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Integrating Genetic Studies of Nicotine Addiction into Public Health Practice: Stakeholder Views on Challenges, Barriers and Opportunities

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Key Words
Genetics · Individualized medicine · Nicotine addiction · Public health · Tobacco control

Abstract
Objective: Will emerging genetic research strengthen tobacco control programs? In this empirical study, we interview stakeholders in tobacco control to illuminate debates about the role of genomics in public health. ***Methods:*** The authors performed open-ended interviews with 86 stakeholders from 5 areas of tobacco control: basic scientists, clinicians, tobacco prevention specialists, health payers, and pharmaceutical industry employees. Interviews were qualitatively analyzed using standard techniques. ***Results:*** The central tension is between the *hope* that an expanding genomic knowledge base will improve prevention and smoking cessation therapies and the *fear* that genetic research might siphon resources away from traditional and proven public health programs. While showing strong support for traditional public health approaches to tobacco control, stakeholders recognize weaknesses, specifically the difficulty of countering the powerful voice of the tobacco industry when mounting public campaigns and the problem of individuals who are resistant to treatment and continue smoking. ***Conclusions:*** In order for genetic research to be effectively translated into efforts to minimize the harm of smoking-related disease, the views of key stakeholders must be voiced and disagreements reconciled. Effective translation requires honest evaluation of both the strengths and limitations of genetic approaches.

Introduction

Genetic and neuroscience research continues to enhance our understanding of the biological bases of addiction and tobacco dependence. In order for this increased knowledge to decrease smoking-related harms, it must be integrated into clinical and public health practice. However, the usefulness of genetic information to improve health at a population level is in dispute, as seen in a variety of public forums and exemplified by public debates in the pages of *Science* and the *Journal of the American Medical Association* [1–6]. Genetic epidemiologist Kathleen Merikangas and statistical geneticist Neil Risch sparked intense discussion among genetic researchers when they argued in *Science* that there were several diseases, including nicotine addiction, for which traditional public health measures would always be more effective than therapies based on genetic research [5]. This senti-

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ment was reiterated, albeit with moderation, by physician Chris Carlsten and medical geneticist Wylie Burke in the *Journal of the American Medical Association* [3]. This viewpoint stands in stark contrast to that held by some genetic researchers, as set out in a response to Merikangas and Risch, who argued that 'employing the power of genetic studies in understanding the underlying biological, behavioral, and environmental factors will enhance research on etiology, treatment, and prevention for these complex diseases' [1].

A similar response followed Carlsten and Burke's paper [2]; both responses closely mirror the 'disease of the brain' paradigm endorsed by the National Institute on Drug Abuse – a perspective that foregrounds and privileges research on molecular mechanisms of addiction [7]. A similar tension, population-based tobacco control versus a focus on the 'basic science' of addiction, lies at the heart of the controversy that erupted following the recent proposal that the National Cancer Institute's Tobacco Control programs be moved out of the National Cancer Institute and into a new National Institute of Health institute devoted to substance use disorders. Anticancer advocates were chagrined, arguing that one of the most effective prevention strategies would no longer be part of the National Cancer Institute and potentially vulnerable to defunding [8]. What is the correct approach to integrating genetic information about a complex phenomenon like smoking behavior into traditional population health approaches? Tensions are fueled by the hope and perceived hype of genetic technology for personalized medicine given the promises made, but not yet fulfilled, that the knowledge gained in the Human Genome Project will immediately yield cures for countless diseases and disorders [9, 10].

In this paper, we investigate – through the eyes of key stakeholders – how an emerging genetic understanding of smoking could play out in the clinic and in public health programs. We use tobacco control as a case study to identify the benefits and challenges of integrating genetics into public health programs. Considering that both traditional public health measures (e.g. higher taxes on cigarettes and smoke-free work places) [11–14] and medical technology (e.g. pharmaceuticals and nicotine replacement therapies) have had some success in reducing smoking rates, tobacco use can serve as a case study to illustrate the issues that must be addressed when reconciling public health measures with the genetics of complex behaviors. Thus far neither public health nor genetics can claim decisive victories: only 3% of smokers quit each year, and because the number of new smokers approximately matches the quit rate, the prevalence of smoking has declined only modestly in recent years [15].

We will begin this paper with an overview of the science that undergirds a genetic understanding of smoking behavior. Next, we catalogue the ways genetic knowledge is already being used in public health and note the difficulties faced in integrating a genetic perspective into public health strategies that target a complex behavior such as smoking. We then describe the results of interviews with stakeholders: individuals who are responsible for developing, advocating for or against, and implementing these new developments in the laboratory, pharmaceutical industry, health care industry, clinic, and public health setting – i.e. representatives of social domains that are key in determining the path genetic research takes as it moves from bench to bedside and beyond. Our focus in this paper is on unresolved issues: how and in what ways should public health incorporate genetics into its programs; will genetic research influence policy; will genetic research undermine funding for traditional public health programs; will genetic research shift our perception of responsibility for smoking away from larger social processes (and industries) and onto the individual; are therapies and tests created from genetic knowledge supported by solid evidence and cost effective? Our data suggest that stakeholders understand that genetic research may be helpful in creating new cessation aids and targeting scarce resources to those who need them most. Yet, they express concerns that infusing genetics into the public health sector brings the possibility of unintentional consequences such as: compromised privacy, stigma, increased health insurance costs for those deemed 'at risk' or the siphoning of money away from successful, traditional public health programs and toward genetic screening and pharmaceuticals assumed to be 'magic' cures. The possibilities of integrating genetic knowledge into public health programs lie in providing evidence of efficacy and cost-effectiveness of new technologies and in the ability of 2 disciplines with differing worldviews and priorities to work together in evaluating emerging evidence.

Background

The science behind the genetic basis of smoking behavior has evolved from seminal twin studies [16, 17] to investigations of the relationship between variants in specific candidate genes and smoking behavior [18], the latter of which has had limited success [19]. However, ad-

vances in tools, techniques and costs have allowed scientists to perform genome-wide association studies [20], and meta-analyses of these studies [21], with promising results. An important justification for and hope of public health genetics is that genetic research has the potential to create new cessation aids and target scarce resources to those who need them most: those who continue to smoke due to susceptibility to nicotine addiction [22, 23]. Though this body of research is achieving solid results, the low predictive power of the genetic discoveries to date and the need for replication and characterization of candidate genes indicates that much work remains to be done [24, 25]. Moreover, the identification of genetic associations does not necessarily mean that clinically useful outcomes will follow; the path for integrating knowledge on complex disorders is less clear than it has been for single-gene disorders [26, 27]. As Hudson [28] points out, clinical applications are often a distant goal of much genetic research [29].

The potential value of genetic information in public health programs has been laid out clearly by Khoury et al. [27, 30–32], the director of the National Office of Public Health Genomics at the Centers for Disease Control and Prevention, and others [23, 33–35]. Areas for partnerships between the 2 fields include a dedication to prevention; and a strong commitment to evidence-based health approaches and health services research [31]. This vision of cooperation is gaining momentum; half a dozen universities have established public health genetics programs. A strategy for integrating genetics into public health must include: training the workforce to make this transition, building partnerships among stakeholders, committing to interdisciplinary communication [23, 30, 31, 33, 36], and creating a long-term plan of translational research to develop evidence-based guidelines [28, 31–33, 36].

In some public health areas (e.g. newborn screening or cystic fibrosis carrier testing), genomic approaches serve as a logical extension of a variety of diagnostic and screening tests already performed in the clinic. However, integrating genetics into public health programs that target diseases such as lung cancer or emphysema, which stem from a behavior (i.e. smoking), creates additional challenges. Such diseases have long been targeted through traditional preventive public health programs and strategies and present a significant deviation from public health programs, like newborn screening, for which genetic knowledge is integral. In addition, scholars often point to the need to navigate ethical, legal and social concerns including privacy, adequate informed consent, accessibility, and accuracy of tests or individualized information [34, 37]. Scholars also recognize that accurately communicating information to health educators, clinicians and the public about genetic tests and technologies is of utmost importance [30, 33, 38].

A small body of empirical research explores how individuals will respond to genetic information about individual risks for tobacco dependence or smoking-related disease. Though these studies indicate that test results may increase an individual's motivation to quit smoking, there appears to be no increase in long-term quit rates [39–44]. It is less clear how predictive tests might affect smoking *prevention* efforts. Indeed, other analyses suggest that though genetic information may be medically beneficial for select individuals – pharmacogenomic targeting of cessation therapies is most often mentioned – the population uses of genetic knowledge, especially predictive uses, are currently not efficacious or cost-effective [45, 46]; public health educators remain skeptical of its utility in public health [47].

Finally, these debates occur in the context of fiscal realities; discussion of evidence and cost-effectiveness go hand-in-hand [27, 48]. Debates often occur about the best use of public funds for research, prevention and clinical care [1, 3–5, 49]. Disputes stem in part from prevention specialists' experiences with losing funding over the past years [50, 51]; scientists are similarly concerned about the effect of budget cuts on their ability to continue research [52]. Scholars in public health genetics point out that there is far more funding allocated to basic research than to translational research and call for this disparity to be alleviated [28, 31, 33, 36]. Some analysts point out that traditional public health strategies, like smoke-free public areas and increased taxes, have not been fully implemented either in the United States or globally but that doing so would yield significant positive health effects [53, 54]. The social context also shapes debate. Funding disputes are argued within a political economy dominated by a multi-billion dollar industry that heavily promotes its products. Within this complex environment, understanding the views and concerns of stakeholders in tobacco research and control is vital when considering how genetics might affect tobacco control and smoking cessation strategies.

Methods

For this research, we utilized a sample of stakeholders as 'key informants', a strategy commonly used in qualitative research [55–57]. Interviews with key stakeholders will tell us not only what they think and how they understand genetic research, but

Table 1. Description of sample and recruitment

Title	Description	Sampling and recruitment	Number of interviews
Scientists	Psychiatrists (n = 13), neuroscientists (n = 4), geneticists (n = 1) and other researchers (n = 2) who investigate neurogenetic links to nicotine addiction	Identified through scientific publications, professional meetings, and National Institutes of Health (NIH) grant awards, participation in Transdisciplinary Tobacco Use Research Centers (TTURCs), and by 'snowball' sampling	20
Clinicians	Clinicians and researchers involved in smoking cessation, tobacco management, and the treatment and prevention of tobacco-related disease	Sampled from each of the ten regions outlined by the department of Health and Human Services (HHS), with two participants from each region [67]	19
Tobacco prevention specialists	Policy-makers in the public and private spheres, including federal (n = 2), state (n = 19) and local-level (n = 2) health policy officials in tobacco control and health prevention; public health educators involved in developing and administering nationwide tobacco prevention programs (n = 2)	Sampled from the ten geographic regions defined by the HHS [67] as well as federal sources; two stakeholders from each HHS region 1, 3, 5, 6, 7, 8, 10; three from HHS region 9, four from HHS region 4, one each from HHS regions 3 and 2; two from federal sources	25
Health payers	Individuals involved in making coverage decisions for large health care providers	Identified using internet resources and company media contacts; participants had ties with medical assistance programs or worked for one of six large health care companies: state Medicaid program in HHS Region 1 (n = 1); state-level private health care companies in region 9 (n = 4); state-level private health care companies in region 5 (n = 1); national-level private health care companies (n = 5)	11
Pharmaceutical employees	Bench scientists in research and development (n = 5), clinicians and others running trials (n = 4), communication and advertising specialist (n = 1), and drug representative (n = 1)	Recruited through personal contacts; represent 6 different pharmaceutical companies that market or are developing tobacco cessation products	11

given their positions in policymaking, what they might do in the face of emerging genetic findings. Their viewpoints are therefore critical in examining the potential impact of genetic research on smoking policy at the national, state and local levels, as well as on clinical practice guidelines, and on prevention, education and tobacco-control programs. Interview subjects were chosen from 5 areas of tobacco control: scientists, clinicians, tobacco prevention specialists, health payers, and pharmaceutical industry employees. Stakeholders were identified based on their substantive interests in tobacco and the type of work they do. We used a type of 'purposeful' and 'maximum variation' sampling that, while not allowing us to make generalizable claims about all groups of stakeholders represented, does allow for an *in-depth* understanding of stakeholder views [56]. By interviewing stakeholders throughout the United States in a variety of positions relevant to translational research, we were able to identify central themes held across this diverse set of informants [57]. Our results do not quantitatively represent stakeholders, but our utilization of open-ended interviews allowed us to probe for differing opinions and to create a strategic sample that includes the likely *range of opinions* that exist in the tobacco research and control community. Interviews were conducted until theoretical saturation was achieved (i.e. until no new theoretical or conceptual domains were forthcoming from the interviewees, and all domains had been fully explored and contextualized) [58, 59] (table 1).

Interviews were semi-structured and conducted primarily by telephone. Interviewees were asked about their beliefs about smoking and addiction etiology, the possible applications of this science in clinical and public health settings and the potential effects of genetic research on stigma associated with smoking, public policy and the tobacco industry. Relevant questions from the interview guide include:

- How might the recognition of a genetic component to smoking behavior influence public policy toward smoking and tobacco control?
- Do you think that genetic explanations of nicotine addiction or tobacco-related diseases would influence how the government sees its responsibility for preventing smoking-related disease?
- Some have suggested that identification of risk genes for smoking behavior will not have as much public health benefit as societal change, such as media campaigns, cigarette prices or smoke-free work places. What do you think about this suggestion?

Interviews lasted between 30 and 60 min. Each interview was transcribed and coded by 2 researchers. Initial codes were created both by identifying the range of responses to specific questions asked of all respondents and by seeking to identify new and emergent issues throughout the interviews. Memos, where data is distilled from initial codes into more cohesive descriptions and analysis of the coded segments of text, were developed. To ensure quality of analysis, we utilized triangulation in the ways suggested by Farmer et al. [60]: a range of perspectives were collected and multiple investigators coded interviews. Every effort was made to identify variation within the themes and select illustrative quotes that represented key themes, including identifying marginal opinions, sometimes called 'counter-themes' or 'negative cases', which are statements that contradicted or did not support the dominant opinion [61]. This variation is included in the analysis below.

Results

How Will Genetic Research Be Utilized in Public Health Programs? Background Beliefs about Strengths and Weaknesses of Genetics versus Public Health

A strong theme found in our sample was the belief that policy intervention was more important than genetics in lowering smoking rates and incidence of smoking-related disease. These individuals (about half of health payers, pharmaceutical employees and prevention specialists, but only a third of clinicians and a few scientists) mentioned several strategies that they believed were effective: large-scale public programs that worked to denormalize tobacco use, increased taxes, community interventions, smoke-free workplaces, banning the legal sale of cigarettes, implementation of and coverage for cessation programs, and media campaigns. One health payer verbalized this sentiment:

> What is going to be far more effective is to change the social norms around this behavior. And, these kinds of genetic tests, the possibilities that we've talked about are … a minor blip in my opinion. It's a social problem. (Health payer: director of research and evaluation at a large health care company in the Midwest)

In contrast, only 2 stakeholders in our sample, both health payers, dismissed policy interventions, believing that they were either ineffective or overly punitive:

> We use excessive taxes on cigarettes as a deterrent to smoking. I'm not aware that that *has* been a deterrent to smoking. That's number one. And I think people would say that if there's a genetic basis, it's a punitive tax on a medical illness. So, where else do we see punitive taxes? Do we have a punitive tax on a candy bar? (Health payer: senior medical director at a large, national health care company)

Others may question the veracity of this assessment, which was voiced by only 2 informants. There were, however, more varied critiques of traditional public health policy, most often offered by clinicians. While clinicians embraced the importance of many social policies, they also saw weaknesses in public health programs' effectiveness in fighting the tobacco companies, getting the right services to individuals and raising money to enact meaningful policies, cessation programs or research.

> Well, I think there's a whole set of public policies that have been shown to be effective in preventing the initiation of tobacco use and … encouraging people to quit. [We need to be] embedding and making aggressively available to people the evidence-based treatments that we know work to help support them quitting, that are being adopted, at best, at a glacial pace in the country and compared to the nimbleness of which the tobacco industry is able to alter its tactics and strategies to get people to use tobacco … One of our core difficulties that we struggle with is that … there's been very little in the way of identifying successful ways to triage people to different forms of service. We struggle all the time, partly because of the lack of sufficient resources in this field, which is actually the core problem. (Clinician in the Pacific Northwest)

This statement also shows that even those stakeholders who believed public health was more important did not necessarily discount genetic alternatives; if public health relies on population-targeted programs, and genetics creates individualized treatment (i.e. pharmacogenomics), perhaps they can complement each other to create effective tobacco control programs. In fact, almost a fourth of our sample, spread relatively evenly across the various stakeholders, refused to choose either tobacco policy or genetic research as 'more important', instead believing that they complemented each other:

> I wouldn't, a priori, say there's any basis for saying, 'A genetic approach is any more or less effective than any of these other activities in isolation.' … I can certainly envision ways in which a genetic story [could be] woven into the overall mix … Smoke-free places and tax increases, and some of the other effective policy measures will have been well-used by then, and kind of work into [the] wallpaper. So you need a new message. And [genetics] could

be the new message. And it could be used in the media campaign. They're not mutually exclusive. (Pharmaceutical employee working in marketing)

This respondent, like many in our sample, embraced both tactics and believed that genetics potentially could be woven into the existing public health framework.

Will Genetics Influence Policy?

Embracing public health programs does not presume a rejection of genetic research. However, embracing 'potential' is different from enacting change. Stakeholders we interviewed often struggled with defining concrete ways public health and genetics fit together.

… unless there's something we can do with [genetic] information, I really don't see it influencing public health at all. If we were able to use it in a way that made sense, then okay. But, until that happens, I don't see how it could influence us. (Prevention specialist working in a tobacco control program at a state public health department, Pacific Northwest)

A fourth of our sample – primarily scientists, prevention specialists and clinicians – did not think that genetic research would influence public policy, either because of the counter-effect of the tobacco industry or the belief that politically data would be 'spun' to support existing and varied political viewpoints on tobacco policy. In other words, informants believed that people have already made up their mind about tobacco policy, that the government either does or does not take tobacco control seriously and additional data will not change those policies or beliefs:

I'm very mindful of the politics involved here. The tobacco industry exerts tremendous influence on politicians, and it's a big business, and I try not to be too cynical about the political aspects of this, but we can have the best evidence in the world and if there's a lot more dollars that the tobacco industry throws at political action committees and legislators and lobbyists and so forth, we may have very little influence, ultimately. (Scientist: professor of medicine and clinical research at a large Midwestern university)

Interviewer: And do you think that genetic explanations of nicotine addiction or tobacco-related diseases would influence how the government sees its responsibility for preventing smoking-related disease?

Respondent: Hm … not in [our state].

I: Why not?

R: For the most part, frankly, it's just not a priority. (Prevention specialist: tobacco cessation specialist at a public health department in the Midwest)

Stakeholders generally believed that genetic knowledge would not influence prevention efforts. Most stakeholders felt that genetic knowledge would not be as pertinent to individuals' choices as peer or other environmental influences:

[Genetic information] won't make a difference. [People are] going to do whatever they want to do. There are some proportions of people, and we don't know how many, who will actually be made more motivated not to smoke by that information. And there are some people who may in fact adopt a fatalistic approach – 'Oh, well, I've got the gene. Nothing I do matters.' (Scientist: head of a genetics lab in a large, southern university)

Teenagers are not able to make informed decisions about anything that has long-term consequences. We *know* that. So why give them the information when there's very little chance that it's actually going to help their behavior in a positive way? That there's a chance that it could well alter it in a negative way. (Prevention specialist: director of a Midwestern state's tobacco control program)

However, a third of our sample embraced genetic research, and the subsequent potential for increased medicalization of addiction, as a positive influence that will strengthen policies, encourage health care companies to cover cessation programs and promote better funding of tobacco control programs.

So, public policy could benefit from the genetic findings in the sense that it may help to influence policy-makers' beliefs that this is a true addiction and not just a bad habit. I think that giving nicotine addiction the kind of credibility as a true medical condition would go a long way and legitimize it in the minds of legislators and policy-makers who can give the kind of money to make a difference. (Scientist: professor of medicine and clinical research at a large Midwestern university)

It is interesting to note that clinicians were more likely, and prevention specialists less likely than other stakeholders, to embrace genomics as part of a process of medicalization of addiction, where addiction is reduced to a biologically-based problem or disease, a point to which we return below.

Only a small number of stakeholders were hopeful that targeted treatments would effectively change public health policies, generally by creating more individualized information:

… The way I always think about genetics and, I guess, policy-related issues, is that it will help individualize therapies, interventions, and presumably, that will improve things because … it's not this 'one size fits all' mentality, and I think that turns a lot of people off … And, in terms of prevention, I think [individualization is] a very important area because it's hard for people to make changes for things that haven't happened, or that *might* happen. And [it's hard for people] to really understand what risk is. And, so I think that the more we can do to try and personalize that information, individualize it, I think the more effective we're going to be in our preventive strategies. (Health payer: worked with a large health care company in California to develop guidelines for genetic testing)

Providing individualized information has long been a part of public health programs, especially those that engage in population screening for genetic diseases (e.g. newborn screening). But questions remain about the cost associated with screening programs for non-mendelian conditions, the speed with which genetic interventions will enter the field and whether an increasing focus on genetic interventions will detract from the overall effectiveness of traditional public health programs. These questions seem especially important for genetic information that is predictive, as opposed to the traditional screening for genetic disorders that are highly penetrant and actionable, which have integrated into public health programs with greater ease.

Will a Genetic Understanding of Addiction Undermine Existing Policy?

Prevention specialists often mentioned fears of losing funding for existing programs due to the appeal of genomic approaches. A minority (10%) of stakeholders worried that spending for genetics may undermine public health funding. No scientists expressed this sentiment.

> Because, the way I look at it in terms of research, people like to do research, bench research. People like to figure out, you know, the ins and outs of nicotine addiction, for instance, to the nth degree. People do not like to do applied research, which is taking a look at this population, and what would work best in terms of approaching this population for a successful tobacco use prevention. And so, it's easy for people to decide that they want to do research around this area and to take away funding from prevention efforts. (Prevention specialist: program manager of a state-wide media campaign in the West)

It is not surprising that scientists did not express this sentiment; even though they recognized the importance of public health programs, they did not see their own work as detracting from tobacco control programs.

Other stakeholders believed that a genetic understanding of nicotine addiction would shift responsibility away from tobacco companies and governments, onto individuals:

> I think [a genetic explanation of nicotine addiction] could cause the government to kind of shirk responsibility, or shift – I shouldn't say shirk – maybe shift responsibility away from the large tobacco companies and onto the individual. (Prevention specialist leading outreach efforts to underserved and vulnerable populations at a nonprofit tobacco control organization)

That genetics may undermine public policy is a small but consistent theme among those in public health.

What Evidence Do We Need, and Will Genetics Be Cost-Effective?

Among prevention specialists and clinicians in our sample, solid evidence, along with cost-effectiveness, were the factors most often noted as critical to the integration of genetic research into public health programs. Two prevention specialists mentioned the disconnect between bench research and clinical practice and noted that there was much work to do to bridge that gap:

> There is some [research] going on, but you're talking [about] more or less taking it from the bench to population-based, and that's a lot of trials in between here and there. So, we have to understand what the mechanisms are. Do we have to define causality? We have to, in terms of what the pathways are. Then, if you're talking about medication, [we have to know], is this effective and safe and all that kind of stuff, too. So, we have a lot of work to do between here and there. (Prevention specialist: oversees tobacco control program for a large city in the Northeast)

This informant asks what qualifies as appropriate evidence: must we define causality; must we know specific pathways? While overt questioning of the nature of evidence is rare in our sample, this interviewee's challenge indicates that scientists and prevention specialists may have a different vision of what qualifies as appropriate and convincing evidence [62].

As noted above, discussing evidence and cost-effectiveness often go hand in hand. Some stakeholders doubted whether a genetic approach would ever be as cost effective as current approaches:

> If … you could get a test … and prevent that heart/lung transplant or something. I mean, that would be different. But we're talking about one hundred dollars of NRT [nicotine replacement therapy] and a few hundred dollars of counseling … How can we make a targeted intervention that requires an expensive test work better than creating smoke-free environments and getting people patches? … I don't think we can. (Prevention specialist: working in a state public health department in the Pacific Northwest)

Two clinicians called into question whether a genetic research agenda to assess risk made sense from a public health standpoint:

> The equivalent would be, in occupational medicine, going into a factory where workers were stirring big open vats of benzene and doing genetic studies to determine who's more or less susceptible to benzene so we could figure out who it's okay to allow to be exposed or not be exposed. (Clinician in the Pacific Northwest)
>
> I mean, what would you do if you did identify [people with higher susceptibility]? So at this point, I wouldn't know what I could do to prevent them from smoking, other than to do what I do anyway, which is to try to give prevention messages, try to do the public health aspect of things, try to, in clinical preventa-

tive visits, talk about it, try to provide information and try to steer people away from that and show them the risks of it. (Clinician, who is also involved in prevention efforts on the East Coast)

Two other clinicians simply emphasized the importance of evidence when adopting genetic technologies into the realm of public health:

What would it take? It would take strong science with good evidence that genetics would make a difference in treatment outcomes. And it's going to take someone paying for it. And ultimately, that's what it comes down to is getting somebody willing to pay for it. But I think if you can – if you have the first two things, you can get the third. (A second clinician working in the Pacific Northwest)

At the heart of these statements are basic epistemological debates about the nature of evidence and what counts as 'productive' knowledge. Such differences illustrate an important challenge to those seeking to integrate genetics into tobacco control.

Discussion

Our analysis of debates about the promise of genetics in lessening the burden of tobacco-related disease serves as a useful example of larger issues confronting those seeking to integrate genetics into public health. Balancing the hopes of personalized medicine with public health approaches will not be easy. Complex, polygenic disorders present a particular challenge. It is unlikely that a test for a single gene will be developed that strongly predicts smoking behavior. Scientists studying the genetics of nicotine addiction instead hope that a better understanding of nicotine's effects on the brain and body will yield new therapies and prevention techniques. If new therapies prove successful and cost-effective, then genetic approaches deserve a place among traditional public health programs. However, in the case of nicotine addiction, an immediate population-level benefit is unlikely; the fruits of genetic research will not be realized in the near future. Funding for these projects must be accompanied by realistic expectations since definitive therapies may take decades to emerge.

Seeking to identify the genetic basis of smoking behaviors as a foundation for developing therapeutics is consistent with the medicalization of a range of substance use disorders [63]. It is not surprising that clinician stakeholders are more – and prevention specialists are less – likely to embrace a disease model in which etiology is located at the level of biological process. Medicalization attracts funding to basic science research and may alleviate stigma, as happened for disorders such as epilepsy and depression. Medicalization also solidifies clinical dominance of certain conditions, while also providing clinicians with tools to treat these disorders [64, 65]. By contrast, prevention specialists are tied to the idea that sociocultural interventions can be effective public health measures. They resist a genetic understanding of addiction for one primary reason: If smoking behavior is inscribed in our cells and molecules, as a genetic vision of addiction implies, then this may lead to an overindividualization of medicine that is reactive of and targeted to individual bodies and behaviors, likely one manufactured by the pharmaceutical industry, not broad social policy change, which seeks to influence large groups of people with the goal of affecting individual and population-level change. Assumptions about the nature of and logical therapies for disease – including judgments about whether a behavior constitutes disease – are, in general, more consistent between basic science and the clinic than between basic science and public health. The integration of new genetic knowledge into public health programs requires surmounting this barrier.

The fact that clinicians and prevention specialists, but not scientists, speak about the importance of evidence as a prerequisite for transitioning basic science into the clinic illustrates the divide that exists at the latter stages of translation. Perhaps scientists did not dwell on the need for evidence because they took for granted its importance. But the varying degree of emphasis speaks to the difference in views of scientists compared to preventionists when evaluating the *challenges* of taking genetic findings from the bench into the realm of action, whether in the clinic or a public health department. Varied interpretations of evidence stand as a central challenge for meaningful integration of genetics into public health programs.

If collaboration between specialists in genetics and public health is to occur, it must be carefully planned and problems anticipated. In order to justify incorporation into large population-based programs, time must be taken to create bodies of research showing solid evidence of efficacy and cost-effectiveness, which is possible only with a commitment to applied research. Care must be taken to avoid unintended consequences – like shifting responsibility for tobacco-related disease onto individuals and away from an industry that actively promotes smoking [66] or the defunding of traditional public health programs. Both scientists and those involved in policy

must be willing to assess honestly the strengths and weaknesses of their tactics. Scientists must accept that discovering associations, or even causation in a limited experiment, does not necessarily yield therapies and that focusing on genetics often inadvertently obscures the social determinants of addiction.

For public health genetics to advance there must be discussion of how to integrate the perspectives of a diverse array of stakeholders. What counts as proof of efficacy? What are the underlying assumptions that different practitioners bring to the table? Merikangas and Risch [5] and Berrettini et al. [1] talk past each other instead of trying to find common ground [62]. Their radically different background assumptions are a major reason that they are unable to come to consensus. A meaningful collaboration between public health and genetics will require a reckoning with these disparate viewpoints.

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