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Depolarizing Innovation: Dynamic Policy Implications for Entrepreneurial Ecosystems in Second-Tier European Regions

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Abstract

Entrepreneurial ecosystem (EE) research has mainly focused on metropolitan regions and neglected second-tier (European) regions. I use a comparative case study approach with a focus on regional public policy to analyze two second-tier European regions: Uppsala and Galway. The results show that EEs can emerge as a by-product of attracting foreign direct investment or investment in higher education and research. In both cases, the R&D activities of multinational enterprises (MNEs) and universities contribute to the emergence and growth of EEs by enabling the creation of spin-offs. Given the limited resources in second-tier regions, EE initially focus on specific industry clusters to maximize resource efficiency. Later diversification increases ecosystem resilience and mitigates cluster risks. However, limited access to growth capital in second-tier EEs leads to increased acquisition activity by MNEs or the relocation of high-growth ventures to metropolitan areas. Policy measures that support second-tier regions' efforts to create local EEs initially focus on promoting R&D, knowledge spillovers, and research commercialization, later include the creation of supportive infrastructure, and finally enable the attraction of growth capital to the region.

Keywords: economic geography; entrepreneurial ecosystems; public policy; second-tier regions; spatial context

1. Introduction

This article focuses on the evolution of entrepreneurial ecosystems in second-tier European regions. Section 1 introduces the context of the article and defines the research question that forms the basis for all subsequent sections.

1.1. Context

Entrepreneurial ecosystems (EEs) have recently gained considerable attention in the academic literature and among policymakers (Roundy, 2017). The interest is motivated by the argument that entrepreneurship can drive economic development, employment levels, and productivity growth (Isenberg, 2010; Szerb et al., 2015). Many studies on EEs tend to focus on the national level (Audretsch et al., 2015). Yet, the regional spatial context of entrepreneurship within a country influences the outcome of entrepreneurial activities due to different social, institutional, and economic factors (Müller & Korsgaard, 2018; Roundy, 2017). Indeed, Glaeser et al. (2011) note that regional economic development can differ greatly from national economic development. Therefore, regional differences that determine the context of entrepreneurial activity should be considered when analyzing EEs (Audretsch et al., 2015).

Certain cities and regions around the world have become hubs for startups and innovation-driven companies. Most of these hubs are located in larger "superstar" metropolitan areas (e.g., Kemeny and Storper, 2020; Atkinson et al., 2019). But when it comes to entrepreneurial activity, smaller cities and regions should not be neglected. On the one hand, growing territorial inequality due to a polarization of innovation

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(Atkinson et al., 2019; Muro & Whiton, 2018), which can be observed, for example, when looking at the spatial distribution of venture capital investments (Florida & King, 2016; Florida & Mellander, 2016), could lead to growing social tensions and the rise of political populism (Rodríguez-Pose, 2018). On the other hand, given the positive impact of entrepreneurial activity on economic performance (Isenberg, 2010; Szerb et al., 2015), dynamic and resilient EEs could be a means for smaller regions to close the gap with superstar regions in terms of job attractiveness, which could prevent phenomena such as brain drain, i.e., the outflow of human capital (see Alston, 2004). Since productive entrepreneurial activity in second-tier regions is likely to improve socioeconomic factors (Robinson et al., 2004), it may also have a positive impact on urban development efforts. Therefore, attempting to establish, grow, and sustain a local EE is a plausible strategy for improving the socioeconomic conditions of a second-tier region. Indeed, there are a growing number of thriving EEs in second-tier regions. Examples that have been analyzed in the literature include the U.S. cities of Chattanooga (Motoyama et al., 2016), Boise (Mayer, 2011), and Newton Falls (Roundy, 2019), and the Canadian cities of Waterloo and Calgary (Spigel, 2017).

Research on EEs often takes a static approach (Borissenko & Boschma, 2016). However, as EEs go through different stages of development (see Mack and Mayer, 2016), the effectiveness of specific support mechanisms depends on the state of an EE. Therefore, it is important to take a dynamic rather than a static approach to EE support and related public policy.

1.2. Research Question

This article addresses the impact of policies on the development of EEs in second-tier European regions. Thriving EEs can lead to improvements in socioeconomic factors, which is one reason why policymakers are increasingly interested in the concept (Roundy, 2017). At the same time, crafting and implementing policies that effectively contribute to a vibrant local EE can be challenging. Hence, the research question that forms the basis for the subsequent literature review and qualitative primary research is as follows:

What policies can second-tier European regions adopt, consistent with their stage of development, to effectively foster a local entrepreneurial ecosystem?

The research question consists of three main components that influence the scope of the research: the focus on Europe, the focus on second-tier regions, and the dynamics of policy measures in relation to the evolutionary development of an EE. The literature review in section 2 considers these three components in detail.

2. Literature Review

The second section provides a literature review of various aspects of an EE, including its foundations, relationship to economic and urban development, and the importance of spatial features. After developing the theoretical foundations of an EE, the literature review highlights the specific facets of the research question, i.e., the focus on Europe, the focus on second-tier regions, and the dynamics of an EE.

2.1. Foundations of Entrepreneurial Ecosystems

According to Roundy et al. (2018), Bahrami and Evans (1995) were the first to compare the Silicon Valley technology cluster to a natural ecosystem. Two years earlier, Moore (1993) stated more generally that firms are embedded in an ecosystem and do not develop in a vacuum. Early work introducing the term "entrepreneurial ecosystem" by Cohen (2006) and practical suggestions for developing an EE by Isenberg (2010) have contributed to the concept of EEs (Kuckertz, 2019) becoming known and attracting interest in both academia and practice (Roundy, 2017). While there are several definitions of the term "entrepreneurial ecosystem" in the literature (for an overview, see Cavallo et al., 2019), according to Cavallo et al. (2019, p. 1300), Stam's (2015) definition "[...] has been widely endorsed in literature [...]" and encompasses essential characteristics of an EE:

> "*The entrepreneurial ecosystem as a set of interdependent actors and factors coordinated in such a way that they enable productive entrepreneurship within a particular territory*" *(Stam, 2015, p. 1765)*.

A second definition that emphasizes dynamic processes within an EE by mentioning both the creation and growth of startups comes from (Spigel, 2017):

> "*[An entrepreneurial ecosystem is] a combination of social, political, economic, and cultural elements within a region that support the development and growth of innovative startups and encourage nascent entrepreneurs and other actors to take the risks of starting, funding, and otherwise assisting high-risk ventures*" *(p. 50)*.

Isenberg (2011a, 2011b) highlights that an EE consists of hundreds of specific elements that can be grouped into six larger areas: Culture, Policy, Finance, Human Capital, Support, and Markets. Isenberg also mentions that the combination of elements varies from EE to EE, indicating the uniqueness of each ecosystem, which in turn requires a specific rather than a generic approach to analyzing EEs. Furthermore, Isenberg (2011b) argues that the interaction of elements is highly complex and idiosyncratic, which limits the value of identifying generic causal relationships. An illustration of Isenberg's understanding of an EE can be found in Figure 1, and a more detailed elaboration of the domains can be found in Appendix 1.

According to Mack and Mayer (2016), it is necessary to consider the evolutionary dynamics of the components of an EE as well as its developmental stages. Several other authors share this view (e.g., Isenberg, 2011b; Kuckertz, 2019; Mason and Brown, 2014). Mack and Mayer (2016) divided

the development of an EE into four stages: Birth, Growth, Sustainment, and Decline. Each of these phases has differences in the number of firm entries and firm exits. Mack and Mayer's development model can be seen in Figure 2. The full figure with some of the effects of the phases can be found in Appendix 2.

Based on the two definitions presented in combination with Isenberg's (2011b) understanding of EE domains and Mack and Mayer's (2016) evolutionary development phases, EEs share some common characteristics, including:

- the interdependence of actors and factors,
- the need for coordination and processes to enable productive entrepreneurship,
- the focus on a particular territory, and
- the need for an evolutionary and dynamic perspective.

After discussing the definition and characteristics of an EE, its major areas and phases of development, section 2.2 focuses on the impact of an EE on the economic development of the area in which it is located.

2.2. Entrepreneurial Ecosystems and Economic Development

A positive relationship between entrepreneurial activity and economic prosperity has been noted by several scholars (e.g., Audretsch et al., 2015; Feldman, 2014; Isenberg, 2011b). In contrast to some authors who focus predominantly on the impact of high-growth startups (e.g., Mason and Brown, 2014), Stam (2015) argues that this focus is too exclusive, as other innovative startups and entrepreneurial workers can also contribute to positive welfare outcomes to some extent. Stam refers to an article by Baumol (1990) that distinguishes between productive, unproductive, and destructive entrepreneurial activities and their respective effects on an economy's productivity growth. Several factors influence the extent to which entrepreneurship contributes to the economy of a given area, with some scholars emphasizing that not all entrepreneurial activities contribute positively to its development (e.g., Mason and Brown, 2014; Nightingale and Coad, 2014). Rather, there are a small number of high-growth startups that contribute positively to overall economic growth and many underperforming firms that "[...] have low productivity and low levels of innovation, and generate churn rather than economic growth" (Nightingale & Coad, 2014, p. 130). In addition, N. Lee and Rodríguez-Pose (2021) found that entrepreneurship can lead to regional poverty reduction when it occurs in tradable sectors, increasing the likelihood of positive regional multiplier effects. Entrepreneurship in non-tradable sectors still has some economic benefits despite the likelihood of local market saturation, but is not sufficient to contribute significantly to regional poverty reduction (N. Lee & Rodríguez-Pose, 2021). Aparicio et al. (2020) emphasize that entrepreneurship, if indeed productive, can be a vehicle for inclusive growth that includes a region's vulnerable communities.

Policymakers can achieve better outcomes by distinguishing between different forms of entrepreneurial activity and taking a systems-based, holistic approach rather than focusing on firm-specific interventions (Mason & Brown, 2014). EEs represent one such systemsbased approach. Several scholars have linked EEs to economic growth (e.g., Isenberg, 2011b; Mason and Brown, 2014). This is driven by the emergence of high-growth startups that are enabled by a supportive ecosystem and contribute disproportionately to the economic development of a region (Mason & Brown, 2014; Nightingale & Coad, 2014), e.g., by creating a significant share of new jobs compared to non-high-growth firms (Coad et al., 2014; Henrekson & Johansson, 2010) and by contributing to the growth of other firms in the same area through knowledge spillovers (Acs et al., 2009; Mason & Brown, 2014). However, this growth takes time, so policymakers need to take a long-term perspective (Nightingale & Coad, 2014).

The arguments presented in this subsection seem to motivate policymakers to promote entrepreneurial activities and establish local EEs. However, an EE may also have implications for urban development efforts in each area, touching on a domain that is generally not directly related to entrepreneurship. The following subsection analyses this relationship.

2.3. Entrepreneurial Ecosystems and Urban Development

Some scholars argue that Jane Jacobs, one of the world's most influential urbanists, was quick to emphasize that cities' ability to attract diverse people provides fertile ground for creativity and innovation, which are key to entrepreneurial activity (Hospers, 2006; S. Y. Lee et al., 2004), economic growth (Florida, 2003, p. 43), and vitality (Auerswald, 2015). Because of the density of labor, capital, knowledge, and other resources, cities enable the creation of young firms, a concept Jacobs calls "new work" (Jacobs, 1969, p. 49ff.). Her concept of new work in the context of urban development therefore created some of the frameworks for EEs found in the modern literature. Moreover, she also described the importance of knowledge spillovers between different industries for the economic growth of cities (Desrochers & Hospers, 2007; Qian, 2018). Indeed, Florida et al. (2017, p. 92) state that "[c]ities [...] are the enabling infrastructure where connections take place, networks are built[,] and innovative communications are consummated." In line with Jacobs' observations, Richard Florida's theory of the creative class suggests that creativity and an open culture are "[...] a spur to societal innovation, entrepreneurship, and economic development" (Florida, 2005a, p. 6). Combining Jacobs' argument of the attractiveness of cities to a variety of people and the availability of resources in cities with Florida's theory of the creative class illustrates the link between EEs and urban development. Florida et al. (2017) summarize this finding by stating that innovation, entrepreneurship, and creativity are essentially spatial rather than individual or firm-level processes.

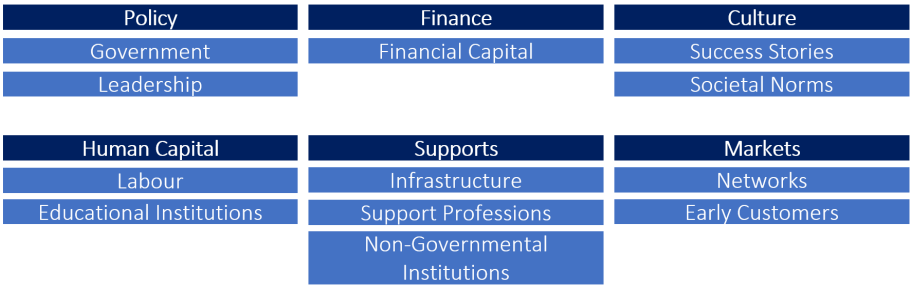


Figure 1: Domains of an Entrepreneurial Ecosystem. Source: adapted from Isenberg (2011b).

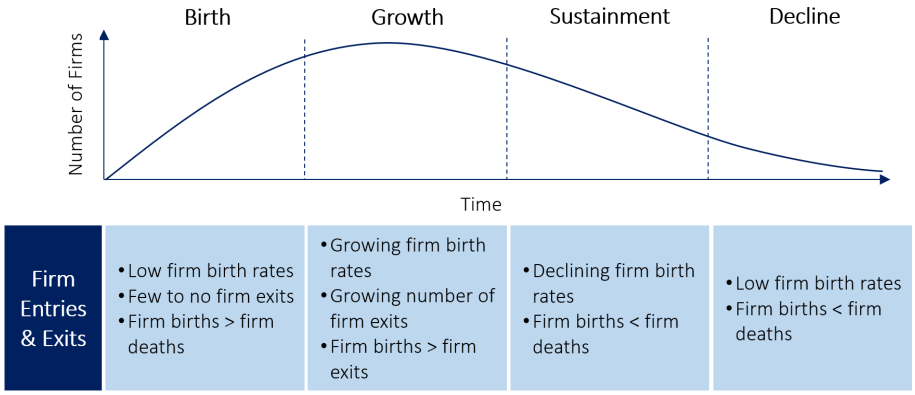


Figure 2: Evolution of an Entrepreneurial Ecosystem. Source: adapted from Mack and Mayer (2016).

As discussed in section 2.2, establishing a thriving EE can contribute to local economic development. This, in turn, has the potential to both increase tax revenues and improve the availability of private capital in a region. As Jacobs (1969, pp. 290-317) noted, urban development in each area requires financial resources, which can come from public or private sources. Therefore, the establishment of a local EE could be part of a broader urban development strategy if an increase in public and/or private funding is anticipated. Similarly, Welter et al. (2008) suggest that promoting entrepreneurship in distressed urban areas, if certain barriers can be overcome, may contribute to their regeneration. As Isenberg (2011b) has noted, each EE is embedded in the context of a particular area and is therefore made up of a unique combination of different elements that interact in complex and idiosyncratic ways. Thus, when attempting to create a local EE, spatial characteristics must be considered.

The section 2.4 highlights the differences between these features and analyzes some of their implications. This sets the stage for the main concern of this article: the unique context and configuration of EEs in second-tier European regions, and the corresponding implications for policy effectiveness throughout the life cycle of an EE.

2.4. Entrepreneurial Ecosystems and Spatial Differences

In this subsection, spatial differences are introduced into the discussion of EEs. First, a phenomenon that affects the geographic inequality of EEs is explained: the polarization of innovation. Then, the focus shifts from a more general consideration of EEs to EEs specifically in second-tier regions. A brief analysis of the uniqueness of the contemporary European context is also provided. This subsection thus introduces the focus of the article: the development of EEs in second-tier European regions.

2.4.1. Polarization of Innovation

In 2005, Richard Florida pointed out in an article in *The Atlantic Monthly* that contrary to the widespread belief that technology and globalization are leveling the global economic playing field, the world has only a few centers where innovation is concentrated, and that this divide is also evident at the national level (Florida, 2005b). He notes that "[p]opulation and economic activity are both spiky, but it's innovation - the engine of economic growth - that most concentrated" (p. 49). Analysis of venture capital investment (VC) in U.S. metropolitan regions, European metropolitan regions, and metropolitan regions around the world (Florida & King, 2016) confirms Florida's original observation of innovation concentration. Florida and King (2016, pp. 6-7) note that only ten metropolitan regions worldwide account for more than half of total global VC investment. Areas in the U.S. accumulated 68.6% of global VC investment, with Silicon Valley alone attracting 25.3% (Florida & King, 2016, pp. 6-11). In the following, this phenomenon is referred to as the polarization of innovation. Figure 3 illustrates the distribution of VC investments worldwide. Appendix 3 illustrates the distribution within the U.S. and Europe in detail.

According to Atkinson et al. (2019), the polarization of innovation leads to a growing gap between superstar metropolitan areas and non-superstar areas, as well as a

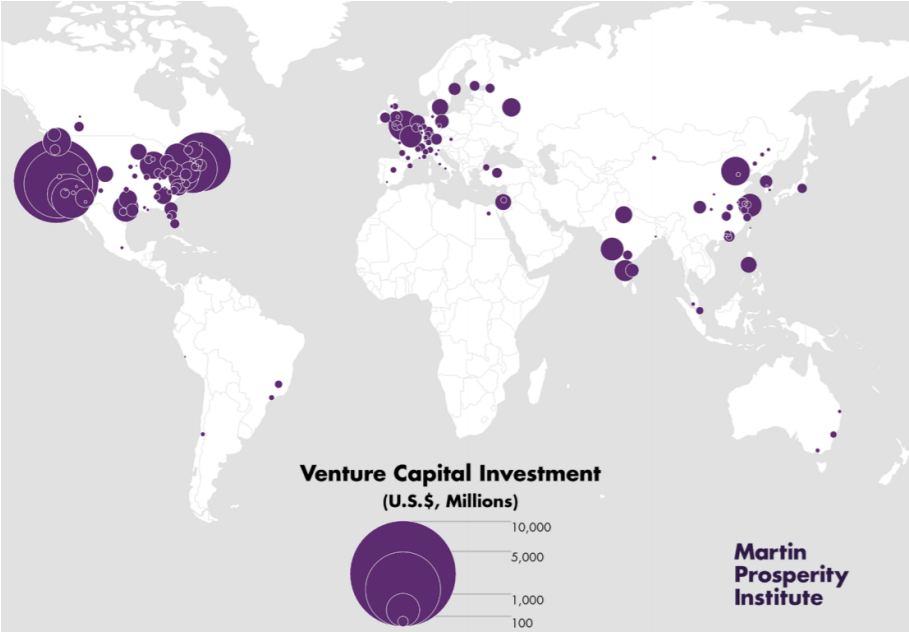


Figure 3: Venture Capital Investments across Metropolitan Areas Worldwide in 2012. Source: Florida and King (2016, p. 10).

concentration of jobs in the innovation sector. This leads to, among other things, higher housing prices and more traffic in superstar areas and out-migration, territorial underdevelopment, and economic exclusion in second-tier and rural areas (Atkinson et al., 2019). Rodríguez-Pose (2018) suggests that such regional disparities even lead to social tensions and political populism based on territorial rather than social foundations.

As discussed in section 2.2, EEs can contribute to the economic development of an area. While most thriving EEs are located in superstar areas, some second-tier regions around the world have managed to build thriving EEs despite innovation polarization. section 2.4.2 focuses on EEs in second-tier regions, while section 2.4.3 highlights the uniqueness of the contemporary European context, which has not yet received much attention in the entrepreneurship literature (Audretsch et al., 2015).

2.4.2. Entrepreneurial Ecosystems in Second-Tier Regions

There are numerous definitions of second-tier cities or regions in both academic and practitioner literature (see Figure 4 for a non-exhaustive overview). In this article, second-tier regions are defined as regions "[...] that are smaller than the large metropolises that dominate regional or national economies [...]" (Wachsmuth, 2008, p. 1), although no minimum or maximum population size is specified, as second-tier regions should "[...] be defined in relation to the first-tier cities with which they coexist" (Wachsmuth, 2008, p. 2).

As Isenberg (2011b) has noted, the design of an EE depends on the local context and conditions. Therefore, it is neither advisable nor feasible to emulate superstar EEs like Silicon Valley, especially for second-tier regions. Instead, it should be recognized that each EE is different and has unique characteristics (Xu & Dobson, 2019). Peripheral places face certain challenges related to their spatial context and availability of resources as opposed to superstar areas (Xu & Dobson, 2019). These challenges may include more difficult access to financial resources and skilled human capital, a less supportive sociocultural environment, lack of certain infrastructure components (such as transportation infrastructure or high-speed internet), limited markets and market access, and ineffective policies (Xu & Dobson, 2019).

In contrast to the innovation polarization phenomenon, and despite the above challenges, there are some examples in the literature of second-tier regions that have successfully built thriving EEs. Such examples include Boise, Portland, and Kansas City (Mayer, 2011), Chattanooga (Motoyama et al., 2016), Newton Falls and Geneva (Roundy, 2019), and Calgary and Waterloo (Spigel, 2017). Summaries of the above case studies can be found in Appendix 4.

2.4.3. European Context

Compared to North America, the contemporary urban context in Europe has been less studied in the academic literature (Audretsch et al., 2015). However, Europe has many small and medium-sized cities, highlighting its unique polycentric urban structure (Dijkstra et al., 2013). Dijkstra et al. (2013) argue that stylized analytical frameworks, assumptions, and policy conclusions derived from them are mostly based on the contexts of North America or the developing world and therefore have limited relevance to the contemporary European context. This in turn hinders the process of policy development in European regions based on textbook models (Dijkstra et al., 2013). Given the importance of spatial context in discussing EEs and the focus of the academic literature on North America and developing countries, this

Source	Definition
Markusen & DiGiovanna (1999, p. 3)	"[...] spatially distinct areas of economic activity where a specialized set of trade-oriented industries takes root and flourishes, establishing employment and population growth trajectories that are the envy of many other places."
Wachsmuth (2008, pp. 1-2)	"The terms 'second-tier city' and 'third-tier city' are frequently used to describe urbanized areas that are smaller than the large metropolises that dominate regional or national economies, but they have no single or accepted definition. In fact, this fluidity is inherent in the concept [...] and [...] can only be defined in relation to the first-tier cities with which they coexist."
Mayer (2011, p. 7)	"Second tier high-tech regions [...] specialize in certain sub-sectors of the high-tech economy and take advantage of the presence of lead high-tech firms."
Parkinson et al. (2012, p. 3)	"[...] cities outside the capital whose economic and social performance is sufficiently important to affect the potential performance of the national economy."
Dijkstra et al. (2013, p. 354)	"Second-tier metro regions are the group of largest cities in the country excluding the capital."
Cardoso (2018, p. 223)	"[...] non-capital, medium-sized cities, which do not play dominant roles in their countries but are economically, culturally and demographically significant [...]."

Figure 4: Selection of Definitions of Second-Tier Regions.

article considers the unique European context as well as the individual contexts of regions within Europe.

Audretsch et al. (2002, p. 4) argue that the U.S. internalized the virtues of entrepreneurship more quickly than Europe and that European countries were relatively slow to adopt a similar mindset. European attitudes toward the entrepreneurial economy developed in five phases (for a summary, see Audretsch et al., 2002, pp. 4-6). Toward the end of the 1990s, European policymakers reached a consensus on the superiority of the entrepreneurial economy in the United States over the old managerial economy in Europe, leading to a commitment to create a new European entrepreneurial economy (see European Commission, 2000, pp. 249-286). In 2013, in response to the 2008 financial crisis, the European Commission presented an action plan to reignite entrepreneurship in Europe through governance mechanisms (European Commission, 2013, p. 3). Szerb et al. (2020) explain that since then, a policy priority setting framework, the Research and Innovation Strategies for Smart Specialization (RIS3) agenda, has emerged in the EU. The RIS3 agenda aims to tailor R&D and innovation-related policies to the capabilities, strengths, and potential of a given region. According to some scholars, RIS3 is an innovative policy approach (Foray & Goenaga, 2013) that is part of a broader regional and place-specific growth policy framework (OECD, 2013; Pugh, 2014). Morgan (2017, p. 569) even describes it as "[...] the most ambitious innovation program ever introduced in the European Union [...]". Szerb et al. (2020) emphasize that the RIS3 agenda recognizes the spatial differences between regions within the EU, resulting in individual contexts that require tailored governance and policy approaches. The same authors then compare RIS3 with the EE approach. While both approaches respect spatial differences, EEs consider a broader range of individual and institutional factors and the interconnectedness of actors within an ecosystem (Acs et al., 2016; Szerb et al., 2020). Nevertheless, Szerb et al.'s (2020) analysis shows that spatial differences are increasingly considered by policymakers in Europe, both at supranational and national levels. Regarding the development of EEs and to fully understand the framework conditions of each region, identify institutional and individual weaknesses, understand the harmonization of the components of an EE, and simulate policies that could alleviate bottlenecks of the regional EE, Szerb et al. (2020) argue that the use of the Regional Entrepreneurship and Innovation Index (REDI) is appropriate (Szerb et al., 2020; see also Figures 5 and 6). For more information on the REDI, see section 2.5, which also highlights the identified research gap.

2.5. Research Gap

Since the early work of scholars such as Cohen (2006), Isenberg (2010), and Feld (2020), many aspects of EEs have been explored in the academic literature. However, research on EEs has mostly focused on nations (Audretsch et al., 2015) or on established ecosystems in large superstar regions (Roundy, 2019). As a result, there are still a wealth of areas that can be further explored in academic research (Cavallo et al., 2019). This article aims to outline policy implications for second-tier European regions that aim to build, grow, and sustain a resilient EE. The importance of a dynamic

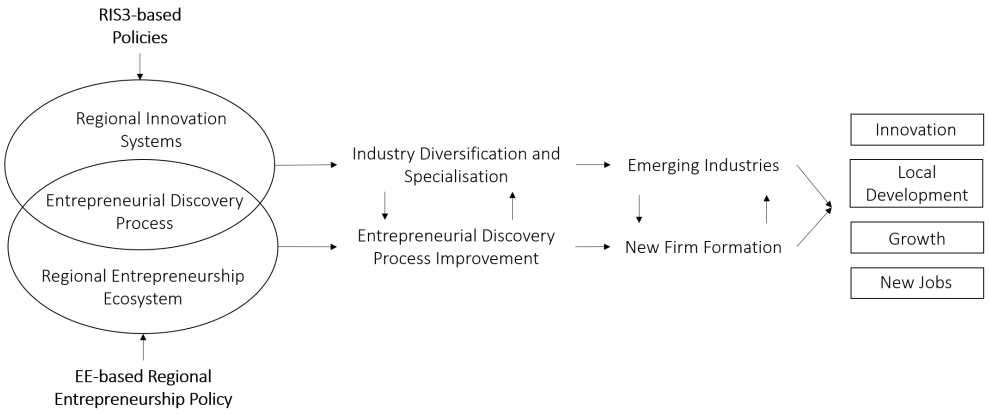


Figure 5: Joint Potential of RIS3- and EE-Based Regional Entrepreneurship Policy. Source: adapted from Szerb et al. (2020, p. 7).

Structure of the REDI: 3 sub-indices/14 pillars		National and regional institution variables	Regional level individual variables
Entrepreneurial Aspiration Sub-index	Financing	Financial Institutions	Informal Investment
	Globalisation	Connectivity	Export
	High Growth	Clustering	Gazelle
	Process Innovation	Technology Development	New Technology
	Product Innovation	Technology Transfer	New Product
Entrepreneurial Ability Sub-index	Competition	Business Strategy	Competitors
	Human Capital	Education and Training	Education Level
	Technology Sector	Absorptive Capacity	Technology Level
	Opportunity Start-up	Business Environment	Opportunity Motivation
Entrepreneurial Attitudes Sub-index	Cultural Support	Open Society	Carrier Status
	Networking	Social Capital	Know Entrepreneurs
	Risk Acceptance	Business Risk	Business Acceptance
	Start-up Skills	Quality of Education	Skill Perception
	Opportunity Perception	Market Agglomeration	Opportunity Recognition

Figure 6: Structure of the Sub-Indices and Pillars of the REDI. Source: adapted from Szerb et al. (2020, p. 9).

approach to research EEs and its underdevelopment in the scientific literature has been noted by several researchers. Both Borissenko and Boschma (2016) and Mack and Mayer (2016) emphasize the need for further research on the dynamics of EEs. Cavallo et al. (2019) emphasize the need to explore the role of policymakers in the dynamic evolution of an EE and how to promote "natural" and self-regulating rather than artificial mechanisms. A call for papers for *Entrepreneurship & Regional Development* by Audretsch et al. (2018) identified the need for papers that address policy issues, such as analyzing how policy influences elements of an EE and how elements of an EE influence policy. Shwetzer et al. (2019, p. 89) additionally articulated two research directions that align with the above pathways for further research, namely "[p]olicymakers' interventions and support to enable and grow EEs" and "EEs creation, growth and how can they be sustained". By elaborating policy implications for European second-tier regions while considering the dynamics of an EE, this article aims to contribute to filling the research gaps mentioned before. By focusing specifically on second-tier European regions, this article also considers the uniqueness of the European context (Audretsch et al., 2015).

After an introduction to the context and challenges European second-tier European regions in establishing an EE, a comparative case study is provided of two second-tier European regions that, contrary to expectations, have managed to establish and develop thriving EEs. The selection of cases is based on the REDI, as it is comparable for all EU regions (Szerb et al., 2013; Szerb et al., 2015). The REDI was constructed to "[...] capture the contextual features of entrepreneurship across EU regions" (Szerb et al., 2015, p. 1) and combines three sub-indices, 14 pillars, and both individual and institutional variables (see Figure 6). Based on these criteria, Szerb et al. (2015, p. 14) created a ranking of regional entrepreneurship that includes the 125 regions of the European Union. The ranking of the top 25 regions can be seen in Figure 7, the original full ranking table from Appendix 5.

Using the REDI, it is possible to identify the second-tier regions that have succeeded in establishing competitive EEs. The regions ranked first through fourth are all superstar regions. However, there are also some regions in the top ten that are not major cities (defined as regions with more than 250,000 inhabitants, according to Audretsch et al., 2015), including:

- 5th place: East Middle Sweden (largest city: Uppsala)

Rank	Code	Region	REDI
1	DK01	Hovedstaden	82.2
2	UKI	London	79.9
3	FR1	Île de France	79.2
4	SE11	Stockholm	73.8
5	SE12	Östra Mellansverige	72.7
6	SE23	Vastsverige	72.2
7-8	IE02	Southern and Eastern	72.0
7-8	DK05	Nordjylland	72.0
9	UKJ	South East (UK)	69.5
10	SE22	Sydsverige	67.3
11	DE03	Berlin	67.2
12	DK03	Syddanmark	65.1
13	BE1	Région de Bruxelles-Capitale	64.9
14	SE33	Övre Norrland	64.7
15	NL3	West-Nederland	64.4
16	DK04	Midtjylland	64.3
17	FR7	Centre-Est (FR)	64.2
18	IE01	Border, Midland and Western	63.4
19	DE7	Hessen	63.3
20	FI1B	Helsinki-Uusimaa	62.2
21	BE2	Vlaams Gewest	62.1
22	UKH	East of England	61.5
23-25	DK02	Sjalland	60.7
23-25	UKK	South West (UK)	60.7
23-25	AT1	Ostösterreich	60.7

Figure 7: REDI Ranking and REDI Scores of the Top 25 European Union Regions. Source: adapted from Szerb et al. (2015, p. 14).

- 7th–8th place: Denmark's North Jutland Region (largest city: Aalborg)
- 9th place: Great Britain's South East (largest city: Brighton and Hove)

When looking at cities with less than 100,000 inhabitants, i.e., small cities (in line with Audretsch et al., 2015), the following regions ranked in the first quarter also seem promising for a more detailed analysis:

- 14th place: Sweden's Upper Norrland (largest city: Umeå)
- 18th place: Ireland's Border, Midland and Western (largest city: Galway)
- 23rd–25th place: Denmark's Zealand Region (largest city: Roskilde)

The author of this article decided to examine the cases of East Middle Sweden and Border, Midland and Western (Ireland) to identify specific factors that contribute to the regions' entrepreneurial success. East Middle Sweden is an interesting case because the region is near Stockholm, the capital of Sweden, yet has been able to develop its own EE, which has produced prominent companies such as Skype and Klarna (see section 4.1 for the detailed analysis). The case of Border, Midland and Western is interesting because it is in a rather rural region on the west coast of Ireland, with an underdeveloped transport infrastructure hampering domestic and international travel (see section 4.2 for a detailed analysis). For linguistic and readability purposes, East Middle Sweden will be referred to as

"Uppsala" and Border, Midland, and Western as "Galway" in the following; however, the surrounding areas as integral parts of the respective EE remain included in the analysis.

After defining the research gap and the two regional EEs that will be analyzed in depth, section 3 describes the research methodology used to analyze the development of the EEs in Uppsala and Galway.

3. Research Method

This section describes the research method chosen for this article, including the research approach, the process of data collection, and the analysis of the data. A more detailed explanation can be found in Appendix 6.

3.1. Research Approach

An inductive research approach was adopted to analyze the dynamic evolution of EEs in second-tier European regions. This approach consists of guiding research questions that determine data collection and analysis (Roundy, 2019). Because there is little research on EEs in second-tier European regions (Roundy, 2019), an inductive, theory-building approach was appropriate (Locke, 2007). Inductive theory building allows the researcher to gain an understanding of the unfolding of processes behind unusual phenomena and explain surprising occurrences (Edmondson & McManus, 2007). The emergence and growth of an EE in a second-tier European region represent such complex processes with multiple variables to consider, such as time, social interactions, and feedback loops (Roundy, 2019).

By choosing a comparative case study approach, similarities and differences in the context, developmental dynamics, and composition of the two EEs in Uppsala and Galway could be derived. While such a "small n" approach (Roundy, 2019) limits generalizability of findings, some scholars argue that comparative case studies generate some degree of generalizability despite a small sample size (e.g., Eisenhardt and Graebner, 2007; Roundy, 2019). However, given the exploratory nature of the research, the goal of this article is particularization rather than generalization (Welch, 2011).

3.2. Data Collection

To gain a deeper understanding of the processes underlying the development of the EEs in Uppsala and Galway, interviews were conducted with representatives from the two

regions. Purposive sampling, a form of non-probability sampling, was chosen to select the interviewees. Given the research objectives and inductive research approach, the sampling procedure did not aim to be statistically significant, but rather to select information-rich cases to gain insight into the nature, processes, and structure of the two EEs (Patton, 2005). Interviewees were selected to allow for the inclusion of different perspectives, knowledge, and experiences of the various stakeholders that comprise an EE (see Isenberg, 2011b; Palinkas et al., 2015). The respective interviewees were identified through a combination of secondary data highlighting key actors within each EE and snowballing (see, e.g., Biernacki and Waldorf, 1981).

The predominant determinant of sample size in qualitative research is information saturation (e.g., Fusch and Ness, 2015; Malterud et al., 2016; Morse, 1995). Because some determinants of information saturation could not be defined a priori, it was not possible to determine a final number of interviews to be conducted at the beginning of the research process. However, as Malterud et al. (2016) mention, a first approximation of the sample size is necessary for research design. Therefore, the author's goal was to conduct at least five interviews in each of the two regional EEs to include the knowledge, views, and experiences of key stakeholders in the EEs. However, the final sample size had to be continuously evaluated throughout the research process and was based on the informativeness of the interviews conducted in relation to the research objectives (Malterud et al., 2016). The final sample table can be found in Appendix 6. The interviews conducted were semi-structured. While a semi-structured interview is more conversational, a list of predetermined questions was used, which provided the opportunity to explore topics in greater depth if deemed important for later analysis of each EE (Longhurst, 2003). The guide used for the semi-structured interviews can be found in Appendix 9.

3.3. Data Analysis

The research for this article was divided into three phases (see Figure 8). Interviews as part of the second phase were conducted via video or phone call due to travel restrictions resulting from the Covid-19 pandemic. To facilitate effective data analysis, verbal transcripts (Matheson, 2007; McLellan et al., 2003; Wellard & McKenna, 2001) were prepared using standard orthography (Kowal & O'Connell, 2004, pp. 249-250). The transcripts can be found in Appendix 11.

The process of coding the interviews followed the suggestions of Schmidt (2004, pp. 254-257). First, the common themes discussed during the interviews were identified and summarized in an analytical guide (see Appendix 10). Then, the interviews were coded accordingly. Based on the coded interviews and by grouping the quotes according to their codes, the relevance of each theme was assessed. Depending on the relevance of the themes, each interview was iteratively analyzed again in depth to understand the meaning of the different interviews and to reach a conclusion as to why each of the two regions studied achieved the establishment of a thriving EE. In addition, following the example of some researchers (e.g., Motoyama et al., 2016; P. Ryan et al., 2021), timelines were used to analyze relevant innovation pathways and the dynamics of each EE. By sequencing secondary data points and adding a temporal layer to the interview coding process, both the creation and subsequent analysis and interpretation of timelines and relevant innovation trajectories became possible.

Interpretive sensemaking was used to analyze the data on Uppsala and Galway. Interpretive sensemaking avoids generalizations and emphasizes the importance of individual context (Welch, 2011). By sequencing relevant innovation trajectories, process-based interpretation, and explanation of the evolutionary dynamics of the two EEs became possible (P. Ryan et al., 2021). The analysis was refined through successive iterations between theory and data (G. W. Ryan & Bernard, 2000, p. 783). By combining the viewpoints and perspectives of the various interviewees, as well as data obtained from secondary sources, "chain[s] of evidence and narrative accounts" (P. Ryan et al., 2021, p. 7) emerged that reveal the evolutionary processes of the two EEs in Uppsala and Galway. The interpretation of the data always considered the spatial context of each case (Roundy, 2019). Figure 9 summarizes the data sources used and their analytical use for this article. The next section presents the results.

4. Findings

This section summarizes the results of the primary and secondary data collected on the EEs in Uppsala and Galway. It also summarizes the similarities and differences between the two EEs. The underlying data structures are presented towards the end of each stage of development; the exemplary quotes can be found in Appendix 8.

4.1. Analysis of Uppsala's Entrepreneurial Ecosystem

Due to its extensive academic history dating back to 1477, Uppsala is primarily known as a university town, and research on Uppsala's economy has focused primarily on the life sciences cluster (e.g., Teigland et al., 2004, 2007; Waxell and Malmberg, 2007). The local EE has not received much attention in scientific research. Therefore, information about Uppsala's EE comes primarily from qualitative interviews with stakeholders within the EE unless otherwise noted. The context of Uppsala is summarized in Figure 10.

4.1.1. Birth: Research Breakthroughs at Uppsala University

The roots of entrepreneurial activity in Uppsala can be traced to significant research findings in biotechnology at Uppsala University in the 1920s and 1930s (Waxell & Malmberg, 2007). These findings led to a growing interest in university-industry collaboration in the life sciences. In 1950, the large Swedish pharmaceutical company Pharmacia decided to move its core business from Stockholm to Uppsala (Eliasson & Eliasson, 2006; Waxell & Malmberg, 2007). The reason for this was the successful R&D collaboration with Uppsala University (Eliasson & Eliasson, 2006), which mainly

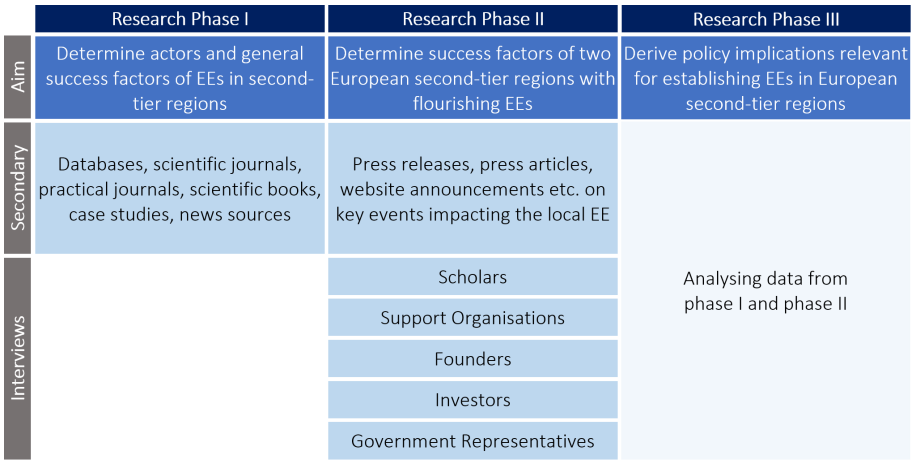


Figure 8: Research Phases. Source: own illustration.

Data Source	Type of Data	Analytical Use
Primary Sources		
Interviews	**Semi-structured interviews in Uppsala (9):** • 1 local government representative • 1 scholar from a local university • 2 representatives from a major support organisation • 1 representative from an industry-specific support organisation • 2 entrepreneurs located in Uppsala • 1 entrepreneur located in Stockholm with activities in Uppsala • 1 representative from an investor network **Semi-structured interviews in Galway (5):** • 1 local government representative • 1 scholar from a local university • 1 representative involved in two major support organisations and a co-working facility • 1 investor and simultaneous representative of a major support organisation, a co-working facility, and a local business network • 1 entrepreneur located in Galway	• Reconstructing the historical development of the EE • Evaluating economic trajectories and key events with an impact on the development of the EE • Mapping the current state of the EE and its context • Evaluating key actors, assessing their roles within, and their importance for, the EE • Outlining the strengths and weaknesses, as well as their (contextual) root causes, of the EE
Secondary Sources		
Scientific papers	Multiple scientific papers on key economic development trajectories and initiatives in Uppsala and Galway	• Reconstructing the historical development of the EE • Understanding the underlying processes of the respective EE's development in Uppsala and Galway • Providing support to data and interpretation
Websites of regional organisations and press coverage	Websites of relevant actors within the respective regional EE and multiple press clippings regarding the development and the state of the regional EE	• Understanding the perception of the respective region in a local, national, and international context • Providing support to the interpretation of economic trajectories and key events • Providing support to the role assessment of key actors

Figure 9: Data Sources and Analytical Use. Source: own illustration.

revolved around two Nobel Prize winners in chemistry (Waxell & Malmberg, 2007). Pharmacia then gradually became one of the most important employers in the region and contributed to the growth of the Uppsala life science cluster.

After Pharmacia moved its headquarters to Uppsala, the company continuously engaged in significant M&A activity (Dahlgren & Valentin, 2007). Then, in the mid-1990s, Pharmacia began spinning off, selling, and restructuring various parts of the company (Waxell & Malmberg, 2007), which attracted two large multinationals to the region (Eliasson & Eliasson, 2006): Pfizer and Cytiva (formerly GE Healthcare). Uppsala's attractiveness to life science companies can also be attributed in part to the increased availability of scientifically trained and industrially experienced people following the dissolution of Pharmacia (Eliasson & Eliasson, 2006), supporting Mayer's (2011, p. 205) observation that MNEs act as "surrogate universities".

The presence of Pharmacia, and later other multina-

Context of Uppsala's Entrepreneurial Ecosystem	
Location	East Middle Sweden (~70 km north of Stockholm, ~40 km north of Arlanda Airport)
Population	City of Uppsala: ~172,000 | Uppsala County: ~367,000
EE Size	378 start-ups in Uppsala County listed on Crunchbase[1]
Funding	USD 361.9m (104 funding rounds) since 2000 listed on Crunchbase[1]
Industry Cluster	Biotechnology (Life Science)
Success Stories[2]	Skype (ICT) | Klarna (FinTech) | MySQL (ICT) | Orexo (Pharmaceuticals)
Universities	Uppsala University (UU) | Swedish University of Agricultural Sciences (SLU)
Support Organisations[2]	STUNS | UU Innovation | Drivhuset
Incubators / Accelerators[2]	Uppsala Innovation Centre
Coworking Spaces[2]	Uppsala Innovation Hub | Green Innovation Park | BASE10
Financial Capital[2]	Almi | Connect Uppsala | UU Holding | SLU Holding | EASME
Notable MNEs[2]	Cytiva (former GE Healthcare) | Fresenius Kabi | Thermo Fisher Scientific

[1] Crunchbase is increasingly being used as a database for scientific research in economics and management (Dalle et al., 2017), which is why its data is used to provide an overview of Uppsala's EE. Access date: 20 July 2020.
[2] Main actors according to interviewees and secondary data; therefore the list is non-exhaustive.

Figure 10: Case Context of Uppsala. Source: own illustration.

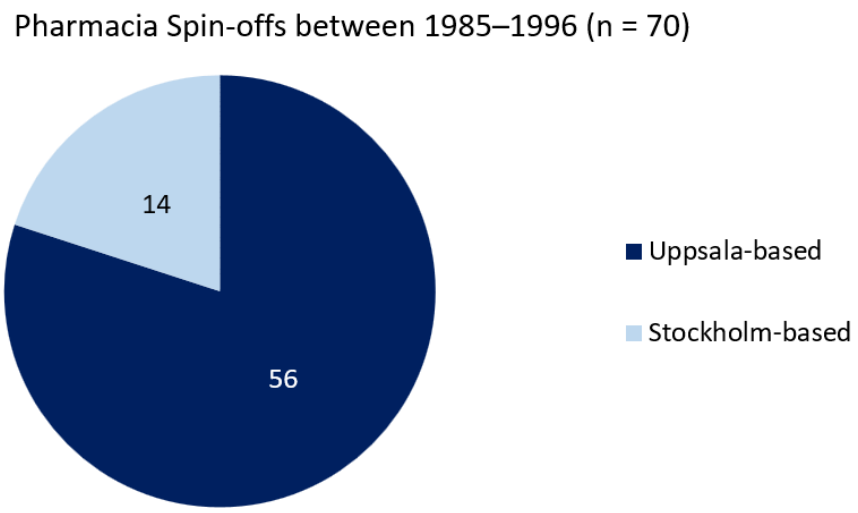


Figure 11: Pharmacia Spin-offs between 1985-1996. Source: own illustration based on Eliasson and Eliasson (2006) and data from Nilsson and Norell (1996).

tionals, in Uppsala has encouraged the creation of spin-offs by former employees of these firms ((Eliasson & Eliasson, 2006); see also Appendix 7 for a non-exhaustive overview of Pharmacia's Swedish genealogy). For example, Pharmacia established 70 companies between 1985 and 1996 (see Figure 11), 56 of which were located in the Uppsala region and 14 in the Stockholm region (Eliasson & Eliasson, 2006), again underscoring Uppsala's attractiveness to the life sciences industry. Even when Pfizer, which acquired parts of Pharmacia during the breakup period, later phased out the research activities started by Pharmacia in Uppsala, former Pharmacia employees continued to establish new companies in the region that were not based on technologies developed at Pharmacia (Eliasson & Eliasson, 2006). For a detailed recapitulation of Pharmacia's history and its aftermath, see Eliasson and Eliasson (2006).

However, the entrepreneurs in Uppsala did not only emerge from the local multinationals during the birth of the EE. The importance of the academic sector in the city ensured a steady influx of domestic and foreign students, as well as professors and researchers. These groups of people were of great importance for the emergence of Uppsala's EE. It is noteworthy that the Swedish legal framework provides university researchers with rights to their results, which is known as "professor's privilege" (see, e.g., Färnstrand Damsgaard and Thursby, 2013). Thus, unlike other countries, researchers at Swedish universities are allowed to commercialize their results without having to deal with legal issues related to intellectual property (IP). According to several interviewees, this mechanism, combined with an emerging support system focused primarily on the life sciences cluster, encouraged professors and researchers to pursue entrepreneurial ventures. Interestingly, most professors and researchers remained employed part-time at the university, resulting in hybrid entrepreneurship (Folta et al., 2010).

4.1.2. Growth: Emergence of an Entrepreneurial Support System

Interviewees attributed the growth of Uppsala's EE to many aspects revolving around activities and initiatives either initiated or supported by government officials. Due to high tax rates and the general importance of the public sector in Sweden, several interviewees stated that the activities of entrepreneurial support organizations in Uppsala have been and continue to be at least partially dependent on public funding. Among government officials, successful university-industry collaboration in research and development has gradually awakened interest in the shared potential of academia, business, and the public sector, as well as in the potential of entrepreneurial activities. One of the major initiatives aimed at harnessing this potential was the creation of STUNS, an independent nonprofit organization dedicated to orchestrating the now emerging local EE. STUNS's founding in 1983 was based on a plan by the governor at the time to create a local science park modeled on Silicon Valley.

Third-level funding and the initiation of STUNS are just two examples of the emerging public interest in local entrepreneurship. As Uppsala grew, other public and semi-public organizations and actors gradually emerged. Examples include Almi, a regional development office that provides financial capital to companies; Connect, an organization that connects entrepreneurs with domestic and foreign investors; Drivhuset, a support organization for student entrepreneurs; and the Uppsala Innovation Centre, a leading international business incubator.

Although many different organizations are involved in Uppsala's EE, there has been no sign of competition between actors within the ecosystem during the growth phase, which has been and continues to be an important regional success factor. Close collaboration between actors within the ecosystem is a major strength of Uppsala, according to several interviewees. Because the city of Uppsala is spatially compact, there are certain geographic locations where entrepreneurial activities are concentrated. The resulting density of the EE facilitates knowledge exchange between different actors within the ecosystem and catalyzes entrepreneurial activity in the region. As one interviewee from STUNS noted:

> *"[...] since [...] Uppsala is a fairly small city, we try to have [...] a no-wrong-door policy. [...] we are a lot of actors within the innovation ecosystem that try to refer people depending on how mature their idea is [...]."*

Due to the above factors and processes that influenced the growth of Uppsala's EE, the region gained some notoriety as the birthplace of companies such as Skype, Klarna, MySQL and Orexo. Such success stories, several interviewees said, were fundamental to Uppsala's EE, e.g., by inspiring and motivating students to become entrepreneurs. Entrepreneurial role models are certainly crucial to the ecosystem even today.

The growth of Uppsala's EE is partly due to its spatial location. The city is close to Sweden's largest international airport, Arlanda, which has been particularly important to the local life science cluster given its global reach. The startups that emerged in the growth phase of the Uppsala industrial cluster, after serving regional markets in the initial phase of the EE, were therefore usually "born globals", i.e., they served several international markets early in their development (Knight & Cavusgil, 1996). In addition, public transportation between Uppsala and Stockholm allows residents to commute to Stockholm in about 30 minutes.

Because real estate prices in Uppsala have historically been lower compared to Stockholm, the capital of Sweden, the transportation infrastructure continues to make it attractive to live and do business in Uppsala today.

4.1.3. Sustainment: Acquisition, Relocation, or Early Initial Public Offering

Several interviewees emphasized that Uppsala's EE has gradually diversified and become less dependent on the life sciences industry, although the cluster is still critical to the region's success. The continued importance of life sciences in Uppsala is supported by the number of people employed in the cluster. In 2012, Uppsala had the highest density of employees in the life sciences industry in Sweden (see Figure 12). In 2016, life science cluster companies in Uppsala employed more than 5,300 people (full-time equivalents), making it the most labor-intensive sector in Uppsala (City of Uppsala, 2015). For a list of the ten life science companies with the most employees in Uppsala, see Table 3.

Despite the importance of the regional life sciences cluster, some of the entrepreneurial success stories mentioned above did not originate in the life sciences industry, but in unrelated fields such as finance (Klarna) and ICT (Skype, MySQL). The entrepreneurs behind such successful indigenous ventures not only inspire the local Uppsala population to also engage in entrepreneurial activities, but according to several interviewees, often engage in other activities that later contribute to strengthening the local EE. These activities include further entrepreneurial endeavors, i.e., becoming

Table 1: Data Structure of Uppsala's Ecosystem Birth.

Uppsala's Entrepreneurial Ecosystem			
Phase: Birth			
Domain	**Sub-Domain**	**Theme**	**Exemplary Quotes: IDs** (see appendix 8)
Culture	Societal Norms	Uppsala's reputation as an academic town	*UE2:1*
Human Capital	Educational Institutions	Research breakthrough in life sciences at Uppsala University	*US1:1*
		Relocation of Pharmacia motivated by university-industry R&D collaboration	*US3:1*
		Professor's privilege as hybrid entrepreneurship enablement	*UU1:1; US3:2*
		University-industry R&D collaboration attracts MNEs	*US3:3; UG1:1; UU1:2*
	Labour	Spin-off activities by former MNE employees	*UI1:1*
Markets	Networks	Dissolvement of Pharmacia attracting MNEs	*UE2:2*

Table 2: Data Structure of Uppsala's Ecosystem Growth.

Uppsala's Entrepreneurial Ecosystem			
Phase: Growth			
Domain	**Sub-Domain**	**Theme**	**Exemplary Quotes: IDs** (see appendix 8)
Markets	Networks	Uppsala's life sciences cluster continues to grow	*UE2:3; US2:1*
Policy	Leadership	Positive sentiment towards entrepreneurial activity among government officials	*UG1:2*
	Government	Significant public investment in entrepreneurial support infrastructure	*UG1:3*
Culture	Societal Norms	Close collaboration between relevant actors within Uppsala's EE	*US2:2; US2:3*
	Success Stories	Successful start-ups from Uppsala inspire nascent entrepreneurs	*UG1:5; UE2:4*
Human Capital	Educational Institutions	University-industry R&D collaboration as an important contributor to Uppsala's attractiveness	*UI1:2; UG1:4*
	Labour	Availability of well-educated human capital	*US1:2; US2:4*
Supports	Infrastructure	Proximity to Stockholm and Arlanda Airport contributes to Uppsala's attractiveness	*US1:3; UE2:5; UG1:6*

Table 3: Employment by Top 10 Life Science Companies in Uppsala in 2016. Source: STUNS Life Science (2016).

Company	**Employees** (2016)	**Activities in Uppsala**
GE Healthcare Bioscience	1,177	R&D, Manufacturing, M&S
Fresenius Kabi	947	R&D, Manufacturing, M&S
Thermo Fisher Scientific	544	R&D, Manufacturing, M&S
Galderma	469	R&D, Manufacturing, M&S
Recipharm Uppsala	203	R&D, Manufacturing
Quintiles	174	Service
J&J (AMO)	121	Manufacturing
GEMS PET Systems	105	R&D, Manufacturing, M&S
Orexo	102	R&D
Oasmia	75	R&D, Manufacturing, M&S
Total	**3,917**	

serial entrepreneurs, taking advisory positions in local start-ups, or becoming investors in regional businesses. In the interviews, these processes, combined with the collaborative mentality prevalent in the region, were described as a kind of pay-it-forward culture that has gradually developed throughout Uppsala's EE.

However, there are certain trends that pose a challenge to maintaining the local EE in Uppsala. It was highlighted

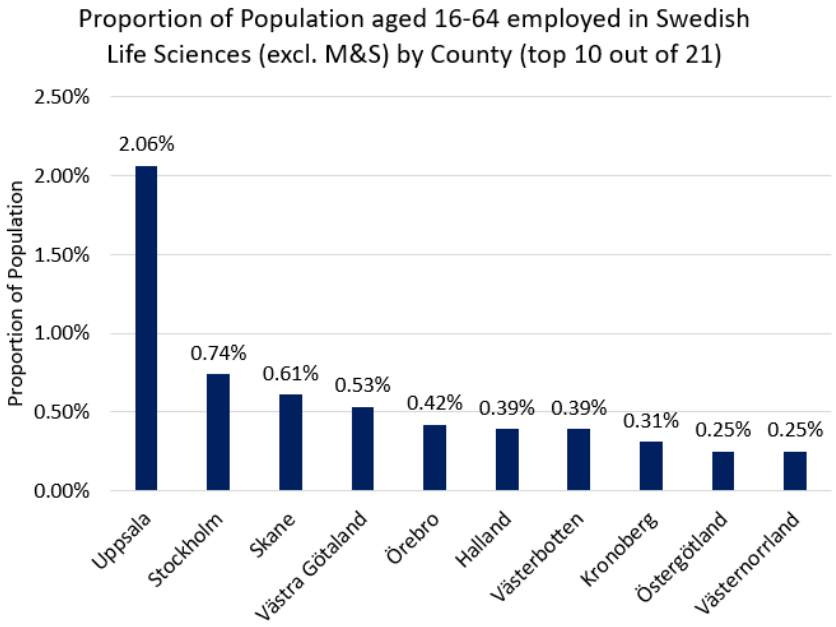


Figure 12: Proportion of Population Employed in Swedish Life Sciences in 2012. Source: adapted from Sandström (2014, p. 117).

in the interviews that despite some successful startups that have emerged from the EE in Uppsala, these companies tend to move either to Stockholm or to other international metropolises during their scale-up phase. This is at least partly due to the lack of availability of financial capital for regional scale-up companies, which limits their growth potential within Uppsala's EE. This was also noted by Eliasson and Eliasson (2006) when they analyzed the aftermath of Pharmacia's dissolution. Therefore, Uppsala may initially benefit from promising startups, but loses them at some point in their growth phase. Moreover, the lack of growth capital also leads to an increase in acquisition activity by local multinational subsidiaries (Eliasson & Eliasson, 2006). However, such acquisitions prevent Uppsala's EE from becoming less dependent on foreign multinationals and strengthen the domestic part of the local EE, as was also pointed out in the interviews. On the contrary, as Eliasson and Eliasson (2006) point out, a lack of qualified venture capitalists with sufficient industry knowledge increases the risk of regional activities retreating to other locations within or outside the country of origin, as well as missing out on technologies with significant economic potential. To date, Uppsala has been successful in retaining local MNE subsidiaries primarily due to university-industry collaboration, availability of skilled human capital, and relatively low wages (Eliasson & Eliasson, 2006). However, the continued dependence on foreign MNE subsidiaries, although less pronounced than at the beginning of the EE, poses a risk to Uppsala's economy, as one interviewee pointed out:

> "*Our main issue is that they [foreign-owned MNE subsidiaries] are all owned by American risk capital firms, so we are just a little dot. If they say, we do not want this little dot in this little town anymore because it is far away up north, then our whole ecosystem probably falls.*"

However, there is a notable alternative to VC investing in Sweden in the form of a small-cap venture exchange called First North (see Carpentier et al., 2010). This specialized exchange allows young companies to go public at an early stage and raise money through an initial public offering (IPO). While some regional companies make use of this alternative, according to several interviewees, Uppsala-based startups in their growth phase still largely aim for a takeover by a multinational company or relocate to a metropolis.

4.1.4. Summary

In summary, the analysis of Uppsala's EE shows that an EE depends on different actors and can emerge from processes that are not directly aimed at promoting local entrepreneurship. The emergence of Uppsala's EE can be attributed to Uppsala University's strength in life science research. This strength has led large life science companies, particularly Pharmacia, to locate in Uppsala and collaborate with the university on research and development. Through the creation of spin-off companies, these processes have led to the emergence of a strong life science cluster that continues to play an important role today, distinguishing the ecosystem from that of nearby Stockholm.

Through mergers and acquisitions, the subsequent breakup of Pharmacia has attracted other multinational companies operating in Uppsala, predominantly R&D. In addition, former employees, usually highly qualified and experienced, have contributed to Uppsala's EE growth by establishing spin-off companies. Government initiatives to support startups in Uppsala, both financial and non-financial, have enabled the emergence of such companies.

Table 4: Data Structure of Uppsala's Ecosystem Sustainment.

Uppsala's Entrepreneurial Ecosystem			
Phase: Sustainment			
Domain	**Sub-Domain**	**Theme**	**Exemplary Quotes: IDs** (see appendix 8)
Markets	Networks	Gradual diversification of Uppsala's EE	*US3:4; US1:4*
Culture	Societal Norms	Pay-It-Forward type culture fosters indigenous start-ups	*US1:5; UE1:1; UI1:3*
Finance	Financial Capital	Lack of growth capital in Uppsala	*UE2:6; UI1:4*
		Possibility of an early IPO at a small-cap venture exchange called First North	*UE2:7*
		Lack of growth capital leads to relocation of indigenous start-ups in the scale-up phase	*UG1:7; UI1:5; UI1:6*
		Lack of growth capital leads to increased acquisition activities by local MNE subsidiaries	*US1:6; US3:5*

Uppsala has also benefited from its size and spatial context, which has resulted in a high density of highly skilled human capital, geographic proximity of relevant actors within the EE, and proximity to relevant infrastructure. This has facilitated collaboration, for which Uppsala's inherent pay-it-forward culture has played an important role by minimizing competition within the system.

The case of Uppsala furthermore sheds light on problems that other second-tier regions may also face. Because Uppsala has a strong academic past, the city's reputation depends largely on its two local universities. As a result, Uppsala is perceived primarily as a university town, which to some extent discourages people from considering the region for their careers. In addition, the size of the region, combined with its proximity to Stockholm, makes it easier for both companies and individuals to relocate, making it difficult to retain companies and talent attracted by the allure of such a global metropolis. Another contributing factor is that Uppsala does not have access to growth capital, which would be important for startups looking to scale up. As a result, it is difficult for Uppsala to both convince thriving companies that have originated in Uppsala to stay in the region rather than move to a larger city, and to convince non-local startups and aspiring entrepreneurs to choose Uppsala as a location for their entrepreneurial endeavors. Figure 13 provides an overview of the development of Uppsala's EE.

4.2. Analysis of Galway's Entrepreneurial Ecosystem

Various aspects of Galway's medical technology cluster have been analyzed in the academic literature (Evers & Giblin, 2017; Giblin & Ryan, 2012; P. Ryan & Giblin, 2012; P. Ryan et al., 2020, 2021). The analysis of Galway's EE therefore combines secondary data with information obtained through qualitative interviews with actors within the Galway EE. The context of the Galway case is summarized in Figure 14.

4.2.1. Birth: Monetary Incentives Attract MNEs to Galway

As highlighted both in the literature and by interviewees, Galway's EE has grown rather organically (see, e.g., Evers and Giblin, 2017, p. 112). While the first foreign-owned medical technology company in Galway was established in Galway in 1973 (P. Ryan et al., 2021), the first pivotal event occurred in 1982 when CR Bard (acquired by Medtronic in 1999, hereafter referred to as Medtronic for simplicity) established a manufacturing facility in Galway (P. Ryan et al., 2021; P. Ryan et al., 2020; Evers and Giblin, 2017, p. 112; P. Ryan and Giblin, 2012). After CR Bard filed the first medical technology patent in the region in 1991 (P. Ryan et al., 2020), Boston Scientific, the second major MNE in the region, established a manufacturing site in 1994 (P. Ryan et al., 2021; Evers and Giblin, 2017, p. 112; P. Ryan and Giblin, 2012; Giblin and Ryan, 2012). Both multinationals were attracted to the region by IDA Ireland initiatives such as a low corporate tax rate, grants, and research incentives (P. Ryan et al., 2021; Evers and Giblin, 2017, p. 110; P. Ryan and Giblin, 2012; Giblin and Ryan, 2012), access to European markets, English-speaking labor, and a relatively low cost base (P. Ryan & Giblin, 2012). With the aforementioned incentives, IDA Ireland aimed to attract foreign direct investment (FDI) to benefit from the knowledge spillover from abroad (Evers & Giblin, 2017, p. 111; see also Figure 15).

Some interviewees have also linked IDA Ireland's efforts to attract foreign multinationals to a series of events related to Digital Equipment Corporation, a major player in the minicomputer industry. In 1971, the company opened an assembly plant in Galway (Van Egeraat & Jacobson, 2004). The assembly plant closed in 1993, and although Digital Equipment Corporation maintained a software development function in Galway (Van Egeraat & Jacobson, 2004), the plant's closure resulted in the loss of over 700 jobs in the region (Coughlan, 2017). As some interviewees pointed out, and although some of those laid off later became entrepreneurs in the region out of necessity, a local task force in collaboration with IDA Ireland worked to attract large new employers to the region after the closure (Coughlan, 2017), eventually succeeding with the arrival of Boston Scientific. Boston Scientific, which was also attracted by Medtronic's successful operations in Galway, then took over the empty premises previously occupied by Digital Equipment Corporation.

	Birth	Growth	Sustainment
Pull Factors	• Breakthrough research in biotechnology at Uppsala University • Relocation of Pharmacia to Uppsala	• Establishment of MNE subsidiaries within life sciences • Emergence of government-led EE support system	• Expansion of support system • Quality of life combined with proximity to Stockholm and Arlanda Airport
		Success stories and entrepreneurial recycling	
Policy	• University-industry R&D collaboration • Professor's privilege facilitates research commercialisation	• Publicly-financed innovation support organisations • Improvement of EE support processes (e.g. issuing of permits and licenses)	• Infrastructure development projects • Location marketing to initiate change of Uppsala's perception as mere university town
Finance	Government-led via university funding and private sources primarily coming from Pharmacia	Government-led, emergence of private investment	• Government-led with continued private investment • Lack of growth capital
		• Possibility of early IPO via small-cap venture exchange • Acquisitions by MNEs	
Culture	Strong academic reputation, entrepreneurial spirit rather limited	Entrepreneurship starting to gain traction	Entrepreneurship as a valid career path
		• Success stories contribute to continuous growth of interest in entrepreneurship, especially among local university students • Pay-It-Forward type culture emerges early on within the EE • Collaboration rather than competition between EE actors	
Support	University-based research commercialisation support system	Emergence of public and private support organisations	Extensive collaboration between different support organisations within the EE
		Increase of university-led research commercialisation efforts	
Human Capital	R&D crucial to emergence of entrepreneurial endeavours	Some competition for talent with Stockholm	
	• Influx of students and researchers • University researchers may engage in hybrid entrepreneurship		
	Pharmacia's gradual dissolvement leaves highly skilled human capital with industry experience		Economic potential in Uppsala starts to get noticed
Markets	• Clear focus on life sciences industry driven by academic research and presence of Pharmacia • Life sciences as a globalised industry	• Life sciences cluster continues to grow • MNEs open subsidiaries • Emergence of indigenous firms with a rather regional focus in the beginning	• Life sciences cluster still crucial, but start of EE diversification in industries that also benefit from university-industry R&D collaboration • Emergence of indigenous firms with a born global internationalisation approach

Figure 13: Development of Uppsala's Entrepreneurial Ecosystem. Source: own illustration, format adapted from Mack and Mayer (2016).

While the two multinationals initially established only manufacturing facilities in Galway, Medtronic established an R&D center in 1996, followed by Boston Scientific's product development center in 1997 (P. Ryan et al., 2021). The establishment of innovation-oriented facilities was critical both to the survival of the multinationals' subsidiaries and to the development of Galway's EE as a whole, as one researcher interviewed pointed out. While early local start-up activity in the 1980s and 1990s focused predominantly on supplying the two multinationals (Evers and Giblin, 2017, p. 114; P. Ryan and Giblin, 2012), it was indigenous firms founded by former employees of the multinationals that designed and developed their own ideas in areas unrelated to the industry (P. Ryan & Giblin, 2012; P. Ryan et al., 2021). The former Medtronic and Boston Scientific employees benefited from the connections they made and the management skills they developed while working for the MNEs (P. Ryan et al., 2021; Evers and Giblin, 2017, p. 118; P. Ryan and Giblin, 2012). These connections and skills, along with the international exposure, quality compliance experience, and credibility they built as business professionals, enabled them to identify business opportunities leading to spin-off activities in Galway (P. Ryan et al., 2021; Evers and Giblin, 2017, p. 118; P. Ryan and Giblin, 2012). Because the medical technology market is global, international connections were critical to commercial success (Evers and Giblin, 2017, p. 118; Giblin and Ryan, 2012). However, spin-off activities were not limited to former MNE employees. As mentioned by interviewees, researchers from

Context of Galway's Entrepreneurial Ecosystem	
Location	West of Ireland (~210 km west of Dublin, ~215 km west of Dublin Airport)
Population	City of Galway: ~80,000 | County Galway: ~258,000
EE Size	198 start-ups in County Galway listed on Crunchbase[1]
Funding	USD 448.2m (122 funding rounds) since 2000 listed on Crunchbase[1]
Industry Cluster	Medical Technology
Success Stories[2]	Altocloud (ICT) | Creganna (MedTech) | Aerogen (MedTech) | Planet (FinTech)
Universities	National University of Ireland, Galway (NUIG) | Galway-Mayo Institute of Technology (GMIT)
Support Organisations[2]	GMIT Innovation Hub | NUIG Innovation Office | Galway City Innovation District | SCCUL Enterprises | WestBIC
Incubators / Accelerators[2]	EI New Frontiers at GMIT | StartLab Galway | BioInnovate at NUIG
Coworking Spaces[2]	PorterShed | Galway Technology Centre | SuperPixel Labs
Financial Capital[2]	Enterprise Ireland | Western Development Commission | NDRC | EASME
Notable MNEs[2]	Medtronic | Boston Scientific | Electronic Arts

[1] Crunchbase is increasingly being used as a database for scientific research in economics and management (Dalle et al., 2017), which is why its data is used to provide an overview of Galway's EE. Access date: 20 July 2020.
[2] Main actors according to interviewees and secondary data; therefore the list is non-exhaustive.

Figure 14: Case Context of Galway. Source: own illustration.

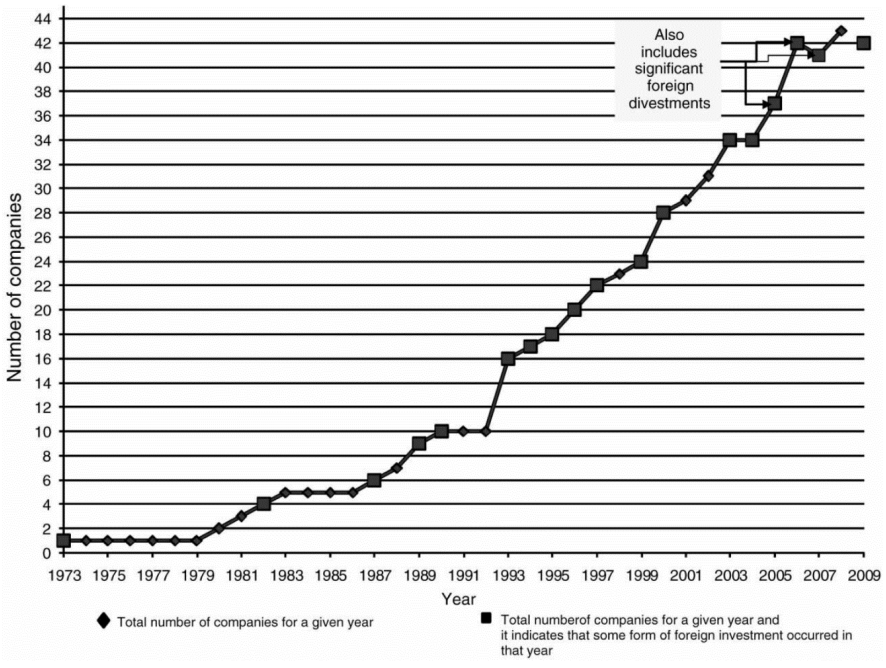


Figure 15: Medical Technology-Related Companies in Galway from 1973-2009. Source: Giblin and Ryan (2012, p. 251); the typing error in the figure's legend ("total number of") has been noted.

local universities also began to participate in the start-up processes. This then accelerated during the growth phase of the EE when local universities began to establish specialized research centers that began to attract highly qualified students and researchers to the Galway region.

Table 5: Data Structure of Galway's Ecosystem Birth.

Galway's Entrepreneurial Ecosystem			
Phase: Birth			
Domain	**Sub-Domain**	**Theme**	**Exemplary Quotes: IDs** (see appendix 8)
Policy	Government	Monetary incentives to attract MNEs	*GU1:1; GU1:2*
		Business-friendly regulatory environment	*GE1:1*
Human Capital	Educational Institutions	Local universities provide skilled human capital	*GS1:1*
		R&D activities at local universities lead to spin-off activities by students and researchers	*GI1:1; GS1:2*
	Labour	R&D activities within local MNE subsidiaries lead to spin-off activities in related industries	*GI1:2; GU1:3; GS1:3*
Markets	Networks	Influx of MNEs from the MedTech field and their shift from production to R&D enable the development of an industry cluster in Galway	*GG1:1; GG1:2*

4.2.2. Growth: NUI Galway Adapts to Emerging MedTech Cluster

While the main local university, NUI Galway, did not initially function as an anchor within the EE, it has continually responded to economic developments in Galway. Since the establishment of an engineering department in 1980 (P. Ryan et al., 2021), NUI Galway has become a major research partner and a provider of specialized human capital. In 1998, the university introduced a biomedical engineering degree program (Giblin & Ryan, 2012; P. Ryan et al., 2021), and in 1999, the National Centre for Biomedical Engineering Science (NCBES) was established to foster university-industry collaboration (Giblin & Ryan, 2012; P. Ryan et al., 2021). In 2003, NUI Galway established the Regenerative Medicine Institute (REMEDI) to further enhance public-private collaboration, and in 2009, a dedicated postgraduate diploma in medical device science was introduced (Giblin & Ryan, 2012; P. Ryan et al., 2021). Shortly thereafter, in 2010, the university initiated the BioInnovate Ireland training program aimed at producing indigenous medical device startups (P. Ryan et al., 2021). Since then, NUI Galway has continued to increase its importance to the local EE, for example, by introducing a master's degree program in biomedical engineering in 2013 and establishing the Irish Centre for Cell Manufacturing (ICCM) and the Centre for Research in Medical Devices (CURAM) in 2014 (P. Ryan et al., 2020, 2021). Overall, the two local universities, NUI Galway, and the Galway-Mayo Institute of Technology (GMIT), were important sources of skilled human capital and frequently collaborated with both foreign and local companies, for example, through research, student placements, or the provision of office space (Giblin & Ryan, 2012; P. Ryan & Giblin, 2012). These activities were not limited to the medical technology industry. As noted by several interviewees, both NUIG and GMIT contributed to the development and subsequent diversification of the EE by attracting financial resources, establishing research centers, attracting graduate students and high-level researchers, and providing startups with the infrastructure they needed to develop.

Following the establishment of subsidiaries by CR Bard / Medtronic and Boston Scientific, Galway's EE has developed rather organically and naturally. While the two multinationals were initially attracted by incentives from IDA Ireland aimed at attracting and retaining FDI, the availability of skilled human capital, research collaboration with local universities, and a growing medical technology cluster have contributed to the growth of the EE. Former employees of multinationals have started their own businesses, first in related and later in unrelated industries, which has enabled the gradual diversification of the region and the growing independence from multinationals. This has also been enabled by several local support organizations that have formed, as well as other relevant actors, such as investors, who began to get involved in the growth phase of Galway's EE. However, as several interviewees emphasized, the growth of the local support system for startups and future entrepreneurs has been driven more by initiatives of key private individuals than by larger local government initiatives. Nevertheless, the importance of public funding that contributed to the growth of EE should not be underestimated, particularly the funding provided by actors such as Enterprise Ireland, IDA Ireland, and the Local Development Office, especially in the early stages of venture development.

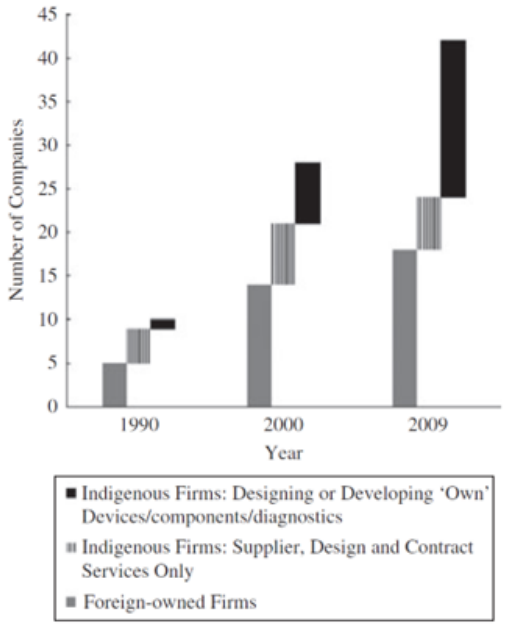
4.2.3. Sustainment: Acquisition as Favored Exit Strategy

Because an EE is made up of diverse actors engaged in innovation, knowledge transfer, research, and other entrepreneurial activities, multinational companies alone, which in the case of Galway initially served as anchor organizations and surrogate universities, were not sufficient to build an active ecosystem (Evers & Giblin, 2017, p. 120). The EE in Galway, while initially focused on a subset of the medical technology industry, has diversified over time, preventing phenomena such as technological lock-in, cluster hollowing-out, and overspecialization (Evers and Giblin, 2017, pp. 117-120; Clancy et al., 2013). Diversification and capability development within Galway's EE have also contributed to growing independence from local MNE subsidiaries (P. Ryan and Giblin, 2012; P. Ryan et al., 2020; see also Figure 16) .

In particular, domestic global companies have developed

Table 6: Data Structure of Galway's Ecosystem Growth.

Galway's Entrepreneurial Ecosystem			
Phase: Growth			
Domain	**Sub-Domain**	**Theme**	**Exemplary Quotes: IDs** (see appendix 8)
Human Capital	Educational Institutions	University-industry R&D collaboration as an important contributor to Galway's attractiveness	*GG1:3; GU1:4*
	Labour	Preparation of local human capital for the local industry by universities	*GS1:6*
Supports	Infrastructure & NGOs	Continuous development of support infrastructure by a group of volunteers and their non-governmental institutions	*GI1:3; GS1:4*
Policy	Government	Higher education funding as crucial investment in Galway's EE	*GE1:2; GS1:5*



Note:
(i) "For the purposes of this graph, the design or development of 'own' devices, components or diagnostics by indigenous firms refers to those firms that are developing their own ideas as opposed to being solely a supplier or contractor. The output may not necessarily be sold or aimed to be sold in the marketplace under the company's own name.

Figure 16: Activity of Indigenous Ventures in Galway's Medical Cluster for Given Years. Source: P. Ryan and Giblin (2012, p. 1334).

products and services that target market niches and use novel technologies (Evers & Giblin, 2017, p. 119) to avoid competition with local MNE subsidiaries. The creation of such companies and the frequent mergers, acquisitions, and management buyouts underscore the dynamic nature of the ecosystem (P. Ryan & Giblin, 2012). Evers and Giblin (2017, pp. 122-123) also find that the founders of born global firms in Galway are more likely to seek the acquisition of developed and commercialized technology by an MNE than to grow independently. According to several interviewees, this is at least partly due to the difficulty of raising capital in Galway, given the lack of local growth capital providers. In cases where ventures do want to grow independently, there is a tendency for these companies to relocate to metropolitan areas during their scale-up phase. The founders of local startups that nevertheless decide to stay in the region tend to later either become serial entrepreneurs, participate in mentoring programs, or engage in investment activities (Evers and Giblin, 2017, pp. 115-116; P. Ryan and Giblin, 2012). In the literature, such processes are referred to as entrepreneurial recycling (Mason & Harrison, 2006).

4.2.4. Summary

The Galway case shows that an EE can emerge organically and as a byproduct of more disjointed structured policy approaches (Evers & Giblin, 2017). The evolution of Galway's EE demonstrates that new businesses in the start-up and early growth stages require structurally embedded support and leadership programs to ensure their long-term survival, which in turn directly impacts local employment security (Evers & Giblin, 2017). However, in addition to public and

Table 7: Data Structure of Galway's Ecosystem Sustainment.

Galway's Entrepreneurial Ecosystem			
Phase: Sustainment			
Domain	**Sub-Domain**	**Theme**	**Exemplary Quotes: IDs** (see appendix 8)
Markets	Networks	Gradual diversification of Galway's EE	*GG1:4; GS1:7*
Culture	Success Stories	Local success stories inspire others to start entrepreneurial ventures	*GU1:5; GU1:6*
	Societal Norms	Entrepreneurial recycling strengthens the local EE	*GU1:7; GU1:8; GI1:4*
Finance	Financial Capital	Lack of growth capital in Galway	*GI1:5; GG1:5*
		Lack of growth capital leads to relocation of indigenous start-ups in the scale-up phase	*GE1:3*
		Lack of growth capital leads to increased acquisition activities by local MNE subsidiaries	*GG1:6; GI1:6; GU1:9; GG1:7*

private support from volunteers and nonprofits, and due to the importance of spinoff activities in Galway, corporate-level initiatives are also needed to foster innovation and entrepreneurship in the region, such as management and commercialization training (Evers & Giblin, 2017). Furthermore, when considering the role of NUI Galway and the Galway-Mayo Institute of Technology in Galway's EE, university-industry collaboration in research and development and the availability of specialized human capital are critical to entrepreneurial activities, which can be ensured through sufficient higher education training and research funding.

When a government invests in the local EE, it must also ensure that technology developed by indigenous startups ultimately leads to the creation of a new business in the region that creates local jobs and reduces dependence on multinational enterprises (Evers & Giblin, 2017, pp. 122-123). In Galway, researchers have observed that after developing a new technology, founders are more likely to seek an acquisition by an MNE than to develop their businesses independently (Evers & Giblin, 2017, p. 122). However, such acquisitions do not help an EE becoming less dependent on MNEs. Therefore, a government should provide incentives to local entrepreneurs to build independent indigenous ventures rather than selling technology early. Policymakers also need to take a holistic approach. Instead of focusing only on jobs created by existing companies at a given time, job creation by serial entrepreneurs must also be considered (Evers & Giblin, 2017, p. 122). Therefore, policies should take a multiyear perspective and focus on human capital development over a longer period.

Interviewees also pointed out the weaknesses of Galway's EE. First, the geographic distance to a major international airport and the underdeveloped transit infrastructure are a major disadvantage for entrepreneurs focused on international markets, as the long travel times both domestically and internationally require large time and financial resources. Second, the lack of financial growth capital in the region leads to increased M&A activity by MNEs and relocation in the scale-up phase, which prevents the emergence of large domestic companies. Third, entrepreneurial support in Galway driven by individuals and organizations is constrained, at least in part, by other stakeholder commitments, as local EE support is dependent on volunteer labor. Fourth, while there are several public policies and strategies aimed at promoting economic development in the Irish regions, some interviewees feel that there is too much focus on Dublin, limiting public funding and thus the development potential of the Galway region.

The Galway case shows a development of technological and intangible capabilities, such as expertise in management and networking at the international level (P. Ryan & Giblin, 2012). Awareness of their own strengths, sufficient foresight, and adequate knowledge were critical for local decision makers, private volunteers, and nonprofit organizations to enable the emergence and growth of Galway's EE (P. Ryan & Giblin, 2012), illustrating the complexity, long-term nature, holistic nature, and spatial contextuality of such processes. Figure 17 provides an overview of the evolution of Galway's EE.

4.3. Comparative Analysis of Uppsala and Galway

While there are some similarities in the analyzes of the EEs in Uppsala and Galway, there are also relevant differences that have policy implications for other second-tier European regions seeking to establish and grow an EE.

In terms of commonalities, both EEs initially revolved around a specific industry cluster and later diversified into related and unrelated industries, mitigating cluster risks. The two clusters, medical technology, and life sciences / biotechnology, both primarily serve international markets, so export-enhancing spatial characteristics have been important in both regions, and emerging new firms in these industries often identify as "born globals." In addition, both regions demonstrated the importance of anchor organizations in general, even if the nature of these organizations differed. In both regions, however, multinationals and large corporations played an important role in the development of the local EE, attracted skilled workers, and facilitated the creation of spin-off companies by former employees. Both regions also benefited from a quality of life perceived to be better compared to their respective capitals, which provided an incentive for skilled workers to stay and build a livelihood, e.g., by starting

	Birth	Growth	Sustainment
Pull Factors	• IDA Ireland incentives for MNE subsidiaries • Presence of CR Bard and Boston Scientific	• Relocation of MNEs R&D activities to Galway • Emerging MedTech cluster	• Expansion of support system • University-industry collaboration
Policy	Tax incentives and research grants to attract MNEs	• Continued investment in higher education and research • Low corporate tax rate and general facilitation of doing business in Ireland	
		Local government rather passively involved in EE	EE starts to get more attention by local government
Finance	Mainly driven from the private side due to attraction of FDI by providing monetary incentives to MNEs	Driven by FDI	Lack of growth capital
		• Early-stage capital provided to new ventures from both public and private funds • Acquisitions by MNEs as entrepreneurs' primary exit strategy	
Culture	Large MNEs establishing subsidiaries in Galway provide job opportunities for local workforce and are seen as key to economic welfare in the region	First successful indigenous ventures motivate other skilled people to start own companies	Entrepreneurship is seen as crucial aspect of regional economic development
Support	Only a few entrepreneurial support systems in place which are mainly driven by private individuals and their organisations	Support system starts growing, mainly driven by private individuals and their organisations with moral support of local government	Local government starts focusing more on entrepreneurial activity, main drivers of support network remain private individuals and their organisations
Human Capital	Relocation of MNEs production facilities indicate availability of "productive" workforce	Specialisation of NUI Galway to provide local economy with highly skilled human capital in MedTech areas	Industry-aligned specialised research and teaching at local higher education institutions facilitate recruitment of skilled human capital
Markets	• Production focus within MedTech industry • Little R&D activity by local MNE subsidiaries • MedTech as a globalised industry	• Growth of local MedTech cluster • R&D activities gradually expand within MNEs • Emergence of indigenous firms focusing on supplying local MNE subsidiaries	• Continued diversification of EE and decreasing importance of foreign-owned MNE subsidiaries • Emerging indigenous firms with a born global internationalisation approach

Figure 17: Development of Galway's Entrepreneurial Ecosystem. Source: own illustration, format adapted from Mack and Mayer (2016).

their own businesses, despite job losses in the subsidiaries of multinational enterprises. Moreover, the presence of large companies accelerated the development of the respective industrial cluster and contributed to employment prospects in the regions. In addition, university-industry partnerships, especially in R&D activities, proved to be crucial for the ecosystems. Regarding the sustainment of the EEs, both regions have struggled to attract growth capital, resulting in indigenous companies either being acquired early by larger companies or relocated after reaching the scale-up stage. In Uppsala, however, small companies can go public early through a dedicated stock exchange, which provides an alternative to raising venture capital.

A notable difference in the formation phase of the ecosystems is that companies were attracted to Uppsala by significant scientific findings from Uppsala University, while Galway attracted companies by monetary incentives provided by a government agency, IDA Ireland. This is also the reason why Uppsala companies moved R&D activities to the region from the beginning, while Galway companies first moved mainly production and only later R&D activities. There are also differences in the companies that were relevant to the emergence of each EE. Pharmacia was a domestic company, while both CR Bard and Boston Scientific were large U.S. corporations and thus foreign companies.

The later development of the two EEs revealed further differences. The EE in Galway grew more organically, with multinationals acting as anchors and incubators for new businesses. In Uppsala, growth was due to a combination of government initiatives and processes within large companies that also led to the creation of spin-off companies. The importance of local universities in the different stages of development also varied across the regions. In Uppsala, Uppsala University was a key player in the early stages of the ecosystem (action), while NUI Galway gradually gained importance by specializing in areas relevant to the local industry cluster

(reaction).

Even if both regions are considered second tier, there are relevant differences in spatial characteristics that influence both EEs. Uppsala's proximity to Stockholm and Arlanda Airport has a predominantly positive impact on the ecosystem by facilitating internationalization and increasing the available labor pool, although there is some competition for skilled labor between Uppsala and Stockholm. Galway's geographic location, on the other hand, limits competition for human capital with Dublin, the Irish capital. However, due to its distance from a major airport and the lack of a high-speed train connection, both domestic and international travel is longer compared to Uppsala, which negatively impacts Galway's attractiveness to startups whose employees need to travel frequently. An overview of the similarities and differences in the development processes that characterize the EEs in Uppsala and Galway can be found in Figure 18.

After analyzing and comparing the EEs in Uppsala and Galway, and by combining the findings with the literature review in section 2, the section 5 addresses the resulting policy implications for second-tier European regions seeking to establish and grow a local EE.

5. Policy Implications

In an empirical analysis of the quality of EEs in the U.S., Vedula and Kim (2019) showed that the quality of an EE affects the chances of firm survival. Nascent entrepreneurs benefit significantly from high-quality EEs, while serial entrepreneurs are less dependent on the quality of an EE. Vedula and Kim's analysis implies that nascent entrepreneurs in particular need to be strategic in their location decisions to maximize the chances of firm survival. Even for entrepreneurs already located in a lower-quality EE, moving to a higher-quality EE brings additional challenges, such as acquiring knowledge about the new market, building a good reputation, creating new networks, and mobilizing resources (Vedula & Kim, 2019). Therefore, location decisions in the early stages of venture development are particularly important for nascent entrepreneurs. This underscores the need to create and maintain a high-quality EE in regions that want to leverage entrepreneurship for regional economic growth.

As highlighted in earlier sections, policymakers must keep in mind that not all entrepreneurial activity contributes positively to a region's economic development (Acs et al., 2016; Baumol, 1990; Mason & Brown, 2014; Nightingale & Coad, 2014). While entrepreneurship in tradable sectors increases the likelihood of positive local spillover effects that benefit people not directly involved in entrepreneurial activities, entrepreneurship in non-tradable sectors shows a weaker impact on local economic growth and its effects, such as poverty reduction (N. Lee & Rodríguez-Pose, 2021). However, as Aparicio et al. (2020) have noted, innovation- and opportunity-driven entrepreneurship has the potential to contribute to social inclusion and inclusive growth, including in vulnerable communities.

Policies should be embedded in a larger framework aimed at encouraging local entrepreneurial activity. An EE, as explained in section 2.1, consists of several actors that influence its quality. Government actions therefore represent a part of the larger ecosystem, which underscores the need to synchronize government actions with incentives and support from other actors (Spigel, 2017). As Acs et al. (2016) point out, certain policies that can be highly effective in promoting local entrepreneurial activity may not be immediately recognizable as such, such as education policies or social security (Acs et al., 2016). Therefore, policymakers should take a holistic and systems-based approach to policy development and implementation. Policymakers should also ensure that policies are dynamic, as the ecosystem is constantly evolving and the sources of incentives for entrepreneurial activity change over time.

Combining the literature review on EEs in section 2 and the analysis of EEs in Uppsala and Galway in section 4 identified policy approaches that second-tier regions have used to establish and promote local EEs. Although spatial differences and a region's individual context must be considered, the following policy approaches can help second-tier regions develop a local policy framework and establish support systems that help create, grow, and sustain a thriving EE. The implications are divided according to the stages of development of an EE, which were presented in section 2.1 (Mack & Mayer, 2016). The decline phase was excluded because the policy implications for a declining EE are similar to those of the previous phases and are aimed at either rebirth or renewed growth. Figure 19 provides a brief overview of the key findings relevant for regional decision makers, while the following subsections provide a more detailed elaboration of the policy approaches and their respective implications.

5.1. Birth Phase

As the analysis of Uppsala and Galway, as well as the regions described in Appendix 4, has shown, second-tier regions tend to focus on a particular subset of an industry during the birth phase to build a solid knowledge base and specialize their activities. Given limited resources such as financial and human capital, it is likely necessary to build an EE around an existing industry cluster to benefit from comparative advantages (Giblin & Ryan, 2012). In addition, policymakers need to understand local strengths and weaknesses to recognize the region's capabilities and identify areas for smart specialization (P. Ryan & Giblin, 2012; Szerb et al., 2020). Furthermore, as Szerb et al. (2020) mention, policymakers should avoid focusing only on a region's strengths. Instead, mitigating weaknesses may be a necessary condition for realizing the full potential of regional strengths. The REDI presented in sections 2.4.3 and 2.5 can help regions in the EU identify such constraining pillars and design policies that alleviate existing bottlenecks (Szerb et al., 2020).

Next, policymakers should take a long-term perspective when attempting to establish an EE (P. Ryan & Giblin, 2012). Such ecosystems, as this article has repeatedly emphasized, go through various stages of development, and it likely takes

Theme	Similarities	
Industry Cluster	Both EEs revolve around a specific industry (Life Sciences/Biotech in Uppsala, MedTech in Galway)	
R&D Activities	R&D activity, within academia and/or within MNEs, was a prerequisite for the emergence of both EEs, also highlighting the importance of university-industry R&D collaboration	
Gradual Diversification	A gradual diversification is observable in both EEs	
Importance of MNEs	MNEs and large corporations, especially their R&D activities, played a major role in the EEs' development	
Regional Size	Both regions benefit from their limited size in terms of community building facilitation, a higher perceived quality of life by key actors, and cost benefits compared to the respective capital city	
Entrepreneurial Recycling	Entrepreneurial recycling and a Pay-It-Forward type culture are key phenomena in both EEs	
Success Stories	Regional success stories positively impact the emergence of nascent entrepreneurship in both EEs	
Growth Capital	There is a lack of growth capital in both EEs, leading to increased acquisition activities by MNEs and/or the relocation of scale-ups	
Theme	**Uppsala**	**Galway**
MNE Attraction	MNEs attracted to the region by research strength of local university	MNEs attracted to the region by monetary incentives provided by a government agency
Ownership of First Large Organisations	The first large organisation with a major impact on the emergence of the EE was native to Sweden	The first large organisations with major impacts on the emergence of the EE were foreign-owned
EE Development	EE development was spurred by both private and public initiatives	EE development was rather organic and driven by private initiatives
Anchor Organisations	Local university and Pharmacia acted as anchor organisations	MNEs acted as anchor organisations
Timing of MNEs R&D Activities	Large organisations and MNEs relocated R&D activities early on, production activities have not played a major role	Large organisations and MNEs relocated production activities early on and only later expanded into R&D activities
Spatial Context / Infrastructure	Proximity to Stockholm and Arlanda perceived as a positive factor for international travel and human capital availability, but some competition for talent with Stockholm	Lack of proximity to Dublin and international airport negative factor for international travel, skilled human capital is provided by local universities, and little competition for talent with Dublin

Figure 18: Comparison of Entrepreneurial Ecosystems in Uppsala and Galway. Source: own illustration.

several years for the effects of a local EE to become apparent when analyzing regional economic and financial indicators. Policy approaches should therefore be based on a long-term commitment to ensure the viability and resilience of the local EE, while also emphasizing the need for positive attitudes toward entrepreneurship among government officials and the public.

In the case of Galway, a low corporate tax rate, grant incentives, and research incentives motivated multinationals to establish subsidiaries in the region. The attraction of anchor organizations as a policy approach also worked in the cases of Portland, Boise, and Kansas City, although these case studies are not subject to the European context (see Appendix 4), again underscoring the need for contextual sensitivity. In any case, R&D activities in local affiliates of MNEs are particularly important to benefit from value-added spin-off activities. Moreover, trade policy enabled multinationals as well as emerging born global startups in Galway to do business outside of Ireland and provided international networking that is particularly important for small economies (P. Ryan & Giblin, 2012). Furthermore, the importance of networking in the birth phase, especially between existing and nascent entrepreneurs (Mack & Mayer, 2016), should not be underestimated.

The attraction of a large organization has also spurred entrepreneurial activity in Uppsala. The anchor in Uppsala's case, however, was its world-renowned university, which engaged in university-industry collaboration in research and development. Following the dissolution of Pharmacia, a number of highly qualified former employees who wished to remain in the region established their own entrepreneurial ventures. These processes were supported by a solid entrepreneurial support network, driven by both private and public actors. In addition, Uppsala encouraged spin-off activities and the commercialization of research results through the establishment of technology transfer offices at local universities to assist researchers in commercializing research. Although most researchers remain employed part-time at the university, support for research commercialization has produced hybrid entrepreneurs who work simultaneously in

	Development Stage		
Domain	Birth	Growth	Sustainment
Policy	Build on local strengths, mitigate weaknesses, and foster positive sentiment towards entrepreneurship among government officials	Facilitate new venture creation and research commercialisation via legal framework, promote the growing EE and local capabilities	Adapt the local policy framework and support mechanisms to cater for the needs of an increasingly diversified EE and local industry
Finance	Ensure early-stage capital availability for entrepreneurs from public and private funds	Incentivise private investment in early-stage and growth-stage ventures, start attracting skilled VCs and other growth capital providers to the region	Attract skilled growth capital providers to the region, ensure the accessibility of growth capital in the region to prevent high-growth start-ups' relocation or acquisition
Culture	Encourage networking between existing and nascent entrepreneurs	Establish collaboration-promoting physical spaces for relevant actors within the EE, look after serial entrepreneurs to foster entrepreneurial recycling	Use local success stories for promotional activities to encourage further regional entrepreneurial activity
Human Capital	Provide sufficient third-level funding to ensure the availability of skilled human capital and enable the commercialisation of research findings	Ensure alignment between higher education institutions' activities and the needs of the local industry cluster	Ensure continued third-level funding and universities' development to utilise strengths, mitigate weaknesses, and cater for the needs of the local industry
Supports	Establish support programmes helping nascent entrepreneurs develop necessary entrepreneurial skills	Develop physical infrastructure to ensure the attractiveness of the region to MNEs and born global start-ups, incl. regional, national and international transportation	Engage in conversations with entrepreneurs to determine and close gaps in the support system, ensure high-quality infrastructure
Markets	Focus on a specific industry subset to build a cluster, build an attractive business environment, attract MNEs, foster university-industry R&D collaboration	Enable the gradual diversification of the local industry via industrial, regional, science, and technology policy mechanisms	Incentivise the independent commercialisation and growth of regionally developed new technologies to avoid MNE overdependence

Figure 19: Overview of Policy Implications by Ecosystem Development Stage. Source: own illustration.

academia and business. The Swedish concept of professor's privilege has enabled these processes by preventing IP protection issues. A list of policy approaches to EE creation in second-tier European regions is shown in Figure 20.

While the policy approaches listed in Figure 20 contribute to the birth of an EE, the continuation of most of these policies is necessary during subsequent phases of development. In particular, sufficient third-level funding, university-industry collaboration in R&D, and commercialization of research results were also important for the growth and sustainment of the EEs in Uppsala and Galway.

5.2. Growth Phase

By investing in higher education, policymakers in Galway ensured that the medical technology cluster had access to skilled human capital. Similar processes around local universities, as discussed in Appendix 4, were also observed in Calgary (Spigel, 2017) and Chattanooga (Motoyama et al., 2016). In addition, in both Galway and Chattanooga (Motoyama et al., 2016), the gradual development of the local university to serve and collaborate with the emerging cluster of foreign and local companies was observed. Thus, not only companies but also universities specialized in activities that were aligned with the local cluster.

As the Galway and Uppsala cases have shown, policies that create incentives for current employees of local MNE subsidiaries, as well as for employees of local higher education institutions, to engage in spin-off activities can contribute to the growth of the EE (P. Ryan & Giblin, 2012). Such policies may relate, for example, to developing current production capacity, facilitating the creation of new ventures, training the necessary skills, regional, national, and international networking (P. Ryan & Giblin, 2012), and facilitating the commercialization of research results.

As Giblin and Ryan (2012) note, policy can also focus on attracting more FDI by promoting both the capacity and capabilities of emerging domestic firms, thereby creating incentives for foreign investors to further exploit these local capabilities. This also underscores the importance of geographically concentrated technological capabilities (P. Ryan & Giblin, 2012). Policies aimed at further developing these capabilities can therefore maximize the resulting external economies (P. Ryan & Giblin, 2012). Moreover, to ensure the resilience of the developing EE, policymakers should not focus exclusively on the emerging industry cluster, but should develop industrial, regional, science, and technology policy mechanisms that allow for technology and industry diversification (P. Ryan & Giblin, 2012). Gradual diversification of the EE mitigates cluster risks, so policy approaches aimed at diversification are also important in the sustainment phase.

Both Galway and Uppsala have benefited from their reputation in a particular industry. However, neither EE is particularly well known outside these industries. Therefore, using marketing techniques to increase awareness of the existing supportive ecosystem for entrepreneurs can help regions attract prospective and early-stage entrepreneurs, as well as other relevant stakeholders such as investors, to locate in their respective second-tier regions. In doing so, the advantages of the local EE should be highlighted. Second-tier re-

Birth	
Policy Approach	**Impact**
Focus on a specific subset of an industry	Build a solid knowledge base, specialise activities and create an impactful cluster
Comprehend local strengths and weaknesses	Identify the region's capabilities and identify areas of smart specialisation
Take a long-term approach to EE development and dynamically adjust policy measures	Prevent surrender if policy measures do not have an immediate (measurable) impact
Implement targeted (monetary) incentives and create an attractive environment to do business	Incentivise MNEs to establish local subsidiaries
Implement attractive trade policy and an infrastructure facilitating international trade	Incentivise MNEs to establish local subsidiaries and aid native born global firms' inception and growth
Encourage networking between existing and nascent entrepreneurs	Foster indigenous venture creation by local population
Establish and fund organisations dedicated to supporting existing and nascent entrepreneurs	
Encourage university-industry R&D collaboration via funding mechanisms	Attract MNEs and indigenous ventures to the region, encourage spin-off activities
Ensure sufficient third-level funding	Ensure the availability of highly skilled human capital and local R&D capabilities
Facilitate research commercialisation via technology transfer offices at universities and IP regulation	Encourage spin-off venture creation by researchers

Figure 20: Policy Approaches for Second-Tier Entrepreneurial Ecosystem Birth. Source: own illustration.

gions, such as those found in Uppsala and Galway, tend to benefit from dense networks, collaboration rather than competition, a sense of community, and a pay-it-forward culture. This also underscores the need for community development in second-tier EEs, as this can be a competitive advantage over EEs in superstar regions. A list of policy approaches for growing an EE in second-tier European regions is shown in Figure 21.

Overall, to grow a second-tier EE, having a support system in place that aids current and nascent entrepreneurs is necessary. Awareness thereof and collaboration within the ecosystem are also crucial to ensure the development of a sustainable competitive advantage. Related to this, and since a competitive advantage must be evaluated relative to competing EEs (Porter, 1985, pp. 1-30), competing regions should be analyzed thoroughly and continuously.

5.3. Sustainment Phase

As highlighted in Galway's EE analysis, sustaining an EE requires avoiding phenomena such as technological lock-in (see also, e.g., Maggioni, 2004). Thus, policies should focus on diversifying the ecosystem to mitigate cluster risks. Mack and Mayer (2016) suggest networking the local EE with other EEs at the national and international levels to avoid entering the decline phase. Seeking international networks and sharing ideas and experiences with other second-tier EEs was also highlighted by a government representative as a goal of Galway's economic policy.

In both Uppsala and Galway, a lack of local growth capital has been observed as a particular risk that can lead to stagnation and/or entry into the decline phase. This is also a challenge highlighted in a paper by Xu and Dobson (2019) on second-tier EEs. Due to their limited size, second-tier regions are not necessarily on the radar of growth capital providers such as VCs, at least outside the original industry cluster. As a result, promising startups tend to either seek acquisition by a multinational or relocate to superstar regions where growth capital is available. This can be seen in both Uppsala and Galway. One strategy that can help second-tier regions retain homegrown companies is to establish an exchange that allows small companies to go public relatively early. Examples of such venture exchanges include First North, which has launched in Denmark, Sweden, Iceland, and Finland, and the TSX Venture Exchange in Canada (Carpentier et al., 2010). The introduction of tax incentives or other monetary benefits for growth capital investors may also increase the attractiveness of investing in regional companies scaling up.

By retaining ventures with scaling potential, a second-tier region should aim to create an outstanding indigenous company that can serve as an inspiring example of local success. Such examples, as highlighted by interviewees from Galway and Uppsala, can inspire others to pursue entrepreneurial endeavors, creating a positive cycle of local entrepreneurial achievement. In addition, successful entrepreneurs sometimes become serial entrepreneurs or use their accumulated wealth to invest in other local startups, a process known as entrepreneurial recycling (Mason & Harrison, 2006).

As emphasized throughout this article, policymakers must continually adapt the policy framework and support mechanisms to ensure the sustainability and resilience of the EE. This will ensure that the needs of key stakeholders within the local EE are addressed to prevent the EE from entering

Growth	
Policy Approach	**Impact**
Encourage university-industry R&D collaboration via funding mechanisms	Attract and keep MNEs and indigenous ventures to/in the region, encourage spin-off activities
Ensure sufficient third-level funding	Ensure the availability of highly skilled human capital and local R&D capabilities
Facilitate research commercialisation via technology transfer offices at universities and IP regulation	Encourage spin-off venture creation by researchers
Ensure alignment between university research and teaching focus with local industry cluster	Ensure availability of highly skilled human capital for local economy and university-industry collaboration potential
Facilitate new venture creation via legal framework and infrastructure investments, and enable regional, national and international networking	Encourage spin-off venture creation by employees of large organisations and researchers at local universities
Develop and promote the capacity and the technological capabilities of emerging indigenous companies	Attract more FDI by incentivising foreign investors to further tap into the geographically concentrated local capabilities
Ensure sufficient funding for key actors within the local EE	Enable the continuous growth of the local EE
Promote the growing EE and its supportive infrastructure on a national and international level	Attract relevant actors, incl. nascent and early-stage entrepreneurs, to the region
Encourage collaboration among ecosystem actors, e.g. by creating attractive physical spaces that ensure density	Foster community development and a Pay-It-Forward type culture
Analyse the strengths and weaknesses of competing regional EEs	Ensure sustainable competitive advantage development relative to competing regions
Ensure the availability of relevant resources to current and nascent entrepreneurs and their awareness thereof	
Develop industrial, regional, science, and technology policy mechanisms that allow for technology and industry diversification	Ensure resilience of the growing EE, avoid technological lock-in, cluster hollowing-out and over-specialisation

Note: a dotted line indicates a policy approach already mentioned in a previous development stage that has been included again to emphasise its fluidity and relevance observed across development stages in flourishing second-tier EEs.

Figure 21: Policy Approaches for Second-Tier Entrepreneurial Ecosystem Growth. Source: own illustration.

Sustainment	
Policy Approach	**Impact**
Develop industrial, regional, science, and technology policy mechanisms that allow for technology and industry diversification	Ensure resilience of the growing EE and avoid technological lock-in, cluster hollowing-out and over-specialisation
Seek international networks and exchange ideas and experiences with other second-tier EEs	Generate ideas to avoid technological lock-in and diversify the local EE to ensure its resilience
Establish a small-cap venture exchange	Enable indigenous ventures to access growth capital and prevent them from MNE acquisition or relocating
Introduce tax incentives and/or other monetary benefits for venture capital investors and other growth capital providers	Attract venture capital investors and other growth capital providers to the region and thereby increase the availability of growth capital to local scale-ups
Use local success stories for promotional activities	Inspire the local population to start entrepreneurial ventures and attract entrepreneurs to the region
Ensure the wellbeing of local entrepreneurs by engaging in conversations and providing them with what they need	Foster entrepreneurial recycling and trigger a virtuous cycle of local entrepreneurial success
Adapt the policy framework and support mechanisms to cater for the needs of an increasingly diversified EE	Ensure the resilience of the local EE and prevent its decline

Note: a dotted line indicates a policy approach already mentioned in a previous development stage that has been included again to emphasise its fluidity and relevance observed across development stages in flourishing second-tier EEs.

Figure 22: Policy Approaches for Second-Tier Entrepreneurial Ecosystem Sustainment. Source: own illustration.

the decline phase. A list of policy approaches for sustaining an EE in second-tier European regions is presented in Figure 22.

The above policy approaches, their underlying mechanisms, and their respective effects were observed in existing second-tier EEs. However, as highlighted throughout the article, each EE is subject to a unique spatial context that must be considered when attempting to build, grow, and sustain a thriving ecosystem to support entrepreneurial activity. The next section summarizes the findings of this article and discusses the limitations of the results.

6. Conclusion and Limitations

Through a thorough literature review and the creation of a comparative case study of two regions, this article sought to derive dynamic policy implications for second-tier European regions seeking to effectively foster a local entrepreneurial ecosystem. While the importance of spatial differences was emphasized throughout, there are certain patterns that recur not only in the two second-tier European regions analyzed in this article, but also in the second-tier North American regions previously analyzed in the academic literature. First, it became clear that the establishment of thriving EEs in second-tier regions is possible despite polarization trends in innovation, but the emergence of an EE need not be intentional. Both Uppsala and Galway benefited from certain processes that later enabled the emergence of their respective EE. Thus, their creation was more accidental and a by-product of university-industry collaboration in Uppsala and attracting foreign direct investment in Galway. Both processes required government activity, but this varied between the regions. In Uppsala, the government was involved primarily through funding for higher education, while in Galway, the government created, among other things, a policy framework that provided incentives for multinational enterprises to locate in the region.

Second, the importance of R&D activities of local MNE subsidiaries and higher education institutions cannot be overstated. It was the transition from manufacturing to R&D by the subsidiaries of the multinationals in Galway, driven by the specialization of research at one of the local universities, that enabled the emergence of the EE. In Uppsala, on the other hand, it was the research strength of one of the local universities that attracted large companies to the region in the first place. R&D was thus a prerequisite for the birth of the EEs in Uppsala and Galway.

Third, another result revolves around the impact of innovation polarization on later stages of EE development. Both Uppsala and Galway suffer from a lack of access to growth capital. In both regions, this leads to increased acquisitions by multinationals and the relocation of scale-up ventures to national or international superstar regions. This finding seems particularly important as it underscores that location decisions by entrepreneurs have a direct impact on the growth potential of ventures. In addition, limited access to growth capital likely increases costs for scale-up ventures not operating in the region's focus industry if they attempt to find investors locally. This is due to a lack of qualified and experienced investors for the company's specific target industry. Such an increase in the cost of money results in either lower investment amounts or the loss of a larger portion of the venture itself, neither of which is beneficial to the entrepreneur. Therefore, the availability of growth capital should be an important criterion for entrepreneurs' location decisions, which means that the availability of growth capital should be a priority for regional decision makers, especially during the growth and sustainment of an EE.

The results of this article have certain limitations. By comparing two EEs, a "small n" method (Roundy, 2019) was chosen, which limits the degree of generalizability of the results. Given the different circumstances in the two regions, the results are subject to spatial context. However, as Eisenhardt and Graebner (2007) argue, this method nonetheless allows for an assessment of the presence and consistency of findings across cases, which provides some degree of generalizability. Moreover, both EEs revolve around subsectors of the life sciences. Focusing on this specific industry may limit the transferability of certain findings to other industry foci. However, by combining the insights gained from the comparative case study with a literature review on EEs in general and EEs in second-tier regions in particular, a more holistic picture was drawn from which policy implications for other second-tier European regions can be derived. Nonetheless, the findings may be sector-specific to some extent.

By exploring dynamic policy implications for second-tier European regions seeking to establish, grow, and sustain an EE, this article sought to contribute to research on the importance of the spatial context of EEs, as well as on the life cycle of EEs. The findings can help local policymakers develop policy frameworks and support mechanisms that enable an EE to emerge, grow, and sustain in a second-tier region. Given the link between entrepreneurship and economic development, the results of this article can contribute to the economic and social well-being of regions as well as their urban development plans.

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