the generation of new physiological and biochemical knowledge, so even knowledge of their false starts and failures may help to shape one's own research programme. Thus, the impact of interfirm spillovers on research productivity in the pharmaceutical industry may have increased over time. The authors argue that before 1978 the benefits of spillovers were realised primarily within narrow therapeutic areas, while after 1979 the reverse appears to be true. The authors argue that programmes benefited primarily from work conducted by their competitors in related therapeutic areas, rather than research focused on same disease targets. As the authors conclude, "modern theory ascribes a central role to interfirm spillovers as drivers of economic growth, so it is reassuring to find them present in research intensive industry such as pharmaceuticals" (page 56).

Aharonson et al. (2003) use detailed data on Canadian biotechnology entrants in the 1990s to explain the dichotomous variable of whether or not to enter in a postcode area in a given year. One of the explanatory variables is the intensity of incumbents' inventive activity, measured as R&D spending and number of R&D employees. The authors argue that new entrants are influenced systematically by factors promoting the benefits of co-location, and seek locations that would allow them to benefit positively from knowledge spillovers.

For the third spillover effect of private R&D (reduction of costs), Levin and Reiss (1984) estimate that a 1% increase in the R&D spillover causes average cost to decline by 0.05%. Berstein and Nadiri (1989) show that average cost decline (on average) by 0.2% in response to a 1% growth in R&D spillovers. However, there are differences on the impact of cost reduction across the different industries analysed (chemicals, petroleum, machinery and instruments) and in the short run and long run. For instance, in the long run, a 1% increase in the intra-industry spillover caused average cost to decline by around 0.1% for instruments and machinery and by approximately 0.2% for chemicals and petroleum (estimates twice as large as in the short run). Spillover-receiving firms gained a 0.27%, 0.22%, 0.15% and 0.14% variable cost reduction in the petroleum, chemical, machinery, and instruments industries respectively as a result of a 1% increase in the intra-industry spillover.

4.3 The role of social networks as a source of spillovers

Powell (1990) argues that social networks offer a highly feasible means of utilising and enhancing such intangible assets as tacit knowledge and technological innovation. Powell also argues that the exchange of distinctive competencies – be it knowledge or skills – is more likely to occur in networks. Breschi and Lissoni (2006) carry out a reassessment of the arguments and tests in support of exercise and magnitude of local knowledge spillovers proposed by Jaffe et al. (1993). They add both new data (Italian patents) and new measurable variables (social proximity between inventors, and inventors' mobility across firms). Breschi and Lissoni interpret their results as an indication that localisation effects tend to vanish where citing and cited patents are not linked to each other by any network relationship. On the contrary, knowledge flows, as evidenced by patent citations, are strongly localised to the extent that labour mobility and network ties also are. These authors conclude by arguing that geography is not a sufficient condition for accessing a local pool of knowledge, which also requires active participation in a network of knowledge exchanges. Agrawal et al's (2006) results are also consistent with the conjecture that social relationships facilitate knowledge spillovers.

Owen-Smith and Powell (2004) highlight the importance of knowledge networks in the biotech sector. These authors claim that within regional economies, contractual linkages among physically proximate organisations represent relatively transparent channels for information transfer. Also, they argue spillovers that result from proprietary alliances (i.e. formal networks in this case) are a function of institutional commitments and practices of members of the network.

Feldman (2000) also defends the importance of social interactions, although she argues that we do not know exactly how economically useful knowledge is created as a result. Breschi and Malerba (2005) reinforce the importance of social networks and argue that one of the key issues raised by all of the approaches in the literature is that learning through networking and by interacting is seen as the crucial force pulling firms into clusters and the essential ingredient for the ongoing success of an innovative cluster.

Feldman and Kelley (2006) argue that that successful strategies for learning abut technical advances outside a company's internal R&D efforts may depend on the breadth of collaborative links with other enterprises, connections to universities and the adoption of university norms of publishing research; and, probably more important, that knowledge flows both ways along these pathways. Along the same lines, Martin and Tang (2007) cite a number of papers highlighting how "through these networks, scientists can quickly and effectively contact acknowledged experts on a particular issue to obtain from them information or advice" (page 11).

5. Public and Private R&D: Substitutes or Complements?

There are a limited number of studies measuring the positive pay-off generated by publicly funded medical research. The recent studies published by Toole and colleagues, based on US data, show that basic research supported by government and public agencies, mainly undertaken in university and non-profit laboratories, stimulates and supports significantly private investment on R&D in the pharmaceutical and biotech sector. In particular, Toole (2005) provides evidence on the complementary effect of public basic research on the level of private investment on R&D. The study is based on an empirical model where the level of private investment is a function, among other things, of basic scientific knowledge generated by public research. The estimated long run elasticity of public research measures the impact on the level of private R&D investment in response to an increase in public investment in basic research. Results indicate that "a dollar increase in public basic research stimulates an additional $8.38 in pharmaceutical investment after eight years" (Toole, 2005).

Toole (2000) examines the impact of public research on pharmaceutical innovation using a production function approach, linking new molecular entities (NMEs) approved by the US Food and Drugs Administration (FDA) with the stock of public basic research (number of awards granted by the National Institutes of Health (NIH)) and private pharmaceutical R&D. Public research has a positive and significant impact on discovery of NMEs: elasticity estimates are in the range of 2-2.4 implying that a 1% increase in the stock of basic research leads to an average 2-2.4% increase in the number of approved NMEs. The results also show there is a lag of 17 to 19 years between investment on public research and new products approval.

There are a number of empirical studies that attempt to support the hypothesis of complementarity between public research and private R&D. As discussed previously, Toole (2005) reports evidence of public research stimulating additional private investment on pharmaceutical R&D. Crespi and Geuna (2004) focus on the impact of higher education R&D spending on science productivity (not specifically on the pharmaceutical sector) and attempt to estimate any crowding-in or crowding-out effect of different sources of funding. Because of the need for more robust country level data, however, they do not find any significant evidence of this phenomenon.

Beyond the empirical estimates, it is important to understand why an increase in public expenditure on research has a positive effect on private R&D in the biopharmaceutical sector. In other words, what are the key characteristics of R&D for health care technologies that make it so important for the public sector to intervene though specific policy mechanisms? What is the role of public funding supporting biomedical basic research?

The development of innovative technology in the pharmaceutical and biotech sector is characterised by:

- high level of uncertainty due to a significant scientific challenge at early stage (basic research and pre-clinical) and recurrent risk of failure at clinical phases;
- large investment required compared to other sectors. The average out-of-pocket costs of a new product approval is $400 million (Di Masi et al., 2002) whilst in other highly innovative sectors, such as IT and communications technologies, an investment of £4 million allow companies to bring new products to the market (Cooksey, 2006).

Investors in the pharmaceutical and biotech sectors (shareholders and venture capitalists, respectively) need to assess the expected returns on their investments, which is particularly problematic at the basic research stage where the outcomes of research efforts are very uncertain, and to generate returns as quickly as possible. Venture capitalists, who represent key funders of early-stage biotech firms, have a time horizon of three years for a particular investment compared to 10-12 years required to companies to develop and market successful health care products (Pisano, 2006).

Against this background, various reports commissioned by government authorities have attempted to illustrate and explain why publicly funded medical research can stimulate and complement private investment on R&D in the pharmaceutical and biotech sectors. Factors considered by private companies as important include:

- potential collaborations with research centres and universities supported by government funding are associated with "cost-sharing and risk reduction opportunities" (NERA, 2007, CRA, 2004). For example, public resources can be used to finance fixed capital costs (e.g. laboratories and other infrastructures) and private funds can cover variable cost of research projects (Crespi and Geuna, 2004);
- returns may be subsidised by public investment on research and clinical trials. The NIH in the US, investing $4.2 billion a year, is often cited as an example of government funds effectively complementing venture capitalists investments in the biotech sector.

6. Conclusions

It is important to consider wider economic gains as well as health gains when assessing the economic benefits of medical research. Part of these wider gains arise from the spillovers generated by R&D.

We have reviewed the literature on R&D/knowledge spillovers. Spillovers have been identified and measured both in general and in the medical and biopharmaceutical sector specifically. This literature is unambiguous that spillovers exist and are important, and need to be taken into account when measuring the economic value of any R&D carried out. The literature is more ambiguous about the quantification of spillovers than about the mechanisms through which they travel. The literature shows that publicly funded medical research is complementary to private pharmaceutical R&D investment.

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