Editorials

Widening Disease Definitions: What Can Physicians Do?

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Disease definitions are often broadened over time to include milder and earlier cases.[1] A strong driver for such definitional changes is the belief that they will benefit patients by preventing more severe disease or future complications. Family physicians must ensure that these claims are rigorously evaluated to show clinically meaningful reductions in morbidity and mortality and that the potential harms of widening disease definitions are not ignored. *Table 1* includes examples of widened disease definitions.[2-6]

Why Are Widening Disease Definitions a Problem?

Widening disease definitions cause harm by exposing more patients to the adverse effects of treatments, triggering investigation and prescribing cascades, increasing anxiety, and placing a financial burden on patients and the wider society.

Advocates for widening definitions, including authors of guidelines, often argue that the diagnosis and treatment of earlier and milder disease will result in better health outcomes for patients. They assume that evidence of benefits in more severe cases applies (or is even greater) in patients with milder or earlier disease, when in fact benefits are likely to

TABLE 1

Examples of Widened Disease Definitions

Disease	Cause of change	Change made	Estimated change in disease prevalence	Potential benefits	Unintended consequences/harms
Hypertension[2]	Change from professional society recommendation or guideline	Threshold lowered to blood pressure of 130/80 mm Hg	32% increase in U.S. adults (37% to 49%)	Improvement in diet and physical activity Earlier initiation of blood pressure–lowering treatment	Increased anxiety and depression Preexisting condition for insurance coverage Hypotension, syncope, renal failure from drug treatment
Polycystic ovary syndrome[3]	Change from professional society recommendation or guideline	Diagnosis if two of the following are present: reduced ovulation, hyperandrogenism, ultrasound evidence of disease (previous definition was based on only reduced ovulation and hyperandrogenism)	100% increase in patients 27 to 34 years of age (9% to 18%)	Relief of symptoms Improvement in diet and physical activity	Altered self-perception Worry about future health and fertility
Breast cancer[4]	Introduction of more sensitive testing	Increasing use of three-dimensional mammography (tomosynthesis)	38% relative increase in the cancer detection rate of women screened (0.64% to 0.88%)	Earlier detection of breast cancer	Increase in women treated for breast cancers that would not have caused clinical symptoms (overdiagnosis)
Autism[5,6]	Change in implicit threshold of disease	Difference in symptoms between children with autism and a control group declined from 1990 to 2020	276% relative increase in eight-year-old children in the United States from 2000 to 2016 (0.67% to 1.85%)	Increased access to educational and other supports	Effect of lifelong label of disease, including stigma

Information from references 2-6.

be smaller or nonexistent. Examples include claims that increased detection of nonalcoholic fatty liver disease will reduce future incidence of cirrhosis or that diagnosing a patient with hypertension will lead to improvements in diet and physical activity that prevent cardiovascular events. At the same time, potential physical and psychological harms of diagnosis and treatment are often underestimated or not evaluated.[1]

Much of the burden of managing these millions of new cases of disease falls to primary care clinicians. There is a substantial opportunity cost, diverting attention and resources away from patients who would benefit most. What appear to be small changes to disease definitions cause large changes in disease prevalence and create a demand for unproven, ineffective preemptive services. This contributes to the increasing number of tasks a family physician is expected to perform, such that a physician would need to work more than 13 hours a day to provide care for 1,500 patients.[7] As Margaret McCartney states in *The Patient Paradox*, "Too much testing of well people and not enough care for the sick worsens health inequalities and drains professionalism, harming both those who need treatment and those who don't.[8]

Recent increases in the prevalence of chronic diseases are well described, although the contribution of widened disease definitions is rarely acknowledged. The incidence of diabetes mellitus, usually attributed to population lifestyle factors, increased substantially for several years after the change in the fasting plasma glucose threshold was lowered from 140 to 126 mg per dL (7.77 to 6.99 mmol per L) in 1997. This trend has been used to forecast ever-increasing numbers, even though incidence has stabilized or even reduced in most populations since the mid 2000s.[9]

Widened disease definitions cause the false impression of an overall improvement in health for people with the condition, even if there are no actual improvements in care delivery. Because milder cases are less likely to result in death and serious complications, the number of significant health outcomes per cases diagnosed is reduced. For example, screening for prostate cancer will cause an apparent increase in prostate cancer survival rates, even if screening has no effect, as patients with clinically insignificant cancers are added to both those who survive cancer (numerator) and the number of cases of prostate cancer (denominator). The same effect is seen with foot amputations in diabetes or obstetric complications in gestational diabetes. This apparent success is then used to support the usefulness of detecting earlier and milder disease, in an ever-increasing cycle.

Why Does This Problem Arise?

The drive for widened disease definitions generally comes from specialist groups. They are often accompanied by warnings about "epidemics of disease," "silent killers," and the dangers of undiagnosed disease. Specialist groups see more patients with advanced disease and late complications. It is natural that they will advocate to try to reduce this burden. Some changes are driven by good intentions. But financial and other conflicts of interest are often at play, with key opinion leaders and patient advocacy groups having ties to industry or profiting in other ways by increasing the profile of their particular disease of interest.[1,10]

We have also fostered a widespread belief in the community that early detection saves lives. Widespread detection and treatment of elevated blood pressure and cervical cancer screening are two examples for which early detection has successfully improved health outcomes. But explaining to patients that more testing and early detection of other conditions may have no benefit and may even be harmful is complex, especially in the context of several decades of public messaging saying the opposite.

What Family Physicians Can Do About It

Recognizing the problem is the first step in tackling it. In particular, family physicians should not blindly accept new definitions and testing guidelines without an adequate understanding of the harms and benefits of the changes and the implications for our patients and wider practice.[11]

Some of the questions family medicine physicians need to ask are[12]:

- How many people will this affect?
- What is the risk that patients diagnosed using this new testing guideline or disease definition will develop more severe disease or complications?
- What is the evidence that early treatment will prevent serious disease or complications?
- What are the potential harms of diagnosis and treatment? ▶

Conclusion

Now is the time to reassess the importance of what we are doing in our practices. We need to push back against misdirected low-value care, incentives, and changes to practice. We are not here to passively enact specialist recommendations. Instead, we need to more assertively act as advocates for our patients and our communities.

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References

1. Moynihan RN, Cooke GPE, Doust JA, et al. Expanding disease definitions in guidelines and expert panel ties to industry: a cross-sectional study of common conditions in the United States. *PLoS Med*. 2013;10(8):e1001500.
2. Bell KJL, Doust J, Glasziou P. Incremental benefits and harms of the 2017 American College of Cardiology/American Heart Association high blood pressure guideline. *JAMA Intern Med*. 2018;178(6):755-757.
3. Copp T, Jansen J, Doust J, et al. Are expanding disease definitions unnecessarily labelling women with polycystic ovary syndrome? [published correction appears in *BMJ*. 2017;359:j5380]. *BMJ*. 2017;358:j3694.
4. Marinovich ML, Hunter KE, Macaskill P, et al. Breast cancer screening using tomosynthesis or mammography: a meta-analysis of cancer detection and recall. *J Natl Cancer Inst*. 2018;110(9):942-949.
5. Rødgaard EM, Jensen K, Vergnes JN, et al. Temporal changes in effect sizes of studies comparing individuals with and without autism: a meta-analysis. *JAMA Psychiatry*. 2019;76(11):1124-1132.
6. Maenner MJ, Shaw KA, Baio J, et al. Prevalence of autism spectrum disorder among children aged 8 years - Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2016 [published correction appears in *MMWR Morb Mortal Wkly Rep*. 2020;69(16):503]. *MMWR Surveill Summ*. 2020;69(4):1-12.
7. Altschuler J, Margolius D, Bodenheimer T, et al. Estimating a reasonable patient panel size for primary care physicians with team-based task delegation. *Ann Fam Med*. 2012;10(5):396-400. Accessed August 23, 2020. https://www.annfammed.org/content/10/5/396.long
8. McCartney M. *The Patient Paradox: Why Sexed-Up Medicine Is Bad for Your Health*. Pinter & Martin; 2012.
9. Magliano DJ, Islam RM, Barr ELM, et al. Trends in incidence of total or type 2 diabetes: systematic review. *BMJ*. 2019;366:l5003.
10. Fabbri A, Parker L, Colombo C, et al. Industry funding of patient and health consumer organisations: systematic review with meta-analysis. *BMJ*. 2020;368:l6925.
11. Moynihan R, Brodersen J, Heath I, et al. Reforming disease definitions: a new primary care led, people-centred approach. *BMJ Evid Based Med*. 2019;24(5):170-173.
12. Doust J, Vandvik PO, Qaseem A, et al.; Guidelines International Network (G-I-N) Preventing Overdiagnosis working group. Guidance for modifying the definition of diseases: a checklist. *JAMA Intern Med*. 2017;177(7):1020-1025. ■