Cost-effectiveness of nanomedicine: estimating the real size of nano-costs

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“Nanomedicine could contribute significantly to affordable care, but a first step is performing proper evaluation by updated cost-effectiveness analyses”

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The nanomedicine market: small particles; tremendous potential

Nanoparticles have already demonstrated their clinical potential, showing their ability to change the course of diagnostics and therapy [1,2]. The number of products with enhanced therapeutic efficacy due to their nanoscale dimensions is skyrocketing. The availability of nano-based therapeutics on the rapidly emerging nanomedicine market is growing, while an even greater number of nanodrugs are undergoing clinical investigation [3–5].

The big business of nanomedicines had an estimated value of US\$53 billion in 2009 [6]. The industry is projected to reach a total market value of approximately US\$334 billion by 2025 [7,8]. Soon, the first-generation nanodrugs will start going off-patent, while an increasing number of new generation nanotherapeutics (around 40% of nanodrugs are currently in Phase II clinical trials) will enter the market, creating more market value [7,9]. According to the Grand View Research Report, the USA remains the leader in the nanomedicine industry, owning 46% of the total international nanomedicine revenue in 2016 [9], followed by Europe [10]. Japan is considered an emerging but attractive nanomedicine player [10]. Major industry players in the market include Pfizer Inc. (NY, USA), Ablynx NV. (Ghent, Belgium), Nanotherapeutics Inc. (FL, USA), Nanoviricides Inc. (CT, USA), Abraxis Inc. (USA), Arrowhead Research Inc. (CA, USA), Celgene Corporation (NJ, USA), Bio-Gate AG (Nürnberg, Germany) and Merck (NJ, USA) [9].

The major portion of nanomedicine market revenue is for therapeutics, consisting of drugs, devices and drug delivery systems. The anticancer agents segment is still the most advanced and largest niche of the nanomedicine market, accounting for almost 50% of revenue, and this niche is expected to continue fueling the nanomedicine market in the future [10]. However, an increasing number of nanotherapeutics have been investigated for their potential use as targeted drug delivery agents across a wide variety of diseases. Emerging segments for nanodrugs include chronic respiratory diseases, anti-inflammatory delivery, cardiology and vascular diseases, neurology, anti-infectives, diabetes and regenerative medicine.

Economic challenges of the nanomedicine market

Although the nanomedical market has enormous potential and attracted interest from the scientific community around the world, successful translation of nanodrugs from bench to bedside remains challenging. Commercialization continues to be driven mainly by small and medium-sized enterprises (SMEs), addressing the extremely lengthy and costly validation of the concept as well as the navigation through clinical trials [11], while Big Pharma remains on ‘low profile’, showing apparently low interest in these emerging drugs [9]. Once SMEs demonstrate the potential of the new concept with validated drugs or devices, Big Pharma increases interest by buying more of the SME [11]. For the SMEs, collaboration with larger pharmaceutical companies and academia is crucial, capitalizing the unique strengths of each collaborating partner [12]. If we investigate the 2018 nanomedicine investments, we see the EU Framework Program 7 and Horizon 2020 in Europe invested €430 million in 84 research projects, divided over 1000 labs and 250 SMEs [13], while the NIH in the USA invested an equivalent amount of US\$445 million [14].

Industry investors will rarely invest money in the 'risky' projects and technologies. Industrial investments start when extreme risks have been mitigated by others. Once a drug or technology has demonstrated significant potential, private industry starts investing, shifting the balance 'public' (or philanthropic) funded projects to commercially funded.

Price poses an important challenge for companies producing nanotherapeutics. Nanodrugs are significantly more expensive to manufacture than conventional medicines [15–17]. These diseconomies of scale lead to significantly higher selling prices, or acquisition costs for hospitals, hampering nanomedicines' everyday success. High acquisition costs can, however, be justified by the nanotherapeutics' improved cost–effectiveness. If not, the nanodrug will fail to be reimbursed. However, the challenges of nanomanufacturing go beyond money. The expertise to intervene with nanomedical technology is also limited in supply. The time and space required to manufacture nanodrugs is constrained. In European countries where medicines are selected and funded out of public sources upon rational selection, a high acquisition cost may be a serious obstacle for reimbursement. In these countries, highly priced nanomedicines have an extremely low chance to reach the market – and thus the patient. Another barrier of expensive interventions is the nearly complete separation between costs of care and the patient in the for-profit healthcare industry. The intermediaries between patient and healthcare – health insurers and hospitals – have taken control over healthcare expenditures. These intermediaries are driven by profit and strive to keep costs down. This is an unfortunate situation in the USA, where private insurers are lowering the possibility of highly effective but costly nanomedicines to be reimbursed.

Finally, most developed countries are facing skyrocketing healthcare costs. An ageing population, increasing prices of medicines and treatments, and inefficient use of medical services are partly responsible for the continuously rising costs [18]. However, the main factor responsible for the spiraling healthcare costs are the chronic diseases, such as cancer and diabetes, and 'epidemic' rates worldwide, fueling healthcare spending [18]. Chronic diseases overwhelm patients physically, emotionally and financially, but they also have a significant impact on society in terms of healthcare costs – income losses for patients and caregivers. Rising healthcare spending puts increasing pressures to improve the efficiency of public healthcare services, which should encourage policy-makers and health administrators to stimulate more efficient healthcare. This clearly demonstrates the need for an efficient allocation of healthcare resources to contain the growth of healthcare spending while making new drugs and treatments, such as highly effective nanodrugs, available at reasonable costs.

Comprehending cost–effectiveness comprehensively: is something missing?

The success of bringing highly priced nanotherapeutics to the patient – and thus uptake into the market – can be significantly improved by employing specific decision-making frameworks. The use of comprehensive, standardized cost–effectiveness analyses shifts the focus toward restraining healthcare expenditures while maintaining quality of care [19], creating value for money in the healthcare market. Value for money is created for society by integrating and reimbursing cost-effective interventions, in other words, treatments or drugs which have the lowest cost per given health effect.

An important drawback of current cost–effectiveness research in the field of nanomedicine is that almost all studies continue to account for only the direct costs of treatment, ignoring indirect costs completely. A quick search of scientific databases (PubMed, Medline, the Cochrane Library and ISI Web of Science) confirms that the cost–effectiveness analysis comparing first generation PEGylated liposomal doxorubicin with gemcitabine [20] continues to be the sole comprehensive study in nanomedicine; it demonstrated 'expensive' liposomal doxorubicin is cost saving when considering all costs. Prompt action is urgently needed in the nanomedicine market to demonstrate 'expensive' nanodrugs of newer generations are also cost effective or even cost saving for society using a comprehensive cost taxonomy. Moreover, the hospital perspective continues to frame the assessment of costs in the field of nanomedicine. As a consequence of this frame, indirect costs are never assessed, penalizing the more effective nanodrugs, since less production and transportation costs from fewer treatment-related adverse events and long-term complications can result in huge savings. More effective nanomedicines can also result in significantly lower forgone interests due to a premature death, since survival can be improved. Moreover, the indirect patient visiting costs for family and friends can drastically decrease, since patients could spend significantly fewer days in the hospital, lowering hospital administration costs. Direct costs for additional therapies and drugs could also decrease due to fewer treatment-related adverse events and long-term complications of the disease. The 'human loss', or the indirect, intangible cost in pain and suffering could be significantly decreased (though this cost should ideally be included in quality of life estimates). A final point of concern is the large variation in cost definitions,

which hinders cross-study comparisons. There is urgent need for an updated cost model, where costs are ideally assessed from a societal perspective, combining direct and indirect costs regardless of who bears them.

Future direction: comprehensive cost-effectiveness of nanomedicine

Although the number of cost-effectiveness studies in the nanomedicine field have increased significantly, cost-effectiveness research of nanomedicines is still in its infancy and only limited progressions have been realized. Comprehensive, standardized cost-effectiveness remains a missing link between the development of excellent new drugs and the efficient allocation of scarce financial resources. Ultimately, the model could be validated and applied to any new intervention. Once accepted by major payers, the decision-making model could be used for policy decision-making.

The current and apparently 'unbreakable' barrier to efficient commercialization could, however, be torn down even in these times of shrinking budgets. Nanomedicine could contribute significantly to affordable care, but a first step is performing proper evaluation by updated cost-effectiveness analyses. Only then will 'unattractive' nanodrugs (those with significantly higher acquisition costs) reveal their potential superiority as cost effective for society. In particular, large direct and indirect savings can be realized by the administration of effective nanodrugs. Without this, 'expensive' nanomedicines – which have the right characteristics to seek reimbursement – will have only little chance of reaching the patient, relegated instead to a valley of 'forgotten' promising therapeutics.

Author contributions

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