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Evaluating Drug Efficacy and Patient Outcomes in Personalized Medicine: The Role of AI-Enhanced Neuroimaging and Digital Transformation in Biopharmaceutical Services

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Abstract

This article concerns the development of statistical software, in Python and R, that is aimed at evaluating the effectiveness of personalized treatment strategies.

This software is a framework for estimating, with quantified uncertainty, how much better a proposed personalized treatment strategy is expected to perform compared to a current strategy for allocating treatments. The framework and software are aimed at researchers or practitioners who have clinical trial data where electronic health records or baseline patient characteristics are sufficient to personalize treatment. Importantly, the software incorporates the last data points of a study and stops the trial when adequate conclusions can be drawn. It serves as a complement to three papers that have explored the theoretical properties of such decision rules.

Keywords: Drug Efficacy, Patient Outcomes, Personalized Medicine, AI-Enhanced Neuroimaging, Pharmacokinetics, Pharmacodynamics, Digital Transformation, Biopharmaceutical Services, Machine Learning in Healthcare, Neuroimaging Data, Genetic Profiling, Clinical Data Integration, Adaptive Dosing, Drug Concentration, Adverse Drug Reactions (ADR).

1. Introduction

Medical patients vary in response to treatments and experience heterogeneous sets of side effects. This is particularly a problem in the current treatment paradigm. The idea that individual treatment decisions can be improved by treating patients based on a heterogeneous set of prognostic indicators has been known for decades. This medical paradigm, called personalized medicine, holds the potential to markedly improve population health by targeting treatments to those individuals most likely to benefit and least likely to be harmed, drastically diming the ongoing and massive costs associated with the conventional trial-and-error approach to treatment.

In recent years, relational collaborative filtering has gained increased interest. In essence, these approaches model treatment effect heterogeneity by estimating the dependence of outcome on patient and treatment features. A basic set-up pursued by many papers considers a single outcome of interest collected in a standard, fixed-dimension monitoring window after treatment initiation. Generalization of the estimation and optimization of dynamic treatment regimes to more than one outcome remains largely open and rarely considered.

The joint modeling of several outcomes is complicated by the nonlinear direct effect of treatment on longitudinal response. Meanwhile, any given treatment effect also enters the joint distribution determining all outcomes, allowing additional model flexibility to be exploited. The possibility of accommodating a binary outcome as a limit of continuous regression outcomes recently garnered interest. This is particularly important for drug treatment applications where some adverse events can be rare. For this reason, a re-analysis of data on a relevant trial is a pertinent endeavor.

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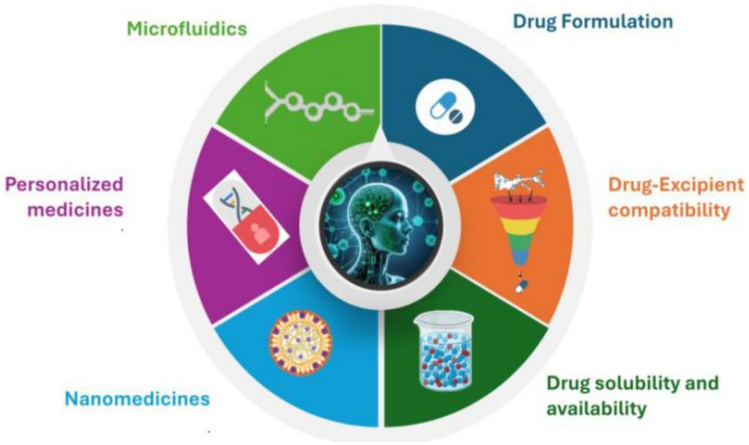


Fig 1: Drug Discovery and Drug Delivery

1.1. Background and Significance

Personalized medicine, sometimes called "precision medicine" or "stratified medicine," is a medical paradigm offering the possibility for improved health of individuals by treating individuals based on heterogeneous prognostic or genomic information. These approaches have been described under the umbrella of "P4 medicine," a systems approach that combines predictive, personalized, preventive and participatory features to improve patient outcomes. A concept encompassed under the personalized medicine rubric is adaptive or dynamic treatment regimes, where randomized comparative/controlled trials are performed at one or more stages to infer when it is best to administer which treatments. The problem of optimal dynamic regime estimation has drawn much attention from researchers of a statistical, epidemiological, and econometric upbringing for its use in patient therapy RCTs. An equivalent concept under a clinical trials framework are adaptive interventions (AIs). Much recent statistical research has focused on how to best estimate DTRs or AIs, strategies that vary treatments administered over time as more is learned about how particular individuals/patients respond to interventions. Important early success in the design of clinical trials to deliver information about dynamic treatment regimens was recognized in the 2000 election platform for the Office of the President of the United States. One important implication of these initiatives is that in coming years many more patient therapy RCTs of this form will be conducted on widely varying diseases. Thus, having a method for a priori RCTs to plan such dynamic regimens is necessary. At present there is no such method, nor are there guidelines for questions typically encountered in the design of such trials.

Personalized medicine is a statistical problem. A clear gap in the literature is the difficulty of assessing how well one model for personalized care performs. Most work has focused on the construction of personalization models, e.g., algorithms or rules that indicate how future patients should be treated based on their prognostic information. There has been some work on point-value comparisons, i.e., under one particular model, the difference in expected outcome measures is studied. However, from a pragmatic perspective, it is undesirable to limit testing to one model. Practitioners require general techniques to assess how well personalization is working and, by extension, how much personalization is warranted given available prognostics. This perspective has been echoed elsewhere; "more targeted research is warranted on the development of tools and guidance for the validation of prespecified adaptive treatment strategies". This paper and its software is an attempt to fill in part of this gap. It addresses the (hopefully) simple end of the problem.

Equ 1: Drug Efficacy Evaluation

$$E(t) = \frac{E_{\max} \cdot C(t)}{C(t) + EC_{50}}$$

Where:

- $E(t)$ = drug efficacy at time t
- $E_{\max}$ = maximum effect of the drug
- $C(t)$ = concentration of the drug in the bloodstream at time t
- EC_{50} = concentration of the drug at which 50% of the maximum

2. Understanding Personalized Medicine

2.1 Personalized Medicine Personalized medicine is the trend in the healthcare industry. In recent years, it has attracted increasing interest from both the healthcare industry and IT research community. Being able to predict the individual outcome is one of the ultimate goals of making things under control. Once we can predict individual responses perfectly,

the following things will be particularly promoted. Medical treatment or healthcare provisions can be taken immediately when some potential risks can be predicted from the individual. Health insurance schemes specialized for the individual can be designed in a way that is suitable with the individual risk, and avoid paying unnecessary high insurance premiums. Despite many research contributions in learning useful information from large-scale patient record databases, most of the existing research is concentrated on deterministic methods. When the model fails, it can give unwanted consequences due to the predicted false result. One possibility to improve this issue is to integrate the stochastic dynamics.
2.2 Current Personalized Medicines and EBP The rise of personalized medicines is suggested by the rapid decline in costs to sequence a human's genome. However, personalized care has been practiced since antiquity in both explicit situations and counter-factually in modeling without deliberately making the underlying assumptions. With the increasing availability and decreasing cost of large amounts of granular data, personalized medicine has generated substantial interest in both the public health community and the general public. The motivation of personalized medicine is that individuals differ in terms of genetics, environment and behavior and the best treatment for one patient may not work for another. Although most recent methods papers in personalized medicine call for a move towards evidence-based procedures, the machinery to rigorously facilitate such changes is scarce.

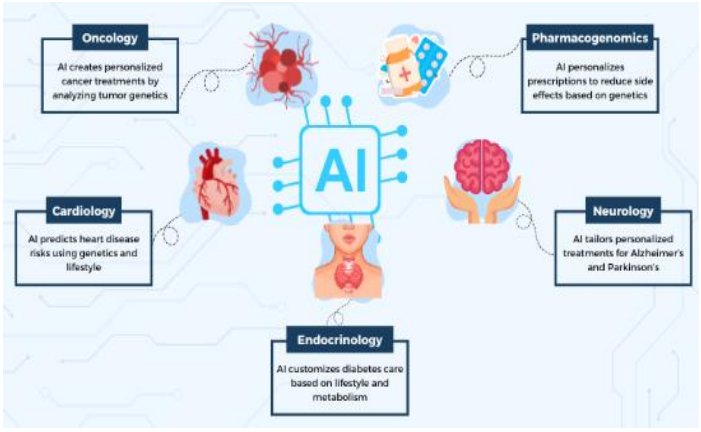


Fig 2: AI-Powered Personalized Medicine

2.1. Definition and Importance

In this manuscript a new method to rigorously evaluate the effectiveness of a binary personalization model using treatment effect ML-EM (TEME) is introduced. In particular, the case with continuous and binary patient subgroups and a binary endpoint is addressed. The method is outlined and is presented. In personalized medicine, personalizations are tailored entirely to the characteristics of a single subgroup unit. Alternatively, group-level personalizations relevant to characteristics common across the group are referred to as a model of 'binary personalizations'. The effectiveness of such a binary personalization model can be assessed related to the explicit binary patient subgroups. Model misspecification can be detected, and hypothesis-driven identification of informative subgroups and gradient estimates can be performed. Estimates of improvement are produced that are large-sample consistent and asymptotically normally distributed. The methodology is exemplified on both simulated data and in the context of a comparative effectiveness trial in Major Depressive Disorder. Finally, suggestions for extensions and applications are given. Concern with 'horizontal misspecification'. That is, because they are tailored to individuals, evaluation of binary personalization models against binary patient subgroups can broaden the scope of model checks to those more likely to go undetected by the common cutoff-free methods.

2.2. Historical Context

The possible value of the disease endophenotype concept, in association with the disease risk geno phenotype of the individuals, relative to the drug-induced gene expression mechanism affecting the response and the outcome of a drug, is explored. Personalized medicine or tailored therapy is an approach, the main aim of which is to use an individual's genetic and environmental information in order to improve the efficacy and safety of treatment. The wide practice of personalized medicine has been, so far, hampered by the unfinished understanding of the individual specifics of an organism relative to drug response and treatment outcome. The biomarkers affecting, predisposing or reflecting these specifics have not been sufficiently characterized yet. Drug toxicity and low/no efficacy are major causes of drug failure, causing unsafe and insufficient medications. Once an inappropriate drug therapy is prescribed, the mechanisms inducing adverse drug reactions (ADRs) could affect geno phenotype and endophenotype of the patient, affecting the outcome, as well. Pharmacogenomic factors are key determinants in drug efficacy, predicting variability regarding drug response. However,

almost all the pharmacogenomic studies conducted so far investigate the genetic basis of the individual differences relative to the therapeutic drug alertness. Nevertheless, the exposure of an organism to a certain medication could harm biological systems concerning the drug itself but also regarding deviations from the homeostasis it attracts. Drug response could be perceived as an induced disease, in which a patient is in a recovering process.

3. Drug Efficacy Evaluation

In the field of lifestyle diseases, national medical expenses have been continuously increasing as the leading cause of death worldwide. However, treatment strategies for lifestyle diseases such as diabetes, hyperlipidemia, and hypertension are still decided at the doctor's discretion. This study presents a comprehensive method to evaluate the potential outcomes of using a newly prescribed drug based on a medical history in terms of overall drug efficacy and patient outcomes, by defining and simulating the flow of patient data through medical records, referrals, prescriptions, and testing the proposed methodological framework with detailed data on diabetes drugs.
Personalized medicine with individual patient characteristics has always been the ultimate goal. Innovation in this area includes biomarker-based patient selection in clinical drug development. Pharmaceutical companies are developing investigational drugs with companion diagnostics, which can make a better prognosis for a patient by grouping them according to the genomic characteristics, and are conducting clinical development in combination. In addition to companion diagnostics, there are many investigational new drugs for which predefined patient enrichment biomarkers are present, and of approved drug products, pharmacogenomics (PGx) biomarkers and other biomarkers are listed for patient selection. The recent environment of drug development is noted with the rise in R&D costs for pharmaceutical companies and the decrease in the number of approved drugs since the early 2010s. The advent of innovative methods, given the stagnant productivity of new drug development in comparison with the increase in investment, in order to discover new drugs is always a hot topic in the pharmaceutical industry. Recent research tends to focus on the problem of complexity.

3.1. Methods of Evaluation

Evaluating the effectiveness of personalized medicine has been a burgeoning area of statistical research, with a focus on estimating dynamic treatment regimes (DTR). Implementing a DTR requires software that will provide doctors or patients with a treatment decision based on an assignment of treatments for future patients as well as the option of very quick results in the form of a website. The goal of the software is to optimize patient outcome by assigning the treatment that maximizes the mean potential outcome as a function of future covariates and outcomes. There are ten available public pieces of software that estimate an optimal DTR. Many of these are developed by statistical researchers for the analysis of a DTR in the context of a specific data set, and are thus not suitable for widespread or immediate use. From a clinical practitioner perspective, the goal of a DTR is to use historical data to economically assign treatment options for future patients, such that the expected prognosis is optimized. On the flip side, software is needed that can answer two fundamental questions that practitioners will need. The two fundamental questions are as follows: 1) How much better is this personalization model expected to perform compared to previous strategies? 2) How confident can practitioners be in this estimate? This compares a given model for a DTR against a treatment allocation model based on treatment as usual or a predefined split. Commonly, a practitioner will be interested in making treatment decisions only for subsets of the patients for whom there is randomized controlled trial (RCT) data. Implementing this in the context of the software means the DTR should only be compared against the “Always” or “Splitting Covariate” randomization rules.

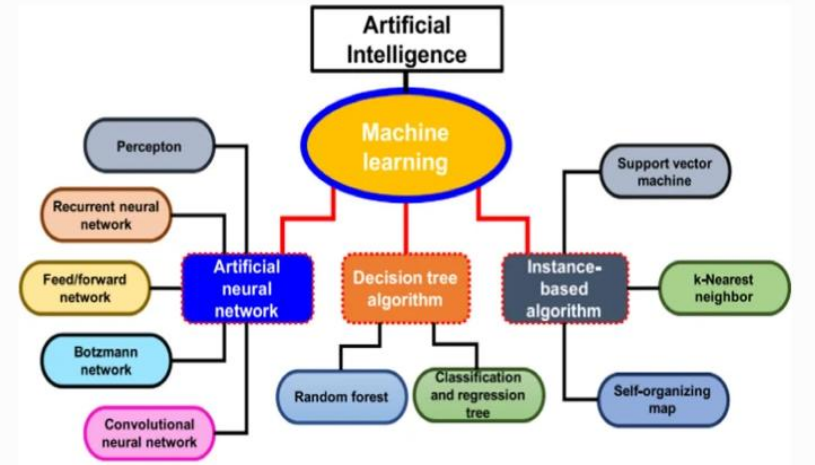


Fig 3: Evaluating the effect of artificial intelligence

3.2. Challenges in Assessment

Recently, personal and predictive medicine, often termed "individualized medicine," has been evolving with technological advances. In particular, genome-wide association studies have opened the gate for pharmacogenetic parameter applications in personalized medicine. These studies have shown hereditary variability in drug treatment response; indicating individual patient-specific dosing strategies are needed. Since genetic markers are passive parameters, there is growing interest in more active measures to adapt drug treatment to the patient and monitor and possibly predict treatment response. Live monitoring of treatment response is proposed and implemented for the choice of anticoagulants such as coumarins. Drug-dosing and assessment are controlled by the coagulation state of the patients. This novel perspective of drug monitoring could be extended to a wide range of drugs for several indications. For full realization, the pharmacokinetic-pharmacodynamic models need to be formulated. To this end, inlet-absorption-topology (IAT) models are proposed for drugs in blood within personal pharmacogenetics framework. Coupling IAT with the active treatment concept suggests new monitoring concepts for the control of drug dosing in personalized medicine and enables integration of features found in a model-based design. Algorithm performance is verified through integration on a mobile phone.

Equ 2: Adaptive Dosing Model

$$D_{\text{adapted}}(t) = D_{\text{base}} \times \left(1 + \alpha \cdot \frac{I(t)}{I_{\text{baseline}}}\right)$$

Where:

- $D_{\text{adapted}}(t)$ = adjusted drug dosage at time t
- D_{base} = baseline drug dosage
- α = adjustment factor (tuned based on clinical experience and AI
- $I(t)$ = current neuroimaging-based measure of brain activity
- I_{baseline} = baseline neuroimaging measure (e.g., before treatment)

4. Patient Outcomes in Personalized Medicine

An immense amount of effort will go into the design and understanding of effective personalized medicine. However, a fundamental driver of adoption, quantitative assessment of personalized treatment strategies, has been greatly oversimplified in the current literature, focusing largely on the results of simple patient subgroup analyses and abstracting away the critical connection to treatment strategies. It is illustrated that the efficacy of personalized treatments can also be estimated using outcomes on non-randomized patients and the availability of matched pairs. The theory shows that simple subgroup analysis helps estimate personalized treatment effects consistently, but efficiency is sacrificed when the estimand is far from the target of interest. The benefit of matching is demonstrated in this context and more broadly in Monte Carlo research involving a large number of simulation scenarios. With increased availability of patient-level information and advances in biomedicine, there has been a recent flurry of activities in the application of individualized treatment strategies based on patient characteristics. The emergence of personalized medicine for the treatment of breast cancer is a case in point. Traditional treatment approach consisting of combination chemotherapy is replaced by a gene expression array or assays using a panel of 21 genes to test the probability of a recurrence in distant organs. This new test helps to decide whether to use chemotherapy to treat the patients.

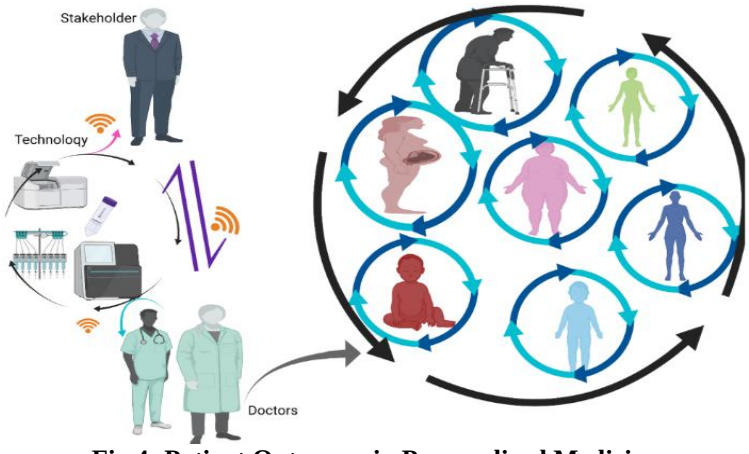


Fig 4: Patient Outcomes in Personalized Medicine

4.1. Measuring Patient Outcomes

Personalized medicine is generally understood as a health care model that tailors medical decisions, practices, interventions and therapies to each patient by basing treatment administrations on an individual's phenotype, genotype, environment and lifestyle. Despite its promise, the potential benefits of personalized medicine are challenged by the difficulty in defining and evaluating its effectiveness. Existing approaches to evaluating drug efficacy and patient outcomes may not be appropriate for personalized medicine. This section argues why current methods for evaluating drug efficacy are unsuitable for personalized medicine and suggests alternative approaches. It is essential to better understand and evaluate the effectiveness of personalized medicine.

Patient outcomes defined by health or causes of health have seen increased use in medical research and evidenced-based decision-making in health care. The benefits of patient outcomes are undeniable in that they provide the primary end goals in clinical trials, quantify the impact of treatment benefits, and ameliorate patient care. Evaluating patient outcomes is normative in standard medical statistics, even if the treatment is individualized. However, there are many issues: the individual treatment benefits derived are often not actionable, there is a dearth of valid and reliable instruments to measure treatment benefits, and inference on individual treatment effects is under-powered. There is agreement that in any full and fair comparison of care, patient outcomes should be used. Hence, the benefit or harm of different drug treatment options needs to eventually specify patient outcomes that are being considered in the treatment comparison. There is ample medical and philosophical discourse on defining and measuring health, with some consensus that health can be measured broadly within physical, mental, and social domains. Each domain should comprise q distinct measures where q is large; highly reduces the necessity to estimate the population value of any one measure. In addition, averaging across domain-specific measures helps to ensure that outcomes are relatively robust to process measure error.

4.2. Factors Influencing Outcomes

How patients respond to drug therapy in practice can differ given factors such as the setting of care, the quality of care, the cost of care, lifestyle, overall morbidity and co-morbidities, lifestyle, levels of adherence and prescribing, and what, if any, pharmacogenomic testing is undertaken. Preferences of the payer and the government regarding access to innovative therapy and fixed budgets are likely to be more influential. Restrictions on utilization are increasingly well-respected in countries with mature health care systems, possibly because such decisions are generally taken by experts and made transparent with input from professional health care groups. Decisions in this area should be well-informed and clearly communicated both to domestic health care professionals and health care authorities in other countries to avoid the impression that cost concerns take precedence over patient health needs and to avoid counter-productive reactive measures. Innovative therapies such as the class of personalized or precision-patented drugs are a recent introduction to the market and their utilization is expected to follow a different pattern from traditional drugs. Additional knowledge about their long-term impact on patient outcomes, including the economic benefit or how their risk-benefit balance compares with the previous standard of treatment. The high cost of innovative therapies raises a number of social issues, such as how to ensure equitability and sustainability of access to these treatments. Several countries have started to explore innovative pricing strategies, like performance-based risk-sharing agreements. Such schemes should not be imposed on other countries in an apparently arbitrary manner but tacit acceptance should be sought, based on the realization that different countries have different health care systems and policies.

5. Technological Advances

A broad and detailed roadmap has been laid out above for the administration of precision medicine, from the foundational understanding of the molecular underpinnings of health and disease to the clinical application of novel formulations of treatment. Central to this framework is the generation of tailored blueprints of disease for individual patients, which use the genomics and proteomics of cancer and normal tissue to predict disease behavior and treatment responses. As machinery and methods for detection and analysis become more advanced, questions about the clinical validity and utility of this novel field can be credibly addressed. However, the ultimate aim for all of these endeavours is the tangible delivery of improved patient outcomes in a cost-effective manner.

Precision medicine has enormous implications for the patient population and how they get sick, are diagnosed, and get treated. It is therefore not surprising that that very term, 'precision medicine,' has entered public discourse and inspired the launch of a major new national institute with a mission of spearheading research in this field. Unfortunately, the word itself is often employed in a nebulous, hyperbolic, or misleading way. Beyond the excitement generated from investments, it is easy for developers of new drugs and diagnostic tests to overstate the magnitude of the clinical value and evidential backing of this new field, despite strong marketing pressures. The ability to evaluate personalized approaches alongside standard of care regarding costs and outcomes will be crucial in translating the scientific method from a hypothetical to a practical one. This will necessitate new approaches in the design and implementation of studies, as the current state of affairs places formidable burdens on a single entity attempting to create and validate a new field. Such complex trial

designs require the collaborative efforts of a diverse array of stakeholders, many of whom will be involved in novel research interests.

Equ 3: Risk Stratification and Safety Evaluation

$$R_{\text{ADR}} = f_{\text{AI}}(G, X_{\text{patient}}, C_{\text{brain}}(t), I(t))$$

Where:

- R_{ADR} = predicted risk of adverse drug reactions
- f_{AI} = machine learning model that predicts ADR risk based on multiple
- G = genetic data of the patient
- X_{patient} = other clinical patient factors (age, comorbidities, etc.)
- $C_{\text{brain}}(t)$ = concentration of the drug in the brain
- $I(t)$ = neuroimaging data that might show early signs of adverse effects

5.1. Applications in Drug Development

The importance and broad potential of personalized medicine will be discussed in this review, with a focus on drug development and the resulting therapy. An efficient and integrative approach may incorporate selections of genetic information in patient stratification and treatment planning, and could build a pan-cancer genome-wide association study for individual predictions. Providing insight into the tumor is the most comprehensive and sophisticated record of tumor-mutated regions, molecular pathways, and cellular networks. Knowledge on rare targets or pathways may require in-depth genetic screening of the tumor. Analysis of the peripheral blood circulating tumor DNA allows monitoring the progress and response to treatment. Nevertheless, genetic alterations in non-coding tissues may lead to complex disease and should not be underestimated as disease factors. Personal genomics might facilitate early phase detection of tumors, monitor cancer recurrence, and develop new strategies for therapy.

Advances in sequencing techniques, cheap sequencing costs, and large omics initiatives render it possible to analyze a large number of germline genetic variants and investigate their impact on disease risk and phenotypic traits. In the spirit of the approach, which lists the discoveries of genetic variants and diseases, a database of drug response on drugs and its corresponding genome-wide study is built. With this database, bedside drug prescriptions can be carried out by taking patient genomics, and potentially offer insights into new therapeutic strategies via network biology-based integrative analysis.

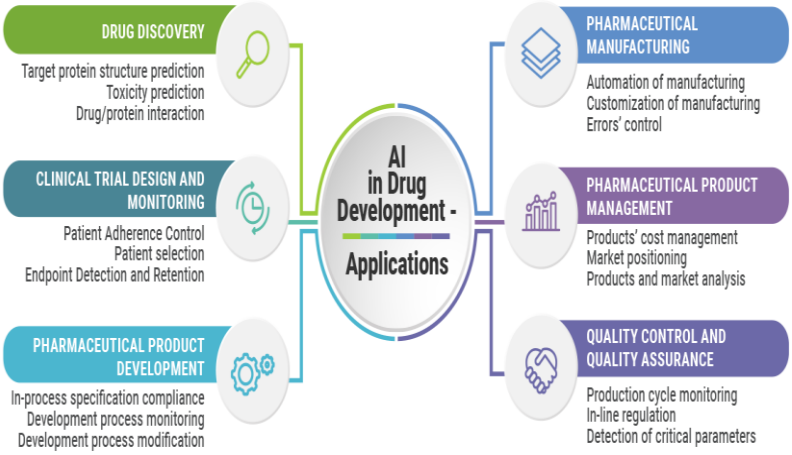
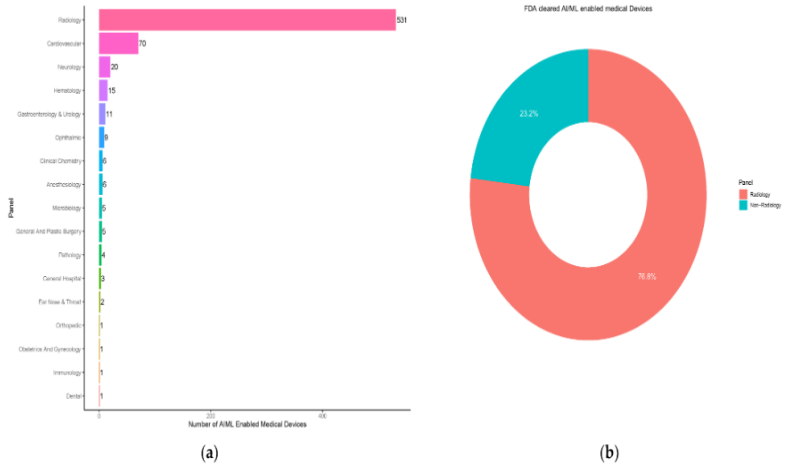


Fig 5: Applications in Drug Development

6. Digital Transformation in Biopharmaceutical Services

Life sciences and pharma industry is witnessing high regulatory scrutiny along with challenges involving drug discovery, safety, production and commercialization. Companies in the pharmaceutical sector face issues of protecting competitiveness of products due to patent expiry. On the market front, investment in research and development (R&D) is a must in order to introduce novel pharmaceuticals efficiently. Between R&D and commercialization, pharma companies need to engage in a rigorous process of clinical trials. On the digital front, emerging trends towards personalized care and digital health signify a shift in business models – from just drug discovery and fabrication to a wider spectrum of services, such as collection and processing of real-time patient data from different medical devices. Along this chain of drug innovation, several additional biomedical services or service types are emerging. In this context, the biopharma (broadly including the biotech) branch of the pharmaceutical industry is still growing despite patent expirations and intense

regulatory conditions for drug approval. As part of the efforts embodied within the third and fourth generation of the innovation theory (characterized by systemic/societal effects), this text posits that the increasing economic value of biopharma services might also be in the analytic field of health data generated within the drug lifecycle. The new 'digital' encompassed transformation entails big data biotech mining; dimensionality reduction and biomarker discovery; dynamic systems-oriented analysis for drug mechanism and effects; as well as prediction model construction for drug efficacy and patient outcome. It is argued that digital biopharma services will be crucial for maintaining competitiveness in the pharmaceutical sector. To the knowledge of the author, such issues have not been hitherto addressed in the academic literature.



(a) (b)

Fig : (AI/ML)-Enabled Medical Devices

6.1. Overview of Digital Transformation

The digital transformation characterizing our century has forced manufacturers and tech industries to adapt their business model while dealing with upcoming disruptions. The healthcare sector had to face an evolving trend while coping with a series of additional challenges; hence, to survive disruption, the identification of novel value propositions and innovative solutions is needed. It is essential to investigate future technological and clinical developments in healthcare. One means to get the needed insights is to conduct regular surveys among professionals in the sector. The collected insights concern market trends, novel approaches, and upcoming disruptions. Nowadays, care delivery gets out of clinics, hospitals, and homes. The advent of remote sensors and wearables brings care to homes, transforming care delivery into a decentralized and digital ecosystem. Moreover, the introduction of AI technologies into clinics and diagnostic procedures supports healthcare providers to make more accurate decisions for the best possible patient outcome. In times of a global pandemic, businesses, and industry sectors should strategize post-pandemic operational approaches. Balance must be maintained for optimization of benefits and outcomes while adapting to unforeseen scenarios. Established series of strategies under sub-themes such as Innovation, Safety Net, and Business Economics. In this backdrop, the overall study architecture evolved notionally. For the next steps, discussions with relevant stakeholders including companies, academic bodies, governmental institutions, and financing agencies will be initiated to refine the study approach and implement the proposed strategies.

6.2. Case Studies in Biopharmaceuticals

During Phase II, the most promising drug candidates are selected, and therefore Phase III studies should be intended to demonstrate the efficacy and safety of the selected candidates in a larger number of volunteers. However, several drugs do not satisfy the desired efficacy and safety criteria in pivotal trials. The root causes for their failure are heterogeneous, including the biopharmaceutical formulations, doses, pharmacokinetics, patients' compliance with the dosing schedule, and patients' population itself—extent of the disease, age, gender, comorbidities, polymorphisms, etc.—, or the statistical design followed in the trial. This diversity of potentially influential factors calls for specific methodologies to investigate the relative importance of, and dependence between, the myriad variables that intervene in the drug efficacy and patient's outcome.

The design and the data arising from the computerization of the clinical trials implemented by the Drugs Directorate of the European Commission of the Joint Research Centre, have made possible the application of specific mathematical models to the evaluation of the 'good clinical practices' of cancer therapeutic clinical trials. A modeling and simulation framework has been developed to investigate in silico the role played by the physico-chemical and biopharmaceutical properties of the VC in the anthracycline-based chemotherapy in treating a homogeneous group of patients affected by small-cell lung cancer. This combined information has allowed us to define a set of accepted rules that can be useful to

interpret the experimental results, understand and criticize the up-to-now adopted therapeutic protocols, and foresee possible pharmaceutical interventions that might enhance future patient's outcomes.

7. Conclusion

Healthcare systems worldwide face similar pressures with ageing populations and increasing expectations regarding available health services. Health budgets are under pressure in many countries, notably within Europe. This is being compounded by the spiraling costs of new premium priced medicines being launched, straining health authorities' resources and their ability to ensure patients receive equitable access to all aspects of care. This has resulted in new initiatives such as risk sharing, in addition to encouraging the use of generics in those countries where no automatic generic substitution takes place to enhance the prescribing of international non-proprietary names.
There is a considerable variety in how different patients respond to treatments, including many of continued proven medical need, and in many instances no response. This has resulted in the use of more novel approaches to health care, involving a more tailored approach to individual patients. Personalized medicine is already happening in certain disease areas and is likely to accelerate with ongoing developments of an additional 10% on top of small molecules and monoclonal antibodies. However, the promise of personalized medicine has not always translated into real world benefits in terms of the care experienced by the patient, with many obstacles hindering the introduction of personalized care. This also includes the lack of required diagnostics in many instances to provide the necessary guidance to tailor therapy. Thus, a need to integrate current knowledge and best practice from the perspective of a payer to help better guide future policy is being considered.

7.1. Future Trends

The variety in how patients respond to treatments will accelerate a move towards a more tailored approach, and there is a need to integrate current knowledge from a payer's perspective both for now to prioritize care and future guidance. Overall this has the potential to revolutionize care. There is considerable variability in how individual patients, including children and adolescents, respond to pharmacological treatments, including drugs, surgery and alternative treatments. Differences in patients' individual make-up arising from genetic, biological, behavioral and environmental factors are seen as the main causes of this variability. This variability translates into differences in clinical outcomes between patients including therapeutic benefit, side effects and healthcare resource use, and different dosing regimens may be needed.
In some areas of medicine, entirely different treatments are already specified for groups of patients. Some physician groups currently already specify different treatments and doses taking into account factors such as patients' ages, gender, family history, current comorbidities, weight, liver function, eating habits, genetic markers and specific gene subtypes, co-prescriptions, contraindications and attitudes towards risk, and this is expected to continue. This is despite the fact that many drugs currently used to treat adults have not been sufficiently tested in the pediatric population and the difference in maturation between adult and pediatric populations. So far these individual peculiarities of patients and their potential effects on treatment response have been considered inadequately during drug development, mainly because of a lack of effective tools and approaches to identify, analyze, and model relevant individual variability among patients. More attention is being given to the differences in treatment effects across subgroups of patients and the development of the so-called personalized medicine paradigm that facilitates the development and application of optimal medical treatments and preventive therapies tailored to an individual's personal molecular profile.

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