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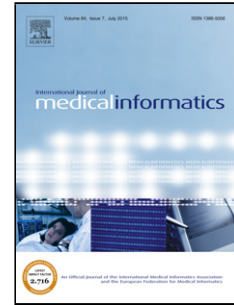
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Anglicization of Hospital Information Systems: Managing diversity alongside particularity

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Anglicization of Hospital Information Systems: Managing diversity alongside particularity

Highlights:

- Tensions exist between ‘standardization’ and ‘localization’ of HIS.
- The complexity of health service provision, drives calls for anglicization of HIS.
- Suppliers to develop sophisticated strategies as they pursue international growth.
- User-supplier links need to be strengthened.
- Usability and productivity are central issues for HIS package procurement.

Abstract

Context: Despite widespread efforts to improve the quality and safety of healthcare through use of hospital information systems (HIS), many healthcare organizations face challenges in implementation and effective use of these applications, in particular when systems have been developed internationally (mainly in the US). Suppliers of these technologies also find it challenging to produce systems that work effectively across a range of geographical, cultural and institutional boundaries. In this paper, we seek to understand the strategies used by suppliers and adopters of HIS to overcome the challenges involved in the development and adoption of generic overseas systems.

Methods: We conducted a qualitative study, by interviewing 176 individuals (eight organizations), observing two user groups, and running a supplier focus group. We used inductive thematic analysis to assess emerging strategies in developing and implementing overseas packaged HIS in English settings.

Findings: The health sector in England has entered a period of potentially transformative change with many international HIS suppliers entering the market. This has provoked call for the ‘Anglicization’ of generic systems. This endeavor, has resulted in emergence of more or less aligned supplier and user strategies to overcome the difficulties in the process. This includes a continuous process of identification and classification of requests (by suppliers), and unification and voicing of needs (by adopters).

Conclusions: The complexity of health service provision, drives calls for customization of technologies in this sector. Consequent tensions between ‘standardization’ and ‘localization’ are requiring suppliers of generic solutions to develop more sophisticated strategies as they pursue international growth of their market.

Keywords: Health Information Systems, Anglicization, Implementation Strategy, Generic Applications

1. Introduction

Despite some recognized benefits of packaged hospital information systems (HISs), including improved patient safety and decreased health care costs^{1,2}, innovation in this sector has proved laborious and the adoption and use of these systems have been slow and challenging³⁻⁸. Many sociotechnical and organizational factors including informational complexity of care processes, organizational structures and practices of healthcare organizations, and the safety criticalness of the sector are among the many reasons that inhibit smooth and timely implementation of HIS⁸⁻¹². The issue becomes even more complex where there is a large cultural, institutional, and geographical distance between the suppliers and adopters of the system, such as when overseas HIS are implemented in settings with particular local needs as the systems are known to be idiosyncratic to the countries of their development¹³. In the wider information system literature, scholars have identified various strategies adopted by suppliers to overcome these misalignment and distance barriers^{14,15}. However, the literature on development, implementation and uses of HIS barely discusses these strategies. It is therefore crucial to explore this issue deeper, in particular as healthcare is known to be slower in development and adoption of technologies than other sectors¹⁶.

We conducted a qualitative study of four commercial computerized physician order entry (CPOE) and clinical decision support (CDS) systems for prescribing that had entered or were in the process of entering into NHS England's market. Through the study of an emerging health infrastructure in England, we aimed to explore the Anglicization strategies by which suppliers managed their entrance and development in a new market of different nationality, often also moving from a private health service to a public health service provider. In this process, we attempted to answer the following questions: a) what are the different strategies used by non-English HIS suppliers to adapt and implement their products for the English market? and 2) what are the strategies adopted by English hospitals to promote and facilitate the

Anglicization process? This study is timely as the UK and many countries are making large investments in digitization of the health sector as well as aggregation of national demands which are likely to impact the supplier's ways of working with the National Health Services (NHS)^{17,18}. The findings have the potential to inform policy as well as helping suppliers and adopters examine and understand the range of approaches.

2. Material and Methods

2.1 Design

This study was a part of a larger program of work into the adoption of CDS/CPOE systems (also known as electronic prescribing) in England. We developed an ethnographic study across multiple settings selected on the basis of provisional theoretical and empirical understanding of the matters under investigation. The scoping of the study and range of sites selected was informed by the strategic ethnography approach^{15,19} for guiding the adequacy of research design in providing in-depth understanding of the complex issues in this context. In studying complex technologies, a multi-adopter ethnographic approach also allows examination of multiple sources of evidence (including vendors and adopters) from different perspectives with the aim of allowing the complexities be revealed^{19,20}.

The term 'Anglicization' was used by our participants. We defined Anglicization as a process involving modification of the CDS/CPOE systems and changes to the implementation practices, which required acts from both supplier and adopter sites, for English NHS markets. These included modification to the underlying processes, data structures, interfaces, and terminology used within the application. This definition thus covers an extended period of time starting from acquisition, implementation, and adoption, to subsequent system use and optimization.

2.2 Institutional Review Board Approval

The study was reviewed by a National Health Service Research Ethics Committee and it was classed as a service evaluation. It received Institutional Review Board (IRB) approval from The University of Edinburgh's Research Ethics Committee. We obtained organizational approvals from case study sites and informed consent from participants of the study. Interview data and observation field notes were anonymized for analysis.

2.3 Sampling and Recruitment of Organizations and Participants

We used our recent study of the English CDS/CPOE market to develop a sampling framework of the current suppliers and adopters of CDS/CPOE applications. Then purposive sampling was used to ensure that we included: 1) products developed in different countries; and 2) products at different stages of their lifecycle (with respect to their entrance and evolution in the English market). To provide multiple perspectives, we also included both suppliers and adopters (hospitals) of these systems in our study. In this process, we contacted eight suppliers and eight adopter organizations of non-English CDS/CPOE systems. Three suppliers and five adopter organizations agreed to take part in the research (Table 1). From each of these organizations, we ensured to interview individuals with experience in implementation of the system in an English hospital.

Table 1. Characterization of Organizations involved in this work

Organization/System Characteristics
<p>Supplier 1/System 1</p> <ul style="list-style-type: none"> - System designed and developed in the USA, Primary User Market: USA, Has been implemented in several English hospitals
<p>Supplier 2/System 2</p> <ul style="list-style-type: none"> - System designed and developed in the USA, Primary User Market: USA, Has been implemented in several English hospitals
<p>Supplier 3/System 3</p>

<ul style="list-style-type: none"> - System designed and developed in a European country, Primary User Market: Europe (not England), Have several implementations in progress in England
<p>Adopter A</p> <ul style="list-style-type: none"> - Rural, acute care, teaching - System 1, CPOE and CDS as part of an integrated hospital information system
<p>Adopter B</p> <ul style="list-style-type: none"> - Urban, acute care, teaching - System 1, CPOE and CDS as part of an integrated hospital information system
<p>Adopter C</p> <ul style="list-style-type: none"> - Urban, acute care, teaching - System 1, CPOE and CDS as part of an integrated hospital information system
<p>Adopter D</p> <ul style="list-style-type: none"> - Urban, acute care - System 2, CPOE and CDS as part of an integrated hospital information system
<p>Adopter E</p> <ul style="list-style-type: none"> - Urban, acute care - System 3, CPOE and CDS as a standalone application

2.4 Data Collection

We used a combination of semi-structured interviews, observations and a focus group to collect data. These methods allowed us to gain insights into the experience of different participants and the nature of the interactions between different entities at different locals. This method allowed us to triangulate the findings and facilitated credibility of the results²¹.

Interviews were carried out with 176 participants from eight organizations (adopters and suppliers). Two out of three systems had origins in the USA and one in Europe. Participants from supplier organizations included UK development leads and UK customer relations. Participants from adopter sites ranged from decision-makers, to implementation teams, information technology staff, and health professionals. Semi-structured interviews were carried out using an interview guide focusing on vendors' strategies in offering and adapting non-

English products to the English market, stages in project initiation through to implementation and go-live, supplier-user relationships throughout the project life-cycle, and managing user expectations. The interview guides were customized to fit the role and organization of the individual interviewee. The interviews ranged from 45 minutes to two hours.

Interview data were complemented by observational data collected from two user groups (two US systems in our sample) and a supplier focus group. The focus group, involving nine participants from six suppliers (two national and four international), focused upon uptake of systems that had been implemented in England. Field notes were recorded in these meetings around three main areas: (a) the technological contents of the discussion, (b) the supplier-user relationships and interactions, and (c) decisions being taken. Data were collected by HM and KC..

2.5 Data Analysis

Data analysis was undertaken using a thematic approach. We analyzed the data collected from each source inductively and we iteratively allowed the emerging themes to feed back into future data collection. The data were analyzed within each data source (as mentioned in Table 1) and then compared across datasets. Through analysis of data, we identified patterns of meanings²² (emerging issues) which were then grouped into themes. Additionally, we cross-analyzed vendor and adopter views to ensure that both perspectives were addressed. This involved discussing similarities and variations across perspectives, as well as investigating potential underlying reasons for differences. In order to present results, we have used direct quotes from the transcribed interviews and observational field notes from user group meetings. Data collected from the supplier focus group was used to validate the findings from the other two sources (interviews and observations).

3. Results

Our previous studies showed that the majority of systems available in England originated in other countries²³ which led to misalignment between system functionalities and internal hospital demands²⁴. Differences in national health systems, financial models, and policies, dissimilarities of organizational practices, and variations in professional roles and authorities were recognized as drivers for Anglicization²⁴.

We often observed creation of workarounds²⁵, loss of user engagement²⁶, and unintended safety threats²⁷ associated with a range of reasons including lack of Anglicization. As a result, the adopting hospitals urged for Anglicization of the systems and the practices surrounding them.

This study builds on these findings, shedding light on the emerging strategies used to overcome these differences. We identified two main types of strategies: 1) the persistent categorization of adopter demands (by suppliers); and 2) promoting demands and facilitating change (by adopters) (Table 2).

Table 2. Summary of Themes and Subthemes Emerging from This Work

Supplier strategies in Anglicization: the persistent categorization of adopter demands	<ul style="list-style-type: none"> - Identification of generic needs - Keeping the ‘Kernel’ Unchanged while Developing an Anglicized Version - Sifting, sorting and prioritizing user demands - England specific versions versus user configurable solutions - Anglicization of the implementation strategy
Adopter strategies in Anglicization: promoting demands and facilitating change	<ul style="list-style-type: none"> - Identifying common needs - Forming a collective voice - Becoming a pilot site/testing partner

3.1 Supplier Strategies in Anglicization: the persistent categorization

In all three cases (the three non-English CDS/CPOE systems), suppliers entered the market with their original non-English applications. At the start there was a tendency to underestimate the extent of differences between these new settings and the context in which the application emerged. It was only gradually, while implementations were taking place in English hospitals, that suppliers responded to the difference between the English health structures and practices and what the systems were offering and acknowledged the need for action.

Bulk of the client base predominantly was born out of the US market and I think that the lessons learned that we see is that there will be behaviors in a private versus publically managed healthcare market, there will be responsibilities between nursing and clinical staff that may differ. (Interview, Supplier 1)

The Anglicization process involved finding similarities and reconciling differences amongst needs expressed by English hospitals. This involved gathering the need of each organization and finding out whether they are generic or local needs.

[...] my job with the team is to ensure that what they're asking for, will be used by all the other clients in the UK as well so it's not just for that client [...] (Interview, Supplier 1)

However, as we observed in the user group events, the suppliers sometimes had problems coping with wide-ranging and sometimes conflicting demands of the adopting hospitals. The suppliers tried to keep particular organizational level customizations to a minimum and only implement the 'generic' needs. This was done through bringing the conflicting views into one room, through meetings or user group events, to (1) identify the actual needs, (2) align the views of different users, and (3) find ways to accomplish a solution that meets the wider requirements.

There's two ways it works. Get the people together who have the differing opinions and sometimes it's between customers, sometimes it's between the customers and [Supplier_2], sometimes there's three different opinions [...]. Is it something that's customizable or like a parameter change. So if you set this change to yes it does it for [Hospital_Name_X] and if you set it to no and it works how [Hospital_Name_Y] wants it to. (Interview, Supplier 2)

However, identification of generic needs did not mean that all these needs would be developed into the system. We observed many instances of negotiation over 'needs' and 'wants' between adopters and suppliers in the user group events. The suppliers then divided the demands into the 'kernel' and 'non-kernel'¹⁵ categories. Demands, which required changes to the kernel and architecture of the systems, which could threaten stability of the package solution or lead to very high costs, were then excluded. For instance, the core architecture was designed on unit-based dispensing (the core design of the system), which was a result of US system being oriented towards billing and insurance concept. Based on this categorization, systems were only exposed to certain level of changes.

So, in the States we have what we call unit based dispensing and basically we supply the patients with medications for a 24 hour period, whereas in the UK you have what you call whole pack dispensing. So basically we in the States we've made the workflow around this unit based dispensing, so they'll have drug cabinets on the floor but essentially the system was built around the unit based dispensing module within [System_1] back in the US. (Interview, Supplier 1)

While keeping the 'kernel' unchanged, the suppliers had strategies to examine the remaining demands. In order to do this, they started by differentiating between what was seen as an Anglicization issue and what was considered a usability issue when going from paper to electronic. After labeling a demand as an 'Anglicization need' they conducted further

examination by identifying the severity of the need based on the labels provided by users (e.g. ‘bug fix’, ‘label fix’, ‘change that’s needed’, ‘workflow issue’, or ‘enhancement’) and availability of supplier resources for development of the change. This ‘sifting’, ‘sorting’¹⁵ and ‘prioritizing’ process meant that whilst some functionalities known as “cannot go live without” were implemented promptly, other demands could be put on hold for months or even years before they were developed into the system.

There’s different levels of proposals as well because there are certain things that are just great ideas that, you know, aren’t really needs or, like isn’t that people can’t function without so we get, as far as the UK group we get a lot of ideas and things like that which we’re always open to and we document them but moving past that it then really just becomes like OK back to the priority stage is this a can’t operate without, can’t function without, a really nice to have or kind of nice to have or it would be great if we got it in a few years, like not a big deal kind of thing. (Interview, Supplier 2)

There were three strategies for responding to change requests: 1) development of England specific version of the products, 2) development of configurable parameters, and 3) declining the requests or postponing them. In the first case, while trying to keep the system as generic as possible, some suppliers bundled demands from English hospitals into one England standard version of the package. The Anglicized versions offered England-specific features which were not available in the original application offered to the customers in the other parts of the world.

[...] we want to put it into the UK standard product, you know, we want to keep all of our customers at the same type of software so that everything is consistent and it’s really more for the market place not for necessarily an individual... we have a UK standard [version] that is different from the US standard [version]. They started about four years ago identically and

then as we needed to we have done. [...] the ability to place a TTO [to-take-home] medication order, that requirement does not exist in America, [...] but in our [UK] ring you can. (Interview, Supplier 2)

The benefit of this strategy was that more England-specific needs could be covered in the product offerings. However, as stated by the adopters, the updates to the original package could take a long time to be developed into the Anglicized version. It also led to more costly maintenance of the system by suppliers. To avoid this duplication of acts, suppliers adopted a different strategy, which was to offer configurable parameters to be set locally in England. However, this strategy was seen as less desirable for many adopters. They stated that the configurable parameters made the system more complex to use.

[System_Name] is far from satisfactory and from what I know of it so far it is a ghastly system, it is not user friendly. (Interview, Adopter A, Consultant)

In addition to system functionalities, both adopters and suppliers sensed a necessity for implementation strategies to be Anglicized. The differences between the health settings, management of human resources, and variations in workforce policies meant that England required an Anglicized version for project management and go-live strategies.

So the ones that I've read about have been ward by ward not 'big bang' so [Supplier_Name] will do it based on their knowledge but actually [their] knowledge is based on the US model not a British model to my great irritation. (Interview, Adopter A, Lead Pharmacist for IT)

We refer to this on-going process of identification and classification of requests (i.e. generic versus local, kernel versus non-kernel, necessary versus optional, Anglicized versus configurable) as the persistent categorization of user demands. This process continued and its results were transformed over time.

3.12 Adopters Strategies in Anglicization: promoting demands and facilitating change

Anglicization was seen as wider process of joint-learning and collaborative customization by the adopting organizations (English hospitals). Therefore, they tried to gather into communities of users who could talk to the supplier using a ‘collective voice’ in order to influence the supplier to modify the products.

There are four or five hospitals saying this is what we want [...] rather than [Hospital_Name_X] wanting one thing, [Hospital_Name_Y] wanting another [...]. If we're all wanting the same thing we present a very united front and that makes it much more likely to happen and they're facilitating that. (Interview, Adopter A, Doctor, Implementation Team Co-chair)

The user communities were formed primarily to identify the common needs and possible solutions, and then to articulate the needs in a similar way. Therefore, as our observation of the user community events showed and our interviews confirmed, sometimes users entered into negotiating demands within their communities until a common framework was formed.

But I think also we're trying to collaborate with other Trusts [hospitals] within the area [...] the EPMA [Electronic Prescribing and Medicine administration, English term for CDS/CPOE] group which meet every month and we sort of air the issues there and try and see if we can, you know, raise, if the same issues that we've all got are sort of ironed out and raised at that point so that it makes things a lot easier to go forward and for the changes to happen. (Interview, Adopter B, Principal Pharmacist)

Whilst community building and collaboration was a common theme, we also identified individual strategies adopted by some hospitals. It appeared that hospitals that were further down the line with the implementation of a system had a better chance of ensuring that many

of their features were incorporated in the Anglicized version. This led adopting organizations to enter into different forms of collaboration with the vendor. One of the main approaches was to become a ‘pilot site’ or a ‘testing partner’ who would be able to test the initial versions of the products and have influence on its design.

Well we will, we're trying to put ourselves so that we become testing partners with [Supplier 1] so those enhancements I put in are things that we test. (Interview, Adopter A, Lead Pharmacist for IT)

As a result of these various strategies, adopter organizations exhibited a combination of individual and community acts, some, earlier in systems implementation cycles, and some further down the line when systems were in use.

4. Discussion

Adoption of ‘generic’ HIS is becoming the norm in healthcare, reflecting the substantial (and growing) set-up, accreditation and maintenance costs of home-grown systems. However, differences in health policy, financing, systems and practices all can lead to a large gulf between standardized solutions offered by vendors and the particular needs of adopter organizations. While there is increasing attention to the misalignment between technology and organization, much of this research is limited to emphasizing consequences of either ‘global’ design and development, or ‘local’ user customization practices. We argue that a dual user-vendor perspective is needed to understand the bridging between the ‘global’ act of vendors (generification) and the ‘local’ operations of adopters (e.g. workarounds²⁵). This paper has, therefore, sought to develop understanding of the role both adopters and suppliers play in internationalizing packaged HIS. Suppliers of packages adopt a spectrum of strategies to bridge the global software-local need gap. Adopters, in turn, take on various activities to drive this forward. Our findings call for reconsideration of how we understand the work of early adopters

of overseas systems and international vendors and their relationships during the global-software nationalization process. Table 3 provides a list of contributions to existing knowledge in this field.

Table 3. Summary Table

Current Literature	Contributions to knowledge
<ul style="list-style-type: none"> • Packaged applications are deigned with ‘generic’ properties; • In generic system development and implementation a complex set of relationships between vendors and users are established; 	<ul style="list-style-type: none"> • Country-specific generification are needed (e.g. Anglo generic) to meet the generic needs of a country. • Suppliers and users have to adopt strategies to enable anglicization. There strategies are sometimes aligned and sometimes conflicting. • In the field of HIS, the user-vendor relationships are yet in their infancy causing numerous problems;

4.1 Transforming from ‘generic’ to ‘Anglo-generic’ application

‘Generification’ of packaged applications, which refers to standardization of software packages to serve an increasing number of organizations needs, is widely discussed by scholars in the field of enterprise systems^{15,28}. Our earlier research showed that, compared to enterprise systems, HIS are still in their early days and as a result (and as we could see in this study) HIS are not made as ‘configurable’^{15,29-31} as enterprise systems^{24,32} making them difficult to be adopted in different health organizations. Also the great specialization of health, its related national laws and regulations, and the safety issues involved in health related activities, resulted

in laborious and lengthy implementation practices. As a result, we observed a number of emerging strategies used by HIS vendors to enter into an international market.

Firstly, we presented how vendors identify generic 'English' needs from organizational preferences (Anglo-generic). On one hand, their lack of expertise in relation to the English market led to protracted, often trial and error, learning for vendors. On the other hand, reconciling the overseas applications with the setting of English hospitals led to acute problems. There were unclear boundaries between national and hospital-specific demands, and while all English hospitals worked under the administration of NHS England (with similar policies and laws), they were arguably diverse in terms of practices and perceived requirements. This made identification of English generic needs difficult. This was made even more problematic when systems embodied conflicting categories and hospitals had valid reasons for sticking to their own processes rather than accepting the generic solutions. Secondly, identification of the English generic needs was not an indicator of what is to be Anglicized. It was rather the beginning of a sifting and sorting process by the supplier. Notably, the English generic needs which were in conflict with the overseas 'generic kernel' design remained untouched. The kernel refers to the backbone of the system on which the logic of the application is built on. The vendor, then, examined and prioritized other English generic needs based on own resources as well as adopters demands. As a result, whilst the extant literature explains how systems developed for a local settings become suitable for several settings^{15,19}, our study revealed a somehow opposite tendency: how generic systems had to be Anglicized to meet the generic needs of a country.

The result was a system which delivered a range of standard features, but also allowed for 'some flexibility'. However, due to the relative newness of the market in England and the varying international supplier-user power dynamics, vendors' emerging strategies for managing the tensions between the 'standard' and the 'flexible English design' were different:

some suppliers, from the outset, believed in adapting the design to offer an English solution, whilst others urged use of the standard system as much as they could. For instance, Supplier 3 emphasized building a full England-specific version of their system in accordance with the needs of one particular hospital (with the view of then extending this to a generic English system). They asked the users to present all their needs and practices to be incorporated into their system. It was only later that users learnt that the responses to their demands were being influenced by the initial design (kernel) of the package. On the other hand, Supplier 1 offered the system as a completely new pre-designed package to the users, which could be configured, (to a certain extent) to meet user needs. However, despite the different entrance strategies, both vendors controlled the principal existing information system to be implemented in each site. In other words systems are ‘made to travel’¹⁵ through different strategies. Users in response established new strategies to take the control back as much as achievable (discussed in the next section).

4.2 Active user strategies: variation of supplier-user distance

In the early days of entrance of non-English systems to the English market, there was a lack of awareness and appreciation of differences between the supplier products and the needs of the English market. We observed commonalities in the history of comparable corporate information systems such as Computer Aided Production Management applications in the 1980s/1990s³³. During the Anglicization process, early-adopters became closer to the vendor and they were actively involved in shaping the English versions of the system. The early-adopters became field study sites for the vendors, and they presented their demands directly to the supplier. Pollock, Hyysalo³⁴ refer to these as ‘reference actors’ who would help the vendor construct the system and at the same time benefit from this close relationship. Suppliers kept the follower organizations more distant. In order to promote their request and urge for solutions, adopter organizations (both early and followers) joined forces to create a common

voice and identify common needs. The greater sharing across hospitals benefitted the vendor in terms of unifying the actual needs. However, at the same time, it forced the vendor to respond to this collective voice. This has been highlighted in the development of packaged applications as change from direct modes of user-vendor relationships to a complex set of relationships which involves formation and reshaping of direct and indirect links between the vendor and its community of users^{14,35}.

4.3 Implications for policy and practice

These findings have implications for broader thinking about strategies for innovation in the field of HIS. First, the suppliers need to understand that the generification process has entered a new terrain. They need to opt for new strategies to incorporate particular needs of different organizations and national systems. They require tactics to manage global/local tensions and introduce 'flexible generification'³⁶ into packaged applications. This requires strengthening the user-supplier links starting with the early introduction of the systems into the country of use and continuing to later adoptions of the systems by followers. This move, from a generic system to catering for the needs of a new country, opens up avenues for long-term development of packages to uncover potentials for a greater array of international markets.

Moreover, the health sector (adopters), should comprehend the concept and attributes of generification. Accordingly, they need to prioritize and regulate their demands. They also need to form networks that manage diversity and drive user innovations or user participation in system development.

Finally, decision makers also need to support driving HIS innovation and streamlining the collaborative processes between suppliers, adopters, and the national health systems. In view of that, they need to put usability and productivity as central issues for package selection and procurement.

5. Conclusions

While generification of packaged applications is well known, the growing complexity of HIS and the particular conditions and needs of the health sector and national health systems, call for customization of technologies in this sector. This results in tensions between ‘standardization’ and ‘localization’. This requires suppliers and adopters of these technologies to develop and improve their strategies to overcome these issues. Whilst some adopter strategies were aligned with suppliers’ approaches, there were also competing interests, which led to conflict of actions. We argue that these emerging strategies are an integral part of the growth of the HIS in international markets. However, they have proved to be inadequate in promoting adequate innovation in this sector.

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Contributorship Statement

AS and RW conceived this work. HM and KC collected data for this study. HM led on data analysis and drafting of the manuscript. All authors have commented on various versions of this manuscript and inputted into the analysis.

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