Scientific challenges for precision public health

Frank Kee, David Taylor-Robinson

ABSTRACT

The notion of ‘precision’ public health has been the subject of much debate, with recent articles coming to its defence following the publication of several papers questioning its value. Critics of precision public health raise the following problems and questionable assumptions: the inherent limits of prediction for individuals; the limits of approaches to prevention that rely on individual agency, in particular the potential for these approaches to widen inequalities; the undue emphasis on the supposed new information contained in individuals’ molecules and their ‘big data’ at the expense of their own preferences for a particular intervention strategy and the diversion of resources and attention from the social determinants of health.

In order to refocus some of these criticisms of precision public health as scientific questions, this article outlines some of the challenges when defining risk for individuals; the limitations of current theory and study design for precision public health; and the potential for unintended harms.

‘Precision’ public health (PPH) is conceptualised as a means of improving population health through the use of new technologies, particularly genomics and digital, which would guide public health practice by generating more individually tailored interventions and policies. The concept of PPH has been the subject of much recent debate, with the Editor of the Lancet recently coming to its defence following the publication of several papers questioning its value. In this essay, we frame some key challenges for PPH as unanswered scientific questions, in an attempt to move the discussion forward.

While numerous articles use the term PPH, there is a lack of a universally agreed definition, with Khoury recently suggesting PPH as a cover-all term for ‘the next generation public health’.

Given the vagueness attending this definition, it is important that we declare, at the outset, the focus of this article. We do not focus on PPH applications, which we believe to be scientifically uncontentious, for example, using information on the genetic profiles of microbes and exposed individuals in communicable disease outbreak detection and management. Nor do we address the curation and analysis of ever more detailed data on populations at finer geographical scales for the purpose of targeting public health interventions on communities, which is, in our view, little more than conventional public health, but with richer data.

Instead, we take our cue from the PPH emphasis in several policy documents in the UK, notably in the recent Green paper on prevention, which spotlights targeted or personalised interventions for lifestyle and behavioural change following individual genetic or digital profiling, for example, using smartphone apps. This version of PPH is our main focus. While the Lancet editor warns against ‘uncritical techno-optimism’ with regard to PPH, he also decries unsustainable ‘pilotitis’, an excess of pilot studies leading to delayed or foregone PPH benefits, and stresses the need for workforce training if the potential of PPH is to be realised. This position leaves us rather confused and raises still further questions. Pilot studies are usually the necessary antecedents of robust scientific studies of mechanisms, efficacy or effectiveness, and it is precisely in this realm that the evidence for PPH remains questionable or at least undercooked. In spite of this, PPH is front and centre in the UK Health Secretary’s forward strategy for personalised ‘predictive prevention’.

What are the main scientific questions that should be answered before launching into workforce training and PPH implementation? Briefly, among the problems raised by PPH that we highlighted in a previous article are: (1) the inherent limits to risk prediction at the individual level, when the uncertainty due to random processes may be conflated with the uncertainty due to limited data or knowledge; (2) the constraints on prevention interventions that rely on individual agency, where such a focus might widen inequalities; (3) the undue emphasis on the supposed new insights gained from an individual’s genetics and their ‘big data’ instead of their own preferences for a particular intervention strategy (4) the diversion of scarce resources and attention away from the social determinants of health.

Building on these issues, recent exchanges have called for a refocusing of the criticisms of PPH as scientific questions. In this essay, we, therefore, outline key scientific challenges relating to defining risk for individuals; the limitations of current theory and study design for PPH and understanding the potential for unintended harms.

DEFINING RISK FOR INDIVIDUALS

We see significant problems in defining risks for individuals (Rose’s ‘causes of cases’) in areas where the epidemiology is just not up to the job. For example, large-scale ‘precision nutrition’ has been proposed as a PPH approach to delivering individualised dietary behavioural change in efforts to address obesity and the health impacts of poor diet. However, data to inform precision nutrition approaches are derived from population-level studies beset with problems of such magnitude that commentators have raised doubts about the possibility of ascertaining the impact of single dietary components on health outcomes. For example, if
we usually have crushed walnuts with our low glycaemic index breakfast cereal and are subsequently observed to have a lower risk of heart disease, to what do we attribute our good fortune? Ioannidis is likely correct in contending that the implausible estimates of benefits or risks associated with specific dietary choices that we typically derive from population-level studies are due to the biases, residual confounding and selective reporting typical of these studies. While innovative approaches have been developed to address the key issue of collinearity among nutrients in our diet, these modern counterfactual based methods merely enable a more principled assessment of causal effects in populations, based on a clearer understanding of the assumptions coded in the underlying directed acyclic graph that the analyst proposes. Their relevance to us as individuals and our own risk, which may change as our dietary fastidiousness or budget changes over the life course, seems unclear.

LIMITATIONS OF CURRENT THEORY

Even if we were able to pinpoint an intervention target for an individual, how would we design and test the optimum intervention? What are the scientific questions and challenges that would need to be addressed in terms of theory and study design? The UK National Institute for Health and Care Excellence (NICE) and Public Health England both endorse the view that intervention design that is informed by sound theory has a better chance of success. Digital technologies that enable frequent, time intensive but tailored behavioural interventions hold some promise, but also pose many challenges to our current health behaviour theories and models.16

First, we lack a clear understanding and theory of factors influencing engagement with digital behavioural change interventions, which is a precondition for effectiveness for many of the interventions promoted through smartphones. Yardley et al rightly highlight the importance of considering how technological and behavioural elements combine to influence engagement.17 Extending our nutritional PPH example above, many time-varying factors (rushing to work, picking up the kids), not to mention personality traits (neuroticism or conscientiousness), may affect engagement with digital interventions to promote a healthy diet and health behaviours themselves. In addition, the behaviours may be subject to compensatory spillover effects affecting other behaviours at the level of the individual.18 Disentangling the influence of a single dietary component from these other influences on health outcomes in an individual is challenging, if not impossible.

Second, we will surely need to develop more complex mechanisms of behavioural change to explain within-person changes over time. By contrast, our current health behaviour theories have traditionally been formulated to explain between-person differences. Inherently, the processes affecting behavioural choices and actions within individuals over time are dynamic, and some have argued that lessons learnt from control systems engineering18 may help us accommodate feedback between underlying psychological constructs and so ‘close the loop’. Relatively scant attention has been given to developing a formal system of behavioural change theories, though the recent paper by West et al is an overdue and very welcome contribution in this regard.19

While commendable, the paper did not give much consideration to timescale and current theories appear to be a poor fit with the more rapid intraindividual dynamics of mobile technology interventions. Even if behavioural change theories can address timescale issues, current theory may be inadequate if, as some believe, behavioural change is better understood through the lens of chaos theory and complex adaptive systems, the key principles of which include unique sensitivity to initial conditions, leading to highly variable outcomes that are difficult to predict, occurring within adaptive systems where multiple components interact to produce results greater than the sum of their parts.

Ecological momentary assessment (EMA) has developed in response to the challenge of understanding behavioural change in individuals over time. EMA sets out to more intensively monitor behaviour and its antecedents over time by measuring moods and behaviours in real time, increasingly using ‘wearable’ technologies.21 The combination of EMA alongside smartphone behavioural change apps has contributed to the drive for digitally enabled personalised prevention and health promotion.22 But this is another area where, despite the policy hype, we believe that technological development may be outrunning the underpinning science.

Reporting standards for EMA studies have only recently been developed, and these should improve assessment of how measurement tools, sampling methods, sampling schedules, sample intensity, prompting strategies and compliance rates might affect study interpretation.23 The same authors developed a checklist and believe that when these key methodological considerations are reported accurately, we may begin to see improved reliability and validity of individual study findings.24 What this checklist does not offer is guidance on how best to analyse EMA data. A variety of statistical methods have been proposed to model and understand, or to predict, the behavioural dynamics in EMA settings, with different researchers opting for, variously, hidden multistate Markov models,24 time series modelling with Markov chains,25 dynamic regression and unified structural equation modelling.26 It would be too easy to dismiss such choices as matters of taste were it not for the fact that they usually materially affect the inferences that can be drawn.27

LIMITATIONS OF CURRENT STUDY DESIGN

Assuming we have appropriated a theory informed optimal design for our PPH intervention, do we routinely use the right study designs to test its effectiveness? The conventional parallel group randomised controlled trial is not up to the task. The leading alternative designs, namely n-of-1 studies and microrandomised trials (MRTs) of Just in Time Adaptive Interventions (‘JITAI’) offer promise but raise ancillary scientific questions with which many researchers and practitioners have yet to grapple.28 N-of-1 studies provide the statistical basis to distinguish interindividual and intraindividual variation, which is crucial for intervention personalisation, offering a scientific basis for tailoring interventions to individuals. While the key design aspect of an n-of-1 study is that an individual is followed for a period of time and their responses measured before and after an intervention, there is in fact currently little consensus on the most effective way to analyse behavioural and psychological n-of-1 studies. In a recent systematic review of n-of-1 studies assessing behavioural change, only 25% of the 39 studies included in the review used appropriate statistical approaches for n-of-1 data analysis.29 30 31 The authors highlighted the challenges inherent in defining a null hypothesis for such studies or quantifying clinically important differences for power calculations.

Designing good tests of PPH interventions is dependent on defining the minimum clinically important difference (MCID) but population-level MICDs are different from individual MICDs, both conceptually, and in the methods that must be leveraged for their estimation.32 This makes it challenging to define a ‘responder’ in the context of personalised interventions. For
example, we ourselves have shown how health professionals struggle to distinguish signal from noise when trying to identify ‘a responder’ to treatment in even simple scenarios. Some tend to overestimate the effects of a patients’ genotype on ‘responder’ status. But even if we properly define an individual-level MCID, the calculation of a final sample size (in this case how many epochs are necessary to observe and characterise the time trace of behaviour) will also depend on an individual’s engagement and willingness to be followed up and record data over prolonged periods. Less literate and less motivated subjects—more likely, perhaps, to be living in disadvantaged circumstances—are likely to have more missing data, and so the quality of predictions and estimates of intervention effectiveness may vary importantly across these groups.

Recently Murphy et al introduced the MRT design, which involves randomisation of interventions at various times and decision points at which an intervention may be effective, based on context or past behaviour. An example is the provision of a tailored activity suggestion to increase step count delivered via mobile phone technology. Microrandomisation of this JITAI for each participant on each day of the study permits an assessment of the causal effect on exercise of providing one intervention compared with an alternative, and whether this effect varies based on context or mood, which is being monitored (as per EMA) via the mobile phone. However, even Murphy et al have acknowledged that novel statistical methods are required to distinguish the effects of participant-determined features, dependent on personal agency, from those of routinely provided behavioural change intervention. This endogeneity problem is compounded when we acknowledge that awareness of being monitored could itself modify the experience and the behaviour—and how to fully address this in the analysis is not yet clear.

Assessing the cost-effectiveness of PPH interventions poses an additional challenge. When new interventions are introduced to the UK National Health Service (NHS), NICE expects a robust cost effectiveness analysis, and adoption decisions are usually based on favourable incremental cost effectiveness ratios (ICERs). Ioannidis et al have pointed out some conceptual difficulties in applying population-level ICERs to individuals because for notionally the same ICER, cost-effectiveness will differ for individuals who have different priorities for specific outcomes, or who have different attitudes toward risk or time discounting. Methods are being developed to cater for such considerations, though it is not clear to us how the NHS should use this information in commissioning PPH. Developing a meta-analytical summary of a series of n-of-1 cost-effectiveness studies would seem to defeat the purpose.

CONCLUSIONS
Before rushing headlong into implementation and workforce training for PPH, we need more insights into the problems and challenges outlined above. Until these issues are addressed, it will not be clear that the benefits of superficial intervention ‘tailoring’ for personalised prevention, common in today’s PPH interventions delivered through mobile technologies, outweigh the harms. Finally, in the current context of declining life expectancy and increasing inequalities in the UK, it is concerning that PPH approaches are being strongly promoted as solutions. We agree with the recent commentary by Olstad and McIntyre that PPH could benefit, conceptually and practically, from a refocus on the upstream social determinants of health. In the meantime, while evidence for sound policy and practice is still being sought, we consider Horton’s diagnosis of ‘pilotitis’ premature.

Acknowledgements The authors thank Davara Bennett for helpful editorial comments.

Contributors FK and DT-R originated the idea, FK wrote the first draft, DT-R developed a second draft, both authors agreed on the final draft.

Funding DT-R is funded by the MRC on a Clinician Scientist Fellowship (MR/P008577/1)

Competing interests None declared.
REFERENCES

1. Horton R. Offline: in defence of precision public health. Lancet 2018;392:1504.
2. Taylor-Dobinson D, Kee F. Precision public health—the Emperor’s new clothes. Int J Epidemiol 2019;48:1–6.
3. Chowkwanyun M, Bayer R, Galea S. “Precision” Public Health - Between Novelty and hype. N Engl J Med 2018;379:1398–400.
4. Khoury MJ, Lademarco ME, Riley WT. Precision public health for the era of precision medicine. Am J Prev Med 2016;50:398–401.
5. CDC. Says DST.precision public health: what is it? Available: https://blogs.cdc.gov/genomics/2018/05/15/precision-public-health-2/. [Accessed 10 Dec 2019].
6. Leguia M, Vila-Sanjuán A, Chain PSG, et al. Precision medicine and precision public health in the era of pathogen next-generation sequencing. J Infect Dis 2019;2:424.
7. Dauwe G, Deribe K. Precision public health: mapping child mortality in Africa. Lancet 2017;390:2126–8.
8. GOV.UK. Advancing our health: prevention in the 2020s – consultation document. Available: https://www.gov.uk/government/publications/advancing-our-health-prevention-in-the-2020s-advancing-our-health-prevention-in-the-2020s-consultation-document. [Accessed 16 Dec 2019].
9. GOV.UK. Prevention is better than cure: our vision to help you live well for longer. Available: https://www.gov.uk/government/publications/prevention-is-better-than-cure-our-vision-to-help-you-live-well-for-longer. [Accessed 14 Jun 2019].
10. Fried LP, Baccarelli AA. Fried and Baccarelli Comment. Am J Public Health 2019;109:1188.
11. Chatelan A, Bochud M, Frohlich KL. Precision nutrition: hype or hope for public health interventions to reduce obesity? Int J Epidemiol 2019;48:332–4.
12. Ioannidis JPA. The challenge of reforming nutritional epidemiologic research. JAMA 2018;320:969–70.
13. Schisterman EF, Perkins NJ, Mumford SL, et al. Collinearity and causal diagrams: a lesson on the importance of model specification. Epidemiology 2017;28:47–53.
14. NICE. Behaviour change: general approaches. Public Health Guidance. NICE, 2007. Available: https://www.nice.org.uk/guidance/ph6/resources/behaviour-change-general-approaches-pdf-5545751717
15. GOV.UK. Improving people’s health: applying behavioural and social sciences. Available: https://www.gov.uk/government/publications/improving-people-s-health-applying-behavioural-and-social-sciences. [Accessed 14 Jun 2019].
16. Riley WT, Rivera DE, Atienza AA, et al. Health behavior models in the age of mobile interventions: are our theories up to the task? Transl Behav Med 2011;1:53–71.
17. Yardley L, Spring BI, Ripper H, et al. Understanding and promoting effective engagement with digital behavior change interventions. Am J Prev Med 2016;51:833–42.
18. Galizzi MM, Whitham I. How to measure behavioral Spillovers: a methodological review and checklist. Front Psychol 2019;10.
19. West R, Godinho CA, Bohlen LC, et al. Development of a formal system for representing behaviour-change theories. Nat Hum Behav 2019;3:526–36.
20. Resinow K, Page SE, Chaos E. Embracing chaos and complexity: a quantum change for public health. Am J Public Health 2008;98:1382–9.
21. Burke LE, Shiffman S, Music E, et al. Ecological Momentary Assessment in behavioral research: addressing technological and human participant challenges. J Med Internet Res 2017;19:e77.
22. GOV.UK. Chief medical officer annual report 2018: better health within reach. Available: https://www.gov.uk/government/publications/chief-medical-officer-annual-report-2018-better-health-within-reach. [Accessed 3 Jul 2019].
23. Liao Y, Skelton K, Dunton G, et al. A systematic review of methods and procedures used in ecological Momentary assessments of diet and physical activity research in youth: an adapted Strobe checklist for reporting EMA studies (CREMAS). J Med Internet Res 2016;18:e151.
24. Koslovsky MD, Swartz MD, Chan W, et al. Bayesian variable selection for multistate Markov models with interval-censored data in an ecological momentary assessment study of smoking cessation. Biometrics 2018;74:636–44.
25. Holmes EA, Bonsall MB, Hales SA, et al. Applications of time-series analysis to mood fluctuations in bipolar disorder to promote treatment innovation: a case series. Transl Psychiatry 2016;6:e270.
26. Ridenour TA, Wittenborn AK, Raff R, BR, et al. Illustrating idiothetic methods for translation research: moderation effects, natural clinical experiments, and complex treatment-by-subgroup interactions. Transl Behav Med 2016;6:125–34.
27. Silberzahn R, Uhlmann EL, Martin DP, et al. Many Analysts, one data set: making transparent how variations in analytic choices affect results. Adv Methods Pract Psychol Sci 2018;1:33–56.
28. Viera R, McDonald S, Araújo-Saeres V, et al. Dynamic modelling of N-of-1 data: powerful and flexible data analytics applied to personalised studies. Health Psychol Rev 2017;11:222–34.
29. Senn S. Statistical pitfalls of personalized medicine. Nature 2018;563:619–21.
30. Sedgwick P. What is an “n-of-1” trial? BMJ 2014;348:g2674.
31. McDonald S, Quinn E, Viera R, et al. The state of the art and future opportunities for using longitudinal N-of-1 methods in health behaviour research: a systematic literature overview. Health Psychol Rev 2017;11:307–23.
32. Davidson KW, Cheung YK. Envisioning a future for precision health psychology: innovative applied statistical approaches to n-of-1 studies. Health Psychol Rev 2017;11:292–4.
33. Zhou Z, Zhao J, Bisson LJ. Estimation of data adaptive minimal clinically important difference with a nonconventional optimization procedure. Stat Methods Med Res 2019;28:2015–24.
34. McMichael AJ, Boeri M, Rolison JJ, et al. The Influence of Genotype Information on Psychiatrists’ Treatment Recommendations: How Experienced Clinicians Know What to Ignore. Value Health 2017;20:126–31.
35. Nahum-Shani I, Smith SN, Spring BJ, et al. Just-in-Time adaptive interventions (JTias) in mobile health: key components and design principles for ongoing health behaviour support. Ann Behav Med 2018;52:446–62.
36. Walsh JC, Corbett T, Hogan M, et al. An mHealth intervention using a smartphone APP to increase walking behavior in young adults: a pilot study. JMIR Mhealth Uhealth 2016;4:e109.
37. Cheung YK, Hseuh P-Y, Qian M, et al. Are Nomothetic or Ideographic approaches superior in predicting daily exercise behaviors? Methods Inf Med 2017;56:452–60.
38. Ioannidis JPA, Garber AM, Analysis IC-E. Individualized cost-effectiveness analysis. PLoS Med 2011;8:e1001058.
39. van Gestel A, Grutters J, Schouten J, et al. The role of the expected value of individualized care in cost-effectiveness analyses and decision making. Value Health 2012;15:13–21.
40. Asaria M, Griffin S, Cookson R. Distributional cost-effectiveness analysis: a tutorial. Med Decis Making 2016;36:8–19.
41. Zucker DR, Ruthazer R, Schmid CH. Individual (n-of-1) trials can be combined to give population comparative treatment effect estimates: methodologic considerations. J Clin Epidemiol 2010;63:1312–33.
42. Bonell C, Jamal F, Melendez-Torres GJ, et al. ‘Dark logic’: theorising the harmful consequences of public health interventions. J Epidemiol Community Health 2015;69:95–8.
43. Mandl KD, Mannai AK. Potential excessive testing at scale: biomarkers, genomics, and machine learning. JAMA 2019;321:739–40.
44. Kaplan M. Happy with a 20% chance of sadness. Nature 2018;563:20–2.
45. Learning one’s genetic risk changes physiology independent of actual genetic risk | Nature Human Behaviour. Available: https://www.nature.com/articles/s41562-018-0483-4. [Accessed 14 Jun-119].
46. Crum AJ, Corbin WR, Brownell KD, et al. Mind over millskahes: mindsets, not just nutrients, determine ghelin response. Health Psychol 2011;30:424–9. discussion 430–431.
47. Emanuel EJ, Wachter RM. Artificial intelligence in health care: will the value match the hype? JAMA 2019;321:2281–2.
48. Rajkomar A, Hardt M, Hosnow MD, et al. Ensuring fairness in machine learning to advance health equity. Ann Intern Med 2018;169:866.
49. Allem J-P, Ferrara E. Could social bots pose a threat to public health? Am J Public Health 2018;108:1005–6.
50. Steel N, Ford JA, Newton JN, et al. Changes in health in the countries of the UK and 150 English local authority areas 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet 2018;392:1647–61.
51. P1 Predictive prevention and the drive for precision public health - Public health matters. Available: https://publichealthmatters.blogs.gov.uk/2018/11/20/predictive-prevention-and-the-drive-for-precision-public-health/. [Accessed 25 Feb 2019].
52. Olstad DL, McIntyre L. Reconceptualising precision public health. BMJ Open 2019;9:o30279.

Kee F, Taylor-Robinson D. J Epidemiol Community Health 2020;0:1–4. doi:10.1136/jech-2019-213311