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THE APPIFICATION OF GENETIC RISK

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ABSTRACT

Appification refers to the development of applications for web and mobile devices. It also represents a process of abstracting complex concepts and systems into discrete and simplified parts. This Essay considers appification as both a reality and a metaphor for disaggregation in the context of the consumer market for polygenic risk scores. It then discusses the policy implications and potential contributions to medical and legal uncertainty.

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I. INTRODUCTION

In 2012, technology startup CEO Steve Newcomb predicted that, in about "10 years, everything [would] be an app."[1] This image of the "appification of everything" was a prescient statement at the time and continues to ring true in the technology sector. Over the last decade, scientific advancements have enabled the appification of an ever-increasing array of domains, and, even today, the promise of appification persists.[2] In 2023, Kian Sadeghi, the founder and CEO of Nucleus Genomics — a startup providing consumers with polygenic risk scores ("PRSs") derived from whole-genome sequencing[3] — said, "It's an inevitability that every single person has their entire human genome on their iPhone."[4] This prediction leads to the question: What happens when we appify genetic risk?

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1. Anthony Wing Kosner, *The Appification of Everything Will Transform the World's 360 Million Web Sites*, FORBES (Dec. 16, 2012, 11:32 AM EST), https://www.forbes.com/sites/anthonykosner/2012/12/16/forecast-2013-the-appification-of-everything-will-turn-the-web-into-an-app-o-verse/?sh=106b384a14bd [https://perma.cc/DAE2-7FX6].

2. *Count of Active Applications in the App Store*, POCKET GAMER, https://www.pocketgamer.biz/metrics/app-store/app-count/ [https://perma.cc/ZPH7-V65S] (providing data on the increasing number of apps available in the Apple App store since 2008); *see infra* note 16 and accompanying text.

3. *Nucleus Genomics Wants to Make Personalized Health Care a Reality*, ILLUMINA (Dec. 13, 2023), https://www.illumina.com/company/news-center/feature-articles/nucleus-genomics-whole-genome-sequencing.html [https://perma.cc/64YC-7R3U].

4. Ashley Smart, *From a Fledgling Genetic Science, A Murky Market for Predictions*, UNDARK (Oct. 27, 2023) (citing Alexis Ohanian (@alexisohanian), X (FORMERLY KNOWN AS TWITTER) (July 14, 2022, 12:06 PM), https://x.com/alexisohanian/status/1547628549674131456?s=20), https://undark.org/2023/10/27/consumer-genetic-testing-science/ [https://perma.cc/X4HN-73HC].

Appification refers to the literal development of applications ("apps") designed for web or mobile devices.[5] An app is a software program that performs specific, often small and limited functions.[6] In contrast to interacting with complex command line interfaces and backend processes, apps enable users to access desired features or capabilities in a simplified way, such as clicking an icon or selecting from a menu of discrete actions.[7] Apps streamline a user's digital experience by condensing what would typically require complex interactions into narrower, more isolated tasks or transactions.[8] The core principle is a shift towards highly focused user experiences compared to traditional multifaceted operating systems or computer platforms.[9]

But Appification is about more than just developing, downloading, or interacting with apps. As Nicolas Terry has observed, Appification is also a useful metaphor for understanding disaggregation and abstraction in different contexts.[10] The direct-to-consumer ("DTC") market for wellness products provides one such example. Instead of conducting complex scientific research or navigating insurance and seeking out a qualified medical professional, DTC wellness products promise to cut out the complicated middle by placing distilled, actionable health information directly into the hands of consumers.[11] While these apps can increase access and facilitate transactions,[12] they can also result in an overreliance on technology that does not account for failure[13] and obscure what have traditionally been important sources of knowledge and understanding.[14]

Appification in both a literal and metaphorical sense is thus an interesting lens through which to consider recent trends in DTC health

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5. *What is Appification?*, EASA (July 28, 2021) https://www.easasoftware.com/democratization/what-is-appification/ [https://perma.cc/7D7B-GWE2].

6. Marshall Gunnell, *Mobile Application*, TECHOPEDIA (May 28, 2024) https://www.techopedia.com/definition/2953/mobile-application-mobile-app [https://perma.cc/FW89-B839].

7. Nicolas P. Terry, *Appification, AI, and Healthcare's New Iron Triangle*, 20 J. HEALTH CARE L. & POL'Y 117, 168 (2018).

8. *Id.*

9. *Id.*

10. *Id.* at 169 ("Appification doubles as a useful metaphor for understanding contemporary attempts to disaggregate healthcare.").

11. *Id.* at 170 ("[Medical apps] disaggregate the complexity associated with traditional healthcare. They peel off various aspects of the healthcare system, frequently aspects that should be made available upstream, and present them in exceptionally easy-to-use software.").

12. *See id.*

13. Amber Case, *The Appification of Everything & Why it Needs to End*, MEDIUM (Sept. 17, 2019) https://caseorganic.medium.com/the-appification-of-everything-why-it-needs-to-end-8a2214c1968f [https://perma.cc/XA6P-FGCT] (providing examples where app-based systems failed, leaving consumers in dangerous or difficult situations without workarounds).

14. David Gerard O'Brien & Megan McDonald Van Deventer, *The Appification of Literacy*, *in* THE HANDBOOK OF RESEARCH ON THE SOCIETAL IMPACT OF DIGITAL MEDIA 417, 417–18 (Barbara Guzzetti & Millinee Lesley, eds., IGI Global 2016).

technologies. If Sadeghi is right and the near future involves the widespread or even universal appification of the human genome and complex measures like PRSs, disaggregated from scientific research and clinical care and delivered by an easy-to-use app, it is worth unpacking the resulting layers of abstraction. While the challenges that arise may simply be part of existing and well-documented problems present across all health apps,[15] articulating abstractions in DTC PRS may shine a light on appification's potential policy implications and help anticipate possible solutions.

This Essay proceeds in three parts. Part II introduces the reality of app development — including the emergence and proliferation of DTC genetic testing and app-based consumer products. Part III then considers appification as a metaphor for disaggregation and considers two examples where DTC PRS is broken off from more complex wholes. The first is when knowledge moves from academic research to consumer products. The second is when we position PRS in a consumer wellness context instead of a patient care context. Finally, Part IV speculates on how these multiple sources of obfuscation involved in the appification of genetic risk could contribute to, and potentially even compound, ongoing legal and medical uncertainty. This Essay then concludes by emphasizing that appification is not merely an inevitability that must be mitigated but, if approached thoughtfully, an opportunity to enhance genomic literacy.

II. THE REALITY OF APPIFICATION

The appification of everything has been taking place across sectors for years.[16] Genetic science is no exception to this phenomenon. Search an app store for "genetics," and several are available for download.[17] Some are associated with companies that handle and analyze biological samples.[18] Others allow consumers who have already taken DNA tests to upload their raw genetic data acquired elsewhere for new analyses.[19]

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15. *See generally* Leah R. Fowler, *Health App Lemons*, 74 ALA. L. REV. 65 (2022) (describing the promises and perils of health apps and how information asymmetries prevent consumers from understanding the risks and limitations).

16. Kosner, *supra* note 1 (describing the trend of appification in 2012); *see also* Emily Stewart, *Do We Really Need an App for Everything?*, VOX (June 1, 2023, 7:50 AM EDT), https://www.vox.com/money/23743915/iphone-android-apps-airline-dentist-pandemic-data-privacy-restaurant [https://perma.cc/DLT4-78XC] (lamenting the proliferation of apps in 2023).

17. Divya Talwar, Yu-Lyu Yeh, Wei-Ju Chen & Lei-Shih Chen, *Characteristics and Quality of Genetics and Genomics Mobile Apps: A Systematic Review*, 27 EURO. J. HUM. GENETICS 833, 838 (2019).

18. *See, e.g.*, 23ANDME, https://apps.apple.com/us/app/23andme-dna-testing/id952516687 [https://perma.cc/K8Z5-ZBCQ].

19. *See, e.g.*, Genomapp. Healthy Ethics., https://apps.apple.com/us/app/genomapp-healthy-ethics/id922937973 [https://perma.cc/9R4E-MYJ2].

Some do both.[20] Some are thoughtfully designed and systematically evaluated.[21] Others are not.[22] The consumer market for genetic testing and its offerings increases with every technological development and scientific advancement. This Part describes how genetic testing has already been and continues to be appified. It begins with the current state of DTC genetic testing, including the newer and growing consumer market for DTC PRS. It then considers the types of abstraction that app development introduces.

A. DTC Genetic Testing

Genetic testing has been appified. DTC genetic testing allows consumers to purchase test kits directly, send in a DNA sample, and receive results on the web, via an app, or in a written report,[23] all without ever seeing a doctor. This subpart discusses DTC genetic testing, including PRS, delivered via an app. Given the small number of studies evaluating genetics and genomics mobile apps, this subpart approaches the subject in generalities.

Though the app phenomenon is somewhat more recent, DTC genetic testing has existed in some form or another for nearly twenty years.[24] According to one survey, by 2022, two in ten Americans had reported taking a mail-in DNA test, and many (forty-five percent) would be interested if it were offered free of cost.[25] Though exact numbers are debated, and there is some question about whether initial uptake was more aggressive than long-term trends can sustain,[26] tens of millions of Americans have already obtained genetic test results from

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20. Cathryn M. Lewis & Evangelos Vassos, *Polygenic Risk Scores: From Research Tools to Clinical Instruments*, GENOME MED., May 18, 2020, at 8 (2020) (giving several examples of companies that provide DTC PRS, including 23andMe, Impute.me, and MyHeritage).

21. Evan D. Muse, Shang-Fu Chen, Shuchen Liu, Brianna Fernandez, Brian Schrader, Bhuvan Molparia et al., *Impact of Polygenic Risk Communication: An Observational Mobile Application-Based Coronary Artery Disease Study*, NPJ DIGIT. MED. (Mar. 11, 2022), at 1.

22. Norina Gasteiger, Amy Vercell, Alan Davies, Dawn Dowding, Naz Khan & Angela Davies, *Patient-Facing Genetic and Genomic Mobile Apps in the UK: A Systematic Review of Content, Functionality, and Quality*, 13 J. CMTY. GENETICS 171, 179 (2022) ("[N]one of the 22 apps we reviewed had been verified by evidence in published scientific literature.").

23. *What is Direct-to-Consumer Genetic Testing*, MEDLINEPLUS (June 21, 2022), https://medlineplus.gov/genetics/understanding/dtcgenetictesting/directtoconsumer/ [https://perma.cc/5GB4-AM6X].

24. *Direct-to-Consumer Genetic Testing FAQ*, NAT'L HUM. GENOME RSCH. INST. (June 14, 2023), https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources/Healthcare-Provider-Direct-to-Consumer-Genetic-Testing-FAQ [https://perma.cc/98SZ-74K9] (identifying 2005 as the year the "first DTC companies were founded").

25. Taylor Orth, *DNA Tests: Many Americans Report Surprises and New Connections*, YOUGOV (Feb. 24, 2022, 7:15 PM GMT), https://today.yougov.com/society/articles/41232-dna-tests-many-americans-report-surprises-and-new- [https://perma.cc/U8ZQ-R6VK].

26. Mary A. Majumder, Christi J. Guerrini & Amy L. McGuire, *Direct-to-Consumer Genetic Testing: Value and Risk*, 72 ANN. REV. MED. 151, 152 (2021).

DTC companies.[27] If venture capital investment is any indication, this number will continue to grow.[28]

With DTC genetic testing, individuals can get genetic insights into health, traits, and ancestry through recognizable companies like 23andMe, Ancestry, Gene by Gene, and MyHeritage.[29] Getting your whole genome sequenced in 2024 is not even particularly expensive. When running a promotion, Nebula Genomics will do it for as little as $99, plus the cost of membership.[30] At that price, the company will provide a basic ancestry report and detect common predispositions.[31] For slightly more, $249 plus the membership fee, Nebula promises to provide a deep ancestry report and to detect all predispositions and rare genetic mutations.[32] Even companies that only conduct one type of test — say, ancestry tests — can make raw genetic data available to consumers, allowing them to submit it elsewhere for independent interpretation and other types of results.[33] For example, if you already have your raw DNA data, Nebula offers DNA expansion and limited analysis for free.[34]

More recently, DTC genetic testing has opened the door to more cutting-edge science, including PRS. Stacey Pereira et al. succinctly define PRS as "an estimate of a person's relative genetic susceptibility to a particular disorder that considers all risk variants present in the person's DNA, weighted by the strength of each variant's ostensible association with the disorder in question."[35] PRS involves the analysis of a few or even hundreds or thousands of genetic variants.[36] Though

27. Tanya Albert Henry, *Protect Sensitive Individual Data at Risk from DTC Genetic Tests*, AM. MED. ASSOC. (Nov. 16, 2021), https://www.ama-assn.org/delivering-care/patient-support-advocacy/protect-sensitive-individual-data-risk-dtc-genetic-tests [https://perma.cc/2SGW-Y43Z] (estimating that over 100 million individuals underwent DTC genetic testing by the end of 2021).

28. Martin Romero, *The $8.8 Billion DTC Genetic Testing Market*, FUTURE HEALTH (Apr. 12, 2024), https://www.thefutureofhealth.co/p/the-88-billion-dtc-genetic-testing [https://perma.cc/4QXU-24JB] (providing examples of venture capital investment in genetic testing companies).

29. Majumder et al., *supra* note 26, at 152.

30. *The First Step*, NEBULA GENOMICS, https://nebula.org/blog/the-first-step [https://perma.cc/K3WB-5XNQ] ("We're offering members of the Nebula community something none of our competitors do, the opportunity to have your whole genome sequenced for free, with the cost paid by researchers who want access to that data. If you'd rather have your sequencing done immediately, you can purchase that directly from us for just $99.").

31. *Id.*

32. *Id.*

33. Majumder et al., *supra* note 26, at 153.

34. *DNA Upload, Expansion, and Analysis!*, NEBULA GENOMICS, https://nebula.org/dna-upload-analysis/ [https://perma.cc/LU7V-T6T8].

35. Stacey Pereira, Katrina A. Muñoz, Brent J. Small, Takahiro Soda, Laura N. Torgerson, Clarissa E. Sanchez et al., *Psychiatric Polygenic Risk Scores: Child and Adolescent Psychiatrists' Knowledge, Attitudes, and Experiences*, 189 AM. J. GENETIC MED. 293, 293 (2022).

36. Lewis & Vassos, *supra* note 20, at 1.

the statistical methods used to compute PRS may vary,[37] the concept involves weighting and summing risk alleles to produce a unitless risk score representing the relative contribution of those variants to an observed phenotype.[38] As many have noted, PRS may appear simple, but they represent a far more complex genetic reality.[39]

Though PRS are relatively new genetic metrics, the consumer market is growing rapidly alongside the genome-wide association studies ("GWAS") that make generating PRS possible.[40] These studies often come from academic researchers. Some DTC companies conduct their own studies using customer survey responses and their proprietary databases.[41] GWAS can also be automated. Consider a Twitter bot called GWASBot.[42] As the Dunn Lab characterizes it, this bot "produces a Manhattan plot of a random phenotype from @uk_biobank data every day and highlights that you can find a GWAS signal in almost everything."[43]

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37. Todd Lencz, Maya Sabatello, Anna Docherty, Roseann E. Peterson, Takahiro Soda, Jehannine Austin et al., *Concerns About the Use of Polygenic Embryo Screening for Psychiatric and Cognitive Traits*, 9 LANCET PSYCHIATRY 838, 839 (2022) (citing to Ying Ma and Xiang Zhou, *Genetic Prediction of Complex Traits with Polygenic Scores: A Statistical Review,* 37 TRENDS IN GENETICS 11 (2021)).

38. Jacob S. Sherkow, Jin K. Park & Christine Y. Lu, *Regulating Direct-to-Consumer Polygenic Risk Scores*, 330 J. AM. MED. ASSOC. 691, 691 (2023); Lewis & Vassos, *supra* note 20, at 2 ("Summing across variants assumes an additive genetic architecture, with independence of risk variants. Although simplistic, this reflects our best estimate of the genetic architecture of common complex disorders, where little evidence of interaction between genetic variants is detected.").

39. Anna Docherty, Brent Kious, Teneille Brown, Leslie Francis, Louisa Stark, Brooks Keshin et al., *Ethical Concerns Relating to Genetic Risk Scores for Suicide*, 186 AM. J. MED. GENETICS PART B: NEUROPSYCHIATRIC GENETICS 433, 434 (2021).

40. Larissa Peck, Kennedy Borle, Lasse Folkersen & Jehannine Austin, *Why Do People Seek Out Polygenic Risk Scores for Complex Disorders, and How Do They Understand and React to Results?*, 30 EURO. J. HUM. GENETICS 81, 82 (2022). ("[P]ublic interest . . . has led companies that already provide direct-to-consumer (DTC) genetic testing online to include PRSs . . . . Third-party services have also emerged which allow users to upload their raw personal genetic information . . . and generate PRSs . . . . Emerging data demonstrates very rapid increase in the usage of these third-party sites.").

41. *See, e.g.*, Aaron Wolf, *Polygenic Risk Score (PRS) Traits*, ANCESTRY, https://support.ancestry.com/s/article/PRS-traits?language=en_US [https://perma.cc/NBS6-LQ79].

42. @SBotGwa, X (FORMERLY KNOWN AS TWITTER), https://x.com/sbotgwa?lang=en [https://perma.cc/8H42-K5EU].

43. *A Look Into the Weird and Wonderful World of Academic Twitter*, THE DUNN LAB, https://www.thedunnlab.com/blog/a-look-into-the-weird-and-wonderful-world-of-academic-twitter [https://perma.cc/K7J7-QMVA]; Smart, *supra* note 4 ("On different days in August, it identified genetic variants linked to people's ability to solve an arithmetic problem, their tendency to feel fed up, and their penchant for taking naps during the day."). The Data Science Genetic Epidemiology Lab at the University of Helsinki manages the account, stating that it "posts every day the results of a genome-wide association study" and that they are "expanding the studies included and the information shared in collaboration with the Neale Lab @ the Broad Institute." Data Science Epidemiology Lab, *Projects*, UNIV. HELSINKI, https://www.helsinki.fi/en/researchgroups/data-science-genetic-epidemiology-lab/projects [https://perma.cc/5N6B-W4R7].

Some large, recognizable companies that dominate the DTC genetic testing market, like 23andMe, already offer PRS.[44] However, much smaller emerging apps focus on specific types of PRS.[45] The proliferation of GWAS has brought with it more data from which to develop consumer PRS tests.[46] For example, GenePlaza, which markets itself as "a marketplace for genetic reports,"[47] hosts apps that predict genetic risk for depression,[48] neuroticism,[49] and intelligence[50] based on GWAS. As GWAS become easier to conduct, the number of possible PRS to commercialize will also grow.[51] In other words, the growth of GWAS means more findings that permit focused DTC PRS to emerge with surprising frequency — even if those test results are only loosely based on the study findings.[52]

B. Apps and Abstraction

One way to think about apps is as abstractions.[53] Appification simplifies complex backend processes and infrastructure, hides more technical details, and makes the consumer experience seamless.[54] While technical discussion of app development is beyond the scope of this Essay, the main takeaway is that abstraction in app development handles "complexity by hiding unnecessary details from the user," allowing users to avoid "understanding or even thinking about all the hidden complexity."[55]

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44. *Understanding Polygenic Risk Scores*, 23ANDME (Sept. 25, 2023), https://blog.23andme.com/articles/better-polygenic-risk-prediction [https://perma.cc/PU49-BM4V] (noting that "23andMe offers more than 30 reports based on polygenic risk models.").

45. *See, e.g.*, *Depression App*, GENEPLAZA (May 29, 2018), https://www.geneplaza.com/app-store/68/preview [https://perma.cc/H8E7-68J2] (showing an app providing a risk score for depression).

46. A.C. Palk, S. Dalvie, J. de Vries, A.R. Martin & D.J. Stein, *Potential Use of Clinical Polygenic Risk Scores in Psychiatry — Ethical Implications and Communicating High Polygenic Risk*, 14 PHIL. ETHICS & HUMANS. IN MED., Feb. 27, 2019, at 2–3.

47. *A Marketplace for Genetic Reports*, GENEPLAZA, https://www.geneplaza.com/ [https://perma.cc/K6BR-K5EZ].

48. *Depression App*, *supra* note 45.

49. *Neuroticism App*, GENEPLAZA, https://www.geneplaza.com/app-store/57/preview [https://perma.cc/8P2Q-YN3V].

50. *Intelligence App*, GENEPLAZA, https://www.geneplaza.com/app-store/60/preview [https://perma.cc/Z4HR-TA8X].

51. Smart, *supra* note 4 (describing a Twitter bot called @GWASBot that "conducted roughly one new GWAS every day, publishing its results on X.").

52. Amy Maxmen, *'Gay Gene' App Provokes Fears of a Genetic Wild West*, 574 NATURE 609, 609 (2019) ("Anyone can take the variations identified by such studies, strip them of caveats and nuance, and market a simple genetic-interpretation tool online.").

53. Terry, *supra* note 7, at 168.

54. *Id.*

55. Thorben, *OOP Concept for Beginners: What is Abstraction?*, STACKIFY (Feb. 28, 2024), https://stackify.com/oop-concept-abstraction/ [https://perma.cc/EY7S-6MBE] (explaining process abstraction and data abstraction).

Consider abstraction in the context of DTC PRS. A consumer submits a file containing raw genetic data and is given a PRS. That DNA raw data will include single nucleotide polymorphisms, the chromosome and genomic location, and the genotype for that variant.[56] However, the consumer does not need to know, and likely does not know, the contents of the data file, only that it is a compatible format to upload. In between the input and the output, the genetic information and identified genomic variants must be considered in combination.[57] Taking information from a GWAS, the company will identify the independent risk variants for a disorder and sum the number of risk alleles at each variant, weighted by effect size.[58] The result is the PRS, which identifies the relative risk of developing a disease.[59] A consumer does not have to know the details of this process, including the source or limitations of the GWAS, to obtain a PRS.

As a result, using apps to deliver DTC genetic information, including PRS, results in a significant amount of abstraction for both developers and end users. In some ways, these abstractions are great. The consumer market and appification of DTC genetic tests offer many benefits, including simplicity and accessibility, information that can help reduce fear and stigma, an increased sense of agency and ability to be proactive about health conditions, and additional levels of privacy in certain narrow contexts like insurance.[60]

But apps do not just make technology easier and more convenient; they fundamentally change how we access and use information.[61] In the process, appification can also prevent the consumer from knowing what is happening in the background and ultimately obscure important sources of knowledge and understanding.[62] As a result, apps themselves may be detrimental to consumer literacy skills.[63] This is potentially true of any app. However, combined with complex metrics like PRS, this

56. *What is the DNA Raw Data and How Does it Look?*, XCODE (June 3, 2021), https://www.xcode.life/23andme-raw-data/what-is-the-dna-raw-data-and-how-does-it-look [https://perma.cc/S64T-H3W6].

57. Lewis & Vassos, *supra* note 20, at 1 ("In a polygenic disorder, a single variant is not informative for assessing disease risk. Instead, a genetic loading conferred by the combined set of risk variants is necessary to obtain a measure that has sufficient information to identify those at high risk.").

58. *Id.* at 2.

59. Docherty et al., *supra* note 39 (defining PRS as measures that "integrate effect sizes from many genetic risk variants to come up with a continuous score for risk of developing a . . . medical condition.").

60. *See generally Direct-to-Consumer Genetic Testing FAQ*, *supra* note 24 (identifying 2005 as the year the "first DTC companies were founded").

61. O'Brien & Van Deventer, *supra* note 14, at 417–18 ("[Appification] refers to a fundamental shift in how we access and use information and media. Specifically, how we are moving from using the Web as a vast information server" to the Web as little more than a "backend service for apps.").

62. *Id.*

63. *Id.* at 423 ("As of yet, it is unclear what sorts of literacy skills and practices are promoted by apps while some traditional reading and writing practices are undermined.").

abstraction may influence whether and how consumers understand their results.

III. THE METAPHOR OF APPIFICATION

As discussed in Part II, in a literal sense, appification refers to the development of web and mobile apps. App development inherently involves abstraction, which can obscure important information and processes. This appification is pervasive in DTC testing and has grown to include PRS. However, we can also consider appification as a metaphor for disaggregation in the context of DTC PRS. This Part considers how DTC testing can fragment PRSs from important context and knowledge sources, independent of how they are presented. First, it considers the disaggregation that occurs when PRSs move from academic research to consumer products. Next, it turns to the disaggregation that takes place when these results move from a health care context to consumer wellness.

A. Academic Research to Consumer Product

The first example of disaggregation that can occur with DTC genetic risk involves the nuance and caveats lost between a scientific research study — like a GWAS — and the information presented to a consumer receiving a result, like an app-based PRS. Here, the PRS may lack the full context of the original finding from which it was derived, including information about the result's limitations.

The details of a GWAS provide important information about how an individual can interpret their PRS. Researchers have noted that "the accuracy of a PRS is a function of both the size of the GWAS and its similarity to the target individual."[64] A PRS derived from a larger GWAS is likely to be more accurate and have a stronger predictive capacity compared to one derived from a smaller study.[65] Accuracy may depend on the similarities between the study population and the target individual, like socioeconomic status, age, and sex.[66] If the GWAS study population differs significantly from the target individual, the accuracy of the PRS may be compromised.[67] As a result, without

64. Lencz et al., *supra* note 37, at 839.

65. Palk et al., *supra* note 46, at 2 ("The power of such studies to robustly identify associations between genetic variants and traits, and thus, to accurately predict disease risk depends primarily on sample size. To achieve statistical significance, such studies require large numbers of samples of both cases and controls.").

66. *See id.* at 4.

67. John Novembre, Catherine Stein, Samira Asgari, Claudia Gonzaga-Jauregui, Andrew Landstrom, Amy Lemke et al., *Addressing the Challenges of Polygenic Scores in Human Genetic Research*, 109 AM. J. HUM. GENETICS 2095, 2095–96 (2022); *see also* Lewis & Vassos, *supra* note 20, at 3.

information about the study from which a PRS is developed, it is difficult to understand what a result really means for an individual.

Alternative sources of information about genetics and genomic science are not always trustworthy. The media may translate scientific advancements through oversimplification and exaggeration, creating a grabby headline rather than conveying the truth.[68] DTC companies may exacerbate the problem by pushing back against the value of experts, viewing them more as gatekeepers than guides, and treating authorities with suspicions of paternalism in an effort to sell products.[69] One reporter observed that "commercial push has created tension between academic researchers who toil to uncover new genetic associations and the entrepreneurs who repurpose the results for profit."[70]

An example illustrates the types of nuance missing when research enters the consumer realm. Consider the "*How gay are you*" app.[71] In August 2019, researchers published a large-scale GWAS aiming to identify genetic variants associated with same-sex sexual behavior.[72] The researchers found that "genome-wide significant loci associated with same-sex sexual behavior and found evidence of a broader contribution of common genetic variation."[73] The study was clear that, in this context, genetics were not determinative, and, in fact, individual-level prediction would be impossible.[74]

Nevertheless, within one month, the online app store GenePlaza hosted the "*How gay are you*?" app designed to provide consumers with a genetic score for homosexuality.[75] There was significant public

68. Paige Brown, Namrata Kotwani, Brian Resnick, David Ransohoff & Richard Ransohof, *Inaccurate Representation of Results in the Media*, THE EMBASSY OF GOOD SCI. (Oct. 28, 2020), https://embassy.science/wiki/ [https://perma.cc/5Q74-DPET] (noting that the media may distort research findings through "oversimplified language, exaggeration, sensationalist reporting, and the avoidance of complex issues").

69. *See* Eric T. Juengst, Michael A. Flatt & Richard A. Settersten Jr., *Personalized Genomic Medicine and the Rhetoric of Empowerment*, 42 HASTINGS CTR. REP. 34, 35, 38 (2012).

70. Smart, *supra* note 4.

71. Dian Kwon, *Scientist Seek to Kill Genetic Test for Same Sex Attraction,* THE SCIENTIST (Oct. 17, 2019), https://www.the-scientist.com/scientists-seek-to-kill-genetic-test-for-same-sex-attraction-66591 [https://perma.cc/F3MP-KWCL].

72. Andrea Ganna, Karin J.H. Verweij, Michel G Nivard, Robert Maier, Robbee Wedow, Alexander S. Busch et al., *Large-Scale GWAS Reveals Insights into the Genetic Architecture of Same-Sex Sexual Behavior*, 365 SCI. 1, 3 (2019) (measured by ever versus never having had a same-sex sexual partner).

73. *Id.* at 7.

74. *Id.* at 1, 5 (emphasizing that "many uncertainties remain to be explored, including how sociocultural influences on sexual preference might interact with genetic influences" and "these scores could not be used to accurately predict sexual behavior in an individual"); *see also* Letter from Benjamin Neale on behalf of his coauthors to the developers of GenePlaza (Oct. 14, 2019) [https://perma.cc/2GVM-9ZTS].

75. Kwon, *supra* note 71.

concern given the subject,[76] and even the study's authors cautioned that the app was dangerous and encouraged its removal.[77] The app's lead developer objected to the criticism.[78] In response, he changed the app's name and added content to clarify that the authors of the GWAS were not affiliated with the app.[79] However, by November 2019, within four months of release, the app was no longer available on GenePlaza.[80]

In light of this trend, many scholars have noted that researchers must ensure their findings are used responsibly.[81] Though public pressures helped motivate the study authors to speak out and control misleading consumer products in this example, apps do not always generate enough attention or pressure for this to occur regularly. As a result, similarly misleading apps may persist indefinitely on the market, remaining disaggregated from the original study and experts.[82]

B. Health Care to Wellness

Another source of disaggregation is when PRSs are removed from a clinical environment with medical providers and genetic counselors and given directly to consumers with no intermediary to help interpret the findings. When this happens, consumers may have a difficult time understanding what a PRS means and what, if any, actions the consumer should take in response.

Even in a clinical encounter and in the presence of physicians, it is difficult to communicate the significance of PRSs.[83] DTC PRSs are often removed from clinical encounters and the presence of experts or comprehensive genetic counseling altogether. Regardless of who presents them, PRSs are probabilistic, not deterministic, and indicate

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76. Megan Molteni, *How Earnest Research Into Gay Genetics Went Wrong,* WIRED (Nov. 18, 2019, 7:00 AM), https://www.wired.com/story/how-earnest-research-into-gay-genetics-went-wrong/ [https://perma.cc/24AR-N858]; Dan Robitzski, *Scientists Call for Removal of App Claiming to Detect Gay DNA*, FUTURISM (Oct. 17, 2019, 10:50 AM EDT), https://futurism.com/neoscope/scientists-against-app-detect-gay-dna [https://perma.cc/L92F-GAJ9].

77. Letter from Benjamin Neale on behalf of his coauthors to the developers of GenePlaza, *supra* note 74.

78. Maxmen, *supra* note 52, at 609.

79. *Id.* ("The next week, Bellenson renamed the app '122 Shades of Gray' and added a note explaining that the authors of the Science study weren't affiliated with the project.").

80. Kwon, *supra* note 71; Maxmen, *supra* note 52, at 610 (noting that Alain Coletta, co-founder of GenePlaza, removed the app on October 24, 2019).

81. Lasse Folkersen, Oliver Pain, Andrés Ingason, Thomas Werge, Cathryn M. Lewis & Jehannine Austin, *Impute.me: An Open-Source, Non-Profit Tool for Using Data from Direct-to-Consumer Genetic Testing to Calculate and Interpret Polygenic Risk Scores*, 11 FRONTIERS GENETICS, June 30, 2020, at 7.

82. Quinn Grundy, *A Review of the Quality and Impact of Mobile Health Apps*, 43 ANN. REV. PUB. HEALTH 117, 122–23 (2022).

83. Lewis & Vassos, *supra* note 20, at 4–5 (explaining the clinical limitations of PRS); *see also* Pereira et al., *supra* note 35, at 297 (showing that only 26.8 percent of a sample of US-based child and adolescent psychiatrists responded correctly when asked to interpret example results).

relative risk compared to the general population rather than absolute risk.[84] And most consumers lack sufficient statistical literacy to interpret lifetime risk or compare relative risks between groups.[85]

Without caution in communicating findings, consumers risk falling into "genetic determinism," leading those same people to ignore important environmental and behavioral contributions to disease development and outcomes.[86] More robust counseling about the risks of false positives and negatives, low penetrance, and predictive value — which cannot be guaranteed in a consumer context — should be part of any return of results.[87]

Given the clear challenges in comprehending PRSs, it is important to understand how DTC PRS companies communicate results and how consumers understand and react to them. Evidence regarding reactions and propensity toward reductive interpretations of PRS results is mixed.[88] One study of the motivations, understanding, interpretation, and psychological impacts of DTC results on real impute.me (now Nucleus Genomics) users found that only about a quarter of participants could answer all understanding and interpretation questions correctly.[89] Concerningly, poorer understanding of PRSs and lower levels of numeracy were associated with a greater risk of experiencing a negative psychological reaction to the information.[90] In that study, over sixty percent of participants reported a negative reaction, and about five percent scored over the threshold for potential post-traumatic stress disorder in reaction to their results.[91]

The likelihood that consumers will not understand or will experience negative psychological reactions to their results is relevant in light of the limited potential benefits of DTC PRS. Importantly, most PRS

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84. Peck et al., *supra* note 40, at 86.

85. *See generally* Gerd Gigerenzer, Wolfgang Gaissmeier, Elke Kurz-Milcke, Lisa M. Schwartz & Steven Woloshin, *Helping Doctors and Patients Make Sense of Health Statistics*, 8 PSYCH. SCI. PUB. INT. 53, 54 (2007).

86. Brent M. Kious, Anna R. Docherty, Jeffery R. Botkin, Teneille R. Brown, Leslie P. Francis, Douglas D. Gray et al., *Ethical and Public Health Implications of Genetic Testing for Suicide Risk: Family and Survivor Perspectives*, 23 GENETICS MED. 289, 296 (2021); Lewis & Vassos, *supra* note 20, at 4 ("An important consideration is the need to avoid presenting a false impression of genetic determinism (the notion that genes alone define biology). This could otherwise detrimentally impact personal choices, harming physical and mental well-being (e.g. diet, exercise, lifestyle), and possibly even education, employment, or family planning.").

87. Kious et al., *supra* note 86, at 296.

88. Palk et al., *supra* note 46, at 7; *see also* Majumder et al., *supra* note 26, at 154 (discussing consumer reactions and interpretations of BRCA testing results).

89. Peck et al., *supra* note 40, at 82, 84 ("Regarding general understanding of the meaning of PRSs, 35.5% (n = 93) of participants incorrectly classified one or more statements. When asked to interpret an example Impute.me result, 61.6% (n = 149) of participants incorrectly identified one or more statements. Overall, only 25.6% (n = 67) of participants answered all understanding and interpretation questions correctly.").

90. *Id.* at 86.

91. *Id.* at 85–86.

lack clinical utility.[92] In some medical contexts, PRS show some promise, at least theoretically.[93] A study of child and adolescent psychiatrists noted that more than half of respondents thought these scores had some clinical utility in their practice, and the vast majority (86.7 percent) believed that psychiatric PRS would become at least slightly useful in child and adolescent psychiatry within the next five years.[94] PRS can also be one part of a multistage screening process in other clinical contexts, but it is not solely determinative.[95]

Notwithstanding those examples, some scientists say that, even with technological advancements, many PRSs will never be able to accurately predict who will or will not develop a given disease.[96] Thus, even if a DTC PRS result encourages a consumer to speak to their doctor or seek out additional diagnostic tests, there is likely nothing a clinician can do with these results.[97] Under the best circumstances, DTC results may generate important conversations between health care providers and their patients, resulting in more robust health education.[98] However, this requires access to care and the necessary specialists in the first place, as well as a physician capable of understanding the results.[99] More likely, though, misleading but catchy language in apps, received without expert guidance or caution, may lead consumers to believe that their results mean more than they do.

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Important nuances and caveats can be lost when genetic risk information is disaggregated from scientific research or clinical care to a consumer context. Without the background information and limitations from a GWAS, it is hard to understand if an individual differs from a

92. Docherty et al., *supra* note 39, at 434; *see also* Lewis & Vassos, *supra* note 20, at 4; Smart, *supra* note 4 (quoting the chief of the public health genomics branch at the Centers for Disease Control and Prevention, Muin Khoury). *But see* Ahmet Fuat, Ella Alden, Mark Monane, Ruth Coll, Sarag Groves, Elizabeth Little et al., *A Polygenic Risk Score Added to a QRISK2 Cardiovascular Disease Risk Calculator Demonstrate Robust Clinical Acceptance and Clinical Utility in the Primary Care Setting*, 31 EUR. J. PREVENTATIVE CARDIOLOGY 716, 720 (2024).

93. Palk et al., *supra* note 46, at 3.

94. Pereira et al., *supra* note 35, at 297.

95. Lencz et al., *supra* note 37, at 840 (giving the example of breast cancer and myocardial infarction).

96. Amit Sud, Rachel H. Horton, Aroon D. Hingorani, Ioanna Tzoulaki, Clare Turnbull, Richard S. Houlston et al., *Realistic Expectations Are Key to Realizing the Benefits of Polygenic Scores*, 380 BMJ, Mar. 1, 2023, at 1.

97. Smart, *supra* note 4.

98. Lewis & Vassos, *supra* note 20, at 8.

99. US-based child and adolescent psychiatrists did not perform much better than consumers when interpreting PRS results. Pereira et al. found that only 26.8 percent of participants responded correctly when asked to interpret example results. Pereira et al., *supra* note 35, at 297.

study population and whether those differences are meaningful.[100] It is difficult to communicate PRS complexity in a clinical setting with medical professionals,[101] but even more so in a consumer context.[102] When this information is delivered via an app, compounding abstraction with disaggregation has the potential to further flatten complex results into data points devoid of context. If professionals do not account for these factors, they may contribute to medical and legal uncertainty.

IV. APPIFICATION AND UNCERTAINTY

Sadeghi's prediction that everyone will inevitably have their genome on their phone[103] may prove true. If so, more people will experience the appification of genetic risk — both through the literal use of apps designed to analyze their data and as a metaphor as the use of that data becomes further removed from scientific research and medical care. In the background of this confluence of abstractions, PRSs already generate significant medical and legal uncertainty.[104] This Part explores how appification could contribute to and potentially compound two facets of that uncertainty. First, it describes how app-based health disclaimers can blur the boundaries between what is "medical" and what is not. Second, it explains how health apps add considerations that further complicate already challenging legal questions about regulatory oversight of DTC PRS.

A. Medical Uncertainty

DTC PRSs can result in significant medical uncertainty.[105] One source of that uncertainty occurs when consumers mistakenly believe

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100. *See supra* notes 65–67 and accompanying text. If the app does not cite a study or provide information about the study population, a consumer would not be able to identify whether they are similar to the study population.

101. Lencz et al., *supra* note 37, at 841 (observing that "communication of these considerations by providers to patients, in clinically meaningful terms that can be readily understood, will likely be challenging").

102. Peck et al., *supra* note 40, at 86.

103. Smart, *supra* note 4 (citing Alexis Ohanian (@alexisohanian), X (FORMERLY KNOWN AS TWITTER), https://x.com/alexisohanian/status/1547628549674131456?s=20 [https://perma.cc/P7TG-VSBT]).

104. *See, e.g.*, Jessica L. Roberts & Sonia M. Suter, *Damned If You Do or Damned If You Don't: The Medical Malpractice Implications of Consumer-Generated Polygenic Risk Scores*, 38 HARV. J.L. & TECH. 417 (2024) (discussing medical uncertainty for physicians); Valerie Gutmann Koch, *Previvorship and Medical Uncertainty*, 38 HARV. J.L. & TECH. 401 (2024) (discussing medical uncertainty for patients); Shawneequa Callier & Anya E.R. Prince, *The Legal Uncertainties of Sociogenomic Polygenic Scores*, 38 HARV. J.L. & TECH. 553 (2024) (discussing legal uncertainty in various contexts); Jin K. Park & I. Glenn Cohen, *The Regulation of Polygenic Risk Scores*, 38 HARV. J.L. & TECH. 377 (2024) (discussing legal uncertainty in regulation).

105. *See supra* note 104.

that DTC PRS results are health advice. Though this type of confusion may be common across all types of health apps, the abstraction and disaggregation identified in this Essay, coupled with the inherent complexity of PRS, may further impede consumer understanding and result in confusion.

Apps disaggregate DTC PRSs from scientific research and medical encounters that can provide counseling and context about the limitations of the results.[106] As a result, it makes logical sense that a consumer may not fully appreciate the distinctions between a genetic result obtained from their physician and one obtained directly from a DTC service. As noted several times throughout this Essay, risk — especially the relative risk conveyed by PRSs — is already difficult to communicate.[107] Appification may compound this problem.[108] Apps often communicate genetic risk in a manner that does not maximize the potential for benefits or in a setting that does not help contextualize consequences.[109] Even websites, which often display more comprehensive information than a smartphone app, do not generally communicate high-quality genetic information.[110] The result may be that consumers are even less likely to understand the medical significance of their DTC PRS when delivered via an app than in other contexts.

Consumers can thus become confused about the appropriate use and limitations of health information obtained from an app. One way for health apps to limit potential liability that can arise from confusion about appropriate use is to provide medical disclaimers in the terms of service ("ToS"). This practice is also common in DTC genetics. George Church, a Harvard professor and co-founder of Nebula Genomics, has told reporters that "Nebula Genomics' reports are not intended for medical or pharmaceutical use."[111] Even the "*How gay are you*" app, described in Section III.A of this Essay, included a disclaimer that it could not be used to predict same-sex attraction, even while the name itself strongly suggested otherwise.[112]

Perhaps predictably, these types of disclaimers and their regular appearance in the ToS fine print do not always work, given the well-documented challenges in finding, reading, and understanding ToS in

106. *See supra* Part III.

107. Sud et al., *supra* note 96, at 5.

108. *See generally* O'Brien & Van Deventer, *supra* note 14.

109. Folkersen et al., *supra* note 81, at 7–8 ("An example of such perspective is that of giving reports by disease score, and not by individual risk variant as is currently the case in most third-party analytics apps.").

110. *Id.* at 7.

111. Smart, *supra* note 4.

112. Maxmen, *supra* note 52, at 609 ("Bellenson says that the idea his test could endanger people is an 'absurd scenario' and notes that the test also included a warning that it could not predict same-sex attraction. . . . He says that because the app has always warned users that it is not predictive, it does not misrepresent the study.").

the first place.[113] *Tompkins v. 23andMe, Inc.*[114] provides a useful illustration of how these types of medical disclaimers can be ineffective. In this case, a class of plaintiffs brought claims against 23andMe, a DTC genetic testing company, for "unfair business practices, breach of warranty, and misrepresentations about the health benefits of 23andMe's services."[115] The plaintiffs claimed that 23andMe "represented and advertised that their DNA Kits would improve consumers' health."[116] 23andMe's response emphasized that "the Company's website and ToS made abundantly clear that the health-related component was for informational purposes only, did not constitute medical advice or diagnoses, and could not be used by customers for diagnostic purposes."[117]

This lawsuit, however, brought no resolution to the issues of alleged breach of warranty and misrepresentations of health benefits.[118] However, *Tompkins* shows that consumers, including those seeking out DTC genetic testing, may not appreciate the limits of their results, even if medical disclaimers appear in the ToS. These disclaimers may also complicate liability if harm results.[119] Thus, the appification of PRS may worsen the medical uncertainty consumers feel when trying to understand their results and reconcile them with disclaimers.

B. Legal Uncertainty

DTC PRSs are also the subject of considerable legal uncertainty, and the appification of genetic risk may further complicate legal and regulatory categorization. Though many regulatory bodies oversee genetic testing[120] and mobile health,[121] this Part focuses narrowly on

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113. Yannis Bakos, Florencia Marotta-Wurgler & David R. Trossen, *Does Anyone Read the Fine Print? Consumer Attention to Standard-Form Contracts*, 43 J. LEGAL STUD. 1, 32 (2014); Leah R. Fowler, Charlotte Gillard & Stephanie R. Morain, *Readability and Accessibility of Terms of Service and Privacy Policies for Menstruation-Tracking Smartphone Applications*, 21 HEALTH PROMOTION PRAC. 679, 682 (2020).

114. 840 F.3d 1016 (9th Cir. 2016).

115. *Id.* at 1021.

116. First Amended Class Action Complaint at 8, Guthrie v. 23andMe, Inc., Nos. 2:14-cv-00168, 14CV01258 (N.D. Cal. Mar. 13, 2014), 2014 WL 10450399.

117. Brief of Defendant-Appellee at 7, Tompkins v. 23andMe, Inc., 840 F.3d 1016 (9th Cir. 2016) (No. 14-16405).

118. *Tompkins*, 840 F.3d at 1032 (the court held that the challenged arbitration agreement was not unconscionable under California law and that their "authority to review portions of the contract outside the arbitration provision [was] limited.").

119. Jessica L. Roberts & Sonia M. Suter, *Damned If You Do or Damned If You Don't: The Medical Malpractice Implications of Consumer-Generated Polygenic Risk Scores*, 38 HARV. J.L. & TECH 417, 427 & n.61 (2024).

120. Majumder et al., *supra* note 26, at 155.

121. Nathan Cortez, *The Mobile Health Revolution?*, 47 U.C. DAVIS L. REV. 1173, 1179 (2014) ("Congress and over half a dozen federal agencies, including the FDA, the Federal Communications Commission ('FCC'), the Federal Trade Commission ('FTC'), the Department of Commerce, the Department of Defense, and various subagencies of the Department

current debates about how the U.S. Food and Drug Administration ("FDA") regulates DTC PRSs. Here, ongoing debates about regulating laboratory-developed tests ("LDTs") and the hands-off approach to regulating low-risk wellness products like health apps collide.

The first piece of this challenge involves contemporary debate about how the FDA regulates LDTs. At present, the regulation of LDTs is in flux.[122] Put briefly, the regulatory landscape surrounding PRS has historically been inconsistent, shared, and dependent on context.[123] The Medical Device Amendments of 1976[124] included genetic tests within the definition of diagnostic tests, putting them under the FDA's purview.[125] However, many genetic tests are developed and analyzed by a single laboratory and marketed as LDTs.[126] Though the FDA has previously asserted regulatory authority over LDTs, historically, it has exercised "enforcement discretion" over them.[127] As a general matter, the FDA has chosen not to enforce applicable regulatory requirements, and, as a result, most LDTs have not undergone FDA review or received clearance, authorization, or approval for marketing.[128]

Although the FDA already regulates DTC genetic tests and arguably has the authority to oversee a broader swath of LDTs more actively if it so chooses, many existing DTC PRSs have evaded regulatory scrutiny.[129] At the same time, the appification of genetic risk raises additional questions. It is less clear the extent to which medical device regulations and other legal requirements extend to DTC websites or apps that do not actually handle specimens but rather calculate PRSs

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of Health and Human Services ('HHS'), have addressed mobile health."). Others have observed that health apps blur the division between the FDA and the FTC and that their functions are both overlapping and complementary. Sarah Duranske, *This Article Makes You Smarter! (Or, Regulating Health and Wellness Claims)*, 43 AM. J.L. & MED. 7, 22 (2017).

122. Jin K. Park & I. Glenn Cohen, *The Regulation of Polygenic Risk Scores*, 38 HARV. J.L. & TECH 377 (2024).

123. Takahiro Soda, Amanda R. Merner, Brent J. Small, Laura N. Torgerson, Katrina Muñoz, Jehannine Austin et al., *Child and Adolescent Psychiatrists' Use, Attitudes, and Understanding of Genetic Testing and Pharmacogenetics in Clinical Practice*, 325 PSYCHIATRY RSCH., at 2.

124. Medical Device Amendments of 1976, Pub. L. No. 94-295, 90 Stat. 539 (1976).

125. Soda et al., *supra* note 123, at 2.

126. *Id.*

127. Sherkow et al., *supra* note 38, at 691 ("[M]any DTC PGSs evade regulatory scrutiny as general wellness products or unregulated software over which the FDA declines to exercise enforcement.").

128. *Id.*

129. *See* Christi J. Guerrini, Jennifer K. Wagner, Sarah C. Nelson, Gail H. Javitt & Amy L. McGuire, *Who's on Third? Regulation of Third-Party Genetic Interpretation Services*, 22 GENETICS MED. 4, 7 (2020); Anna Clark, *Scores of Critical Lab Tests Fall Into a Regulatory Void. The FDA Is Trying to Close It,* PROPUBLICA (June 22, 2023), https://www.propublica.org/article/fda-moves-to-regulate-lab-developed-tests [https://perma.cc/J8KP-A9LD].

from existing consumer data.[130] The FDA takes a risk-based approach for apps that would qualify as medical devices.[131] However, the FDA also exercises "enforcement discretion" over a subset of low-risk wellness products. This means the FDA may still choose not to actively regulate many apps providing DTC PRSs. Further, the 21st Century Cures Act[132] places yet another subset of these products outside of the agency's regulation and oversight altogether. Section 3060(a) of the 21st Century Cures Act amended § 520 of the Food, Drug, and Cosmetic Act ("FDCA") to remove certain software functions from the FDCA definition of a device, including those that "maintain[] or encourag[e] a healthy lifestyle."[133] This is particularly relevant for apps, like those described in Section IV.A, that disclaim any medical or diagnostic functionalities.

Health apps — which can include apps that provide DTC genetic testing — increasingly blur the lines between what counts as a medical device and what counts as a low-risk wellness product or a software function that simply helps users achieve and maintain a healthy lifestyle.[134] The ultimate categorization often hinges on intended use, statutorily defined as the "objective intent of the persons legally responsible for the labeling of an article."[135] Though the FDA can consider any relevant source of information, it often comes down to how a company chooses to market its product.[136] This discretion means that many innovators in this space see it as up to them as to whether they are required to seek any kind of FDA approval. In 2019, 23andMe introduced a PRS for type two diabetes without involving the FDA, arguing that it fell within an exemption for low-risk "general wellness"

130. Clinical Laboratory Improvement Advisory Committee Summary Report 13, U.S. DEP'T HEALTH & HUM. SERVS. (2019) (includes concerns about CLIA not applying to places purely doing bioinformatics); *see also* Guerrini et al., *supra* note 129, at 4 ("But these same agencies have not yet exercised regulatory authority with respect to entities whose services consist solely of interpreting, reinterpreting, or facilitating self-interpretation of individuals' raw genetic data.").

131. *See* 21 U.S.C. § 360(c) (defining Class I as devices with the lowest risk and subject to the least regulatory control; Class II as those with an intermediate level of risk; Class III as devices with the highest risk which generally require premarket approval).

132. 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016).

133. *Id.* at 1130–31. The other four are the following: (1) provide administrative support for a health care facility; (2) serve as electronic patient records; (3) transfer, store, or display data for converting data formats; and (4) provide limited clinical decision support. *Id.*

134. Fowler, *supra* note 15, at 95–97.

135. 21 C.F.R. § 801.4 (2020).

136. David A. Simon, Carmel Shachar & I. Glenn Cohen, *Skating the Line Between General Wellness Products and Regulated Devices: Strategies and Implications*, 9 J.L. BIOSCIENCES 2, 7 (2022) (observing that "regulatory flexibility has also allowed producers to modify and improve upon a strategy they have perfected over many decades: offering device-like products as non-devices using a variety of tactics, including disclaimatory language.").

products.[137] Church and Sadeghi, CEOs of companies like Nebula and Nucleus, also do not believe the FDA has authority over their consumer products.[138] If left up to the market, it seems unlikely that most developers — especially of smaller apps — will seek FDA approval.

Several scholars have argued that, though federal jurisdiction over third-party genetic interpretation services is limited, it may "be appropriate at this time, subject to agency clarification and appropriate exercise of oversight."[139] Others, however, urge that more is needed — especially in the context of DTC PRS, given the unique harms that can arise. As Jacob S. Sherkow, Jin K. Park, and Christine Y. Lu have observed, "[t]he lack of oversight poses harms to consumers because they are at risk of misinterpreting or misusing PGSs in ways that are different — and potentially more harmful — from traditional DTC tests."[140] But to do so, the FDA would have to overcome years of relative inaction, confusing carveouts, and anticipated legal opposition to new rulemaking.

Thus, consumers may be left with the same confusing language hidden in ToS that complicates medical uncertainty when trying to understand what oversight the product they have chosen has undergone and what, if any, protections they should expect. Appification may, therefore, add to the uncertainty.

V. CONCLUSION

If the future involves everyone having their entire genome on their phone, appification is inevitable. The appification of genetic risk, as both a reality and a metaphor, is about the abstraction inherent in the literal development of web and smartphone apps and the effect of disaggregating complex genetic test results from more complicated but more complete sources of information. When PRS leaves the relative safeguards of academia and medicine, it improves access to testing but may also strip it of its full meaning. When delivered via an app, the results may seem simplified and easy, but they may also obscure important sources of knowledge and understanding.[141] At baseline, PRS are already challenging to comprehend even with complete information, and we are only beginning to understand how to communicate

137. Antonio Regalado, *23andMe Thinks Polygenic Risk Scores Are Ready for the Masses, but Experts Aren't So Sure*, MIT TECH. REV. (Mar. 8, 2019, 7:00 AM), https://www.technologyreview.com/2019/03/08/136730/23andme-thinks-polygenic-risk-scores-are-ready-for-the-masses-but-experts-arent-so-sure/ [https://perma.cc/UV99-46M8].

138. Smart, *supra* note 4.

139. Guerrini et al., *supra* note 129, at 5.

140. Sherkow et al., supra note 38, at 692.

141. O'Brien & Van Deventer, *supra* note 14, at 419–20.

their complexities.[142] Appification may further complicate efforts to bring these types of genetic tests to consumers in a meaningful way.

This Essay does not argue against the value of PRS, even in its DTC forms. Instead, it cautions that though apps may be immensely beneficial, we must also consider what we potentially lose in translating complex concepts into simplified outputs often devoid of nuance, context, and support. Apps are not monoliths, and future research should consider which and how DTC PRS products excel and which ones fall short. This inquiry can have real-world value. First, efforts to unpack potential sources of obfuscation may ultimately help ameliorate potential consumer confusion by encouraging app developers to design products that convey important details and provide relevant context. Second, it may help stakeholders remain vigilant to other potential sources of abstraction and anticipate possible challenges. Finally, it may inform how to address medical and legal uncertainty by underscoring how DTC PRS raise similar and different policy considerations from those we have already encountered in the "appification of everything."[143]

142. Docherty et al., *supra* note 39, at 434; Lencz et al., *supra* note 37, at 840.
143. Kosner, *supra* note 1.