BUILDING A BUSINESS

Mapping the European startup landscape

A deep dive into the influence of research output, patenting, venture capital and human capital on startup financing activity in Europe reveals not all countries are equal.

The European life science startup sector differs from its counterpart in the United States in terms of financial and human resources. What is less widely appreciated are the differences in biotech startup formation among the various European nations. Here we set out to map these differences and provide an overview of those European nations that lead and those that lag in terms of biotech startup formation. We chose to focus on what we believe to be four fundamentals underlying research translation: scientific research output, biomedical patent activity, presence of local biomedically focused venture capital (VC) companies, and the abundance of human capital. Our results highlight in particular the importance of a robust scientific base, but also emphasize the need for strength in both financial and human capital.

Bird's-eye view

We start by mapping European startup activity in the biomedical sciences over the past five years. As a proxy for startup activity, we measure the number of startup deals, defined as the first time a biomedical company raised seed or startup venture capital. Results were obtained by examining data from 2013 to 2017 extracted from the GlobalData Pharmaceutical database. We restricted our analysis to those countries with a population size over one million that generated at least two startup deals over this time period.

Over the study period, we found 395 biomedical startup deals across 16 European countries (a combined population of ~470 million people). Our analysis reveals great geographical variation in the number of startup deals, both in absolute numbers (Fig. 1a) and per capita (Fig. 1b).

In absolute numbers, the UK leads the chart, with 129 biomedical startup deals in the dataset, followed at a distance by France (with 51) and Switzerland (37; Fig. 1a). When we correct for population size, it becomes clear that this variability points at intrinsic differences among the countries and is not a mere reflection of size. For example, Switzerland ranks 3rd in absolute number of startup deals but ranks highest on deals per capita, with 43.5 deals per 10 million inhabitants. In contrast, Germany, Europe's biggest economy, ranks 4th in absolute terms with 31 startup deals, but only 13th when correcting for population size. Likewise, countries such as Denmark and Ireland have a lot of startup activity relative to the size of their population (Fig. 1b), whereas other countries, such as Poland and Italy, rank low both in absolute and in relative numbers.

Scientific output

The original discoveries underlying biomedical startup companies are often made in academic research institutes. To probe the relevance of research for startup formation, we mapped the biomedical science output across Europe. As a proxy for research productivity, we used the total number of citable and non-citable documents published in the field of medicine in 2013–2017 obtained from the Scimago Journal & Country Rank.

Much as for its startup activity, the UK has a prolific scientific output (Fig. 2a). However, the UK's performance is average when taking into account population size (Fig. 2b). Leaders per capita in terms of

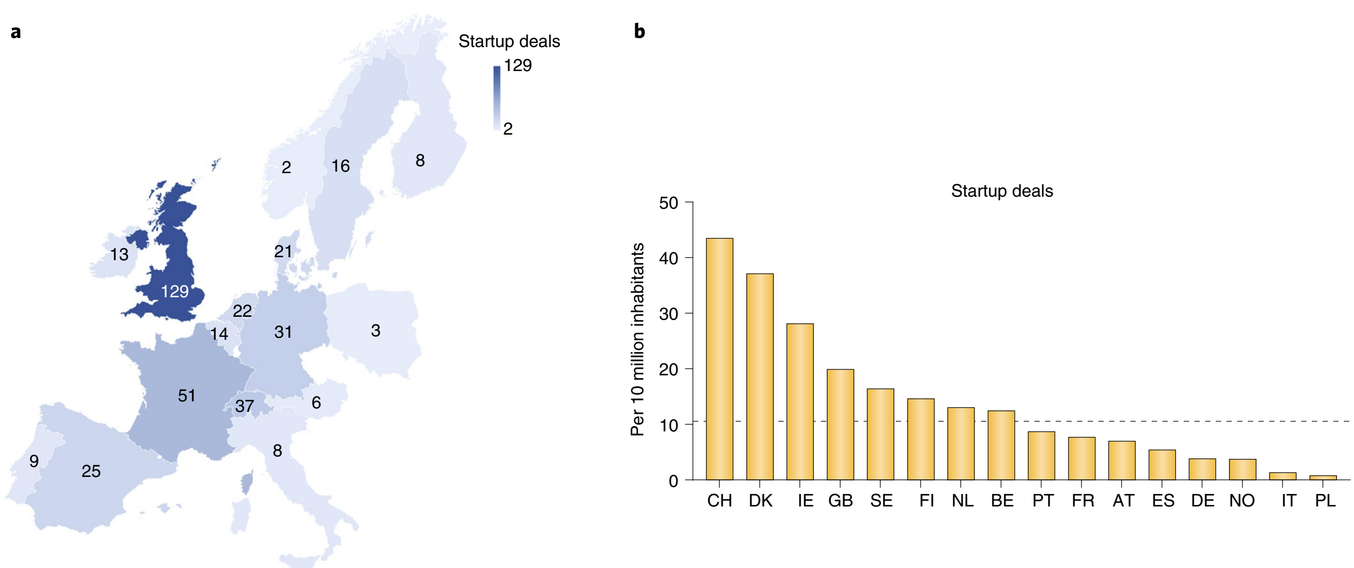

Fig. 1 | Distribution of startup deals among European countries. a, The number of biomedical startup deals in Europe (2013–2017) is indicated by color shading and shown in absolute numbers on the map. **b**, The bars represent the number of startup deals (2013–2017) scaled per capita. The dotted line represents the median. Countries are referred to by their two-letter ISO-2 codes: AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GB, the UK; IE, Ireland; IT, Italy; NL, the Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden.

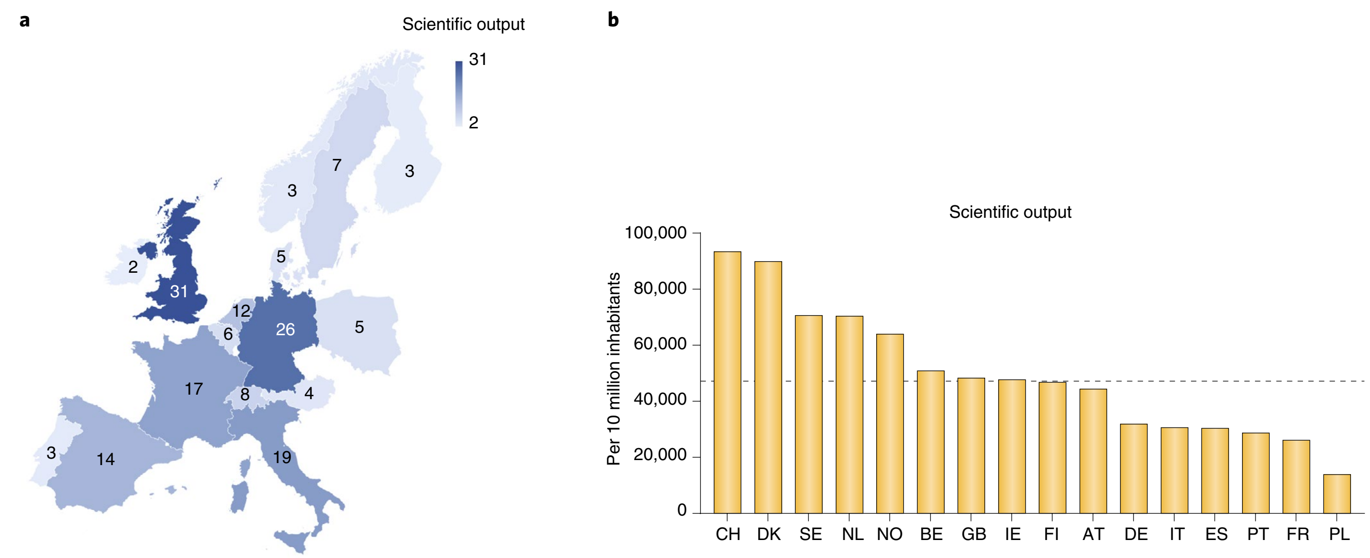

Fig. 2 | Biomedical research output differences across Europe. a, Each country's scientific output is indicated by color shading and shown in absolute numbers on the map. **b**, The bars represent the scientific output scaled per capita. The dotted line represents the median. AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GB, the UK; IE, Ireland; IT, Italy; NL, the Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden.

scientific output are Switzerland, Denmark, Sweden and the Netherlands; laggards are Germany and France, which rank below average, and Poland ranks the lowest (Fig. 2b).

These differences may at least partly be explained by differences in the public budget allocated to research and development (R&D). In 2015, the European countries with the highest R&D spending as a percentage of gross domestic product (GDP) were Switzerland, Sweden, Austria and Denmark, with 3.4%, 3.3%, 3.1% and 3% of GDP, respectively; the counties with the lowest R&D spending were Poland, Spain, Portugal and Italy, with 1%, 1.2%, 1.2% and 1.3% of GDP, respectively (all data from the European Commission).

Innovation is needed for successful research translation. Accordingly, we noted that those countries that excel at both startup activity and science output (Switzerland, Denmark, the Netherlands and Sweden) also appear in the top eight of the 2018 Global Innovation Index by Cornell University, INSEAD and the World Intellectual Property Organization (WIPO).

Patenting activity

Intellectual property protection of academic discoveries is integral to the creation of a startup company. Patent protection allows inventors to recoup their investments in R&D by providing a monopoly on selling any patent-protected invention for a defined period of time. Because of the very high development costs and long timelines of new drug approvals, it is crucial that innovative findings are patent protected well before finding their way to market. Hence we hypothesized that differences in patent output from scientific institutions across Europe may also contribute to differences observed in startup activity in particular jurisdictions. Figure 3 shows the number of patents filed by academic and research organizations between 2013 and 2017 in the field of biomedicine across Europe (see Supplementary Methods for patent definition and search strategy).

Our analysis reveals France as the country with the highest intellectual property output in absolute numbers, with 1,467 filed patents—over twice as many as the UK. This is somewhat of a surprise considering France's lower scientific output. Interestingly, France has one of the most attractive preferential tax treatments for incentivize patenting[1] and was among the first countries worldwide to do so. In contrast, the UK only introduced a preferential tax treatment for patenting in 2013, which may explain the lower relative patent output in the UK.

On a per capita basis, however, Switzerland ranks highest, in line with its leading position in scientific output. However, scientific activity is not necessarily linked with high patent output; for example, academic institutes in Sweden and Finland have filed few biomedical patents in that same period, despite their strong research productivity.

Venture capital availability

Given the risky nature and long time lines of life science ventures, most startups must at some time turn to VC investors to support their development programs. To assess the influence of VC on the chain of research translation, we looked at the number of active VC companies per country.

In absolute numbers, the UK stands out (Fig. 4a), in line with having the most startup deals and strong scientific and patent output. This could be because the UK was the first European country to place intellectual property ownership with academic organizations and to introduce technology transfer offices that manage the intellectual property and license agreements[2]. The UK also performs above average when taking into account the population size, although Switzerland again towers above Britain and all the other European nations (Fig. 4b).

Five of the countries analyzed do not have any active VC companies. These countries also have a below-average output on biomedical research and patenting. These factors are likely strongly linked to each other, as VC companies also offer know-how and access to their networks.

Human capital

Even when a strong scientific base, patents and VC funding are available, it still takes a team of motivated entrepreneurs to drive the formation of a biotech spin-out. This team of bioentrepreneurs needs to negotiate a license agreement, set up a company, find capital to support the company and attract employees and advisors skilled in drug and clinical development. Often, it also involves leaving the certainty of university employment behind and jumping into an uncertain but exciting future.

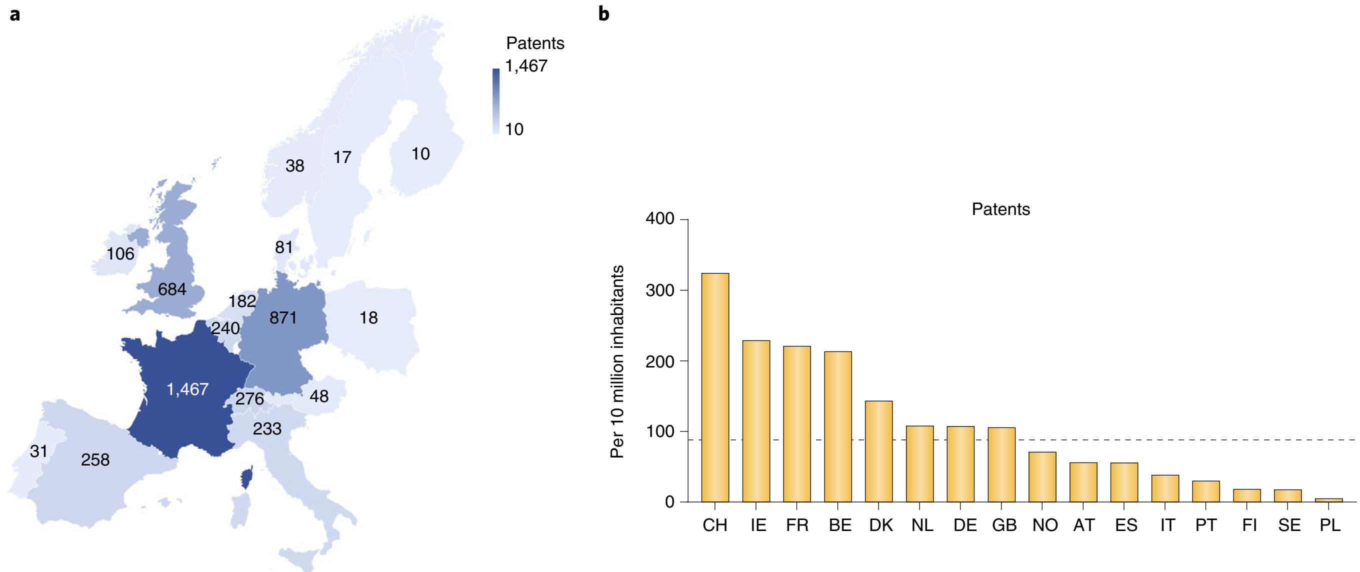

Fig. 3 | Biomedical patent differences across Europe. a, The number of patents in European countries (2013–2017) are indicated by color shading and shown in absolute numbers on the map. **b**, The bars represent the number of patents scaled per capita. The dotted line represents the median. Patents were sourced via Acclaim IP using the following query terms: university, college, research foundation, research organization, institute, school (including translations into European languages) plus our keyword- and Cooperative Patent Classification–based searches to select for biomedical sciences. AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GB, the UK; IE, Ireland; IT, Italy; NL, the Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden.

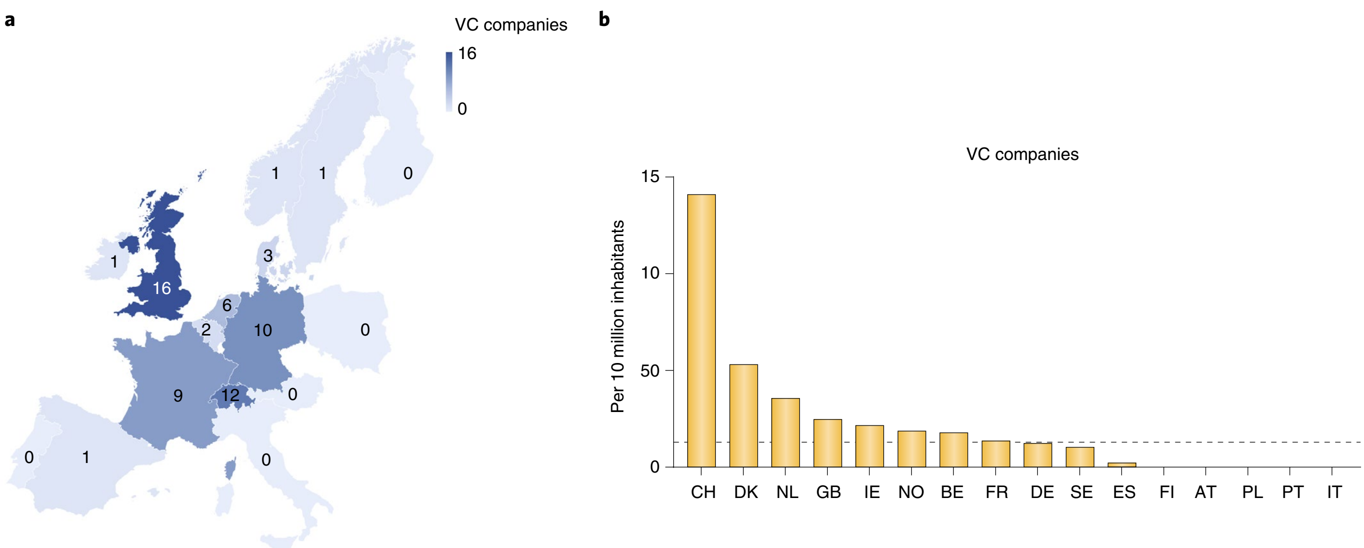

Fig. 4 | The number of biomedical VC companies across Europe. a, Companies in Europe are indicated by color shading and shown in absolute numbers on the map. **b**, The bars represent the number of VC companies scaled per capita. The dotted line represents the median. AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GB, the UK; IE, Ireland; IT, Italy; NL, the Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden.

To gain more insight into the availability of this 'human capital' and its importance for research translation, we considered two factors. First, as a proxy for the availability of all experts skilled in drug and clinical development, we counted the number of principal investigators actively involved in clinical trials. For this, we looked at investigators who have been involved in at least five clinical trials between 2013 and 2017, according to the GlobalData Pharmaceutical database. Second, we mapped nations on the basis of the 2017 Global Entrepreneurship Index[3]. This index, produced by the Washington, DC-based Global Entrepreneurship and Development Institute, measures both the quality of entrepreneurship in a country and the extent and depth of the supporting entrepreneurial ecosystem. The index takes human capital into account, as well as opportunity perception, startup skills, risk acceptance, networking, cultural support, opportunity startup, technology absorption,

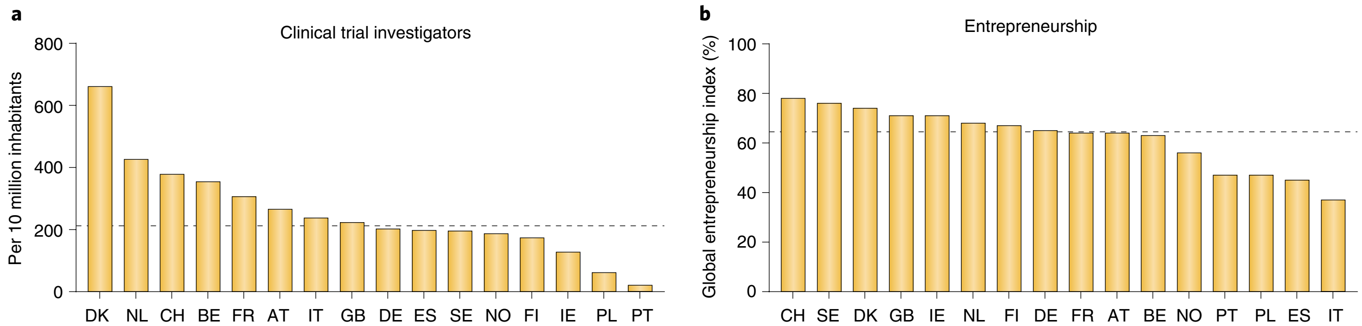

Fig. 5 | Human capital across Europe for biotech startups. a, Bars represent the number of clinical investigators scaled per capita. **b**, Bars represent the Global Entrepreneurship Index. The dotted lines represent the medians. AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GB, the UK; IE, Ireland; IT, Italy; NL, the Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden.

competition, product innovation, process innovation, high growth, internalization and risk capital[3]. Although the Global Entrepreneurship Index is not specific to the biomedical sciences, we believe it is a good representation of the entrepreneurial spirit of a country.

Switzerland and Denmark perform well on both measures of human capital (Fig. 5), in line with their overall strong performance in research translation. Across Europe, we found that countries with few startups, such as Italy and Spain, also have the smallest entrepreneurial ecosystems (Fig. 5b). This may be related to local economic factors, such as high unemployment rates (11.2% for Italy and 17.2% for Spain in 2017, according to Eurostat, European Commission). Nonetheless, Italy and Spain do have a reasonable number of active investigators (Fig. 5a). Poland and Portugal score low on both measures of human capital, consistent with their overall low performance in research translation.

Which ingredients determine success?

We found much variation across Europe in number of startup financings, as well as in science output, patent activity, VC presence and human capital. Using statistical analyses, we set out to disentangle the individual contributions of these variables to startup activity per capita. We analyzed the relation between our independent variables of interest (scientific output, number of patents, number of VC companies, number of clinical investigators and entrepreneurship score) and the dependent variable (number of startups) by applying an ordinary least-squares regression using both bivariate analysis and multivariate analysis (MVA). For the MVA, we included real GDP per capita in 2016 as a control variable (data obtained from Eurostat).

Using five independent linear regression analyses, we found that scientific output, patent activity, VC companies, clinical investigators and entrepreneurship all have a significant influence on the number of startup financings per country (Fig. 6, Supplementary Tables 1 and 2, and Supplementary Methods). However, as anticipated, these variables also strongly relate to each other (see Supplementary Table 2). For example, the science output correlates with the number of patents ($r = 0.43$), VC companies ($r = 0.74$), clinical investigators ($r = 0.69$) and entrepreneurship ($r = 0.71$), and the number of patents strongly correlates with the number of VC companies ($r = 0.74$).

Strikingly, when taking all relationships into account using the MVA analysis, it appears that scientific output is the key determinant of startup success (Table 1). The β coefficient indicates that with every 10,000 papers or documents of science output, the number of startup financings increases by 4.6. This finding appears relatively robust, as we saw a similar coefficient for science output in the linear regression. We found that the MVA model explains 83.8% of the variance in the number of startup deals (Table 1), suggesting that our chosen variables together indeed are fundamental to startup activity. Nonetheless, other explanations can be considered for the observed differences, including the state of the entrepreneurial culture[4], the presence of large pharmaceutical companies (which can offer skilled personnel to facilitate staffing of a new entity), access to cross-border VC companies[5] or availability of alternative sources of startup funding (such as grants, philanthropists, family offices and angel investors).

Conclusions

Mapping of the European biomedical startup scene revealed large differences across Europe. The great majority of the variation in startup financing activity can be explained collectively by science output, biomedical patent activity, the presence of biomedically focused VC companies, and human capital. Several insights arise from our analysis, which may be useful to policymakers, scientists and biomedical entrepreneurs.

First, biomedical research is the dominant feature of startup success, and policymakers wishing to stimulate biomedical startup activity should consider prioritizing biomedical research. Second, good science on its own is not enough for patent activity, as exemplified by countries such as Sweden and Norway. Differences in patenting across different countries may be attributed to several factors, including the nature of the research being done (fundamental or

Table 1 | Multivariate linear regression for the five factors mentioned in this study

Dependent variable (number of startup financings per capita)	MVA β coefficient	Robust standard error of the β coefficient
Scientific output (per 10,000) per capita	4.649*	2.441
Patents per capita	0.055	0.053
VC companies per capita	0.380	1.357
Clinical investigators per capita	−0.019	0.024
Global Entrepreneurship Index	0.227	0.157
Real GDP per capita (×1,000)	−0.360*	0.188
Constant	-11.705*	6.170

16 observations, $R^2 = 0.838$. *$P < 0.1$. P-values are based on a two-sided t-test.

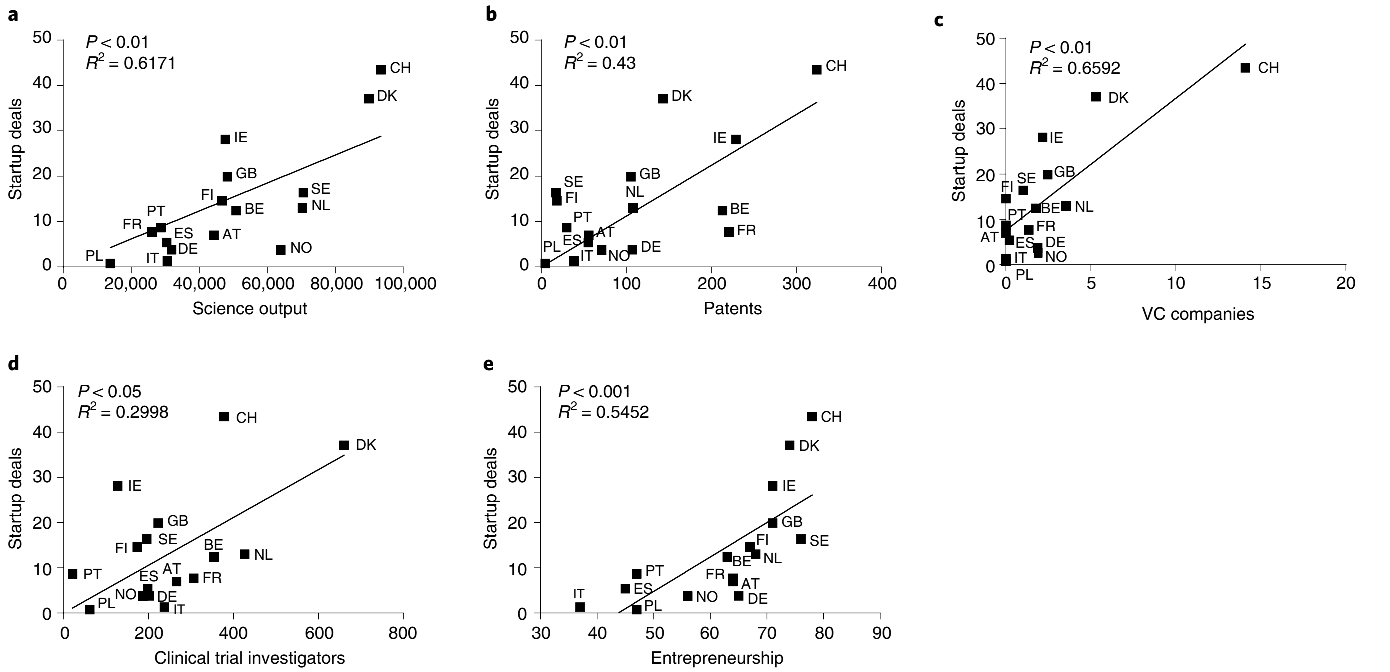

Fig. 6 | Relationship between the number of startup deals and scientific output, patents or VC presence across Europe. a–e, The solid line indicates the predicted relationship between scientific output (**a**), number of patents (**b**), number of VC companies (**c**), number of clinical investigators (**d**) or entrepreneurship score (**e**) and the number of startup deals. Data are normalized to population size (per 10 million inhabitants). *P*-value from two-tailed *t*-test and R^2 of the linear regression analysis are shown. Each country is indicated by a square and its two-letter country code. See Supplementary Methods for details on statistical analysis and multivariate analysis. AT, Austria; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FI, Finland; FR, France; GB, the UK; IE, Ireland; IT, Italy; NL, the Netherlands; NO, Norway; PL, Poland; PT, Portugal; SE, Sweden.

applied), the technology transfer expertise available, the number of skilled patent lawyers in a country, and awareness among scientists of the importance of keeping all science out of the public domain before patents are filed. Academic institutions in some countries may prefer to file patents in national patent offices, extending coverage via the European Patent Office and/or US Patent and Trademark Office only when it appears advantageous to do so, which may be the case in countries such as Finland and Sweden. Patenting activity might also be related to whether scientists see any monetary benefits from their patents. For instance, Germany has strict patent laws that regulate the remuneration of employees who make an invention while employed, whereas in other counties this decision is left to the employer.

Third, presence of a local VC company is beneficial for startup formation. Experienced VC companies tend to be well connected to the pharma industry, patent attorneys, regulatory bodies, contract research organizations and world-leading scientists. VC investors can assist researchers in successfully translating a novel innovation from academia into the clinic and advise bioentrepreneurs on how to make their startup company attractive for investments. Their absence may create a self-defeating cycle whereby a lack of local investors discourages bioentrepreneurs and lack of science and patents in turn discourages investors. Policymakers wishing to stimulate the life science startup scene may think about supporting the start of venture funds in countries where their presence is scarce.

Lastly, given that the distances are not huge in Europe, we encourage bioentrepreneurs to start companies in European regions with high scientific output and a concentration of local VC companies and human capital before attempting to raise money for a startup. Whereas historically money followed inventions and company creation, today's company creation is becoming more and more centered in places where all infrastructure and know-how are readily available. Such migration of teams and startups toward capital is seen in the United States, where San Francisco and Boston have become the true biotech hubs of the country. Despite the formation of smaller bioclusters, this phenomenon is less visible in Europe. ❐

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Competing interests

B.v.W., S.v.D. and R.W.R. are employed by Forbion Capital Partners, which invests in biotech ventures.

Additional information

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