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**European Disparities in
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European Disparities in Regional Health R&I Performance

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Abstract. Health represents one of the thematic priorities for smart specialisation. Until now the difficulty in properly measuring research and innovation (R&I) in Health sector has represented a barrier to address specific policies in favour of less performing regions. This is due to two factors: a lack of available data particularly at regional level; and the difficulty in clearly defining the boundaries of the Health sector. Data provided by European Commission, focusing on Health as FP7 thematic priority, as well as recent data on ongoing clinical trials and Health infrastructure at regional level developed by university of Trieste allow the use of a novel regional and sectorial breakdown to deeper investigate the mechanisms supporting R&I in European Regions. The paper provides an analysis of possible determinants of EU regional Health R&I inequalities, disentangling the factors related to publications propensity from those related to patents propensity. The results show that despite one of the most relevant determinants of R&I in the Health sector remain the level of R&D expenditure, other factors such as the size or degree of Health specialisation of the region should also be taken into account. While patenting activity in this sector remains a prerogative of regions with already technological and industry capacity, publications activities result less context specific being present also in peripheral regions. Our results are in line with the new place-based smart specialisation-type policy thinking.

Keywords: Health, patents, scientific publications, regions, smart specialisation, Europe

JEL Classification Numbers: O33, O34, R11, R58

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1. Introduction

One of the goals of the European economic growth umbrella strategy Horizon 2020 is to address the inequalities in the Health sector and find the right strategies to promote Research and Innovation (R&I) regional convergence in the EU. Along this line, smart specialisation was introduced into the reformed EU Cohesion Policy as a method helping to prioritise investments in innovation and knowledge-related activities to promote economic growth and increase public spending efficiency (McCann and Ortega-Argilés, 2015; McCann et al., 2017). Research and Innovation Strategies for Smart Specialisation (RIS3) are focused on the exploitation of regional endogenous capabilities based on smart evolution and technological related diversification, in order to support long-term sustainable regional economic development. Smart specialisation benefits and builds on insights from different approaches: related variety, systemic approaches as well as competitiveness which links performance of sectors to their trade patterns and also the geography of their input and output markets (McCann and Ortega-Argilés, 2017). Not by chance, Health appears as one of the top policy investment priorities chosen by the RIS3 in EU member states and their regions (Sörvik and Kleibrink, 2015), although they might target it from very different perspectives. That is, referring to Health when dealing with *smart growth* looking at the competitiveness of the Pharmaceutical, Biotech or Medical technology sectors; under the umbrella of *inclusive growth* when dealing with ageing population; or dealing with *sustainable growth* when addressing Healthcare innovation, such as e-Health governance. Until now the difficulty in clearly define the boundaries of the Health sector together with the lack of available data with a breakdown at sectorial and regional level, have represented important constraints (Charlesworth et al., 2011; Røttingen et al., 2013). Suggested policies have been mainly based on limited quantitative analysis assessed mainly on national specificities (e.g. the region located in a widening¹ or non-widening EU country) or qualitative analysis on very deep case studies applicable only for that particular regional case (see for instance the Stairway2Excellence project undertaken by the JRC).

One of the main challenges in implementing RIS3 is linked with the processes of strategic priorities selection as well as monitoring and evaluation of the specific Health R&I capacity of the regions. Although several works have already targeted Health R&I performance as their topic of analysis, these have been done mainly at the national or international level (e.g. WHO, 2013)². Regarding the

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¹ According to the Horizon 2020 Work Programmes, Widening countries are those “ranked below 70% of the EU average of the composite indicator of Research Excellence”. See <https://ec.europa.eu/programmes/horizon2020/en/h2020-section/spreading-excellence-and-widening-participation> for further clarification on this distinction.

² See also the activities carried out by RICYT, PAHO and UNESCO institutes, presented at a workshop in February 2013: <http://www.who.int/research-observatory/workshop/en/>.

regional case, very general measures of R&I regional performance have been considered entitling the risk to underestimate the potentialities of some EU regions that show good performances only in a partial sub-set of outcomes³. Disentangling the different typologies of performances associated with R&I propensity becomes a priority to address regional inequalities in a more appropriate way.

Thanks to recent data provided by the European Commission and other new data developed by University of Trieste in the framework of a Horizon 2020 project, the paper aims to have a better understanding of the EU regional performance differences in Health R&I.

The aim of the paper is therefore to *understand which are the main factors influencing different European regional performances in Health R&I, while looking at different Health R&I outcomes: scientific publications and patents activities related to Health thematic priority.*

After having identified the key factors, which could explain the divide among Health R&I regional performance, the paper will provide some indications on which policy decisions might help supporting the Health R&I in the framework of regional innovation and smart specialisation policy strategies. The rest of the paper is structured as follows: section 2 discusses the theoretical framework, section 3 presents the methodology and the empirical analysis, section 4 is devoted to discuss the finding while section 5 concludes with some reflections about policy implications.

2. Theoretical framework

2.1 The main determinants of research and innovation

There is a quite substantial literature in innovation studies investigating the R&I production capacity of firms and industries in relation to a wide range of determinants, including: R&D expenditure, quality of human resources, available infrastructures, degree of internationalization and collaborations, the composition and specialisation of the industry as well as quality of institutions (e.g. Amin and Thrift, 1994; Audretsch and Feldman, 1996; Bronzini and Piselli, 2009; Buesa et al., 2010; Cantwell and Iammarino, 2000; Furman et al., 2002; Hagedoorn, 2002; Rodríguez-Pose and Crescenzi, 2008). Recent literature investigating these factors in European NUTS2 regions has shown that knowledge outcomes are explained by the different elements underpinning their innovation systems: their (National and Regional) economic environment, the

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³ Poor values for some regions in relation to some aggregated standard measures may sometime due because those regions may have a relatively weak or even non-systems scoring in those measures (Cooke et al., 1997; Evangelista et al., 2002).

innovation capacity of their industrial structure, the university potentiality as well as their expenditures in R&D (Iammarino, 2005; Sterlacchini, 2008; Buesa et al., 2010; Crescenzi and Rodríguez-Pose, 2011).

2.2 Regional and industrial specificities

Although regions are embedded in national innovation systems (Freeman, 1987; Lundvall, 1992 and Nelson, 1993; Pavel and Pavitt, 1994; Edquist, 1997) they have very peculiar local propensity to develop knowledge, to innovate and to advance technologically in their socio-economic system (Acs et al., 2002; Iammarino, 2005). Regions may have local governance settings prone to promote specific innovation initiatives, organizations and agents with different attitude to knowledge collaborations, often driven by *ad hoc* regional policies; contextual educational and R&D institutions, professional tradition, and experiences which relate to the specific economy in play, training, schooling and financial organizations as well as specific networks of dominant innovative companies, supplier and customers (Amin and Thrift, 1994; Hotz-Hart, 2003; Asheim and Coenen, 2005; Asheim and Gentler 2005). Therefore, differences in the attitude of regions to acquire knowledge and innovate are mainly due to the specific setting of regional organisations and institutions (Amin and Thrift, 1994; Cooke, 1997; Asheim and Coenen, 2005). This implies that in Europe – considering the heterogeneity that exists among regions – national factors are surely important but not enough for grasping what can sustain less performing regions in their R&I performances.

The maps below (fig. 1) give already an idea of the heterogeneity of R&I capacity for Health in relation to the geographical aggregation. These maps show the propensity of EU countries and regions to patent and publish in Health; and are based on the original data provided by the European Commission, where all patents and publications are assigned an FP7 thematic priority. As it is possible to observe, while the country-level map clearly divides Europe (North-West against South-East), the regional breakdown shows that: 1) many widening countries have some good performing regions; and 2) less performing regions exist also in non-widening countries.

Fig. 1 - R&I output propensity in the Health sector

Source: Own elaboration on European Commission DG Research and Innovation data. Patents and publications have been classified by FP7 thematic priority (in our case only Health thematic priority is considered). Publications are in fractional counts. Patents are EPO patents applications by country of inventor. Data are expressed in quartiles and refers to a mean calculated for the years 2008-2010. Lighter colour indicates the first quartile 0.25 (less performing regions). In the regional map related to patent data, Croatian NUTS2 regions are missing.

The novel labelling of patents and publications, according to FP7 thematic priorities, is particularly useful for confirming some theoretical insights. In fact, as stressed by a large part of the literature, innovation systems, knowledge and innovation dynamics are quite different not only across regions,

but also across industries. Different industries follow different patterns of knowledge and have different capability in R&I (Asheim and Coenen, 2005; Malerba 2002, 2005; Moodysson et al., 2008; Martin and Moodysson, 2013; Pavitt 1984). Thus, the determinants of R&I propensity may be very different from one industry to another. Asheim and his colleagues (Asheim and Coenen, 2005; Martin and Moodysson, 2013; Moodysson et al., 2008) have developed a Knowledge Based taxonomy (analytical, synthetic and symbolic). Health falls into the category of *analytical knowledge*, characterized by scientific knowledge and rational processes, which represents strategic knowledge (although not exclusive) in sectors such as biotechnology and life science.

Indeed, innovation scholars have analysed many peculiar aspects of the R&I processes in Health industry and its sub-sectors (pharmaceuticals, biotech, medical devices, etc.). Gambardella (1992) studies the dynamics of the US pharmaceuticals industry to assess the capability of the private sector to take advantage, via R&D and patents, of the public knowledge generated by scientific publications. Malerba and Orsenigo (2002) apply a history-friendly model to the pharmaceuticals and biotech sectors, finding that the cumulativeness of innovation in this sector reinforces its concentration, despite the growing role of small and new biotech firms. Pammolli et al. (2005) employ several indicators – including patents and publications – to assess the relevance of the innovative process in the medical devices sector. Their results confirm those of Cohen et al. (2000) who find that “medical equipment industry turns out to be the one where patents are considered the most effective mechanism for appropriating returns from product innovation”. Ali and Gittelman (2016) propose that laboratory science and clinical research represent fundamentally different research paradigms being an important engine of innovation. Using patent and data licenses from two USA Medical Centers over a 30 year period, they analyse the propensity to licensing by looking at the composition of team of researchers. They found that teams composed with different types of knowledge (medical as well as pure academic members) were more successful in patenting their research. Although industries draw upon a combination of different knowledge bases, and Health industry has its peculiarities, it is clear that it is mainly a science-driven sector governed by analytical knowledge. We expect in this case that factors such as strong investment in R&D as well as international cooperation become very important to sustain the R&I of the region in those sectors (Martin and Moodysson, 2013).

Baesu et al. (2015) provide a specific literature review on the regional determinants to support high-tech sector performance in which we can include Health industry. Among the usual factors such as finance capacity (that can be attributed mainly to the R&D investments in the region), they indicate that other relevant factors are also human resources and favourable institutions and infrastructures.

In other words, we expect that R&I performances in this science-based sector are influenced not only by high level of R&D investment and international cooperation in innovation. Indeed we believe that also more widespread indicators related to the regional system in terms of organizational, institutional and human resources potential for the production of knowledge – such as the presence of knowledge workers as well as the presence of good functioning institutions in the region – might increase the propensity to generate R&I outcomes. We expect therefore that:

H1: *Important factors influencing Health R&I performance in Europe are regional high investment in R&D, a good attitude to international collaboration, but also a regional system with a qualitative pool of human resources and good organizational and institutional potential.*

2.3 Different outcomes: Science vs. technological performances

The regional maps (fig 1) presented in the previous section, besides providing an idea of the heterogeneity of R&I capacity for Health in relation to its geographical aggregation, show also clear regional performance disparities looking alternatively at patents or publications. That is, some regions outperforming in patenting may underperform in publications and vice versa. Therefore, regional aggregated data on R&I performance or evaluations based on one indicator only, often the base for policy decisions, give a partial image of what is happening in the region. Indeed several studies have found a negative correlation between highly cited academic publications and valuable patents (Gittelman and Kogut, 2003; Rothermel and Hess, 2007; Subramanian and Lim, 2013).

This is not surprising. In fact, it is very well known that science and technological realms are driven by different incentives and aim to answer to different goals (Dasgupta and David 1987, 1994). On the one hand, one of the main goals of advancement in science in the Health sector through research – particularly if sustained by public support – is to reach a better welfare state and provide improvement in Human Health (Frankel report, 2004). For doing so, mechanisms and incentives should not be so strongly market-driven, and this has to be reflected in an outcome that goes beyond market as well. Usually, scientific publications represent this science realm since researchers involved in publications are usually paid independently by the results of their research, which is usually independent of any business logic (Callon, 1994).

In general, basic scientists receive deep scientific training but do not engage in interaction with living patients as part of their professional practice. The National Science Foundation definition thus identifies the main objective of basic research as the acquisition of knowledge without the

obligation to apply it to practical ends (McGartland Rubio et al., 2010). Basic researchers have fewer opportunities than their clinical counterparts to make valuable connection between the lab, the clinical observations and the market opportunities (Ali and Gittelman, 2016). *Clinical research* is defined by the National Institute of Health as patient-oriented research conducted and interacting with human subjects including: mechanisms of human disease, therapeutic interventions, clinical trials, or development of new technologies. McGartland Rubio et al. (2010) define *translational research* as research that fosters multidirectional integration of basic research, patient-oriented research, and population-based research, with the long-term aim of improving the health of the public. In the last years, several translational research institutes have been developed around Europe proving the success of combining different type of research. Therefore, it is expected that having good research infrastructures such as medical schools or translational research centres at regional level may be fundamental for sustaining good performances in science.

However, measuring the output of research groups only in terms of the numbers of papers published in the international literature can give us a sense of the volume of output but not of the quality of this output. As Rigter (1986) pointed some types of health research (e.g. epidemiology) are more time consuming and elaborated than others (e.g. biochemistry) and thus generally produce fewer publications per unit of researcher of time. Therefore, additional output variables should also be considered.

Technological outcomes⁴ can be better represented by patenting activities where differently from the science realm there is usually (although not always) a stronger need to answer to market logic strategies. Some other authors will argue that although patents are good indicators of new technology creation, they do not measure the economic value of the technologies (Hall et al., 2001). Technology often awards profit organizations able to handle the innovative process using risk and resources that are more difficult to handle in the public sphere (Barba Navaretti et al., 1998). When research becomes potential, such as in the case where inventions are translated into patents applications, research becomes closer to this market logic. Literature stresses, in particular, that knowledge production related to patenting may be functional, for example, to the presence of a high-tech innovative milieu in the region as well as high-tech clusters and agglomerations (Baesu et al., 2015; Buesa et al., 2010).

We have to acknowledge that not all research is of course patented by profit organizations and not all scientific activities follow ‘no market’ mechanisms. But, usually, there exist some closeness of

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⁴ Technology is here intended in a broad sense including intangible and service elements as well (see Arora et al., 2001).

scientific publications to the science realm and of patents to the technological realm. In this paper we aim to test if this analogy is also valid for the Health thematic priority supported by EU strategies.

H2: *Factors determining patents and publications propensity in Health may be of different nature.*

3. Methodology and Empirical Analysis

3.1 Data and variables

Our research overcomes the data availability problems of place-based analysis with an industrial focus. As already mentioned, quality data with a double regional and sectoral breakdown covering an extensive number of regions are usually very difficult to find. Eurostat, for example, offers data with a broad definition of Health (i.e. Human Health and social work activities) and only partially available for some European regions, making impossible to develop representative and robust analysis.

This research is based on a novel dataset of Health patents and scientific publications classified on the basis of the Health thematic priority targeted by European Union in the previous FP7 projects⁵.

Health is a very complex sector that involves both product and service activities ranging from the development of drugs to the development of medical devices as well as Health care activities. Classifications such as the IPC or NACE allow investigating only some partial aspects of the Health sector (e.g. manufacture of pharmaceuticals, manufacture of medical equipment).

Defining Health as the thematic priority used by European Union - although far to be a perfect classification - allows at least contributing better through the analysis to rethink policies in line with European target and economic growth prospects included in their regional innovation and smart specialisation strategies.

Because of data limitations and the added difficulty to give borders to the sector, some other variables used in our analysis are coming from secondary sources (e.g. Eurostat, other EU DGs) and have been maintained without a sectoral breakdown. These other variables are in the literature

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⁵ Data on patents and publications assigned to FP7 thematic priorities (including Health) at the national and regional level come from two studies commissioned by the EC DG Research and Innovation: “Measurement and analysis of knowledge and R&D exploitation flows, assessed by patent and licensing data” (2014) and “Analysis and Regular Update of Bibliometric Indicators” (2013).

generally associated to the development of R&I in high-tech and knowledge intensive sectors so that we should expect that a relation exists with the Health sector, too.

Additional efforts have been devoted in gathering novel data at regional and sectoral levels. Using data from the FAIMER International Medical Education Directory (IMED) for the list of medical schools in Europe, and from the CenterWatch database for the list of all current ongoing clinical trials, a complete map for those indicators across EU regions has been developed.

As the dependent variables we use two sectorial specific indicators that capture, as discussed above, important aspects of the technological and scientific performances in Health. On the one hand we use the number of publications in fractional terms indexed in Scopus that have been specifically assigned to the Health thematic priority; on the other hand we use the number of EPO patent applications by region of inventor related to the same thematic priority (see footnote 5). The choice to use patents applications instead of granted patents allow us to capture better the regional technological potentiality even if not completely exploited⁶. In order to ensure comparability among patents and publications propensity both indicators refer to the specific year 2010⁷. The two indicators, as other variables related to knowledge, are expressed when possible in natural logarithmic terms (ln). This allows us to avoid potential problems related to the presence of outliers illustrated by the high skewness of patent data distribution.

The independent variables are a large set of contextual and sectoral indicators that literature considers relevant when analysing the R&I capacity in knowledge intensive and high-tech industry: share of R&D expenditures over GDP, quality of human resources expressed in terms of knowledge workers⁸, available infrastructures (proxied by the number of active medical schools in EU regions), degree of internationalization and networking (proxied by Health priority co-patenting activities with global partners as well as participation in Health FP7 projects), the composition of the industry (proxied by the presence of firms in projects related to Health priority, clusters in advanced Health sectors⁹). Since literature stresses that the quality of the regional innovation system determines the

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⁶ Data on application in patents does not suffer of the same time lag as data for granted patents, given the fact that in the EU patents are published not before 18 months to the priority date (Hinze and Schmoch, 2004, p. 218).

⁷ We decided to refer to this specific year because it is the best recent year in terms of reliability we could use for patent data.

⁸ Knowledge workers are, in the ILO definition, “persons whose education and high level of technical expertise qualify them for employment in knowledge-based industries”. Such a variable has been used here because of good quality of data of this indicator but also because it can be considered a good proxy of the ability of human resources to create and use knowledge throughout the regional economy since it refers to the professional profiles of the knowledge workers more than the knowledge workers per se.

⁹ It is very difficult to provide an overall map of all EU clusters in the Health sector or in Life Science because there are different interpretation of what is Health or Life Science in different EU regions. For this reason we preferred to give a flag to the regions that have been considered by the EU cluster observatory the top performing regions in two of the ten

propensity of R&I in the region, some proxies related to the quality of regional institutions and organizational system are also considered. We use 1) the effectiveness of government and 2) the typology of regions on the basis of their technological specialisation (low-tech region, advanced service, advanced manufacturing or technological advanced region). The latter variable is based on the classification developed by researchers at Politecnico di Milano (ESPON, 2011) using Eurostat data. The presence of ongoing clinical trials that may serve for new knowledge creation in the sector may also relate directly and indirectly to the development of patents/publications in Health. For this reason we use here the log of the number of ongoing recruiting clinical trials¹⁰. For the two different outcomes patents and publications, we crosschecked also the experience of the region in patenting when investigating the publications propensity and in publications when investigating the patents propensity.

To test whether different factors affect R&I differently according to the country typology we consider their classification into widening and no widening countries. Other controls are related to the degree of specialization of the region in the Health sector (HI index) and its size (expressed here in terms of population and in terms of potential market).

Overall, the analysis is based on information from a wide sample of EU regions. Some variables – such as publications, ongoing clinical trials or medical schools – are available for all EU regions, while other independent and control variables show some missing values. The final sample for the analysis consists of 206 regions in the case of patents and 205 regions in the case of publications out of 266 regions originally considered¹¹. In total, missing observations are few compared to the average of quantitative studies at regional level (e.g. Buesa et al., 2010). Moreover, our sample guarantees the coverage of regions for all EU countries except for Croatia. As regards the time coverage, the outcome and control variables refer to year 2010, while independent variables are related to previous years, whenever possible. The appendix illustrates in details the variables of the sample considered, their descriptive statistics (table A) and the correlation matrix among the variables (B).

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identified emerging industries and that are specifically related to Health: biopharmaceutical and medical devices (European Cluster panorama, 2014).

¹⁰ We were able to track ongoing clinical trials at NUTS2 level in relation to only active recruiting clinical trials present in the database CenterWatch. The data are not referable to a specific time period but only to the current situation (as of end of year 2015). Moreover they are fractional, therefore it is not possible to take account of different hospitals or centers that in the region may be involved in the same clinical trials. In this respect this proxy is more a map of the capacity of the regions to participate in different clinical trials teams and not of participating in clinical trials per se.

¹¹ We have excluded from the analysis the regions related to France's overseas as well as the Spanish Ceuta and Melilla while included the mono-regions NUTS00 Cyprus, Estonia, Lithuania, Luxemburg, Latvia, Malta. In the analysis of publications we had an additional missing value for Cantabria region (ES13) that reduced the sample to 205.

3.2 The model

To investigate the causal relationship in the EU regions between the two different Health R&I outcomes expressed in terms of patents and publications propensity, and all the different factors that may have an influence on those outcomes, we run simple linear regression estimations for Health patents propensity and for b) Health publications propensity, both expressed in logarithmic terms.

The two regression models have been developed in two steps: first we have included only regional effects and second we have controlled for the effect of belonging to a widening country, therefore with already a potential difference at national level for R&I activities. In this way we can disentangle better if and how this supra-regional effect may capture part of the effect of the other variables on the outcomes. We have run different test to control for multicollinearity, heteroscedasticity and normality of the different models. The inclusion of robust standard errors and the use of White's test confirm the validity of the model against heteroscedasticity, while the VIF test confirms the validity of the model in relation to multicollinearity. For what concerns the normality test, due to the reduced number of observations, we have opted for a graphical examination of residuals in terms of qnorm (Quantiles of residuals against quantiles of normal distribution) and pnorm (Standardized normal probability plot). For both types of residuals we observe a general alignment of values (only few observations are not well aligned) although the normality becomes worst in the case of publications. The quality of the models is anyway guaranteed by the very high value of the adjusted R^2 (particularly in relation to publications as an outcome).

Table. 1 - Determinants of Health patents propensity and Health publications propensity for EU regions

	Health Patents propensity		Health Publications propensity	
	All regional effects Model A (I)	Widening effect Model A (II)	All regional effects Model B (I)	Widening effect Model B (II)
Widening effect		-0.492** [0.224]		-0.101 [0.148]
Population	0.030*** [0.006]	0.029*** [0.006]	0.015*** [0.004]	0.015*** [0.004]
Potential market size	0.000 [0.000]	0.000 [0.000]	-0.000* [0.000]	-0.000* [0.000]
Health Specialization Index	0.491** [0.224]	0.375* [0.215]	0.780*** [0.161]	0.755*** [0.154]
R&D expenditure on GDP	0.242*** [0.063]	0.218*** [0.061]	0.131*** [0.041]	0.128*** [0.040]
Medical schools	-0.061 [0.039]	-0.058 [0.037]	0.026 [0.033]	0.026 [0.033]
Experience in Health publications	0.234* [0.125]	0.188 [0.124]		
Experience in Health patents			0.198*** [0.054]	0.187*** [0.057]
Ongoing clinical trials	-0.032 [0.085]	0.011 [0.089]	0.277*** [0.057]	0.285*** [0.059]
FP7 project participation	0.002 [0.001]	0.002* [0.001]	0.003*** [0.001]	0.003*** [0.001]
EFPIA participation in FP7 projects	-0.001 [0.006]	-0.001 [0.006]	-0.007** [0.003]	-0.007** [0.003]
Firms participation in FP7 projects	0.009*** [0.003]	0.008** [0.003]	-0.012*** [0.002]	-0.012*** [0.002]
Biopharmaceutical top cluster	0.379*** [0.144]	0.375*** [0.140]	-0.052 [0.100]	-0.048 [0.100]
Medical Devices top cluster	0.677*** [0.181]	0.652*** [0.181]	-0.070 [0.095]	-0.070 [0.095]
Knowledge workers	0.014 [0.016]	0.028* [0.017]	0.012 [0.010]	0.015 [0.011]
Health International tech collaboration	0.438*** [0.071]	0.415*** [0.068]	-0.018 [0.042]	-0.018 [0.042]
Government effectiveness	0.281*** [0.091]	0.207** [0.100]	-0.090 [0.054]	-0.102* [0.054]
Advanced service region	0.241 [0.246]	0.160 [0.256]	-0.119 [0.158]	-0.133 [0.161]
Advanced manufacturing region	0.404 [0.281]	0.422 [0.270]	-0.404*** [0.154]	-0.394*** [0.150]
Technologically advanced region	0.509** [0.251]	0.421 [0.262]	-0.148 [0.167]	-0.162 [0.170]
Constant	-2.356*** [0.623]	-2.397*** [0.638]	2.849*** [0.418]	2.797*** [0.447]
N	206	206	205	205
Adjusted R-squared	0.6746	0.6818	0.7916	0.7911
P	0	0	0	0

* $p < 0.10$, ** $p < 0.05$, *** $p < 0.01$, denote 10%, 5% and 1% significance level respectively. Robust standard errors in parenthesis

4. Empirical findings

Table 1 presents the main results of our analysis. The results clearly show that the propensity to obtain innovation outcomes in the Health industry is influenced by regional as well as characteristics of the Health sector.

In general, the Health Specialisation Index shows that regions more specialised in the Health industry tend to patent and publish more in the same area. Another general condition that seems to favour both outcomes is R&D intensity. Finally, the models also capture the positive effect of the critical mass represented by population.

Our results also point out that the regional conditions for promoting patenting and publishing in Health activities should be different. Patenting activities seem to be more linked with private sector activity and technological assets while publication activities seem to be more linked to public sector activities, in particular education and hospitals. Patenting appears to be related to the industrial technological strategies and the quantity and quality of public policy support schemes; while publication processes are more linked to previous stages in the patenting and commercialisation processes, such as basic science (“bench”) to tangible medical innovation (“the bedside”) (captured by R&D and clinical trials).

Regarding Health patents, our results mainly point to two main determinants: critical mass and collaboration. Critical mass is important in favouring patenting activities. It can be seen in the general positive effect of R&D intensity, population and Health specialisation. Being a technologically advanced region and promoting cluster creation also clearly favour the production of Health patents. In particular, policy support measures aimed at creating critical mass and promoting collaboration in Health industries such as the existence of Medical Devices or Biopharmaceutical top clusters seem to favour the propensity to patent. Regarding public support, patenting in Health seems to be positively affected by regional contribution to FP7 programmes, in particular in case of firm participation. The results also present the benefit of collaboration to promote regional Health patenting activities, e.g. the importance of collaborating at the local/regional level with the implementation of cluster policy schemes as well as at the international level with the positive effect of FP7 industry-university collaborations and Health international technological collaboration patterns. Finally, as can be seen in the results from Model A, government effectiveness contributes to regional Health patenting success.

Model B in table 1 presents the main regional and industrial factors influencing the regional propensity to produce Health publications. As mentioned before, critical mass in the form of population, investment and Health specialisation appear to be important factors promoting innovation outcomes. Publication favouring conditions are linked with the Health history of the region. Positive effects are linked to regional path dependency in Health: Health specialisation index, experience in patenting and current clinical trials. Publications seem to be clearly affected by public support schemes. Having an active participation in clinical trials in the region as well as participation of knowledge provider organizations to international projects related to Health (such the FP7 ones) are relevant for increasing the publication propensity, but not for increasing the patenting propensity. The coefficients related to the participation in those international projects by EFPIA firms and other firms (including SMEs) are negative in model B meaning that what mainly counts here is the participation of other types of organisations, such as research centres and academia.

While having previous experience in publications seems not so fundamental for the capacity of the regions to patent, the propensity to publish is instead significantly related to previous experience in patenting in the sector. This suggests that new technological advancements performed in this sector and in the regions give start to new scientific research to be conducted. However, the presence of some agglomeration economy as well as the presence of a certain general technological capacity of the region, particularly if dedicated to manufacturing activities, is not relevant (the coefficient for the variable related to advanced manufacturing region is negative both in model B I and B II).

What it emerges clearly is that the *relationship between the determinants and the two different outcomes vary in a substantial way*. Although R&D expenditure, the size as well as the specialization of the region matter in general for Health R&I, a chi-squared test across the different regressions for comparing the coefficients shows that at least size and R&D expenditure have a different degree of relation with the two outcomes. The R&D expenditure on GDP seems also to be more related to patents propensity than publication propensity. A deeper look at the relation between the different nature of the R&D expenditure and the two different outcomes allows us to understand better which type of R&D expenditure contributes more to the two distinct outcomes (see table 2). As we can observe from the simple correlation coefficients, business R&D expenditures that have usually a private sector nature relate more with patents, while government and higher education R&D expenditures (that have usually a more public sector nature) are more linked with publications.

Tab. 2 - Correlation coefficient between different typology of expenditure in R&D and patents and publications propensity

R&D expenditure	Health Patents	Health Publications
BERD R&D (n 83)	0.7555	0.6140
GOVERD R&D (n. 113)	0.5640	0.6956
HERD 0509 (n. 116)	0.6006	0.8666

Source: own elaboration EU DG data and EUROSTAT data. BERD (business expenditure in R&D), GOVERD (government expenditure in R&D) and HERD (higher educational R&D expenditure) are calculated on the average of previous 5 years to the referred year 2010 for patents and publications. All variables are in log terms. Correlations are significant at 1% level.

After having looked at the regional variables we can also say something about supra-regional factors through models II. Belonging to a Widening country does not affect the publications performances but it penalizes the patents performances. It also reduces the relevance of some regional factors such as the specific effectiveness of regional institutions and organizations with respect probably to national institutions. Overall, what it emerges from the analysis allows confirming H2: the determinants of patents propensity are different from the determinants of publication propensity.

5. Conclusions and policy implications

Following the recurrent selection of the Health sector as one of the policy priorities in the Regional Innovation and Smart Specialisation Strategies in Europe, our paper aimed at contributing to a better understanding of the Health sector in European regions. Through the use of novel data at regional and sectoral level, the paper has analyzed for the Health sector targeted as a priority for EU S3 the propensity to produce research and innovation outcomes measured as publications and patent counts. Our findings are clearly in line with the notion that agglomeration plays a crucial role in promoting innovation at the regional level. Scientific publications and patents are two different outcomes in the innovation process and their promotion require differentiate inputs and regional conditions.

Our analysis shows that the nature of these two innovation outcomes differs: while patenting activities are linked with industrial private sector and commercialization purposes, publications are mainly related to public basic research (“bench”) and experimentation in the form of clinical trials (“bedside”). These results are in line with previous research done in the subject, confirming it with the use of a novel regional and sectorial breakdown.

Agglomeration economies in the form of population density, technological mass, higher presence of the sector and path dependency appear as key determinants to promote patenting activity in the Health sector in Europe. Agglomeration can be promoted by the use of policy measures supporting the creation, transformation, and diversification of sectors such as cluster approaches or smart specialization strategies. Additionally, other measures that facilitate the private-public cooperation (locally or internationally) seem to be fundamental to multiply the positive effects of economic agglomeration and industrial specialization in patenting in Health.

Although we can find a higher propensity to patent in non-widening countries, regional factors have also an important role in widening countries. Our analysis shows that for increasing patent capacity more than disposing of a good pool of knowledge workers in the region, it is important to have a vital industrial structure that is not only dominated by few large firms but populated by SMEs. The patent propensity depends also on the capacity of the regional industry to develop international cooperation (mainly of technological nature) with global players. Nevertheless, this capacity seems to remain a prerogative only of those regions that have already a certain minimum level of absorptive capacity to confront with partners far away (Cohen and Levinthal, 1989; Fu et al., 2011).

The analysis also shows that good performances in publications can be found in regions belonging to widening countries or peripheral. This is not surprising since codified knowledge, as it can be a large part of knowledge contained in scientific publications, it is usually less linked to the territorial aspects (Polanyi, 1983) if not directly related to support the experimentation of new knowledge (through supporting clinical trials or building on knowledge already patented in the region). From a policy point of view, this result brings a twofold message: on the one side, EU support to scientific excellence has been successful also in catching-up regions; on the other side, the lack of private investments in the same regions might prevent the translation of such excellence in innovative outcomes. Therefore, identifying the difference between patents and publications' determinants becomes crucial for developing correct policy instruments across EU regions.

Our paper, in line with previous empirical evidence, advocates the benefits of specialisation, agglomeration and internationalisation. The development of a good industrial strategy is a priority to support innovation activities in all the sectors in general and in the Health sector in particular. Given its peculiarities, a good industrial strategy may include policies supporting different R&D&I support schemes such as pre-seed funding to foster emerging healthcare industries.

Our analysis is also in line with the current policy debates on the importance of analysing the characteristics of favourable innovation and entrepreneurship ecosystems for the development of

emerging industries and clusters in the area of health care and related industries (Angelis et al., 2015). Cluster initiatives are determinant in the case of European Health industries as they nurture several emerging healthcare niches at the same time, rely on local and international collaboration platforms and favour the cross-disciplinary skills well needed in healthcare businesses.

The relevance of different typologies of international networks calls for different typologies of supporting initiatives to the internationalization strategies. While for increasing regional patent performance what matters is a long distance network of technological nature, for publication performance what need to be supported is a more active participation in international research projects (favouring for example coaching activities with best performing regions and their organizations).

Last but not least, since the analysis shows that higher performances both in patenting and publications are related to those regions that have already some specialization in the sector with respect to other sectors, it is important to remark that investments for smart specialization should be done in regions that show a real potential and not only that have targeted Health as a thematic priority to exploit among others. Looking specifically to less performing regions that have a real potential to exploit policy initiatives, they should also go in the direction of reducing the gap between publication and patent outcomes through the promotion of technology transfer through cooperation among university and local industry.

This research provides some important messages to policy makers but better data at regional and sectorial level are desirable to disentangle more the effect of some determinants for the Health R&I, such as the role of large firms with respect to small firms or the brain drain processes which is characterizing strongly this sector.

Future research should be devoted to better look at the composition of the sector (for instance through the analysis of specific NACE subsectors or through qualitative case studies). This will allow also to go more in direction of policies that can take account of the specific variety of subsectors that may be related and that can create cumulative paths of growth of the regions with an already potential to exploit (Frenken et al., 2007).

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Appendix

Tab. A - Descriptive statistics

Typology	Variable name	Variable description	Source	Unit of measure	Obs.	Mean	Std Dev.	Min	Max
Dependent variables	Health patents	Number of EPO patents application by region of inventor classified on the bases of the Health thematic priority (year 2010)	EC DG-RTD (Framework contract)	ln	206	1.905	1.528	-2.996	5.241
	Health publications	Number of publications (frac) classified on the basis of the Health thematic priority (year 2010)	EC DG-RTD (Framework contract)	ln	206	6.114	1.146	3.060	9.051
Independent variables	R&D expenditure on GDP	Intramural RD Expenditure % of GDP 2009		%	206	1.807	1.257	0.200	7.900
	Medical schools	N of medical schools in the region with active graduation until year 2009	Own elaboration FAIMER (IMED) database	number	206	1.481	2.050	0	18
	Experience in Health publications	Number of publications (frac) classified on the basis of the Health thematic priority (mean: years 2005 - 2009)	EC DG-RTD (Framework contract)	ln	206	6.054	1.174	2.771	9.068
	Experience in Health patents	Number of EPO patents application by region of inventor classified on the basis of the Health thematic priority (mean: years 2005 to 2009)	EC DG-RTD (Framework contract)	ln	205	2.140	1.593	-4.605	5.525
	Ongoing clinical trials	Number of recruiting ongoing clinical trials * (year 2015)	Own elaboration CenterWatch database	ln	206	5.031	1.074	0	7.327
	FP7 projects participation	Number of FP7 project participation in the region (excluding duplication)	EC DG-RTD (Framework contract)	number	206	43.087	63.329	1	433
	EFPIA participation in FP7 projects	Percentage of EFPIA in the region participating in the FP7 projects on total participants	EC DG-RTD (Framework contract)	%	206	1.802	8.216	0	76.471
	Firms participation in FP7 projects	Percentage of firms (including SME) in the region participating in the FP7 projects on total participants	EC DG-RTD (Framework contract)	%	206	24.188	22.935	0	100
	Biopharmaceutical top cluster	Cluster specialization (flag for Europe's top clusters in Biopharmaceuticals). Dummy equal to 1 if in the region there is the presence of top clusters, 0 otherwise.	European Cluster Observatory: European Cluster Panorama 2014	dummy	206	0.131	0.338	0	1

	Health International tech collaboration	Number of international co-patents involving the given inventors NUTS2 region and third countries inventors for EPO patent applications classified on the bases of Health thematic priority (mean: years 2005-2009) *	EC DG-RTD (Framework contract)	log	206	0.072	0.334	0	3.620
	Government effectiveness	Govern effectiveness: standardized index of quality and fairness of local public school and healthcare system (year 2009) High numbers means higher perception of government effectiveness	EC DG Regio project on QoG	standardized index	206	0.343	0.857	-2.640	1.870
	Low technologically advanced region	1 Low technologically advanced region; 0 otherwise (year 2007)	Eurostat, Politecnico di Milano	dummy	206	0.199	0.400	0	1
	Advanced services region	1 Advanced services region; 0 otherwise (year 2007)	Eurostat, Politecnico di Milano	dummy	206	0.350	0.478	0	1
	Advanced manufacturing region	1 Advanced manufacturing region; 0 otherwise (year 2007)	Eurostat, Politecnico di Milano	dummy	206	0.189	0.393	0	1
	Technologically advanced region	1 Technologically advanced region; 0 otherwise (year 2007)	Eurostat, Politecnico di Milano	dummy	206	0.262	0.441	0	1
	Control variables								
	Widening effect	dummy value equal to 1 if Widening country; 0 otherwise	EC	dummy	206	0.175	0.380	0	1
	Population	Population expressed in habitants (year 2010)	Eurostat	100000 of habitants	206	21.214	16.092	3.199	117.862
	Health Specialization Index	Specialization in Health with respect to other sectors. (year 2010) Index above 1 means that the country is specialised more in Health with respect to other sectors that the relative specialization of the world, while an index below 1 means the opposite	EC DG-RTD (Framework contract)	standardized index	206	1.098	0.318	0.300	2.360
	Potential market size	Potential market size in GDP (pps) (year 2009) (EU27=100) high numbers mean higher potential	EC Eurostat, DG Regional Policy estimates	Standardized index	206	236.169	247.990	2.100	1280

*In order to keep 0 values, we have transformed our measures into $\ln(\text{var} + 1)$

Tab. B - Correlation matrix of the sample variables

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)
Health patents (1)														
Health publications (2)	0.5959*													
R&D expenditure on GDP (3)	0.5501*	0.3516*												
Medical schools (4)	0.3066*	0.5735*	0.0406											
Experience in Health publications (5)	0.5979*	0.9944*	0.3636*	0.5624*										
Experience in Health patents (6)	0.9132*	0.6426*	0.5729*	0.2990*	0.6484*									
Ongoing clinical trials (7)	0.4642*	0.6855*	0.1828*	0.4495*	0.6874*	0.5028*								
FP7 projects participation (8)	0.5567*	0.7109*	0.3651*	0.7127*	0.7054*	0.5700*	0.5013*							
EFPIA participation in FP7 projects (9)	0.1848*	0.1004	0.1857*	-0.0261	0.1106	0.2046*	0.0734	0.1374*						
Firms participation in FP7 projects (10)	0.1897*	-0.2460*	0.1482*	-0.1510*	-0.2346*	0.1905*	-0.0380	-0.1246	-0.0363					
Biopharmaceutical top cluster (11)	0.4171*	0.2945*	0.2594*	0.2112*	0.2914*	0.4205*	0.2228*	0.3597*	0.2149*	0.0488				
Medical Devices top cluster(12)	0.3894*	0.2148*	0.2936*	0.0432	0.2053*	0.3665*	0.2143*	0.1618*	0.0339	0.0549	0.3099*			
Knowledge workers (13)	0.5246*	0.3230*	0.4997*	0.1162	0.3442*	0.5636*	0.1843*	0.4769*	0.2722*	0.2030*	0.3226*	0.1646*		
Health International tech collaboration (14)	0.2923*	0.1712*	0.1405*	0.0816	0.1744*	0.2965*	0.1618*	0.1573*	0.0950	0.0508	0.2887*	0.0912	0.1250	
Government effectiveness (15)	0.3845*	0.0521	0.4246*	-0.1333	0.0706	0.4061*	-0.0682	0.1353	0.0982	0.2504*	0.1288	0.1568*	0.4570*	0.0999
Potential market size (16)	0.4219*	0.2926*	0.1878*	0.2294*	0.3064*	0.4680*	0.2390*	0.4448*	0.3359*	0.1795*	0.2850*	0.1327	0.6168*	0.0468
Low technologically advanced region (17)	-0.4082*	-0.1803*	-0.3332*	0.0137	-0.2098*	-0.4449*	-0.1919*	-0.2132*	-0.1074	-0.1071	-0.1215	-0.1224	-0.5348*	-0.0926
Advanced services region (18)	0.1017	0.1571*	0.0488	0.1215	0.1685*	0.1465*	0.0201	0.2441*	0.0795	-0.0089	-0.0132	-0.1028	0.3325*	-0.0684
Advanced manufacturing region (19)	-0.0805	-0.1704*	-0.0836	-0.0651	-0.1643*	-0.0832	0.0819	-0.1609*	-0.0883	0.0519	-0.1143	0.0508	-0.2589*	0.0582
Technologically advanced region (20)	0.3320*	0.1451*	0.3241*	-0.0861	0.1542*	0.3156*	0.0794	0.0722	0.0900	0.0607	0.2264*	0.1774*	0.3557*	0.1063
Widening effect (21)	-0.4147*	-0.2463*	-0.2838*	-0.0519	-0.2690*	-0.4676*	-0.0322	-0.1870*	-0.0985	-0.1430*	-0.1408*	-0.1509*	-0.1571*	-0.0937
Population (22)	0.4281*	0.6214*	0.0313	0.6449*	0.6104*	0.4125*	0.6317*	0.5235*	0.0897	-0.0645	0.1711*	0.1185	0.0419	0.1302
Health Specialization Index (23)	0.3209*	0.4535*	0.0441	0.2160*	0.4678*	0.3527*	0.2607*	0.3409*	0.0638	-0.0889	0.1503*	0.1090	0.1595*	0.0609

	(15)	(16)	(17)	(18)	(19)	(20)	(21)	(22)	(23)
Government effectiveness (15)									
Potential market size (16)	0.2020*								
Low technologically advanced region (17)	-0.4524*	-0.3231*							
Advanced services region (18)	0.2677*	0.2030*	-0.3654*						
Advanced manufacturing region (19)	-0.1866*	-0.1699*	-0.2409*	-0.3542*					
Technologically advanced region (20)	0.2866*	0.2246*	-0.2971*	-0.4369*	-0.2880*				
Widening effect (21)	-0.4638*	-0.2578*	0.2188*	-0.1765*	0.2344*	-0.2162*			
Population (22)	-0.2463*	0.2206*	-0.0038	0.0143	-0.0065	-0.0063	-0.0491		
Health Specialization Index (23)	0.2463*	0.2642*	-0.1941*	0.1965*	-0.1171	0.0675	-0.3889*	0.0763	

* $p < 0.05$