Self-centric and altruistic unmet needs for Ebola: barriers to international preparedness

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Abstract

Objective Barriers to international Ebola preparedness may be elucidated by identifying heterogeneities in arguments to invest in countermeasures during “peace time”.

Methods For each patent family concerning Ebola and published until end 2014 the oldest patent document was analysed. Grounded theory coding identified five unmet needs; for: (i) vaccines and therapies; (ii) control of outbreaks in endemic areas; (iii) detection and control of outbreaks in non-endemic areas; (iv) better understanding of filoviruses and (v) protection against bioterrorism. Odd-ratios for unmet needs by geographical regions and institution types were compared using Pearson’s Chi-square test.

Results Statistically significant heterogeneities in unmet need profiles were found. US applicants combined self-centric and altruistic arguments, focusing on medical unmet needs and bioterrorism protection. Russian and Asian applicants emphasized self-centric motives, specifically detection and control of non-endemic outbreaks. A clear, statistically significant mismatch between industry and academia was found; while industrial applicants focused on bioterrorism and neglected detection and control of non-endemic outbreaks, academic applicants did the opposite.

Conclusions This research identified heterogeneities in articulated needs between geographical regions and stakeholder types. Structural unmet need articulation may form the basis for attuning stakeholder engagement strategies while progression across the demand-driven value chain might necessitate international concordance.
6.1 Introduction

Strictly implemented public health measures are likely to control Ebola virus outbreaks locally should it emerge in industrialized countries. Where such measures are insufficient, as recently in West Africa, virus-specific antiviral compounds and vaccines become essential to complement these measures. These medical interventions, however, are hard to develop in a timely fashion during “war time”, i.e., at the heart of an emerging epidemic.

Some of the barriers to developing such countermeasures during “peace time” relate to motivational drivers. For industrial stakeholders a major barrier to the development of medical interventions has been the “industry paradox”: the largely self-limiting nature of filovirus outbreaks seems prohibitive for return on private sector investments (219). Public health officials prioritize diseases with higher current unmet medical needs over diseases with limited current health impact, even though the latter may emerge to pandemic proportions with large impacts on society (220). A final barrier appears related to the slow start of international aid campaigns implementing public health measures to contain recent outbreaks (221). This last barrier may at least in part be due to the self-centric focus of some states in terms of biological threat response mechanisms (222).

Although differences in motivational drivers clearly pose barriers to international outbreak preparedness and speculations on these differences exist (222), no systematic research has been conducted on how these drivers actually differ between institutions and geographical regions. This is problematic since strategies attuned to pre-outbreak motivations could be the key to effective stakeholder alignment during “peace time”, necessary for medical preparedness. In turn, this may also improve stakeholder engagement for international aid during the initial phases of outbreaks. To address this knowledge gap, the current research looks into the primary patent literature to analyse documented motivations from stakeholders that have invested in developing countermeasures in a pre-outbreak stage.

6.2 Methods

6.2.1 Measures

All patent documents (215) published until end 2014 with the term “Ebol*” or “filovir*” in title or abstract were retrieved from the Espacenet database. This database includes more than 90 million patents from 92 patent issuing organisations worldwide and is considered by experts to be all-inclusive (D. Van Harte, Dutch RVO, personal communication, January 22, 2015). Priority numbers were used to identify the primary patent document (with the oldest application date) for each family (i.e. related documents that differed only by limited alterations to the same invention). This resulted in 150 primary patent documents, constituting the complete population of patent families that were applied for before July 1st, 2013 (during “peace time”), as well as 7 patent documents published between July 1st, 2013 and December 31st, 2014 (i.e. before the end of the 18-month confidentiality period).
Primary patent documents were subjected to full-text analysis – with a specific focus on the “background” and “field of invention” sections – to identify unmet needs. During this analysis, 26 primary patent documents were excluded for not involving Ebola or filoviruses as a target (exclusion criteria in supplemental material S6.1). Based upon grounded theory coding and inductive text analysis five unmet need categories were identified: (i) the medical unmet need for vaccines and disease-specific therapies, the societal unmet needs for (ii) detection and control of outbreaks in non-endemic areas, (iii) for control of outbreaks in endemic areas and (iv) for protection against bioterrorism, and (v) the technical unmet need for better understanding of filoviruses. Using these five categories, the text from all patents was categorized by blinded review (classification criteria in supplemental material S6.2).

Applicants that were also mentioned as inventor (i.e. non-institutional applicants) were removed. The remaining institutional applicants were classified as industry, academia or government. The country code indicated for these applicants was used to define the geographical region(s) from which the patent originated.

16 patent documents did not mention an institutional applicant. For 13 of these patent documents an institutional applicant was found in another patent document belonging to the same patent family or via an online search identifying the affiliation of the inventors during the time of patent application. Geographical origin for this latter group was derived from the inventors’ country codes. 3 patent documents for which no institutional applicant could be found or derived were excluded from the institutional analysis. Countries with less than 10 patent families each (Australia, Canada and South-Africa) were excluded from the geographical analysis. This included 7 patent families in total.

6.2.2 Statistical methods

The geographical analysis included 117 patents. The institutional analysis included 121 patents. Patents that mentioned multiple unmet needs were counted once for each unmet need. Patents with applicants from multiple geographical regions or from multiple organization types were counted once for each region or organization type, respectively. Pearson’s Chi square test ($\chi^2$) and Fisher’s exact test (FET) were used to determine statistical significance (p<0.05) on 2x2 contingency tables.

6.3 Results

Medical unmet needs were described in nearly all patent families (92%). Three societal unmet needs were mentioned: the need for control of outbreaks in endemic areas (47%), for detection and control of outbreaks in non-endemic areas (37%) and for protection against the threat of bioterrorism (30%). Bioterrorism was first mentioned in 2002 (after 9/11) and subsequently as frequently as other societal unmet needs. 31% of the patents mentioned technical unmet needs (see Figure 6.1).
While Russian applicants were the first to patent an Ebola-related invention in 1992, currently the US are overrepresented in the patent literature with 68% of all patent families having US applicants. Other patenting regions included Europe (13%), Asia (10%) and Russia (9%). Institutional applicants were either academic (64%), industrial (44%) or governmental (29%).

The unmet need profiles of applicants from different regions showed statistically significant heterogeneities (see Figure 6.2). US applicants had two unmet needs of primary interest. More than applicants from other regions, they focused on the altruistic medical unmet need for vaccines and therapies (95% of patents from US applicants; OR=4.44; p=0.029, FET) and furthermore showed a highly significant (p<0.001) and strong (OR=10.54) interest in the self-centric need for protection against bioterrorism (40%; χ2(1)=13.17). This latter unmet need was fully absent in Russia-based patents (p=0.017, FET). In contrast, Russian and Asian applicants mentioned the more self-centric need for detection and control of non-endemic outbreaks in the vast majority of patents, resulting in statistically significant ORs (OR=9.58; p=0.001, FET and OR=8.39; p=0.006, FET, respectively). In turn, this unmet need was of far less importance for US and European applicants (29%; OR=0.20; χ2(1)=14.41; p<0.001 and 13%; OR=0.19; χ2(1)=5.59; p=0.018, respectively). Although Asian applicants also seemed to show relatively much interest in control of endemic outbreaks, these differences were statistically non-significant (OR=3.56, χ2(1)=3.70; p=0.070).
Chapter 6 - II

**Societal unmet need: protection against bioterrorism**

**Societal unmet need: control of outbreaks in endemic areas**

**Societal unmet need: detection and control of outbreaks in non-endemic areas**

**Technical unmet need: better understanding of filoviruses**

**Medical unmet need: vaccines and therapies**

* * significant at p<0.05; ** significant at p<0.01; *** significant at p<0.001

**FIGURE 6.2** Percentage of patents per country (A-E) and per type of organization (F-J) that addressed the specified unmet needs (with odds ratios and 95% confidence intervals).
Further statistically significant heterogeneities in unmet need profiles were found between different institution types. Industrial applicants emphasized the need for protection against bioterrorism (55%; OR=5.91; χ²(1)=18.71; p<0.001), an unmet need that was scarcely mentioned by academic applicants (17%; OR=0.25; χ²(1)=11.48; p<0.001). In contrast, industrial applicants were less interested in detection and control of outbreaks in non-endemic areas (25%; OR=0.42; χ²(1)=4.40; p=0.036) than their academic and governmental counterparts (44% and 41%, respectively). Governmental applicants demonstrated a stronger interest in the control of outbreaks in endemic areas (76%; OR=4.89; χ²(1)=11.92; p<0.001) than industrial and academic applicants (36% and 44%, respectively) and, surprisingly, also in technical unmet needs for a better understanding of filoviruses (55%; OR=3.92; χ²(1)=10.00; p=0.002) than academic and industrial applicants (30% and 23%, respectively).

6.4 Discussion

This study revealed heterogeneities in motivational drivers to invest in Ebola-related medical preparedness between different geographical regions and institution types. These identified heterogeneities may form the basis for tailored actions to improve medical preparedness and outbreak response.

US applicants were overrepresented in the patent literature and primarily mentioned the medical unmet need for vaccines and therapies and the societal unmet need for protection against bioterrorism. This is consistent with the US being ranked as the largest donor of international support for the current Ebola outbreak (137) and may indicate that US stakeholders combine self-centric arguments with a global-oriented perspective on Ebola-related unmet needs. In contrast, Russian and Asian applicants showed a less altruistic and more self-centric profile, with a relatively large focus on diagnostics and the prevention of outbreaks in non-endemic areas. China’s efforts to prevent an outbreak of Ebola in their region (223) may be associated with this more self-centric perspective.

Differences in unmet need articulation between geographical regions impact international coordination. A recent example is the Global Health Security Agenda (GHSA), a partnership launched to complement the WHO International Health Regulations (IHR) treaty in capacity building for detection and response to public health threats (224). The strong focus on health security by the US-led GHSA has been a point of concern for other countries within both the GHSA and the IHR (224). The current study underlines that bioterrorism indeed has been a major point of focus for the US and that this unmet need is not shared by all regions.

From an opposite perspective, in the recent Ebola crisis, the US took six weeks to allocate budget and resources to contain the epidemic after the Public Health Emergency of International Concern (PHEIC) declaration from the WHO (221). A tailored call to action that triggered intrinsic US motivational drivers, as explicated in the current study, might have reduced this delay in response.

Heterogeneities between different institution types seem to be of particular importance for medical preparedness. Industrial applicants tended to articulate Ebola-related unmet needs in
terms of bioterrorism protection, which – as has been suggested in the non-scientific literature – relates to a possibility for a return on investment (136). Interestingly, industrial stakeholders rarely mentioned the need for detection and control of outbreaks in non-endemic areas, thus indicating that they hardly considered this as a potential market. In comparison with academic applicants a clear mismatch in unmet need articulation was found. Whereas industry focused on bioterrorism and neglected the need for detection and control of outbreaks in non-endemic areas, academic applicants did the opposite: 17% of their patents mentioned bioterrorism while almost half of their patents mentioned detection and control in non-endemic areas.

Since interactions between public and private institutions are essential to effective product development (219), mismatches in the demand articulation between public and private institutions can hamper the translation of research findings into new products and services. Agenda-setting is an often overlooked – but essential – step in addressing unmet needs via research and innovation (90). A neglect of specific medical, societal or technical unmet needs may therefore hinder innovative progress, a case which has been exemplified by the increased budget the US Congress allocated for GHSA initiatives and the simultaneous decrease in budgets for research on pathogenesis and epidemiology (224). Heterogeneities in unmet need profiles of different institution types likely resulted in such articulation mismatch in the field of Ebola, contributing to the lack of medical preparedness.

Eventually, the amount of funds allocated by private companies to respond to the current epidemic crisis have reached relatively high values (137), which may indicate an industrial change in perspective on societal unmet needs. Considering the huge impact that societal demand articulation has on stock prices of private companies (225), this is of great importance: such changes may provide the incentives for industrial actors to invest in medical preparedness for a broader range of unmet needs than solely those related to the threat of bioterrorism and thereby improve the alignment with other stakeholders.

6.5 Conclusion

This research provides a first systematic overview of geographic and institutional differences in motivational drivers for engaging in Ebola-specific medical preparedness. During early stages of outbreaks, stakeholder engagement strategies attuned to geographical unmet need profiles may aid in timely outbreak response efforts. A clear understanding of mismatches in this unmet need articulation may furthermore assist in overcoming some of the barriers to the development of new medical interventions against emerging infectious diseases, well ahead of “war times” and epidemic crises. Unmet medical, societal and technical needs are inadequately addressed when political and funding priorities of governments, academia and industry across geographical regions are not connected to unmet need driven development. Structural thinking in which these unmet needs are articulated will contribute to progression across the demand-driven value chain. International and institutional concordance will be a vital part of this.
Ebola: Self-centric and altruistic needs