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The internationalization of innovation towards the South:

A historical case study of a global pharmaceutical corporation in China (1993-2017)

ABSTRACT

Intensified competition means that multinational enterprises (MNEs) are increasingly concerned with locating innovation activities in the most appropriate locations. This had led to emerging economies in the South becoming an important destination of R&D-related foreign direct investment (FDI), departing from their traditional role as low-cost production sites. Thus far, however, our understanding of this transformation process is limited. The purpose of this article is therefore to explore the process by which foreign MNEs' low-value-adding operations in the South are transformed into high-value-adding R&D operations. Drawing on the current literature, we construct a framework of evolution consisting of four major waves of R&D internationalization and corresponding R&D objectives. To better understand how these waves have evolved over time, we focus on the South and trace the process of change using a single historical case study: AstraZeneca in China between 1993 and 2017. We find evidence of idiosyncratic location-bound conditions offering both opportunities and resources. The gradual development of these favourable conditions, along with AstraZeneca's deepening local knowledge, triggered a transformation process in their operations in China. Our study thus offers important historical insights, which present a platform for future research providing more nuanced theoretical explanations of the four waves of R&D internationalization.

Keywords: R&D internationalization, emerging economies, North and South, historical case study.

Introduction

The fast-changing global environment in recent years, including competition from multinational enterprises (MNEs) originating in emerging economies (which we term the 'South') and development of the Southern economies, has led to noticeable changes, both inside advanced-economy (which we term the 'North') MNEs and in host countries (Mudambi *et al.,* 2014; Awate *et al*., 2015; D'Agostino, 2015; Jha *et al*., 2015; Nair *et al*., 2015; Zedtwitz *et al*., 2015). These include the increasing need to monitor and understand new global trends and hence to engage in multi-sourcing of knowledge inputs, a trend reinforced by rising R&D costs and a shortage of R&D personnel in the industrialized countries (Reddy, 1997; Chen, 2004). This has led to a strategic re-focusing of international innovation to simultaneously maximize the value of home-based knowledge and capture and synthesize local-based knowledge, both in the North (Zander, 1999; Chen, 2004) and in the South (Liu and Chen, 2012; Shin *et al.,* 2016). In addition, market and institutional conditions in the South have substantially improved (though at varying speed), including an increased supply of qualified R&D personnel and skills, government support, emergence of regional innovation systems, preferential policies, and an increasingly sophisticated consumer demand (Guan *et al*., 2009; Li, 2009; Liu *et al*., 2011). The combination of these factors, as well as wider developments in the advancement and availability of information technologies in knowledge management (Yu, 2011; Mabey and Zhao, 2017), are driving the shift in innovation locus towards the South (Haour and Jolly, 2014; Haakonsson and Ujjual, 2015), with the aim of developing more sustainable competitive advantages by aligning internal and external knowledge networks globally. Consequently, in recent years MNE global innovation networks have extended to encompass the South (Liu and Chen, 2012; Jha *et al*., 2015; Jha *et al*., 2018) as is clearly evidenced by a recent study published by PriceWaterhouseCoopers (2015) that identified Asia as the top destination for corporate R&D expenditure, ahead of North America and Europe.

Although this emerging trend is gaining a growing level of attention, research on R&D internationalization to date nevertheless takes a predominantly North-centric view. In comparison, studies addressing this trend using a South-centric lens remain sparse, with a few recent exceptions including Awate *et al*. (2015), Jain *et al*. (2015), Zedtwitz *et al*. (2015) and Mudambi and Santangelo

(2016). However, none of these studies were intended to provide the level of depth and detail that our article offers. Our historical case study approach is better able to capture the incremental changes in the South over a considerable length of time. It thus sheds new light on the historical development of four distinct waves of R&D internationalization derived from the current literature. As such, the objective of our study is not to test or re-examine the literature-informed waves. Instead it extends current literature on R&D internationalization towards the South by offering historical and contextual evidence of a micro-level study, i.e. AstraZeneca (AZ) in China, to be used for further theory development and empirical testing across other MNEs and/or Southern economies.

We first construct an overarching framework of R&D internationalization, which encompasses innovation in both the North and the South. Extending existing literature, our framework integrates four major waves of R&D internationalization and their distinct R&D objectives through time. It moves from a North-North wave for home-based knowledge augmentation and a North-South wave for home-based knowledge exploitation, to a South-South wave for local-based knowledge exploration and a South-North for home-based knowledge augmentation. Building on this, we apply a historical (longitudinal) lens to the case of AZ in China to trace and analyze changes in its R&D activities from its first entry in 1993 to 2017. In so doing, our article answers the following two research questions: 1) How have AZ's operations in China evolved between 1993 and 2017 leading the country to play an increasingly active role in AZ's R&D configuration?; 2) What can be learnt from the case of AZ in China in light of the existing literature and theories on R&D internationalization?

Our article makes several key contributions. First, we construct a literature-informed comprehensive framework offering a classification of R&D internationalization waves and their corresponding R&D objectives. This framework explicitly illustrates and integrates four waves of R&D internationalization and their distinct R&D objectives in each wave, depicting the overall process of R&D evolution in the South. Second, in light of this framework we present a more complete picture of the R&D evolution process and the mechanisms underlying this process using the case of AZ China in the period between 1993 and 2017. Our comprehensive case study evidence offers new insights into how the South (in this case, AZ in China) has upgraded its role in R&D internationalization, thus focusing in particular on the last three waves of our framework of R&D

internationalization. It thus addresses the limitations of existing research, which lacks a solid micro-level understanding of the incremental changes an MNE may experience inside a fast-changing Southern economy such as China. Third, by exploring the context of China, we offer new insights into the idiosyncratic institutional and market transformation of the country that impacted on AZ's local R&D evolution. Whilst China is known to represent unique opportunities for MNEs, studies exploring its historical impact on MNE innovation activities remain sparse. Our article is one of the first to apply a longitudinal case study approach to reveal contextual details of R&D evolution in the South. Lastly, our article contributes to the methodological development in research on R&D internationalization research by way of applying a longitudinal historical approach to the study of R&D internationalization, a rather neglected approach (Welch and Piekkari, 2017). We demonstrate the suitability of a single case study in exemplifying 'context' in qualitative research (Siggelkow, 2007; Doz, 2011; Welch *et al*., 2011), when the phenomenon in question is relatively new or difficult to study. The empirical evidence of our study is not intended to generalize across the industry or across other Southern economies, but instead is to be used for further theory development to advance our understanding as to whether the case of AZ in China and the proposed pattern of R&D evolution towards the South are typical.

In the remainder of this article, we first review the literature on R&D internationalization and construct an evolutionary framework. Then, we discuss our methodological approach and the background of our research context. This is followed by our case study findings. Finally, we discuss these findings and conclude with our contributions to theory development, implications for practice, and our recommendations for future research.

The internationalization of R&D: Literature review and conceptual framework

Literature review: R&D locations and objectives

Dunning (1958), Safarian (1966) and Brash (1966) were amongst the first to discuss the act of internationalization of R&D displayed by some first-mover MNEs at the time. Soon after, an empirical study by Creamer (1976) provided clear evidence that a variety of overseas R&D activities were

performed by MNEs from the North. Cordel (1973) and Ronstadt (1978) offered typologies of different overseas R&D activities. Subsequently, Behrman and Fischer (1980), Hakanson (1981), Hood and Young (1982), Niosi (1999), and Edler (2007) recorded a shift of global innovation activities from MNE headquarters towards the active participation of foreign subsidiaries, which became more prominent as an important source of new knowledge generation (Feinberg and Gupta, 2004; Griffith *et al.,* 2004).

Initially, these strategically important locations for new knowledge generation were typically either geographically close or institutionally similar countries, so that MNEs could retain close control over key activities whilst also benefiting from locational advantages (Song and Shin, 2008; Song *et al*., 2011). Hence, a large majority of MNEs chose to locate their international innovation activities in developed countries, particularly in the USA, Europe, and Japan, while also transferring innovations to and back from other developed countries (Niosi, 1999; Edler, 2007; Haour and Jolly, 2014; Haakonsson and Ujjual, 2015). Although these studies provided valuable theoretical and empirical insights at the time, they were predominately underpinned by North-centric developments and thinking, whilst the South remained an 'outsider' in the MNE global innovation network (Liu and Chen, 2012). Drawing on the terminology of 'waves' from the works of Coe *et al*. (1997) and Jha *et al*. (2015), we classify this trend as the North-North wave which is mostly reflecting 'home-based knowledge augmentation' (HBKA-N) within Northern economies.

A second stream of literature has noted innovation-related knowledge transfer from headquarters to less developed economies in the form of production offshoring paired with on-site technical support and backup required to ensure timely problem-solving (Florida, 1997). Furthermore, the global investment environment witnessed significant changes, such as increasing international competition and advancing information technology (Castellani and Zanfei 2006; Yu, 2011). We classify this development of limited R&D activities in the South as the North-South wave, which is closely aligned with Vernon's (1966) product life cycle model whereby existing product knowledge is further exploited in new locations. Consequently, for the first time, the South became a destination for R&D activities, though this was generally viewed as more of an 'operational necessity', restricted to production (Cantwell, 1992; Pearce and Papanastassiou, 1997). Drawing on previous literature on the

objectives and characteristics of R&D internationalization (Kuemmerle, 1999; Bas and Sierra, 2002; von Zedtwitz and Gassmann, 2002; Liu and Chen, 2012), this wave can be identified to reflect the main objective of 'home-based knowledge exploitation' (HBKE-S) in supporting the development of new markets and foreign production sites.

As home-based knowledge exploiters, MNEs chose to locate their R&D units close to large foreign markets or manufacturing sites to ensure on-time support. The main tasks of these R&D units tended to include assimilating knowledge transferred from the headquarters, modifying existing manufacturing processes, or modifying existing products to meet the local market conditions in the host countries (Pearce and Papanastassiou, 1999; Athreye et al, 2016). By doing so, MNEs could gain economic return from utilizing their existing proprietary knowledge (generated in the North) in overseas locations (such as the South), while home-based R&D units continued to define the product specifications and design the manufacturing processes (Schmiele and Mangelsdorf, 2009; Liu and Chen, 2012).

A third and fourth stream of literature has emerged in recent time which suggests the increasingly crucial role of emerging economies in undertaking innovative activities for MNEs by incorporating the development of global innovation networks that excel at tapping into new centres of knowledge (Dunning and Lundan, 2009; D'Agostino and Santangelo, 2012; UNCTAD, 2012; Castellani et al., 2013; Jain et al., 2015; Mabey and Zhao, 2017). What makes these two streams significant is that Southern economies are no longer viewed only as the location for low-cost labour or primary resources, but also potential sources of new knowledge (Prabhu and Jain, 2015). Some of the latest studies further support the growing proportion of FDI now devoted to strategic innovation in emerging economies, particularly Asia (Altenburg *et al*., 2008; Castellani *et al*, 2013; Athreye *et al,* 2014; Prashantham and Dhanaraj, 2015; Bresciani *et al.,* 2016). These innovation investments target both the local market (we term this the 'South-South' wave) and the global market (we term this the 'South-North' wave). This significant development has been the focus of some of the latest research (e.g. Awate *et al*., 2015; Jha *et al*., 2015; Jha *et al*., 2018; Mabey and Zhao, 2017).

In terms of the South-South wave, the main objective of the MNE concerns 'local-based knowledge exploration' (LBKE-S) in support of the development of new products for local and

regional markets (Jha *et al*., 2015). R&D units under the South-South wave are focused on the seeking and development of knowledge useful in providing products to local markets (Jha *et al*., 2015). In situations where market demand is high and the availability of products is low, an opportunity arises for local-based R&D units to fill this gap by developing market-specific products. This leads R&D units to seek localized knowledge from entities such as research institutions, universities, local firms, and customers (Awate *et al*., 2015), and combine this knowledge with its existing internal capabilities to realize new or improved products that are market-specific. In terms of the South-North wave, MNEs are mainly engaged in 'home-based knowledge augmentation' (HBKA-S) in support of the development of complementary and novel knowledge for the global market. R&D units under the South-North wave are concerned with the development of long-term innovative capabilities by taking advantage of novel or complementary knowledge in foreign locations, which is gaining growing importance and is driven by the pressure of knowledge-based competition (Jha *et al*., 2015; Jha *et al*., 2018). To augment their home-based technologies, MNEs set up their R&D units overseas with an aim to access the host countries' knowledge for their headquarters (Asakawa and Som, 2008). One main objective of these units is to engage in knowledge sourcing and to benefit from potential knowledge spillovers (Almeida and Kogut, 1999; Feinberg and Gupta, 2004).

Nevertheless, both these waves reflect a picture that is dramatically different from the conventional view of R&D internationalization. MNEs no longer regard the South only as a target for market expansion and production, accompanied by limited R&D activities, but also as an important location for knowledge augmentation. Reverse knowledge transfer from the South to the North thus becomes a distinct possibility (Govindarajan and Ramamurti, 2011; Govindarajan and Trimble, 2012). This departs from the product life cycle understanding of knowledge exploitation and moves towards a global innovation network arrangement of differentiated and distinct R&D units worldwide (Mudambi and Santangelo 2016). These R&D units, located in the North and the South, span across a wide variety of R&D activities.

Drawing on the four streams of literature, Table 1 summarises our classifications of each of the four waves and associated R&D objectives.

Table 1. Classification of the four major waves in MNE R&D internationalization

North: advanced economies (e.g. US, UK, Germany, Japan)
South: emerging economies (e.g. China, India, Brazil)

	Location	*R&D objectives*
Wave 1	North-North	Home-based knowledge augmentation in the North (HBKA-N)
Wave 2	North-South	Home-based knowledge exploitation in the South (HBKE-S)
Wave 3	South-South	Local-based knowledge exploration in the South (LBKE-S)
Wave 4	South-North	Home-based knowledge augmentation in the South (HBKA-S)

2.2. An overarching conceptual framework: the internationalization of R&D towards the South

Whilst the four waves of R&D internationalization have been identified in prior research, they have remained largely independent as most studies focused on issues *within* the respective waves. In conventional North-North and North-South innovation paradigms, R&D stayed largely in the North whilst MNE activities in the South were predominantly driven by knowledge exploitation to meet growing local market demand. This reflected a highly hierarchical relationship between the North and the South. However, in the latest development of MNE R&D internationalization, Southern economies such as China (Bruche, 2009; Liu and Chen, 2012) and India (Kumaraswamy *et al*., 2012; Awate *et al*., 2015; Jha *et al*., 2015) have emerged as high-profile destinations in attracting inward innovation FDI. Some of the latest evidence (e.g. Liu *et al*., 2011; Liu and Chen, 2012) suggests that MNE R&D mandates in these locations have increasingly gone beyond the traditional pattern of knowledge exploitation. Pearce (2004; 2006), Dunning and Lundan (2008), and Zhang *et al*. (2018) have found that technological dynamism tends to shape the internal organisational structure of the MNE, which often explains the initial and subsequent strategic motivations of overseas subsidiaries. The strategic motivation underlying the establishment of subsidiaries in different countries depends on the locational opportunities and advantages that are present at the time of the initial investment. For instance, initially, market- and efficiency-seeking subsidiaries were mostly established in the South whilst knowledge-seeking subsidiaries were established in the North. Market- and efficiency-seeking motivations, which are underpinned by the strategic rationale of asset exploitation (Bartlett and Beamish, 2013; Dunning and Lundan, 2008), are intended to benefit from local resource abundance by investing in a particular country or region to supply goods or services to local, regional, and/or global markets. A knowledge-seeking motivation, on the other hand, concerns "*the pursuit by MNEs of new*

technological capabilities, scientific capacity (research facilities) and creative expertise (e.g. dimensions of tacit knowledge) from particular host countries, in order to extend the overall competences (product range and core technology) of the group" (Manea and Pearce, 2004:4). As the local environmental conditions in the South continue to evolve, benefits of an embedded innovation capacity for developing goods in and for host markets and regions become apparent. As a result, initial motivations of market- or efficiency-seeking can often shift towards local innovation through 'asset augmenting' activities (such as knowledge-seeking) (Bartlett and Beamish, 2013; Cantwell *et al*., 2010; Dunning and Lundan, 2008; Zhang *et al*., 2018).

Recent work by von Zedtwitz *et al.* (2015) extends the concept of 'reverse innovation' by asserting that emerging economies are not simply locations for innovation adoption but also for new knowledge development. This implies that apart from knowledge exploitation (wave 2), local-based knowledge exploration (wave 3) and home-based knowledge augmentation (wave 4) are seen to take place in the South as R&D units become deeply involved in the local context with increased benefits of access to external knowledge, hiring of local personnel, and support of the local government.

Drawing on previous literature (Cantwell and Iammarino, 1998; Cantwell and Janne, 1999), one explanation for this development could be that countries with abundant innovation resources and a favourable supporting environment can influence the mandate of local R&D units (Ito and Wakasugi, 2007; Liu and Chen, 2012). In the case of certain economies in the South such as India and China, this is increasingly evident (Lu *et al*., 2008; Dodgson, 2009; Castellani *et al.,* 2013). For instance, institutional conditions for innovation in these countries are fast improving through the efforts of national and local governments. Several pro-innovation factors can be identified: investment in higher education and the retention of skilled native and foreign researchers and managers (Yang and Jiang, 2007), development of clusters (encompassing local firms and support systems), and the establishment of national systems of innovation (encompassing MNEs, indigenous firms, public and private research institutions, universities, involving in a variety of innovation activities) (Archibugi and Iammarino, 2002; Lundvall 1992; 2007; Dodgson, 2009). As a result, these economies benefit from an accumulation of innovative capabilities (Lema *et al*., 2015). As part of these changes, subsidiaries in these locations are offered the opportunity to improve their innovation capabilities. Indeed, a recent

study by Zhang and Pearce (2012) finds that subsidiaries in China are not solely receivers of MNE knowledge, but also generators of new knowledge by working closely with local universities, firms, and research institutions. In particular, they argue that while market-seeking subsidiaries are frequently found in emerging economies, some of these economies have developed impressive innovation capacity for generating new knowledge, contributing *de novo* to the MNE's technological trajectory. Thus, new knowledge generated in the South not only better captures the Southern market but can also be valuable to MNE global competitiveness (Mudambi and Santangelo, 2016). The locational hierarchy between the North and the South is thus flattening, whereby the South is starting to become part of MNEs' global innovation network for knowledge augmentation (Chen, 2004; Liu and Chen, 2012). Nevertheless, this changing relationship between the North and the South, and the shift towards R&D in the South, does not happen instantly; instead, MNE R&D internationalization from the North to the South is likely to go through an evolutionary process. However, to date, studies attempting to directly map this pattern across the waves remain scarce (Govindarajan and Ramamurti, 2011; von Zedtwitz *et al*. 2015).

In this study, we assert that the waves in R&D internationalization are not static or unrelated. Instead, they are parts of a dynamic development in which the growth of innovation within MNEs has shifted towards the South. In Figure 1 we illustrate the gradual shift in MNE R&D internationalization from the North to the South. During the first wave (North to North), the global innovation network only spanned across advanced economies, termed the *first-tier* location with the accompanying R&D objective being mainly HBKA-N. Thereafter, the South was considered a *second-tier* location predominantly for the purpose of HBKE-S to meet growing market demand. Subsequently, the increased efforts in improving innovation capability and the fast-growing national economies in the South made them an increasingly attractive hub for LBKE-S, thus adding a *third-tier* location to the global innovation network. In the most recent wave, further strengthening of innovation capabilities in the South has led to HBKA-S and thus a *fourth tier* emerged. In short, the framework proposes that the four waves found in literature can be considered as four *consecutive* processes of R&D internationalization whilst they are also mutually inclusive to represent a multi-layered continuous network of global innovation.

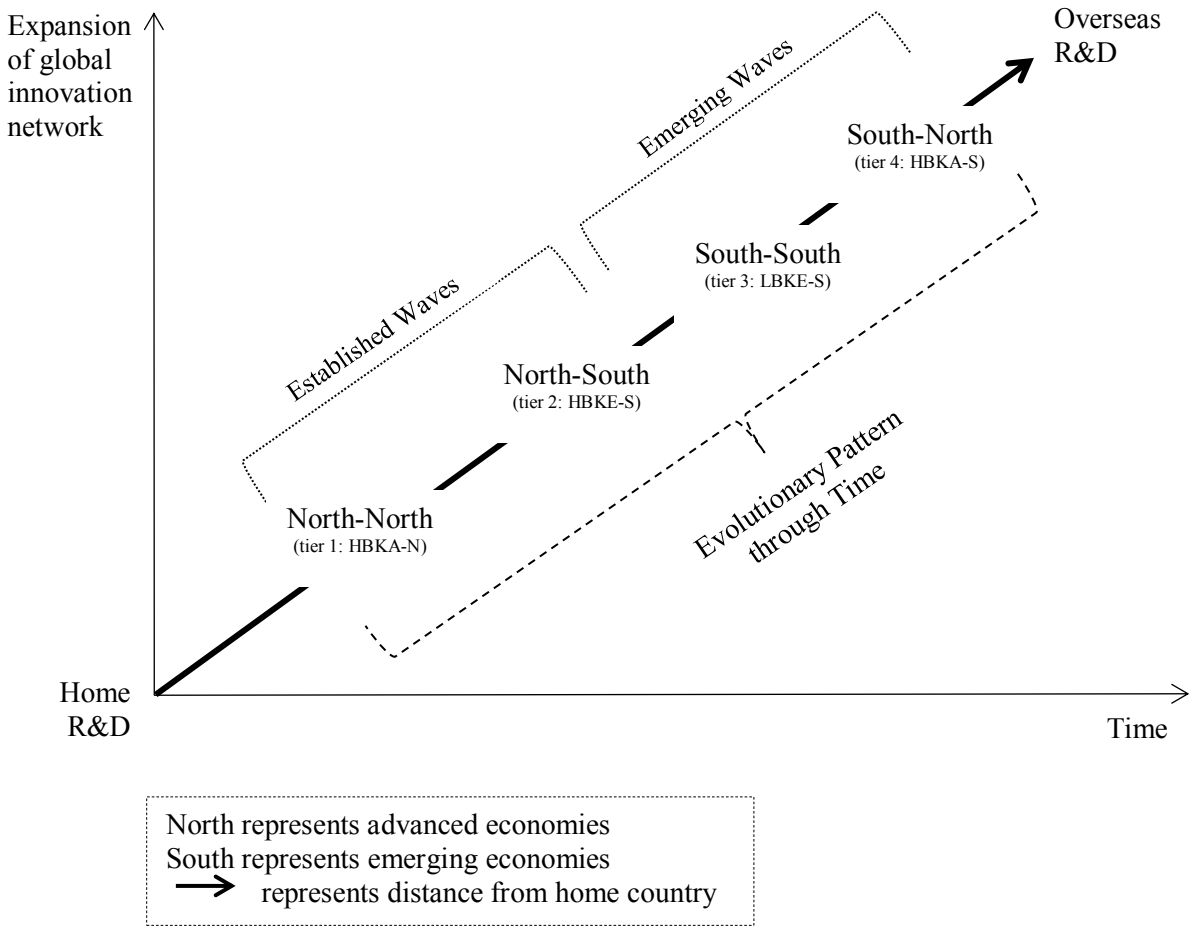

Figure 1. Four-wave framework of MNE R&D internationalization

Therefore, this article proposes that MNE R&D internationalization towards the South is likely to show a dynamic pattern, from HBKA-N and HBKE-S to LBKE-S and HBKA-S. Hence, our empirical study takes MNE subsidiaries in the South as the appropriate unit of analysis in light of this latest development in R&D internationalization (Liu and Chen, 2007; 2012). Furthermore, to address the empirical problem noted by Liu and Chen (2012): "*the spatial distribution of innovation resources and potential is not even… [in the case of emerging economies]*" (p:1109), we take a country-specific approach to better deal with such an unevenness and account for host-country idiosyncrasies. Moreover, since MNEs' decisions to undertake R&D in specific locations are conditioned by both firm and location related factors, a context-specific view of the pattern of MNEs' evolution in their local activities is essential. As each MNE is a nexus of knowledge flows across home and host countries

(Gupta and Govindarajan, 1991), how they pursue certain knowledge objectives by organizing specific R&D activities with local firms, research institutes, and universities in a host country becomes an important question. Nevertheless, studies adopting an evolutionary perspective to explore the pattern of R&D internationalization in the South remain limited. Jha *et al*. (2015), Jha *et al*. (2018) and Kumaraswamy *et al*. (2012) are rare exceptions; however, all focus on India and cover a maximum period of ten years.

In sum, drawing on the literature on R&D internationalization, this article attempts to address the key question of how MNE R&D activities in the South have evolved to play an increasingly active role within the MNE global innovation network, so that new insights into the latest shift in R&D internationalization from the North to the South can be gained. Here, we take a historical lens to identify empirically the potential pattern of change in subsidiaries' innovation activities of a specific MNE, AZ, in the case of a specific Southern economy, China. The next two sections first discuss the specifics of the case study approach (AZ in China), and then provide our empirical findings covering the period between 1993 and 2017.

Epistemology and methodology

To achieve a holistic understanding of the overall development pattern of R&D internationalization in our case study, we decided to adopt a longitudinal historical perspective, which echoes a similar approach taken by Jha *et al*. (2015) and Kumaraswamy *et al*. (2012). We follow Turnheim and Geels' (2013) process-tracing approach to explore the evolution of AZ in China from its initial entry in 1993 to 2017. This approach is particularly useful in capturing the evolutionary pattern we seek to unfold in this study as it "*takes path dependence seriously and goes 'inside the black box' to explain how actions and changing contexts produce event chains*" (Turnheim and Geels, 2013:1754). We adopt an epistemological style commonly used by historians, 'narrative explanation', which is particularly strong in capturing complex social interactions through time and event sequences (Abbott, 2001; Gill *et al*., 2018).

In line with Turnheim and Geels (2013), the narrative explanation style that we adopt in this article is not about simply describing separate events, but involves the tracing of the historical process,

guided by prior literature and the proposed conceptual framework (Figure 1). On the other hand, "*historians rarely perform formal tests of theories; instead, they judge theories and conceptual frameworks for their usefulness in writing plausible and interesting narratives*" (Turnheim and Geels, 2013:1755). Therefore, using a 'thick' descriptive case study (Child *et al*., 2012) allows us to derive insights related to existing knowledge (Doz, 2001:584). Welch *et al*. (2011) proposed that contextualization should not be viewed as a limitation of case study research, but, on the contrary, as a bridge to 'reconcile' the positivist views on the generalizability of findings, which is regarded as fundamentally opposed to 'explaining' and 'contextualizing' (p:743). Applying this to our study, we argue that the contextual details of our case are simply too important to ignore. Thus, in order to fully understand the evolutionary pattern of R&D activities of AZ in China, it is important to complement a 'positivist context-free orientation' with a more contextualized explanation, highlighting causal relationships. The objective of our study is thus to provide an analytical narrative that traces the pattern of R&D internationalization identified in the literature, but then emphasizes the impact of context, thus becoming an 'explanatory' tool of understanding, hence departing from its initial 'exploratory role' (Yin, 2014).

Within case study research, researchers can choose to select either single or multiple cases. The decision on which to use is largely dependent on its appropriateness in dealing with the topic (Yin, 2014; Fletcher *et al*., 2018). As the topic of this study is about drawing on rich contextual details to unfold an evolution pattern, a single case study of AZ in China is chosen. Siggelkow (2007) emphasizes the usefulness of a single case study as an important source for both unique data evidence and theorising. Our chosen case is empirically appropriate for several reasons. First, UNCTAD's (2005) ranking of innovation-related FDI shows that China has become a top inward innovation FDI destination of the South. This is confirmed by a recent report by PriceWaterhouseCoopers (2015) that also identifies China as a recipient of some of the largest global R&D investments. Second, amongst many R&D intensive MNEs, AZ PLC has one of the oldest operating histories in China and was one of the very first to set up a strategic R&D centre in the country (Bernstein Research, 2009), thus providing the longest and richest story.

Case study rigor

In this article, we present a rigorous single case study, relying on the strategies, principles and coding rules described in Cook and Campbell (1979) and Gibbert and Ruigrok (2010). Thus, in Table 2 we present the four validity and reliability criteria, namely internal validity, construct validity, external validity and reliability. These criteria are considered as the 'primary reports' along the horizontal axis. We also discuss the research measures taken in our study for each corresponding criterion, the 'secondary reports' along the vertical axis, drawing on Yin (2014).

Table 2. Primary and secondary reports considered

	Primary Reports (Cook and Campbell 1979; Gibbert and Ruigrok 2010)			
	Internal validity	Construct validity	External validity	Reliability
Secondary Reports (Yin 2014)	Requirement and actions taken: ✓ Literature-informed research framework (refer to 'literature review' section) ✓ Pattern matching with other works (refer to 'discussion' section) ✓ Theoretical triangulation for the conceptualization and interpretation of findings (refer to 'literature review' and 'discussion' sections)	Requirement and actions taken: ✓ Data triangulation (refer to Table 3), cross checks of corporate reports and reports from the Ministry of Commerce, P.R.C., were made to ensure all key activities of AZ were captured; confirmation from two AZ senior scientists ✓ Review of drafts by multiple non-authoring academics	Requirement and actions taken: ✓ Rationale for case selection; evidence of AZ as an appropriate case; embedding the case in the context of China; industry information (refer to 'methodology' and 'AZ in China 1993–2017' sections) ✓ Details on case study context (refer to 'AZ in China 1993-2017' section)	Requirement and actions taken: ✓ Case study database (refer to Table 3) ✓ Name given for the organization in question (AZ PLC) ✓ Case study protocol (refer to the subsection 'data analysis protocol')

With reference to Turnheim and Geels' (2012; 2013) definition of secondary (journal articles and authored books) and primary (newspapers, government reports and company annual reports) data, we draw on a wide variety of secondary and primary sources to highlight and trace activities of AZ during its operations in China. Although these sources cannot always be taken at face value, they do provide some interesting facts for our qualitative analysis, which tracks the gradual changes in the company's operations and it can be said that "This variety in data sources enables triangulation, and allows for a rich analysis…" (Turnheim and Geels, 2013:1755). A comprehensive list of data sources is provided in Table 3.

Table 3. Primary and secondary data sources

Data (in alphabetical order)	**Source**
Books	▪ China Medical and Pharmaceutical Industry Handbook ▪ The Asia-Pacific Biotech Directory ▪ International Directory of Company Histories ▪ Foreign Companies in China Yearbook
Company Annual Reports	▪ AZ PLC ▪ Zeneca Group PLC
Corporate News Releases	▪ AZ Global ▪ AZ China ▪ Ironwood Pharmaceuticals Inc.
Government Reports	▪ China Food and Drug Administration ▪ Ministry of Commerce, P.R.C. ▪ State Intellectual Property Office (China)
Industry Reports	▪ Bernstein Research ▪ Bio Partnerships Asia ▪ Chemical Market Reporter ▪ KPMG Research ▪ McKinsey Quarterly ▪ Thomson Reuters
Newspapers	▪ Asia Pacific Biotech News ▪ CBS News ▪ China Daily ▪ Jiangsu News ▪ The Financial Times ▪ The Independent ▪ The Telegraph ▪ Wall Street Journal ▪ Washington Business Journal

Data analysis protocol

The data analysis process was partially planned and partially emergent as the data collection progressed. Appropriate adjustments were made throughout the study by examining emerging patterns from the raw data, thus making the process interactive. Following a similar approach in Kumaraswamy et al. (2012), our longitudinal case is divided into three distinctive periods (covering waves 2 to 4 of our framework), using the narrative to depict AZ's innovation activities in China. Specifically, period one displays an initial focus on market expansion and production in China together with the necessary low-level R&D activities for local adaptation (i.e. a North-South wave), while period two features a new focus on local and regional innovation and production, and period three is characterised by a shifting focus towards global-driven innovation. We then provide interpretations of those R&D activities undertaken in each period, as well as over the course of the three periods mentioned above in relation to our proposed overarching framework.

Case company: Brief history of AZ PLC

The beginning of AZ can be traced back to 1913 when Astra was an independent company based in Sodertalje, Sweden. It was not until the 1930s, however, that the company started its first small-scale research activities. The company acquired a couple of factories in 1939 and 1942, helping to make Astra the largest Swedish pharmaceutical company. From the early 1990s, Astra started to experience significantly increasing costs for the development of new drugs. Believing that the company needed a more international platform for the future, Astra started to look for partners. It was not long before Zeneca stood out as the ideal partner (The Independent, 1998). This partnering was one of the largest-ever European mergers at the time and made the combined company into the fourth largest pharmaceutical company in the world. The merger also signalled the company's intention to strengthen its innovation and world market share in the long run.

The integration of the two companies' worldwide organizational activities post-merger called for some major structural changes and, consequently, led to the formation of a new group arrangement, whereby a much-widened geographical scale was realized. Specifically, while a new

focus was starting to be placed on the Asia Pacific, Latin America and the Middle-East as younger markets with greater growth potential in the long term, the USA, Canada and Europe remained the three largest and most mature markets for the group. Hence, across these six markets, the overall emphasis was still placed on the North and three worldwide strategic innovation centres in Sweden, the UK and the USA were responsible for the most advanced drug research for the Northern market. This period of operation can be characterized as a part of the North-North wave, with the main objective of HBKA-N. The next section focuses on exploring R&D activities of AZ in China in the context of the North-South, South-South, and South-North waves, and HBKE-S, LBKE-S, and HBKA-S objectives respectively.

Empirical findings: AstraZeneca's R&D internationalization in China, from 1993 to 2017

Three distinctive periods in AZ's internationalization of R&D activities in China can be identified. Below, we discuss each of these periods and the corresponding waves and innovation activities in more details.

Initial expansion in China (1993–2001): The North-South wave and HBKE-S

Since the announcement of 'open door' policy in 1978, China has carried out major economic reforms to move towards a more market-based system of trade and economic growth and to open up for foreign investments in low value-adding and factor-endorsed areas – a reflection of the abundance of low-cost labour and the absence of national innovation capabilities. This shift drastically accelerated China's economic expansion and was the deciding point for Astra to establish its first sales and marketing subsidiary in the country: Astra (Wuxi) Pharmaceuticals Co. Ltd, in Jiangsu Province, not far from Shanghai (Pederson, 2008; World Scientific, 2003).

Jiangsu was an ideal location for Astra for a number of reasons. First, in 1992, many parts of Jiangsu Province were turned into economic zones and Wuxi city established Wuxi New District – one of the largest industrial parks in China. The new district was known for providing strong support for international operations. Second, Jiangsu Province is ideally located next to

trade intensive regions, such as Zhejiang, and is home to hundreds of thousands of businesses. Third, the local government offered many incentives to attract FDI. Hence, the overall business environment of Wuxi made it the ideal location in China at the time of Astra's entry.

In the following year, Zeneca also entered China through a joint venture with Sinopharm, a state-owned corporation. Sinopharm, also known as China National Pharmaceutical Group Corporation, was the largest pharmaceutical and healthcare group in China at the time and already had a well-established network in the country. The initial agreement between Sinopharm and Zeneca was for the sole distribution of Zeneca's leading drugs at the time (Zeneca Group PLC Annual Report, 1994; Heathcote, 1994). Similar to Astra, this move was also an indication of Zeneca's attempt to enter into the Chinese market early as part of their global expansion strategy for existing products. One year into the agreement, Zeneca realized the huge potential of the Chinese market and established its own sales and marketing operations in 1995. Benefiting from the rapid economic growth in China in the following years, Astra and Zeneca both successfully positioned themselves in the Chinese market to be leaders in the sale of specific drugs. They also set up offices in over 20 major cities. However, Zeneca's Chinese joint venture demerged around the same time as Astra and Zeneca merged.

Following the merger between Astra and Zeneca, the new AZ embarked on its most significant Chinese venture at the time, i.e. an accumulative investment of US$270 million (in comparison to a US$121 million investment by GlaxoSmithKline around the same time) in building its first world-class production facility in Wuxi New District, where Astra's previous Chinese operations had been initiated (Chemical Market Reporter, 2001). The new production plant employed 600 workers and produced 95% of all AZ's products sold in the China. It is worth noting that whilst there are other pharmaceutical MNEs with local production facilities in China, AZ was seen to have the largest facility in terms of the scale of investment and the facilities created (Wall Street Journal, 2001; AstraZeneca Annual Report, 2001). This reflects a strong strategic emphasis on HBKE-S in the country and first sign of the North-South wave.

During this period, AZ also made its first investment in R&D in the country – another step under the North-South wave. Between 1996 and 2001, AZ undertook nine international

multicentre clinical trials in the respiratory field in China, with the involvement of over 130 domestic hospitals and institutions. By 2001, AZ had invested US$35 million in clinical trials and conducted 37 clinical research projects involving approximately 20,000 patients at more than 1,000 domestic medical sites. The objectives of these investments were to develop drugs that were effective for Chinese patients with specific diseases. To further its efforts in local innovation, AZ emphasized the importance of strategic partnerships with Chinese research institutions. For instance, AZ and Shanghai Jiaotong University launched a joint research project to investigate the genetic links to neuropsychiatric diseases (AstraZeneca Annual Report, 2001; China Daily, 2001).

Although the research-related activities during this period were not intended to include building its own innovation facilities, AZ was still one of the first foreign companies to commit to market expansion in the form of HBKE-S at the time. This move benefited the company for two reasons. First, China was considered a marketplace where mature drugs could still generate sales long after patent expiration. Second, the common practice in China for drug selection was that once particular branded drugs were accepted by the doctors and patients, there was a strong tendency to stick to them permanently (AstraZeneca Annual Report, 2010; China Food and Drug Administration, n.d.). Hence, the development pattern of this period signals a heavy overall strategic emphasis on market expansion through HBKE-S rather than any other R&D activities, possibly due to the weak institutional conditions at the time, such as the lack of availability of R&D resources and government support policies.

Second period of expansion in China (2002–2008): The South-South wave and LBKE-S

Since 2002, there were two major developments in China. One was the continuation of a series of innovation programmes by the government, including the International S&T Cooperation Program of China; National Key Technologies R&D Program; and the Torch Program for supporting commercialization of high tech products (China Ministry of Science and Technology, n.d.). The other was the fact that the country officially became a member of the World Trade Organization (WTO). This had two major effects – encouragement for increased inward FDI and greater transparency in legal protection for foreign investors. Consequently, AZ deepened its

innovation involvement in China (Ministry of Commerce, P.R.C., 2005; AstraZeneca Annual Report, 2008). Despite China being viewed by most foreign investors as a more attractive destination for production and sales rather than research, extensive local partnering (Table 4) and the establishment of its own Chinese-based research institutions demonstrated AZ's shift of focus in its operation in China from HBKE-S towards LBKE-S, which is indicative of the South-South wave.

Table 4. List of local partnerships

Year of Formation	*Chinese Partners*	*R&D Activities*
2003	Peking University's Guanghua School of Management	To fund the China Centre for Pharmacoeconomics and Outcomes Research
2007	Peking University Third Hospital	To set up the company's first Clinical Pharmacology Unit in the country
2007	Guangdong Provincial People's Hospital	To augment existing clinical research capabilities and to undertake Phase I clinical research
2008	Shanghai Institute of Materia Medica	To establish the Drug Safety Evaluation Joint Research Centre for speedy entry into the market
2008	Pharmatech Wuxi	To synthesize compounds to increase the overall collection of compounds

Specifically, AZ took a major step in 2003 by forming its most significant partnership at the time with Peking University's Guanghua School of Management to fund the China Centre for Pharmacoeconomics and Outcomes Research. This was the first in a series of research and educational programs aimed at supporting reform of China's healthcare system. During the first three years of the partnership, AZ provided over US$360,000 in sponsorship to help set up and establish research, advisory and training programs for government officials, hospital executives and pharmacy directors.

AZ took another major step in its local development by forming a strategic partnership with Peking University Third Affiliated Hospital in 2007 to set up the company's first Clinical Pharmacology Unit in the country (China Daily, 2007). In the same month, AZ and Guangdong Provincial People's Hospital jointly established a research laboratory with a focus on translational

science. The unit was intended to augment existing clinical research capabilities and undertake Phase I clinical research, including clinical pharmacology and safety evaluations – steps necessary for launching new medicines in China. This move accelerated the launch and patient access to new medicines in China. In 2008, AZ reached out to the Shanghai Institute of Materia Medica to establish the Drug Safety Evaluation Joint Research Centre in Shanghai Pudong Science Park of the Chinese Academy of Science. This was also intended to accelerate the speed to market for drugs in the country. In the same year, the agreement between AZ and Pharmatech Wuxi came to a successful end, achieving its intended targets two months ahead of schedule, but AZ decided to extend its contract with the company to continue to synthesize compounds according to AZ's designs to further expand the company's global compound collection.

In terms of establishing its own research institutions, AZ set a number of historical records. For example, AZ was the first company of its kind to launch a localized Clinical Research Unit for the East Asian region in Shanghai in 2002. The significant number of high quality medical talent available in the city was the reason for the location decision. The unit's aim was to oversee East Asian clinical research in mainland China, Hong Kong, Taiwan and Korea, with the clinical research conducted by more than 40 high-calibre Chinese researchers. This signalled that the country would become a critical component of AZ's future global trials and it had the potential to significantly reduce the time it took for drugs to be made available to Chinese patients (AstraZeneca Annual Report, 2002; Ministry of Commerce, P.R.C., 2005).

Another important development came in 2006 when AZ invested more than US$70 million in the establishment of the Innovation Centre China, which again was the first of its kind in the country (Ministry of Commerce, P.R.C., 2006; AstraZeneca Annual Report, 2006; China Pharmaceutical Industry Investment Promotion Report, 2014). It was also one of the most advanced scientific research centres of the Group outside of the UK, Sweden or the USA and provided firm evidence of the company's dedication to research in China, as well as its ambition to have a strong innovation presence in the region. Although the beginning of AZ China did not seem to suggest so, the formation of this innovation centre illustrated that this consideration played a major role in contributing to AZ's global knowledge base. Apart from innovation activities, AZ

further expanded its production scale in 2006 with an additional US$35 million investment in its Wuxi site, which also obtained China and European Union Good Manufacturing Practice certification for exporting to the European Union and other countries adopting the same standards. This development was the foundation of AZ China's important global role later.

In summary, by 2009, AZ employed more than 2,900 staff locally in China, had a network of more than 20 marketing and sales offices, a global manufacturing site in Wuxi, clinical research facilities and multiple collaborations and partnerships with local academic and medical institutions. Their major projects during this period reflected an emphasis not only on market expansion through HBKE-S, but also on LBKE-S to deepen its involvement in the Chinese market in the long run. Apart from improved institutional conditions (e.g. the availability of R&D resources and government support policies), the company's increased local knowledge and experience is likely to have been a reason for the changing emphasis.

Third period of expansion in China (2009–2017): The South-North wave and HBKA-S

This period witnessed the most significant development in terms of localized and global innovation. It also saw the strengthening of the Chinese government's policy and funding support for more advanced innovation activities, including National S&T Major Projects for priority industries, the National S&T Innovation Base Program for establishing new research laboratories and bases, and the establishment of the National Natural Science Foundation of China for improving the funding environment for basic research (China Ministry of Science and Technology, n.d.). During this period, AZ China deepened its involvement in LBKE-S but also initiated activities associated with HBKA-S. In seeking LBKE-S, AZ opened its new Chinese site in Shanghai Zhangjiang Hi-Tech Park (which was commonly known as 'China's Medicine Valley') in September 2009, which included AZ's new Chinese corporate headquarters for China and the Asia Pacific, its marketing operations, its Innovation China Centre, and academic training and regional functions. It became one of only three corporate headquarters of AZ PLC alongside the USA and the UK (AstraZeneca Annual Report, 2009; China Pharmaceutical Industry Investment Promotion Report, 2014). By the end of this financial year, AZ's accumulated sales in China were

more than US$800 million. AZ was confident that with a population of 1.3 billion in China, a burgeoning middle class and an increasing prevalence of Western-style diseases, the Chinese market offered the largest opportunity for growth, and was convinced that new product offerings were the way to further strengthen its position (Thomson Reuters, 2010).

Hence, in order to broaden and improve its product offerings, AZ continued its aggressive innovation localization in a number of ways. First, AZ strengthened its efforts in internal innovation capability building in China. For instance, by 2011, its Innovation China Centre had already built strong capabilities in translation sciences for oncology research for the Chinese market. As a result, the centre embraced the new mission to deliver candidate drugs and ultimate Proof of Concepts and valuable drugs to address the significant unmet medical needs of patients in China, such as for liver and gastric cancer (McKinsey Quarterly, 2012).

Second, AZ also brought in external capabilities to complement its core internal expertise already available at its China centre. One example was an acquisition agreement with a privately-owned generics manufacturing company (BeiKang Pharmaceutical Company Ltd) in 2011, which gave AZ access to a portfolio of injectable drugs used to treat infections suffered by Chinese and Asian patients (China Drug Review, 2012). This move reinforced the company's commitment to bringing original and high quality branded generic drugs to the Asia-region market to increase their accessibility and affordability for patients who were previously underserved.

More importantly, AZ continued to forge extensive and advanced research collaborations with local partners in China for medical breakthroughs. This move was made to not only address the medical needs of the Southern market, but also to seek opportunities to meet global market needs. A list of some of the major collaborations during this period is provided in Table 5. During this period, AZ China entered into several research collaborations for developing drugs for the global market. This move signalled AZ China's first move towards becoming a global contributor of innovation – the start of the South-North wave. For instance, in 2011, AZ and Chi-Med China joined together to co-develop and commercialize a novel cancer therapy called Volitinib (which later turned out to be successful) and, in 2014, it signed an agreement with Tianjin Medical University for cardiovascular research collaboration to explore novel targets against cardiac

fibrosis. Meanwhile, products such as Tagrisso and Brilinta were the outcomes of R&D collaboration between AZ China and AZ's R&D sites worldwide (Greig, 2016; Zhou *et al*., 2017). By the end of 2014, AZ had recorded over 1,500 patents with the State Intellectual Property Office in China (SIPO, 2015). Thus, the increased product offerings and strengthened research collaborations with local partners in the third period show a greater emphasis on local innovation for the local and global markets. This was built on more favourable local conditions and AZ's greater local knowledge and experience.

Table 5. List of collaborations

Year	*Means of Innovation Activity*	*Purpose of Innovation Activity*	*Target Market*
2010	Partnership agreement with Peking University	Discovery and development of new treatments for diabetes, obesity and atherosclerosis	Chinese and global patients
2010	Partnership agreement with No. 1 Affiliated Hospital of Guangzhou Medical College	Basic research on chronic obstructive pulmonary disease	Chinese patients
2010	Research collaboration with BioDuro Clinical Research	Discovery research in respiratory and inflammatory diseases	Chinese and global patients
2011	Research collaboration with Chi-Med China	Development and commercialization of a novel cancer therapy called Volitinib	Global patients
2012	Partnership agreement with WuXiAppTec, and support from AZ's US biotech subsidiary Medimmune	Development and commercialization of a novel biologic for autoimmune and inflammatory diseases	Chinese patients
2012	Research collaboration with Ironwood Pharmaceuticals, Inc.	Development and commercialization of linaclotide for irritable bowel syndrome with constipation and chronic idiopathic constipation	Chinese and global patients
2014	Research collaboration with Shenzhen University Health Science Centre	Pre-clinical research on chronic kidney disease	Chinese patients
2014	Partnership agreement with Tianjin Medical University	Cardiovascular research to explore novel targets against cardia fibrosis	Global patients
2016	Partnership agreement with WuXiAppTec	Advanced research for addressing respiratory, inflammation and autoimmunity, cardiovascular and metabolic diseases, and oncology	Chinese and global Patients

2017	Strategic joint venture (namely Dizal Pharmaceuticals) with Future Industry Investment Fund China	Discover, develop and commercialise new medicines	Chinese and Global patients

(*Source*: www.astrazeneca.com/partnering; China Food and Drug Administration; ThomsonReuters)

From 2016 onwards and in alignment with the introduction of the Healthy China 2030 initiative (Biopharmadive News, 2018; Tan *et al*., 2017), AZ undertook several major advanced R&D projects which further reflect the importance of China as an important R&D location for meeting the needs of both Chinese and global markets. An example worth noting is the strategic alliance AZ formed with WuXi AppTec to produce next-generation medicines by undertaking advanced research in the area of new small molecule development, which is part of AZ's global R&D network and core to AZ PLC (Washington Business Journal, 2017). This project aimed to address the needs of both Chinese and global patients in the main therapy areas of respiratory, inflammation and autoimmunity, cardiovascular and metabolic diseases, as well as oncology. This partnership required not only financial investment but also recruitment of at least 50 world-class scientists to establish a new R&D hub for small molecule research, making China an important location alongside AZ's UK and Sweden R&D centers (AstraZeneca Annual Report, 2016; Financial Times, 2016). By 2017, AZ showed a further 7% growth in sales compared to its competitors. In 2017 alone, a number of key developments took place, illustrating the increasingly important role of AZ China in the global innovation network. For one, the formation of the strategic joint venture of Dizal pharmaceuticals with the Future Industry Investment Fund for discovery, development, and commercialization of new medicines for unmet global needs cemented the expansion of AZ's R&D in China. This occurred at a time when AZ's competitors were consolidating their operations by closing major R&D facilities (Fiercebiotech News, 2017). In late 2017, the research collaboration with Chi-Med led to a global clinical trial for a rare type of kidney disease found worldwide (Chi-Med, 2017; Reuters, 2017). Further, the research collaboration with Ironwood Pharmaceuticals, Inc. led to an application to the China Food and Drug Administration for the development and marketing of linaclotide (Ironwood, 2018), whereas the launch of PT010 for COPD and asthma in China and Japan, ahead of their launch in Europe and the USA, signalled the rise of China as a strategic location for knowledge creation

(Fiercebiotech News, 2017). Most recently, AZ China responded to Chinese institutional reforms in the implementation of the 'digital China strategy' by initiating collaborations with Wuxi National Hi-Tech District and Jiangsu Mobile as well as with China's technology giants, Tencent and Alibaba, to provide 'smart' healthcare services driven by artificial intelligence and internet-enabled technologies (Biopharmadive News, 2018; China Daily News, 2018).

To summarize the three periods analyzed above, Figure 2 illustrates the major changes in AZ's activities in China between 1993 and 2017. In the context of the proposed waves framework (Figure 1), we can identify a case-informed evolutionary pattern. Period one can be characterized as the North-South wave for the main purpose of market expansion through HBKE-S, reflecting a market-seeking motivation. Period two maintained activities of period one while the focus shifted to LBKE-S for meeting distinct local and regional market demands, a reflection of the South-South wave where knowledge-seeking activities emerge. Finally, period three maintained activities of the first two periods while the focus shifted to HBKA-S for meeting global market demand, a reflection of the South-North wave. This became a new variant of knowledge-seeking activities aimed at developing and producing new products that were expected to supply the global market.

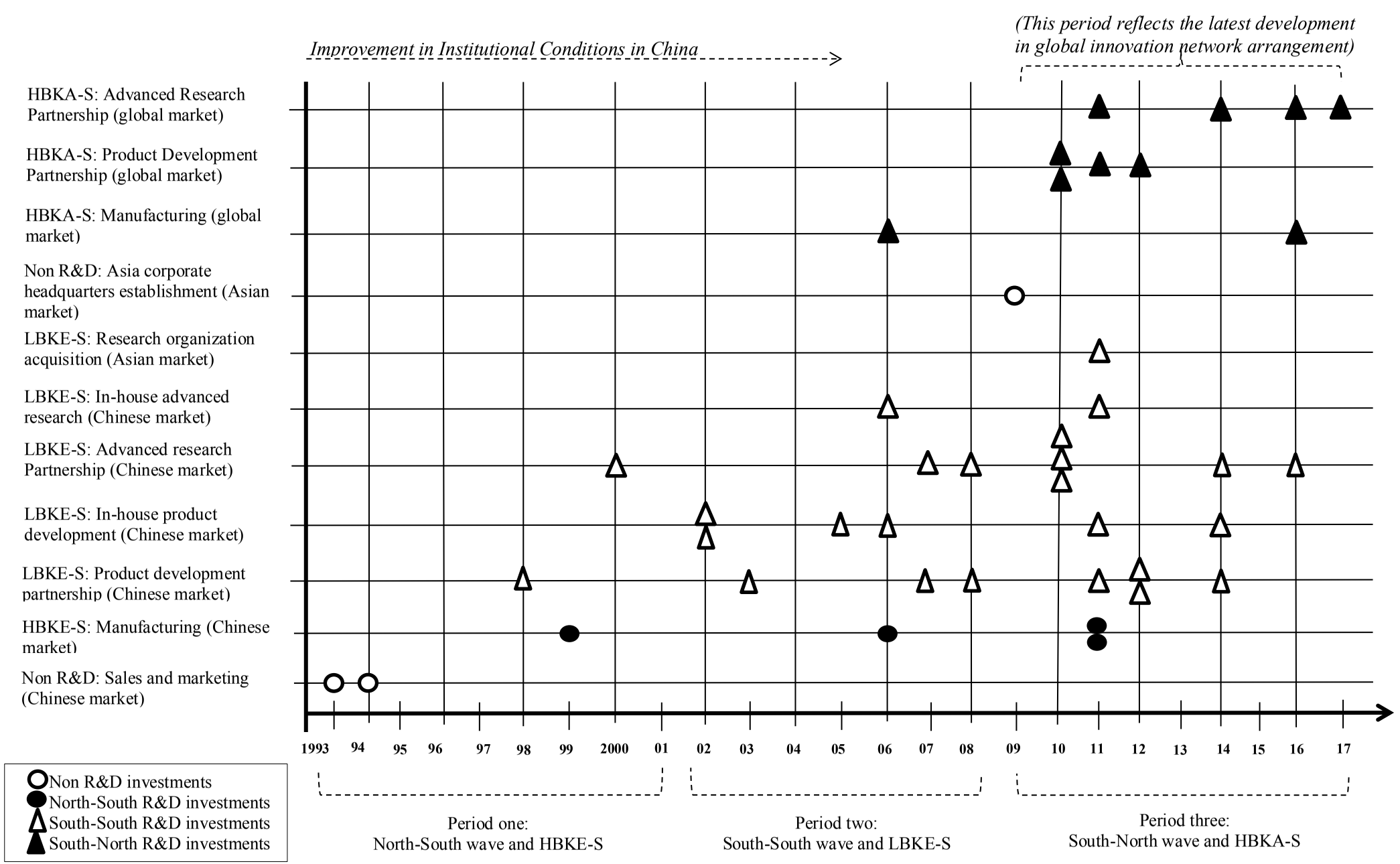

Figure 2. R&D activities of AZ China between 1993 and 2017

Discussion and conclusion

AZ's R&D Evolution in China

Having presented AZ's innovation activities in China in three consecutive periods over the course of more than two decades, we now reflect on each of the three major waves and the overall evolution pattern identified in the case study in light of the proposed framework (Figure 1). We highlight our key findings in order to develop new insights into the latest development in R&D internationalization towards the South.

Period one (North-South wave and HBKE-S): During the period of 1993 to 2001, China remained a location with two distinct characteristics: an emerging market and an abundance of low-skilled labour for low-cost production. Furthermore, we highlighted that although China became a location for AZ's R&D activities, these activities were mainly an 'operational necessity' (Bartlett and Beamish, 2013; Cantwell, 1992; Pearce and Papanastassiou, 1997) and were restricted to product and production-related HBKE-S (Kuemmerle, 1999; Bas and Sierra, 2002; von Zedtwitz and Gassmann, 2002; Liu and Chen, 2012). It could be argued that findings from this period also reflected the wider environmental conditions in China at the time, which could be characterized as having significant weaknesses in the institutional conditions for more advanced R&D activities. During this period, the country showed little or no signs of the availability of R&D resources or supportive government policies.

Specifically, our case study findings show that most of the activities of AZ China during this period were related to assimilating knowledge transferred from the headquarters and modifying existing products to meet the local market conditions in China through extensive localized clinical trials. These activities of product adaptation and localization were achieved in the form of in-house R&D support and collaboration with local Chinese hospitals to ensure safety and suitability of drugs to Chinese patients. Similarly, Zhang and Pearce (2010) and Zhang *et al.* (2018) note that market-seeking subsidiaries in China incorporated a strong element of product adaptation in local operations. Thus, in order to meet the idiosyncratic demand conditions in China, local sourcing of technology became an essential precondition. Furthermore, our empirical

findings also concord with the works of Schmiele and Mangelsdorf (2009) and Liu and Chen (2012) in that MNEs can gain economic returns from utilizing their existing proprietary knowledge (generated in AZ's global R&D centres) in overseas locations (in this case, China).

Hence, we argue that AZ's internal motive for entering China during this period was market expansion, which was strongly facilitated by two co-existing factors at the time: ownership advantages and local conditions (Dunning, 1998; Bartlett and Beamish, 2013). Specifically, the long-established R&D base in the North provided AZ the knowledge-based competitive advantages it needed to target markets of the South in pursuit of market-seeking investments (Cantwell *et al.,* 2010; Kuemmerle, 1999). In contrast, indigenous firms in China were severely lagging behind in terms of innovation. At the same time, China's economic liberalization started to show positive signs, such as growing consumption (Fan and Wang, 2001). This development in the local institutional conditions provided AZ with the opportunity to potentially take over the market by way of offering drugs that were produced with knowledge from the North and labour from the South.

Period two (South-South wave and LBKE-S): Whilst AZ continued to further invest in market expansion activities in China during this period (2002-2008), benefiting from fast economic growth, the company also showed first signs of local-based R&D activities. That is, on top of its existing R&D activities relating to local adaptation in period one, the company initiated new projects into advanced drug testing and discovery specifically targeted at local diseases in China. This is in line with the work of Zhang and Pearce (2012) who find that MNEs in China are not solely receivers of headquarters knowledge, but also generators of new knowledge by working closely with local universities, firms, and research institutions in their effort to augment their market-seeking activities. Following our proposed framework, this development in the case of AZ China signals an important evolutionary step along the continuum of AZ China's pattern of R&D internationalization, where the North-South wave (identified in period one) shifts towards the South-South wave through LBKE-S. China, as an exemplar of the South, is no longer viewed only as a source of low-cost labour, but also a new source of R&D knowledge (Awate *et al*., 2015; Jha *et al*, 2015; von Zedtwitz *et al*., 2015). Knowledge-seeking in the South emerges as a priority for

the company in this wave. Subsidiaries in the South have started to play the role of generating new knowledge, as also evidenced by Zhang *et al*. (2018: 10) who indicate that "*the main sourcing of new technologies is thus expected to be well diversified and come primarily from the [emerging-economy] subsidiary… as well as from subsidiary collaborations with local firms and research institutions*".

The case of AZ China thus shows that this period could be characterized as the seeking and development of knowledge useful in providing new products to the local market. There are two fast-changing forces that contribute to this trend: improvements in both market and institutional conditions in China. In terms of market conditions, the growing market demand and limited availability of effective products called for localized innovation. In terms of institutional conditions, increased availability of R&D resources and supportive government policies provided better conditions for undertaking localized innovation. The imperative to adapt to specific conditions in the Chinese market also concords with the propositions by Zhang and Pearce (2010) that suggest a variant of market-seeking investments whose aim was to allow for the adaptation of these technologies "*to local tastes or needs, to cultural mores and to indigenous resources and capabilities*" (Dunning and Lundan, 2008:70). Though such adaptation also occurred in period one, the way it was implemented at the subsidiary level in period two, and the different sources of technology that were invoked to secure it, may establish a more important role. For instance, our findings show that AZ was able to benefit from increased availability of high quality local medical talent and set up many R&D collaborations with local universities and firms, facilitated by government initiatives. Our findings further show that AZ's localized innovation in China enabled the company to better understand local diseases, conduct trials, and produce more effective drugs for Chinese patients. Consequently, the company was able to retain a secure market share and sustainable economic returns.

Hence, we argue that although AZ's internal motive for continuing to establish itself in China during this period was local responsiveness, this was achieved through knowledge-augmenting rather knowledge-exploiting R&D (Bartlett and Beamish, 2013; Dunning and Narula, 2005). Specifically, the long-established R&D base in the North was no longer the sole source of

competitive advantage (Kuemmerle, 1997). Instead, working with local counterparts during period one enabled AZ to learn more about both the market and the institutional environment (Zhang and Pearce, 2012). Local knowledge access thus became an important channel for enhanced ownership advantage. While in the first period there is a clear dichotomy between MNE ownership advantages (in the form of established home-based knowledge inputs transferred to China) and location advantages (in the form of distinctive demand conditions and the supply of cheap labour and technical skills), the enhanced ownership advantage was the outcome of the interactive collaboration between the company and local knowledge sources, aiming at knowledge-seeking investments (Bartlett and Beamish, 2013). Demand for better products increased significantly in this wave whilst upgrading of knowledge capabilities and improvement of China's legal framework also progressed well. Thus, AZ's shifting internal motive was facilitated and supported by the dynamic and interdependent evolution in ownership and location advantages contributing towards "*the dynamic competitiveness and locational strategy of firms, and particularly the path dependency of the upgrading of their core competencies*" (Dunning, 2000:167).

Period three (South-North wave and HBKA-S): The analysis of period three (2009-2017) data shows the most striking development of AZ China to date. The company intensified its South-South and LBKE-S commitment by innovating for not only China, but also the wider Asian region, both through utilising its existing internal R&D capabilities as well as by collaborating with and acquiring local companies (e.g. Beikang Pharmaceutical Company Ltd). More significantly, during this period, the company showed the first signs of undertaking world-leading R&D for the purpose of addressing knowledge gaps in drug discovery for some of the world's most complex and challenging diseases (via its Innovation China Centre). This finding is in line with existing literature, which suggests that MNEs establish R&D units in locations where they can access host countries' knowledge for their headquarters (Asakawa and Som, 2008). The main objective of these units is to engage in knowledge sourcing and benefit from potential knowledge spillovers (Almeida and Kogut, 1999; Feinberg and Gupta, 2004). At this point, the South-North wave and HBKA-S in support of the development of complementary and novel knowledge for the global market became evident. This development supports the work of Govindarajan and Ramamurti

(2011), Govindarajan and Trimble (2012) and Jha *et al*. (2015) in that R&D units under the South-North wave display the development of long-term innovative capabilities by taking advantage of novel or complementary knowledge in foreign locations. In the case of AZ China, this development shows that MNE subsidiaries located in non-conventional locations can gradually develop strong innovation capabilities and evolve towards being a more active and differentiated player in MNEs' global innovation networks (Mudambi and Santangelo, 2016). We argue that the likely cause of this evolution - as reflected in the AZ China case - is further accumulation of the firm's knowledge on how to best maximize the opportunities offered by improved institutional conditions, such as local R&D firms, R&D talents and preferential policies. For example, our findings of AZ China show that the development of its distinct knowledge base is contingent upon the availability of local R&D resources. The company was able to form long-term partnerships with local universities (e.g. Tianjing Medical University) and research institutions (Chi-Med China), and strategic joint ventures with government funding bodies (Dizal Pharmaceuticals), filling knowledge gaps in the existing global pharmaceutical market. This concords with Liu and Chen (2012) in that a MNE host-country R&D mandate in the South is likely to be influenced by the changing local conditions, changes that in the AZ case had much to do with increased efforts of national and local governments to establish pro-innovation support (Archibugi and Iammarino, 2002; Lundvall, 1992; 2007). This is evidenced by their investment in higher education and training of R&D personnel (e.g. AZ was able to utilize a skilled scientific personnel available in various hospitals and research institutions), the development of science clusters (e.g. AZ was able to benefit from locating in China's Medicine Valley of Shanghai Zhangjiang Hi-Tech Park), and specific policy support (e.g. AZ was able to deepen its involvement in the development of China's national healthcare system with the strong support and facilitation from the government). Another recent investment AZ China made was in the smart healthcare services by collaborating with local technological firms. With respect to AZ's R&D evolution in China during the third period, it is thus fair to argue that the North-and-South location hierarchy for MNE R&D activities is flattening. The South is seen to become an important part of MNEs' global innovation network for knowledge augmentation (Chen, 2004; Liu and Chen, 2012).

Hence, we argue that AZ's internal motive for deepening its involvement in China during this period was worldwide learning (Bartlett and Beamish, 2013; Zhang *et al*., 2018). This strategic shift from market expansion (as found in period one) and local responsiveness (as found in period two) can be attributed to further changes in ownership advantages and local conditions when compared to the two earlier periods. Through the launch of a series of national S&T programmes, a supportive and attractive National Innovation System (NIS) was promoted. Campbell (2013:4) notes that *"the private sector (or semi-private sector) has now taken the lead in innovation from SOEs, and relies on foreign funding along with government support for technology projects. Government-supported research institutions are now spread throughout the country, but innovation leadership in key centers, especially Beijing, Shanghai, and Guangzhou, has passed to private firms"*. It was clear that in such a supportive environment AZ was able to gain local knowledge at a greater scale and scope than before, and combine local and global knowledge for enhanced worldwide ownership advantages. It provided AZ the knowledge-based competitive advantages it needed to target not only the Chinese, but also the global market.

In summary, the discussion of the three consecutive waves of innovation activities in the case of AZ China clearly suggests a dynamic and path-dependent pattern (from North-South to South-South, and to South-North) that concords with our proposed framework (Figure 1). The contextual details of each period reveal evidence that AZ's initial intention of setting up operations in the South (in this case China) was not concerned with strategic knowledge sourcing. It was only through both market and institutional transformation and organizational learning that innovation activities started to be considered seriously (Campbell, 2013). In this very case, our findings imply a possible developmental pattern of co-evolution that has taken place between AZ China and China's various institutions. Drawing on the co-evolutionary perspective (Rodrigues and Child, 2008; Cantwell *et al*., 2010; Child *et al*., 2012), we showed that under conditions of limited organizational knowledge and weak institutions, the activities of AZ China started with the necessary knowledge transfer from headquarters for local production in the early period. This process also 'naturally' contributed to the innovation capability of local counterparts who were involved in AZ's operations in China at the time. As market and institutional conditions improved

(particularly with much stronger involvement and support from the Chinese government) during the second period, innovation activities were upgraded to encompass localized product development and customization for the Chinese market. Meanwhile, this deepening relationship between China and AZ resulted in the Chinese environment becoming increasingly supportive to AZ in the way of new opportunities. This in turn led AZ to invest more capital in China in order to develop R&D capabilities, creating a two-way development pattern for both the Chinese pharmaceutical industry and AZ China. During the most recent period, apart from continuous improvement in market and institutional conditions, AZ's deepened involvement in, and knowledge of, China enabled the company to undertake novel and complementary R&D activities to meet global market needs. At the same time, AZ China contributed to the Chinese pharmaceutical industry's innovation capability development with the support and opportunities offered by the government.

The empirical evidence of the three periods (Figure 2) illustrates that each period is contingent upon the preceding period and AZ's relationship with China. The explanation for this gradual development is likely to be twofold. First, at the firm level, factors such as organizational experience and knowledge of the host-country environment are likely reasons for AZ's growing confidence and R&D commitment in China. At the locational level, factors such as changes to market and institutional conditions of the host country are another likely contributor to the evolution of AZ's R&D activities in China.

In other words, drawing on the co-evolutionary perspective (Rodrigues and Child, 2008; Cantwell *et al*., 2010; Child *et al*., 2012), the AZ China case demonstrates the importance of the linkage between local conditions (external factors) and firm knowledge and motives (internal factors) as potentially co-existing determinants of R&D-related FDI in the South. The local market potential and production benefits in period one attracted AZ to set up sales and manufacturing operations in China, benefiting from HBKE. As AZ became more embedded in the local market with improved market knowledge and an increasingly innovative institutional environment (particularly with the introduction of national S&T programmes), they were able to utilise some of their established local networks (such as partnerships with local hospitals and universities) to carry

out higher-value-adding R&D activities. The strategic objective for AZ China thus shifted towards LBKE-S during period two. Further deepening of AZ's relationship with local counterparts (local firms, research institutions, hospitals, universities, and patients) and continuously improving institutional conditions (government support such as the innovation programmes introduced in period two and three) provided AZ China the opportunity to start seeking HBKA-S during period three. Each of the three periods was successful in achieving AZ's objectives in China and success in each period paved the way for the next period as both firm knowledge and the local environment continuously improved. Thus, we argue that it is the necessary complementarity between internal firm knowledge and the external local environment that has influenced AZ's objectives and performance in China throughout the three periods. The AZ case thus perfectly illustrates the co-evolutionary developmental pattern introduced by prior research (Rodrigues and Child, 2008; Cantwell *et al*., 2010; Child *et al.,* 2012).

Contributions to R&D internationalization theory and literature

Our longitudinal case study of AZ's historical development over the past two decades, with specific reference to the context of China, has offered a rich, contextualized example of a possible emerging pattern in MNE global innovation network arrangements. It can be argued that R&D internationalization by MNEs of the North to economies in the South is too idiosyncratic to be explained by established theories. Most of current understanding is predominantly rooted in the context of advanced economies and far fewer studies have explored the contextual details of R&D evolution from the perspective of the South. Against this background, our study makes a number of relevant contributions.

First, we contribute to the current literature on MNE global innovation networks by constructing a framework that integrates four distinct waves and corresponding R&D objectives to create a more complete picture of the internationalization of R&D (Table 1). Prior developments in an advanced-economy context did not offer the opportunity or need for such definitions. However, the recent shift towards knowledge sourcing from new locations in the South makes such a systematic classification important to inform future research. Moreover, our case study findings are

found to concord with the four major waves and the corresponding R&D objectives. Furthermore, whereas in general, North-centric waves (i.e. North-North and North-South) are established phenomena, research addressing South-centric waves (South-South and South-North) is only recently emerging (e.g. Awate *et al*., 2015; Jha *et al.,* 2015; Jha *et al*., 2018; Liu and Chen, 2012) and still sparse. Hence, our historical longitudinal case study of AZ in China presents new evidence to underpin further discussions on South-centric waves.

Second, we contribute to current theories of MNE R&D internationalization by constructing an overarching conceptual framework (Figure 1) depicting an evolving pattern of MNE R&D activities shifting from the North to the South. The concordance between the waves framework and our case study findings (summarized in Figure 2) suggests that the R&D internationalization pattern is composed of three consecutive (and mutually inclusive) shifts in MNE objectives and operations, from HBKE-S (North-South wave) to LBKE-S (South-South wave), and to HBKA-S (South-North wave). The conceptual framework extends our current thinking in understanding the overall development of the MNE global innovation network arrangement by incorporating the latest trends of R&D in the South (Govindarajan and Ramamurti, 2011; Dhanaraj, 2016). Our study highlights a multi-layered and ever more globalized innovation network arrangement in MNEs in search of sustainable competitive advantages. Additionally, it also reveals the possible role of MNE organizational experience and knowledge in capturing local opportunities offered by the fast-changing market and institutional conditions in the Southern economies.

Our third contribution lies in the context of our study, whereby we focused on China by applying a historical lens to exploring this location for MNE R&D. Whilst China is known to represent unique opportunities for MNEs, to our knowledge no studies have traced the evolution process of R&D by an MNE in the country as closely as we did. Our article is one of the few to apply a longitudinal case study approach to reveal contextual details of R&D evolution in the South. In line with Meyer *et al*.'s (2011) and Liu and Chen's (2012) views on locational differences and the exemplar offered by Wang *et al*. (2012), we offer insights into the idiosyncratic transitions in China from 1993 to 2017, reflecting its importance and distinctiveness as a research

context. Hence, our study highlights the need to appreciate contextual differences among the Southern economies when studying R&D internationalization.

Finally, our article contributes to the recent methodological discussions on qualitative research (e.g. Doz, 2011; Welch *et al*., 2011). In particular, we illustrate the suitability of a historical longitudinal approach and a single case study design in exemplifying 'context' in qualitative research. The case of AZ China illustrates one way of conducting contextually rich research when the target phenomenon is new or difficult to study (e.g. because of company secrecy). The richness of contextual details revealed in this article offers useful empirical insights, and we therefore call for more research to adopt a similar approach to investigating new developments in international business. This is in concert with Verbeke and Kano's (2015:415) suggestion that: *"A business history lens can illuminate the behaviour of developed-economy multinationals"*.

Managerial implications

Our article also has a number of managerial implications. For one, the success of AZ China highlights the potential importance of changing institutional conditions in the case of Southern economies, as well as the possible role of time and experiential knowledge in understanding and deepening R&D-related involvement in the host country. Thus, an important lesson to be learned by other MNEs wishing to tap into the knowledge pool of the Southern economies (such as China) is not to rush into making major R&D commitments at the outset, but instead, to proceed through a more gradual process of learning and trial and error. Whilst many MNEs might have some prior operating experience in the South, the national innovation environment is likely to be constantly changing and therefore should be considered as a completely new territory, requiring effective and accumulated learning. A more incremental approach allows for sufficient time to gain a better understanding of the availability of R&D resources, government support policies, and ways to establish and maintain effective partnerships with local research counterparts.

Limitations and recommendations for further research

Despite its important contributions, our study has several limitations that suggest avenues for future research. First, there are some common concerns associated with our case study design. Despite following a methodological approach found in other studies, the use of a single longitudinal case has the limitation that it reflects the development of the chosen case per se and therefore should always be very carefully considered in relation to others (Child et al., 2012). It is thus likely that another case would reveal a somewhat different picture to the narrative we provided in the present article. However, our initial objective was not to provide generalizable outcomes, but rather to offer a contextually rich analysis of a particular case in light of the recent developments, and based on this, to construct a conceptual framework that can serve as a springboard for future research to investigate this increasingly important topic. To extend our understanding of innovation in the South, it would be of great value if future research could explore the actual mechanisms of the evolution process, as well as the key success factors for the internationalization of R&D towards the South. It would also be insightful to investigate the implications of the South-North wave on MNEs, institutions, and countries, as this wave of development makes the global innovation scene much more complex. Next, it would be interesting to see whether or not AZ China's evolutionary pattern has been followed by other MNEs in either China or other Southern economies. Although we do not see AZ's innovation activities in China as an oddity or outlier, as figures from UNCTAD (2012; 2016) and a study by D'Agostino (2015) clearly show a strong trend of innovation FDI inflows to the South, whether other MNEs have adopted a similar approach in their engagement with Southern economies is an interesting question to pursue. Confirmatory studies (based on larger samples) or comparative studies (across industries or countries) informed by our research findings would be a useful empirical extension of the present study. We hope that the clear delineation of the R&D internationalization waves in our study, using the North and South paradigm, will motivate further empirical research to generate new insights into the global innovation network arrangement of MNEs.

In conclusion, using a detailed historical case study, we presented a contextually rich story of the evolution of an MNE's innovation activities in a Southern economy and evidenced the fast-

growing importance of Southern economies as a new destination for knowledge sourcing. We revealed subsequent waves of North-South, South-South, and South-North in the case of AZ China and identified the latest evolutionary pattern of MNE internationalization of R&D, from North-South (HBKE-S) to South-South (LBKE-S), and to South-North (HBKA-S). We argue that this development has critical strategic implications for the configuration of MNE global innovation networks, as they leverage the availability of lower-cost R&D personnel in the South for local, regional, and global competitiveness.

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References

Abbott, A. (2001) *Time Matters: On Theory and Method*, University of Chicago Press: Chicago

Almeida, P. & Kogut, B. (1999) Localization of knowledge and the mobility of engineers in regional networks, *Management Science,* 45 (7), 905–917.

Altenburg, T., Schmitz, H. & Stamm, A. (2008) Breakthrough China's and India's transition from production to innovation. *World Development,* 36(2), 325–344

Archibugi, D., & Iammarino, S. (2002). The globalization of technological innovation: definition and evidence. *Review of International Political Economy*, *9*(1), 98-122.

Asakawa, K. (2001) Organizational tension in international R&D management: the case of Japanese firms. *Research Policy,* 30 (5), 735–757.

Asakawa, K. & Ashok, S. (2008) Internationalization of R&D in China and India: Conventional wisdom versus reality. *Asia Pacific Journal of Management,* 25, 375–394.

Asia Pacific Biotech News (2001) *AstraZeneca Opens Its Biggest Asian Plant in China*, 5 (10), 179

AstraZeneca PLC (2000 – 2017) *Annual Reports*, AstraZeneca PLC Publications

Athreye, S., Batsakis, G., & Singh, S. (2016) Local, global, and internal knowledge sourcing: The trilemma of foreign-based R&D subsidiaries. *Journal of Business Research*, *69*(12), 5694-5702.

Awate, S., Larsen, M. M., & Mudambi, R. (2015) Accessing vs sourcing knowledge: A comparative study of R&D internationalization between emerging and advanced economy firms. *Journal of International Business Studies*, 46(1), 63-86

Bas, C.L. & Sierra, C. (2002) Location versus home country advantages in R&D activities: some further results on multinationals' locational strategies. *Research Policy*, 31 (4), 589–609.

Bartlett C.A. & Beamish, P.W. (2013) *Transnational Management: Text, Cases & Readings in Cross-Border Management* (7th ed.), McGraw-Hill/Irwin: Burr Ridge, Illinois.

Bernstein Research (2009) *Global Pharmaceuticals: Emerging Markets Should Infuse Badly Needed Revenues for Years to Come*, Bernstein Global Wealth Management: Black Book, 99-104

Biopharmadive News (2018) *AstraZeneca Pins Its Hopes on China*, Published on 02/02/2018, Available at [www.biopharmadive.com]

Bruche, G. (2009) The emergence of China and India as new competitors in MNCs' innovation networks. *Competition & Change,* 13 (3), 267–288.

Cano-Kollmann, M., Cantwell, J., Hannigan, T. J., Mudambi, R., & Song, J. (2016) Knowledge connectivity: An agenda for innovation research in international business. *Journal of International Business Studies*, *47*(3), 255-262

Cantwell, J. (1992) The internationalization of technological activity and its implication for competitiveness. In: Grandstrand, O., Hakanson, A., Sjolander, S. (Eds.), *Technology Management and International Business: Internationalization of R&D and Technology*. John Wiley & Sons: Chichester.

Cantwell, J., Dunning, J. H., & Lundan, S. M. (2010) An evolutionary approach to understanding international business activity: The co-evolution of MNEs and the institutional environment. *Journal of International Business Studies*, *41*(4), 567-586

Cantwell, J. & Iammarino, S. (1998) MNCs, technological innovation and regional systems in the EU: Some evidence in the Italian case. *International Journal of Economics of Business*, 5 (3), 383–408.
Cantwell, J. & Janne, O. (1999) Technological globalization and innovative centres: the role of corporate technological leadership and locational hierarchy. *Research Policy,* 28 (2/3), 119–144.
Cantwell, J., & Piscitello, L. (2000) Accumulating technological competence: its changing impact on corporate diversification and internationalization. *Industrial and Corporate Change*, 9 (1), 21-51
Cantwell, J. & Santangelo, G.D. (1999) The frontier of international technology networks: sourcing abroad the most highly tacit capabilities. *Information Economics and Policy*, 11, 101–123.
Cantwell, J., Dunning, J. H., & Lundan, S. M. (2010) An evolutionary approach to under-standing international business activity: The co-evolution of MNEs and the institutional environment. *Journal of International Business Studies*, 41(4), 567-586
Castellani, D., & Zanfei, A. (2006) *Multinational firms, innovation and productivity*. Edward Elgar Publishing: London
Castellani, D., Jimenez, A., & Zanfei, A. (2013) How remote are r&d labs? Distance factors and international innovative activities. *Journal of International Business Studies*, *44*(7), 649-675.
Child, J., Rodrigues, S. B., & Tse, K. K. T. (2012) The Dynamics of Influence in Corporate Co-Evolution. *Journal of Management Studies*, *49*(7), 1246-1273.
Coe, D. T., Helpman, E., & Hoffmaister, A. W. (1997) North-South R&D Spillovers. *The Economic Journal*, 107(440), 134–149
Cornet, M. & Rensman, M. (2001) The location of R&D in the Netherlands: Trends, determinants and policy. *CPB Netherlands Bureau for Economic Policy Analysis*, Van Stolkweg 14.
CBS News (2009) *AstraZeneca Moves Drug Production to China, Begging Safety Questions for FDA*, Published on 27/11/2009, Available at [www.cbsnews.com]
Chemical Market Reporter (2001) *AstraZeneca Opens Plant in China*, 259 (19), 14-15
Chemical Week (2007) *AstraZeneca Expands in India and China*, 04/04/2007
Chen, S. H. (2004) Taiwanese IT firms' offshore R&D in China and the connection with the global innovation network. *Research Policy*, *33*(2), 337-349.
Chi-Med (2017) Chi-Med and AstraZeneca Initiate SAVOIR, a Global Phase III Trial of Savolitinib in Papillary Renal Cell Carcinoma, Chi-Med News, 29/06/2017
Child, J., Rodrigues, S. B., & Tse, K. K. T. (2012) The Dynamics of Influence in Corporate Co‐Evolution. *Journal of Management Studies*, 49(7), 1246-1273.
China Daily News (2018) Innovation at the heart of development, published on 24/05/2018, available at [http://europe.chinadaily.com.cn]
China Food & Drug Administration (n.d.) *Domestic and Imported Drug Database*, China Food and Drug Administration
China Ministry of Science and Technology (n.d.) S&T Programs, Ministry of Science and Technology of the People's Republic of China
Cook, T. D., & Campbell, D. T. (1979) *Quasi-experimental design: Design and analysis issues for field settings.* Skokie, Il: Rand McNally.
Creamer D. (1976) *Overseas Research and Development by United States Multinationals, 1966-1975*. The Conference Board: New York
Demirbag, M., & Glaister, K. W. (2010). Factors determining offshore location choice for R&D projects: A comparative study of developed and emerging regions. *Journal of Management Studies*, 47(8), 1534-1560.
D'Agostino, L. M. (2015). The neglected effects of R&D captive offshoring in emerging countries on the creation of knowledge at home. *Economia e Politica Industriale*, *42*(1), 61-91.
D'Agostino, L. M., & Santangelo, G. D. (2012) Do overseas R&D laboratories in emerging markets contribute to home knowledge creation?, *Management International Review*, *52*(2), 251-273.

Dhanaraj, C. (2016) Academy of International Business Conference call for paper: The locus of global innovation, Available at https://aib.msu.edu/events/2016/callforpapers.asp], accessed on 02/01/2016
Dodgson, M. (2009). Asia's national innovation systems: Institutional adaptability and rigidity in the face of global innovation challenges. *Asia Pacific Journal of Management*, *26*(3), 589-609.
Doz, Y. (2011) Qualitative research for international business. *Journal of International Business Studies*, *42*(5), 582-590
Dunning, J. H. (1958) American investment in British manufacturing industry, Ruskin House: California
Dunning, J. H. (1993) *Multinational Enterprises and the Global Economy*, Wokingham, Berkshire: Addison Wesley
Dunning, J. H. (1998) Location and the multinational enterprise: a neglected factor?. *Journal of International Business Studies*, 29(1), 45-66.
Dunning, J. H. (2009). Location and the multinational enterprise: a neglected factor?. *Journal of International Business Studies*, *40*(1), 5-19.
Dunning, J. H., & Lundan, S. M. (2008). *Multinational Enterprises and the Global Economy*. Edward Elgar Publishing.
Dunning, J. H. & Lundan, S. M. (2009) The internationalization of corporate R&D: a review of the evidence and some policy implications for home countries1. *Review of Policy Research*, *26*(1-2), 13-33.
Edler, J. (2007) Internationalization of R&D empirical trends and challenges for policy and analysis, *Paper of Prime 3rd Annual Conference*, Pisa, January29/February 1.
Fan, G. & Wang, X. (2001) *NERI Index of Marketization of China by Province*, Economic Science Press: Beijing.
Feinberg, S. & Gupta, K. (2004) Knowledge spillovers and the assignment of R&D responsibilities to foreign subsidiaries. *Strategic Management Journal,* 25 (8/9), 823–845.
Fiercebiotech News (2017) Riding on booming drug sales, AstraZeneca forms $133m China joint venture, published on 27/11/2017, available at [www.fiercebiotech.com]
Firstword Pharma News *(2002) AstraZeneca to open clinical research centre in Shanghai,* Published on 26/11/2002, Available at [www.firstwordpharma.com]
Fletcher, M., Zhao, Y., Plakoyiannaki, E., & Buck, T. (2018) Three pathways to case selection in international business: A twenty–year review, analysis and synthesis. International Business Review, Online First
Florida, R. (1997) The globalisation of R&D: results of a survey of foreign-affiliated R&D laboratories in the USA, *Research Policy*, 26, 85-103
Fors, G. & Zejan, M. (1996) Overseas R&D by multinationals in foreign centers of excellence. *Working Paper No. 111*. The Economic Research Institute. Estocolmo: Stockholm School of Economics.
Generic Drug Report (2012) AstraZeneca buys Chinese generics firm, *Chain Drug Review*, January, 73
Gerybadze, A. & Reger, G. (1999) Globalization of R&D: recent changes in management of innovation in transnational corporations. *Research Policy,* 28 (2-3), 251–274.
Gibbert, M., & Ruigrok, W. (2010). The 'what' and 'how' of case study rigor: Three strategies based on published research, *Organizational Research Methods,* 13, 710-737
Gill, M. J., Gill, D. J., & Roulet, T. J. (2018) Constructing trustworthy historical narratives: Criteria, principles and techniques. *British Journal of Management*, 29(1), 191-205.
Global Sourcing Now (2007) AstraZeneca partners with Peking University Hospital, *Global Sourcing Now*, 09/06/2007
Govindarajan, V., & Ramamurti, R. (2011) Reverse innovation, emerging markets, and global strategy. *Global Strategy Journal*, 1(3‐4), 191-205
Govindarajan, V. & Trimble C. (2012) Reverse Innovation: Create Far From Home, Win Everywhere. Harvard Business Press: Boston
Greig, S. L. (2016) Osimertinib: first global approval. *Drugs,* 76(2), 263-273.

Guan, J.C., Yam, R., Tang, E. & Lau, A. (2009) Innovation strategy and performance during economic transition: evidence in Beijing, China. *Research Policy,* 38 (5), 802–812.
Gupta, A.K. & Govindarajan, V. (1991) Knowledge flow patterns, subsidiary strategic roles, and strategic control within MNCs. In *Academy of Management Proceedings,* 1, 21-25
Haakonsson, S. J., & Ujjual, V. (2015). Internationalisation of R&D: New insights into multinational enterprises' R&D strategies in emerging markets. *Management Revue*, *26*(2)
Haour, G., & Jolly, D. (2014). China: the next innovation hot spot for the world. *Journal of Business Strategy*, *35*(1), 2-8.
Heathcote, M. (1994) Challenging China, *ICIS Chemical Business News*, 14/11/1994
Ironwood Pharma News (2018) *Ironwood Pharmaceuticals Provides Fourth Quarter and Full Year 2017 Investor Update,* 15/02/2018
Ito, B. & Wakasugi, R. (2007) What factors determine the mode of overseas R&D by multinationals? Empirical evidence, *Research Policy*, 36
Jain, S., Nair, A., & Ahlstrom, D. (2015). Introduction to the Special Issue: Towards a theoretical understanding of innovation and entrepreneurship in India.
Jha, S., Dhanaraj, C., & Krishnan, R. (2015) How does multinational R&D evolve in emerging markets? *Working Paper*, International Institute for Management Development, 2015-02
Jha, S., Dhanaraj, C., & Krishnan, R. (2018). From Arbitrage to Global Innovation: Evolution of Multinational R&D in Emerging Markets. *Management International Review*, 1-29.
Jiangsu News (2008) *AstraZeneca Sgned A New Contract with Wuxi*, 11/08/2008
Kuemmerle, W. (1999) Foreign direct investment in industrial research in the pharmaceutical and electronics industries: results from a survey of multinational firms. *Research Policy*, 28 (1), 179–193.
Kumar, N. (2001) Determinants of location of overseas R&D activity of multinational enterprises: the case of US and Japanese corporations. *Research Policy,* 30, 159–174.
Kumaraswamy, A., Mudambi, R., Saranga, H., & Tripathy, A. (2012) Catch-up strategies in the Indian auto components industry: Domestic firms' responses to market liberalization. *Journal of International Business Studies*, *43*(4), 368-395
Kuemmerle, W. (1999) The drivers of foreign direct investment into research and development: an empirical investigation. *Journal of International Business Studies*, 30(1): 1-24.
Lema, R. Quadros, R. & Schmitz, H. (2015) Reorganising global value chains and building innovation capabilities in Brazil and India. *Research Policy*, *44*(7), 1376-1386
Li, J., & Kozhikode, R. K. (2009). Developing new innovation models: Shifts in the innovation landscapes in emerging economies and implications for global R&D management. *Journal of International Management*, *15*(3), 328-339.
Li, X. (2009) China's regional innovation capacity in transition: an empirical approach, *Research Policy*, 38 (2), 338–357.
Li, H. & Cantwell, J. (2012) Innovative firms in emerging markets: country experience (China). In E. Amann & J. Cantwell (Ed.) *Innovative Firms in Emerging Market Countries*, 113-147. Oxford University Press: Oxford
Lim, C., Hemmert, M., & Kim, S. (2017) MNE subsidiary evolution from sales to innovation: Looking inside the black box. *International Business Review*, *26*(1), 145-155.
Liu, M., & Chen, S. (2012) MNCs' offshore R&D networks in host country's regional innovation system: The case of Taiwan-based firms in China. *Research Policy*, *41*(6), 1107-1120
Liu, F. C., Simon, D. F., Sun, Y. T., & Cao, C. (2011) China's innovation policies: Evolution, institutional structure, and trajectory. *Research Policy*, *40*(7), 917-931.
Lu, Y., Tsang, E. W., & Peng, M. W. (2008). Knowledge management and innovation strategy in the Asia Pacific: Toward an institution-based view, *Asia Pacific Journal of Management,* 25(3), 361-374
Mabey, C. & Zhao, S. (2017) Managing five paradoxes of knowledge exchange in networked organizations: new priorities for HRM? *Human Resource Management Journal,* 27(1), 39-57
Meyer, K. E., Mudambi, R. & Narula, R. (2011) Multinational Enterprises and Local Contexts: The Opportunities and Challenges of Multiple Embeddedness. *Journal of Management Studies,* 48: 235–252

Meyer, K. E., & Peng, M. W. (2015) Theoretical foundations of emerging economy business research. *Journal of International Business Studies*,*47*(1), 3-22
McKinsey (2012) Pharmaceutical innovation: AstraZeneca's experience in China, *McKinsey Quarterly*, 1, 93-95
Ministry of Commerce, P.R.C. (2005) China investment guide: Sweden, *Invest in China Serials*, Investment Promotion Agency of Ministry of Commerce Publication
Ministry of Commerce, P.R.C. (2006) I am Jiangsu, *Invest in China Serials*, Investment Promotion Agency of Ministry of Commerce Publication
Ministry of Commerce, P.R.C. (2006) *Drug market: different strategies, same goal, Common News*, Ministry of Commerce Publication
Ministry of Commerce, P.R.C. (2006) *AstraZeneca to expand investment in China,* Common News, Ministry of Commerce Publication
Ministry of Commerce, P.R.C. (2007) *AstraZeneca China Innovation Centre settled at Zhangjiang High-tech Zone Shanghai*, Common News, Ministry of Commerce Publication
Ministry of Commerce, P.R.C. (2011) *AstraZeneca to build $200-mln centre in China,* Europe Report, Ministry of Commerce Publication
Ministry of Commerce, P.R.C. (2014) *China Pharmaceutical Industry Investment Promotion Report*, Ministry of Commerce Publication
Mudambi, R., Piscitello, L., & Rabbiosi, L. (2014). Reverse knowledge transfer in MNEs: subsidiary innovativeness and entry modes. *Long Range Planning*, *47*(1), 49-63.
Mudambi, R. & Santangelo, G. D. (2016) From shallow resource pools to emerging clusters: The role of multinational enterprise subsidiaries in peripheral areas. *Regional Studies*, *50*(12), 1965-1979
Nair, A., Guldiken, O., Fainshmidt, S., & Pezeshkan, A. (2015). Innovation in India: A review of past research and future directions. *Asia Pacific Journal of Management*, *32*(4), 925-958.
Nelson, R. R. & Winter, S. G. (1982) *An Evolutionary Theory of Economic Change*. Harvard Business School Press, Cambridge
Nelson, R. R., & Winter, S. G. (2009) *An Evolutionary Theory of Economic Change*. Harvard University Press: Cambridge
Niosi, J. (1999) The internationalization of industrial R&D from technology transfer to the learning organization. *Research Policy*, 28 (2–3), 107–117.
Pearce, R. D. & Papanastassiou, M. (1999) Overseas R&D and the strategic evolution of MNEs: evidence from laboratories in the UK, *Research Policy*, *28*(1), 23-41
Pearce, R.D. & Papanastassiou, M. (1997) Global innovation strategies of MNEs and European integration: the role of regional R&D facilities, in Pearce (Ed.), *Global Competition and Technology,* St Martin's Press: New York, 123-52
Pederson, J. P. (2008) *International Directory of Company Histories*, St James Press: Chicago
Peng, M. W. (2003) Institutional transitions and strategic choices. *Academy of Management Review*, *28*(2), 275-296.
Peng, M. W., Wang, D. Y., & Jiang, Y. (2008) An institution-based view of international business strategy: A focus on emerging economies. *Journal of International Business Studies*, *39*(5), 920-936
Pharma Times (2006) *China Emerging as Clinical Research Hotspot,* Published on 24/01/2006, Available at [www.pharmatimes.com]
Prabhu, J., & Jain, S. (2015). Innovation and entrepreneurship in India: Understanding jugaad. *Asia Pacific Journal of Management, 32(4), 843-868.*
Prashantham, S., & Dhanaraj, C. (2015). MNE ties and new venture internationalization: Exploratory insights from India. *Asia Pacific Journal of Management, 32(4), 901-924*
PriceWaterhouseCoopers (2015) *Global innovation 1000: Innovation's new world order. Featured Foresignt, PriceWaterhouseCooper PLC.*
Reddy, P. (1997) New trends in globalization of corporate R&D and implications for innovation capability in host countries: a survey from India. *World Development*, *25*(11), 1821-1837.
Reddy, P. (2000) *Globalization of Corporate R&D: Implications for Innovation Systems in Host Countries*. Routledge: London.

Rodrigues, S. B. & Child, J. (2008) *Corporate Co-Evolution: A Political Perspective*, Vol 4, John Wiley & Sons: Chichester
Schmiele, A. & Mangelsdorf, A. (2009) Drivers of international R&D to Asian economies: a perspective from German companies. *Paper for the 6th Asialics International Conference Linkages in Innovation Systems: Global and Local Perspectives*, 6–7 July, Hong Kong University of Science and Technology.
Shin, K., Kim, S. J., & Park, G. (2016). How does the partner type in R&D alliances impact technological innovation performance? A study on the Korean biotechnology industry. *Asia Pacific Journal of Management*, *33*(1), 141-164.
Siggelkow, N. (2007). Persuasion with case studies, *Academy of Management Journal*, 50(1), 20-24
SIPO (2015) *Patent Database*, State Intellectual Property Office, China
Song, J., & Shin, J. (2008) The paradox of technological capabilities: a study of knowledge sourcing from host countries of overseas R&D operations. *Journal of International Business Studies*, *39*(2), 291-303
Song, J., Asakawa, K., & Chu, Y. (2011) What determines knowledge sourcing from host locations of overseas R&D operations?: A study of global R&D activities of Japanese multinationals. *Research Policy*, 40(3), 380-390
Tan, X., Liu, X., & Shao, H. (2017) Healthy China 2030: a vision for health care, Value in Health Regional Issues, *12*, 112-114.
Teece, D. J. (2014) A dynamic capabilities-based entrepreneurial theory of the multinational enterprise. *Journal of International Business Studies*, *45*(1), 8-37.
The Independent (1998) *Has Zeneca Chosen Wisely*? 11/12/1998
The Telegraph (2008) *ICI Finally Consigned to History*, 02/01/2008
The Telegraph (2010) *AstraZeneca Answers the Great Call of China*, 05/06/2010
The Telegraph (2010) *AstraZeneca is Well Placed for the Chinese Boom*, 06/06/2010
Thomson Reuters (2007) *AstraZeneca Agrees to Buy Medlmmune*, 23/04/2007
Thomson Reuters (2010) *AstraZeneca CEO Sees China Growth Doubling*, 26/06/2010
Thomson Reuters (2011) *AstraZeneca and Chi-Med Enter into Global Collaboration to Co-develop and Commercialise Novel Cancer therapy*, Press Release 21/12/2011
Thomson Reuters (2017) *AstraZeneca, Chi-Med take kidney cancer drug into final testing*, *Health News*, 29/06/2017
Turnheim, B., & Geels, F. W. (2012) Regime destabilisation as the flipside of energy transitions: Lessons from the history of the British coal industry (1913–1997). *Energy Policy*, *50*, 35-49.
Turnheim, B., & Geels, F. W. (2013) The destabilisation of existing regimes: Confronting a multi-dimensional framework with a case study of the British coal industry (1913–1967). *Research Policy*, *42*(10), 1749-1767.
UK Trade and Investment (2010) *Opportunities for British and Chinese businesses in science, research and innovation,* Department for Business, Innovation and Skills, Oral Statement to Parliament, published on 08/11/2010
UNCTAD (2005) *World Investment Report: Transnational Corporations and the Internationalisation of R&D*, United Nations: New York and Geneva
UNCTAD (2012) *Technology and Innovation Report*, United Nations: New York and Geneva
UNCTAD (2016) *Investor Nationality: Policy Challenges*, United Nations: New York and Geneva
Verbeke, A., & Kano, L. (2015) The new internalization theory and multinational enterprises from emerging economies: A business history perspective. *Business History Review*, *89*(03), 415-445
Vernon, R. (1966) International investment and international trade in the product cycle, *Quarterly Journal of Economics*, 80, 190-207
von Zedtwitz, M. & Gassmann, O. (2002) Market versus technology drive in R&D internationalization: four different patterns of managing research and development. *Research Policy*, 31 (4), 569–588.
Wall Street Journal (2001) *AstraZeneca Invests $100 Million in China Plant, Its Biggest in Asia*, 29/04/2001

Wang, C., Hong, J., Kafouros, M., & Wright, M. (2012) Exploring the role of government involvement in outward FDI from emerging economies. *Journal of International Business Studies*, *43*(7), 655-676.
Washington Business Journal (2017) *MedImmune gets OK from China to pursue arthritis drug in joint venture deal*, 19/01/2017
Welch, C. & Piekkari, R. (2017) How should we (not) judge the 'quality'of qualitative research? A re-assessment of current evaluative criteria in International Business. *Journal of World Business*, 52(5), 714-725.
Welch, C., Piekkari, R., Plakoyiannaki, E., & Paavilainen-Mäntymäki, E. (2011). Theorising from case studies: Towards a pluralist future for international business research. *Journal of International Business Studies*, 42 (5), 740-762
World Scientific (2003) *The Asia-Pacific Biotech Directory*, World Scientific Publications, New Jersey
Yang, Q., & Jiang, C. X. (2007). Location advantages and subsidiaries' R&D activities in emerging economies: Exploring the effect of employee mobility. *Asia Pacific Journal of Management*, *24*(3), 341-358.
Yin, R. K. (2014) *Case Study Research: Design and Methods 5th*, SAGE: California
Yu, S. (2011) *Information Technology in Multinational Corporations: The Managerial Role of Enterprise Resource Planning System in Headquarters-subsidiary Power Tussle and Local Performance*. LAP Lambert: Germany
Zander, I. (1999) How do you mean 'global'? An empirical investigation of innovation networks in the multinational corporation. *Research Policy*, 28 (2/3), 195–213
Zedtwitz, M., Corsi, S., Søberg, P. V., & Frega, R. (2015). A typology of reverse innovation. *Journal of Product Innovation Management*, *32*(1), 12-28.
Zhang, S. & Pearce, R.D. (2011) *Multinationals in China: Business Strategy, Technology and Economic Development*. Palgrave Macmillan: Basingstoke.
Zhang, S., Zhao, S., Bournakis, I., Pearce, R.D., & Papanastassiou, M. (2018) Subsidiary roles as determinants of subsidiary technology sourcing: Empirical evidence from China, *Economia Politica*, online first
Zhou, C., Wang, M., Cheng, Y., Chen, Y., Zhao, Y., Shi, Y. K. & Wu, Y. L. (2017) 1354POsimertinib in Asia-Pacific patients (pts) with EGFR T790M-positive advanced NSCLC: Updated Phase II study results including progression-free survival (PFS). *Annals of Oncology*, 28(5).
Zedtwitz, M., Corsi, S., Søberg, P. V., & Frega, R. (2015) A typology of reverse innovation. *Journal of Product Innovation Management*, *32*(1), 12-28.