166. Levers & barriers for orphan drug business development: a systematic literature review

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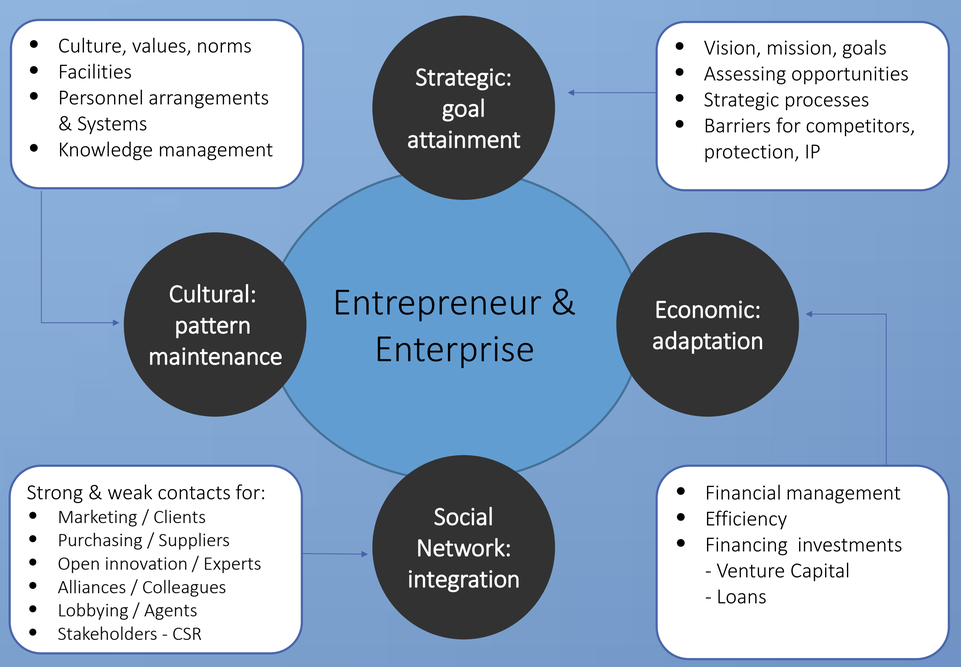
Introduction / Summary

While orphan drug (OD) regulations have proven to be an effective tool in stimulating the development of rare disease (RD) therapies (de Vrueh, 2014), challenges still remain.
Correct diagnosis of a RD is often delayed by many years, there is lack of physicians and healthcare providers with relevant training and experience, and the few treatments available are difficult to access and costly (Benjamin et al., 2017; Grossman et al., 2014). At the same time, companies, like Genzyme and Shire, proved that OD can be the basis of a viable business model (Boon & Broekgaarden, 2013).
As the number of OD's is rising, and they are predicted to account for over 20% of all prescription drugs by 2020 (Benjamin et al., 2017), this calls for a better understanding of the situation: are there opportunities that we are missing?

Social systems analysis

The purpose of this research is to review existing literature concerning the development of drugs for rare, or orphan, diseases. To do so we conduct a systematic review of the available knowledge about the market for drugs for orphan diseases.

We structure our review using the neo-functionalist framework of Groen (2005), see figure below, which suggests that for a system to be viable, it has to maintain four core functions: strategic goal attainment, cultural pattern maintenance, social network interaction and economic optimization of gratification.



Method

- Web of Science (Social Science Index); all years/journals included
- Keywords: "orphan drug" & "rare disease drug"
- 477 records → category refinement → removing
  HIV/AIDS/Drug abuse/Toxicology articles
  Conference abstracts; Open access journals
- 179 records → abstract screening & removing articles not focused on orphan drugs or rare diseases
- 135 records for analysis
- Coding articles on primary dimension (what is this article's primary focus?) and secondary dimension (How is the focus/problem of the article being solved?)

Results: What are we now researching? Where are the gaps?

Strategic dimension

- **Strategic processes & barriers**
  - IP, Market exclusivity

  → Market vs. nonmarket economy
  → Notion of "reasonable profit" needs clarification
- **Goal setting / Decision making**
  - Cost effectiveness
  - Variation across countries
  - Transparency
  - Efficiency, consequences of OD
  - Patient access to treatments

  → Cost effectiveness argument does not matter….
  → Need more integration

Cultural dimension

- **Norms**
  - Most focus on regulations & approval procedures' role & variation across countries
- **Knowledge systems**
  - Changes in technological space: e.g. pharmacogenomics
  - Accumulation of knowledge

  → Need for transformative drugs
  → Public private collaborations
- **Culture and Values**
  - What does it mean to be rare?
  - Should governments prioritize RD?

  → Patients ready to take more risk
  → Discomfort from lack of diagnosis & understanding

Social dimension (SD)

- 1 article focused on networks!
- **As secondary dimension…**
  - SD of learning across patient groups / regulatory bodies / industry
  - SD of Decision making (broader stakeholder involvement; changing corporate practices)
  - SD of financing (venture philanthropy)

  → Recurrent calls for more social collaboration
  → Lack of understanding of the network mechanisms

Economic dimension

- **Expenditures, reimbursements, impact**
  - Low budget impact now, but may increase in future (e.g. impact of pharmacogenomics)
- **OD sales & costs analysis**
  - Few very expensive drugs
  - Volume comes from OD's with non-orphan indications

  →How correct are the figures?
- **Profitability**
  - Strategies for (relabeling, salami slicing)
  - Funds for (philanthropy; VC profitability)

  → Focus on malpractice, not new solutions

Discussion & Conclusion

- **OD literature** appears to be fragmented across outlets (70 outlets for 135 articles in this review), and researchers (4 research groups, with majority of unique contributions)
- **Strategic processes & goal setting:** regulations (e.g. market exclusivity) create conditions of economic sustainability, but do not *motivate* companies to enter in RD space. → Plea for the role of families and philanthropies, for social entrepreneurship. Evaluation & approval procedures face a conflict for more harmonization, yet more account for diversity of the economies. There are calls for alternative decision making frameworks (beyond pure effectiveness argument – e.g. "rescue rule").
- At cultural (**culture, values, norms and knowledge**) level, much work done in analyzing & comparing the regulatory frameworks across countries and over time. Recently, works on knowledge management for clinical trials and sustainable OD development began to emerge. Public-private partnerships and transformative drugs seem to offer promise for further development. Need to shift of locus of responsibility from the state to society: plea for more social entrepreneurship. Further, culture of OD support is framed within "zero sum game" approach, which needs to change to give space for RD developments. Too few contributions focus on patient experience and role. In RD space role of patients differs: we need to integrate them in the norms and values of the system.
- At **network** level we observe the how and who of multiple stakeholders constituting the ecosystem for the orphan drug development. In contrast, information disconnects hurt knowledge exchange and R&D, leading to missed opportunities in drug development. We need to understand the work of networking mechanisms better.
- **Economics of OD's** is the most discussed issue. However, it is dominated by discussions on cost-efficiency and reimbursement across countries. Lack of attention to successful business models, e.g. repurposing of existing drugs, or the role of non-profits. Call for more focus on responsible business models, not "reasonable profit" focus.

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