Using Precision Medicine to Improve Prevention and Reduce the Cost of Healthcare

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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Recent advances in genomics and computing are enabling a change in how we approach health care. The cost of sequencing a human genome has dropped from $2.7 billion dollars in 2003 to under $1,500 dollars today, making it an increasingly viable option for many individuals (*Human Genome Project FAQ*, 2020; Wetterstrand, 2020). This will enable clinicians to tailor treatment plans to a patient's genetic profile, a practice commonly known as precision medicine. There is a lot of excitement around this new model for health care, since it promises to improve patient outcomes in many different areas of medicine (Collins & Varmus, 2015). However, integration of precision medicine into health care practice remains unrealized, largely due to regulation challenges and concerns about its incompatibility with the American private healthcare system. This paper proposes how linking precision medicine to preventative care could overcome these integration challenges by improving overall health outcomes and reducing costs for patients, insurers, and the government.

How Might Precision Medicine Affect the Cost of Healthcare?

According to the CDC, 32.8 million Americans under the age of 65 lack any form of health insurance (CDC, 2020). If implemented improperly, precision medicine could easily exacerbate this issue. The business model of private healthcare is largely based on uncertainty. In most cases, no one really knows if or when they will be diagnosed with a serious disease or get into a major accident. Since it is better to be safe than sorry, most people purchase insurance throughout their lifetimes to avoid being financially ruined if they do end up in one of these worst-case scenarios. The insurance premiums of those lucky enough to stay healthy go towards paying down the medical bills of those less fortunate, while the left-over money is kept by the insurance company as profit. While precision medicine will never be able to tell if someone is going to get into a car wreck, it could provide much more specific information about

their risks of developing conditions linked to genetics: from cancer to heart disease. This could thereby lead to “adverse selection” of health insurance due to informational asymmetry (Blasimme et al., 2019; Cardon & Hendel, 2001). Adverse selection refers to a scenario where higher risk individuals disproportionately purchase health insurance plans, causing insurance companies to spend more on the average customer.

Insurance companies would likely respond to adverse selection in one of two ways: they could (1) restrict access to insurance for genetically at-risk individuals or (2) drive up prices for all customers to amortize the cost. The first scenario is perhaps the most problematic of the two, as it adds another form of explicit discrimination to a health care system that is already rife with inequalities (Dickman et al., 2017). Being born with a genetic predisposition to disease is hardly within an individual’s control, and as such our health care system should not penalize them for it. Congress foresaw this issue, and has already taken steps to avoid it by passing the Genetic Information Nondiscrimination Act (GINA). This law bars health insurance companies from using genetic information to make coverage, underwriting, or premium setting decisions (NIH, n.d.). It is heartening to see the government taking proactive action to regulate precision medicine. However, it is by no means a perfect fix. GINA essentially leaves insurance companies with no choice but to adopt the second strategy: driving up prices across the board. Considering the number of American’s who already can’t afford insurance, this would only serve to deepen socioeconomic health care disparities. In the end this is only marginally better then introducing genetic discrimination into health care, as in both scenarios many Americans will lose access to the care they need.

The other concern is that precision medicine will require more specialized drug development, since now any given condition will be treated with different drugs depending on a patient’s genetic profile (Stewart, n.d.). Currently, if a drug manufacturer develops a drug with a rare use case, they need to charge exorbitant amounts of money for the drug in order to recoup the cost of development and turn a profit. One extreme case is the drug Zolgensma, a gene-

therapy approved in 2019 for use on a rare childhood disorder (Stien, 2019). There are only about 30 children born with the disorder every year - an extremely small number – and as such the drug is priced at $2.1 million dollars a dose (making it the most expensive drug ever sold). While highly-targeted drugs will be much better for a patient's health, the need to develop so many different specialized drugs could absolutely add to the overall cost to health care. Considering all these different ways that precision medicine is expected to increase health care costs, there is a great need to identify ways in which costs can also be *lowered* using this new approach to health care.

The Cost-Saving Benefits of Preventative Care

In order to prevent precision medicine from deepening health care disparities, America needs to find a suitable way to implement the practice. Using precision medicine to improve preventative care could be the key to achieving this goal. Preventative care (a.k.a. preventative medicine) is a health care approach where disease prevention is prioritized, leading to reduced need for treatment down the road. Preventative care can include anything from diagnostic tests, to lifestyle advice, to prophylactic medicines (Healthcare.gov, n.d.). For example, vaccines, contraception, and colonoscopies all fall under its scope. Preventative care is still largely lacking in America, although in recent years it has been gaining traction (Benjamin, 2011). Preventative care was a key focus of President Obama's Affordable Care Act (ACA), as the program relies on disease prevention to cut overall healthcare costs (Amadeo, 2021; CMS.gov, 2010). A recent study published in *Lancet Public Health* found that 27.0% of all US healthcare spending was attributable to preventable conditions (Bolnick et al., 2020). This corresponds to $730.4 billion dollars, which is more than the GDP of 171 countries (to put things in perspective) (Galea & Maani, 2020). The conditions currently included in this figure are numerous, running the gamut from obesity, to many forms of cancer, to vaccine-preventable diseases such as hepatitis B.

Much of the medical innovation happening in the United States centers around developing new disease treatments. The development of new therapies is of course important, but perhaps some of our resources would be better used on disease prevention. Consider colorectal cancer. Around 141,000 people were diagnosed with colorectal cancer in 2017, and more than 52,000 people died from it (CDC.gov, 2017). Routine screening - colonoscopies - can identify precancerous polyps that can be easily removed before they turn into cancer. However, only ~60% of people eligible for this screening receive it (White, 2017). It was estimated that increasing this percentage to just 70% would save the government $14 billion yearly on Medicare spending (Goede et al., 2015). Removal of precancerous polyps costs far less then treatment of late-stage colorectal cancer, so identifying more cases early equates to overall cost saving even if it means increased spending on diagnostics. And this is just one of many diseases that have known, but underutilized, prevention methods. Further focus on preventative medicine could be the key to making healthcare more affordable across the board.

Areas Where Preventative Care Could be Improved

So where does precision medicine play into this? By their current definitions, precision medicine and preventative medicine refer to two independent models of healthcare. Modern day preventative medicine generally centers around one-size-fits-all approaches to improve public health. Many preventative practices are broadly applicable to just about all demographics. Things like exercise and nutrition counselling, regular dental cleanings, and flu vaccines all fall under the umbrella of preventative care, and just about everyone can receive significant health benefits from these proactive practices.

However, not all broadly employed preventative care practices actually result in improved health for every individual. Consider once again the example of colonoscopies. These diagnostic tests are recommended for almost all individuals over age 50, which is an extremely broad category. However, the lifetime risk for developing colorectal cancer is only 4.3% for

males and 4.0% for females (*Colorectal Cancer Statistics | How Common Is Colorectal Cancer?*, 2021). While this is a significant number, it still means that the vast majority of colonoscopies technically don't lead to improved health outcomes. Most patients undergo the potentially uncomfortable and expensive test (the average cost is $3081), and do not find any signs of cancer (Anderson, 2016). They essentially would have been no worse off without undergoing the test, besides perhaps the emotional reassurance that comes with knowing you are free of colorectal cancer. Another example of this concept is the use of drug therapies to address high blood pressure. A large number of drugs are commonly prescribed for elevated blood pressure, including diuretics, β-blockers, calcium channel blockers (CCBs), angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers (ARBs) (Gu Qiuping et al., 2006). However, high blood pressure is not a disease in-and-of itself, instead it is a risk factor for many serious conditions such as heart disease and stroke. Some patients would have never developed these more serious conditions despite their elevated blood pressure, yet they must deal with the costs and potential side effects that come along with all these antihypertensive medications. This approach to medicine is essentially probabilistic. Clinicians provide preventative care to broad groups with the expectation that a worthwhile percentage of patients - but not all - will be positively affected.

Of course, this paper is not intended to be an argument against the wide use of colonoscopies or antihypertensives, as these broad preventative approaches still play a key role in reducing overall suffering and mortality compared to no interventions. And as this paper discussed previously, catching and treating conditions early can lead to significant cost reductions, even if it means initially expending more resources to test large swathes of the population. But what if we were able to narrow the category of people for whom colonoscopies or antihypertensives are recommended, without overlooking any individuals who could actually benefit from them?

Ways in Which Precision Medicine Will Make a Difference

This is where precision medicine comes in. Unlike most preventive care practices, precision medicine by its very nature focuses on carefully curated interventions for small groups of patients. In some cases, it has less to do with disease prevention, and more to do with disease treatment. For example, currently just about all patients who have the same type and stage of cancer will receive the same treatment (or patients will receive different treatments based only on arbitrary factors such as who their provider is). However, different patients commonly respond differently to the same treatment (National Cancer Institute, 2015). Through genomics, scientists are starting to identify genetic differences in tumors that account for many of these discrepancies in treatment response. This information can be used to create better targeted therapies for cancer patients at all stages. Genomics has already led to the identification of treatment response biomarkers in many different forms of the disease: pancreatic cancer, breast cancer, glioblastoma, bladder cancer, colorectal cancer, biliary tract cancer, the list goes on (Sun et al., 2019).

The improved treatments that will come about through precision medicine are extremely promising. Targeted therapeutics could reduce suffering and mortality at a never-before-seen rate. However, this particular aspect of precision medicine provides little in the way of health care cost savings. Research and development of precision medicine therapies are more expensive than traditional medicines since they are less broadly applicable and require companion diagnostics and genetic testing (Anastasi, 2018). In other words, a traditional one-size-fits all approach to disease treatment, while ineffective for many patients, can be cheaper to implement. But, luckily, precision medicine will enable new mechanisms for not just treating disease, but *preventing* it.

The central way precision medicine can be used for preventative purposes is through improved risk factor identification. Genetic testing can help to identify hidden risk factors in otherwise healthy patients. On the individual level, this will enable people to take proactive

measures to avoid serious disease down the line. An early example of this relates to the BRCA1 and BRCA2 gene mutations, which have been closely linked with breast cancer. Women who possess just one of these mutations have a 50-85% chance that they will develop breast cancer before age 70 (*BRCA1 & BRCA2 Genes*, n.d.). However, if these mutations are identified early through genetic testing, affected women have the option to reduce their risk of developing breast cancer by 95% by undergoing a prophylactic mastectomy. With the advent of improved genetic testing this procedure is becoming more and more common: more than tripling in the last decade (Breastcancer.org, 2016). The procedure not only prevents the suffering that comes with having breast cancer, but it also reduces lifetime healthcare costs as it minimizes the need for consistent surveillance (via mammograms) and avoids the exorbitant costs associated with eventual cancer treatment (Mattos et al., 2015).

This example illustrates the effects of precision medicine on disease prevention on an individual level, but what about on a macro scale? Recall how increasing the percentage of eligible people who receive colonoscopies from 60% to 70% would decrease Medicare spending by $14 billion through early disease identification (Goede et al., 2015). These cost savings occur despite the fact that increasing this percentage would mean more spending on conducting the test themselves. But what if we could improve early disease identification while simultaneously *lowering* the number of colonoscopies conducted every year? This could be possible through precision medicine. As mentioned before, colonoscopies are recommended for all adults over the age of 50. If researchers are able to identify the underlying genetic biomarkers of colorectal cancer, only those that carry these biomarkers – and are therefore at significant risk of developing cancer – would need to undergo regular colonoscopies. This would mean more early-cancer diagnoses per colonoscopy conducted, which would result in cost reductions even beyond those brought about through the traditional preventative medicine approach of increasing testing across the board. This has broad implications beyond just colorectal cancer. If we can identify precise risk groups for various diseases, we can

supercharge traditional preventative care techniques by focusing all diagnostic and preventative treatment efforts on only those who could actually benefit from these interventions.

Blending Precision Medicine with Prevention

Being that precision medicine is such a new field, its scope is not yet clearly defined. Some consider precision medicine to be synonymous with genomics-driven medicine, while others say precision medicine must also incorporate non-genetic factors such as environmental and social determinants of health. Discussion of precision medicine's relationship with preventative medicine, the focus of this paper, is still somewhat lacking and no expert consensus has been reached. In a 2018 *JAMA* viewpoint article, Psaty and coauthors (2018) present precision medicine and preventative medicine as two distinct approaches to health care. They distinguish precision medicine as being deterministic in nature, while preventative medicine is probabilistic. They claim that while both models can be useful, they are useful in different contexts. For instance, while precision medicine provides excellent tools for targeting specific biological deficits, preventative medicine provides tried and true methods for addressing broader public health issues. They posit that the traditional one-size-fits-all approach to preventative medicine is here to stay, since these methods have been proven to improve public health, and we are far from maxing out their benefits.

Some other experts dispute this view that precision medicine and preventative medicine are mutually exclusive. Dr. Muin Khoury (2019), the director of the CDC's Office of Genomics and Precision Public Health, wrote a response to Psaty et al's. article in which he claims that "preventative medicine can be more precise and precision medicine can be more preventative". In other words, there is no need to establish a dichotomy between precision medicine and preventative medicine; the two models build off each other. Khoury also mentioned how other researchers have recently defined "precision prevention" to incorporate aspects of each model. In their 2018 review article, Biro et al. claims that precision prevention involves the use of

biological, genetic, behavioral, socioeconomic, and epidemiological data to reduce disease incidence and mortality (Bíró et al., 2018; Rebbeck, 2014). This definition shows how precision medicine does not stand alone, and can be used to build upon many well-established health care techniques.

The view on prevention vs. precision medicine presented by Khoury and Biro et al. is more in line with the stance presented in this paper; precision medicine can be used to enhance traditional preventative approaches. However, these experts do not make the connection between precision medicine and the cost saving benefits associated with improving preventative care. Considering the many concerns regarding the financial impact of precision medicine, it is surprising that the economics of this relationship have not been discussed more in the literature.

Conclusion

The theory that's presented here - that a focus on improved prevention through precision medicine will lead to cost savings - should merely serve as a jumping off point for further research. The economics of health care is an increasingly complex topic; numerous convoluting factors make predicting the financial impact of any given technology extremely difficult. For example, many proponents of the Affordable Care Act speculated that it would reduce emergency room visits, since hospitals are required to provide emergency care regardless of the patient's insurance status (therefore, insuring more patients through the ACA would cause these patients to go to a doctor's office for many health issues instead of the ER). This was one of the ways that the ACA was expected to lower overall healthcare costs, since ER visits are much more costly than primary care visits or visits to urgent care centers. In practice however, the opposite was shown to be true; emergency room visits *increased* after the ACA was implemented (Nikpay et al., 2017). Health care policy can often have unanticipated effects like this, regardless of how much research is conducted before implementation. With this in mind, it is important to consider unexpected alternatives when developing the nation's strategy for

implementing precision medicine. Indeed, any cost savings achieved through improving preventative care may not make up for the expense of new precision drug development and the adverse selection of health insurance. However, this approach is worth consideration and research as we navigate the early challenges that come with this new area in medicine.

Few doubt the life-saving potential of precision medicine. Too much of modern medicine is still based on inference and speculation, but the technologies being developed today are about to change that. Treatments will soon be specifically tailored to each individual's genetic profile and medical background, thereby maximizing the chance for positive outcomes. However, many still question how this medical paradigm shift will fit within the context of America's convoluted private healthcare system. The reduction in uncertainty brought about by genomics and the increased need for specialized drug development could raise the costs of care taken on by insurers, which will then translate to higher premiums for all Americans. It is important that we implement precision medicine in way that mitigates these potential cost increases. As illustrated in this paper, a focus on preventative medicine could hold the key. While the terms "preventative medicine" and "precision medicine" currently refer to two independent healthcare models, they are not mutually exclusive. Precision medicine could lead to significant improvements to preventative care, which in turn could lead to overall cost reductions. Focusing on the preventative aspects of precision medicine could in this way provide a viable option for implementing the new model within the current healthcare system, thereby allowing all individuals to reap the many benefits of precision care.

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