Population-based mortality from breast cancer is determined by incidence and case fatality (survival). Screening increases incidence at early follow-up due to lead time and also reduces case fatality due to early detection. A sufficiently long follow-up period is needed to evaluate the true effect of screening on mortality from breast cancer because it takes decades to accumulate all screen-prevented breast cancer deaths. On the other hand, treatment such as adjuvant therapy contributes only to the case fatality rate. Hence, the effect of adjuvant treatment can be calculated after a much shorter follow-up time than the time required to evaluate the effect of screening. Relying on a short follow-up time may particularly influence the analysis of full-field digital mammography. The study period for digital mammography was only between 2000 to 2012, and use only reached 50% in 2009 (Figure 1B in the article).

The authors evaluated screening and treatment by molecular subtype. However, using molecular subtypes is deceptive as this information will only be known after the breast cancer has been diagnosed and will influence the choice of treatment. How can screening affect molecular types?

The authors should quantify the association of screening with the rate of advanced breast cancers after the introduction of screening because the incidence of advanced breast cancer would not be affected by treatment. The authors could also evaluate tumor-size–specific case fatality rates and that way separate the effect of treatment from the effect of screening. This approach would require reliable information about the detection mode (exposed vs not exposed to screening).

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

1. Plevritis SK, Munoz D, Kurian AW, et al. Association of screening and treatment with breast cancer mortality by molecular subtype in US women, 2000-2012. *JAMA*. 2018;319(2):154-164.

In Reply Dr Chen's main concern seems to be that our study does not have sufficient follow-up time. We used the longest follow-up times available from clinical trials and observational registries to estimate the relative contributions of screening and treatment on the reduction in US breast cancer mortality up to 2012. Chen was specifically concerned that the effect of the transition to digital mammography was not fully realized by 2012. To model the relative contributions of digital mammography on breast cancer mortality for several decades would require making assumptions about changes in clinical practice well beyond 2020. Screening with tomosynthesis and treatment with immunotherapy are a few examples of promising advances on the horizon in breast oncology that could affect the relative contributions of screening and treatment on breast cancer mortality over the next few decades. However, our analysis focused only on actual practice patterns.

Chen makes inaccurate statements about our study. First, he states that "the effect of adjuvant treatment can be calculated after a much shorter follow-up time than the time required to evaluate the effect of screening." That has not been true for hormonal therapies such as tamoxifen for which effects require follow-up times comparable with those in screening trials.

Second, Chen describes our study as "deceptive" because it relies on molecular subtype. He asks, "How can screening affect molecular types?" Clearly, screening cannot affect molecular subtype, but molecular subtype can be used to evaluate the association between screening and breast cancer mortality. For example, it is well documented that method of detection is differentially prognostic in estrogen receptor (ER)+ vs ER– tumors. Moreover ER– tumors are more likely interval cancers. Hence, knowing the molecular subtype of screen-detected and interval-detected cancers is critical when evaluating screening benefits.

Third, Chen proposes that population-level analyses of the effect of screening quantify the rate of advanced-stage cancers and calculate the effects of screening and treatment based on tumor-size-specific case fatality rates (survival). However, numerous studies have shown that relying on stage-shift and survival to assess the benefits of screening produces incorrect conclusions because of lead-time and length biases.

Fourth, Chen implies that we did not have reliable information on the mode of detection. This is not true. We used data from the Breast Cancer Surveillance Consortium on the mode of detection for over 2 million women undergoing screening.

We stand behind our results, the validity of our approach, and the unique value of comparative modeling analyses for public health policy and practice.

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Reducing Calories to Lose Weight

To the Editor In a Viewpoint,[1] Dr Guth said that the challenge of weight loss is to "convince patients to consume fewer calories" and benchmarked weight loss success against the 3500 kcal per pound rule. This view suggests that small decreases in diet calories will progressively result in substantial

weight losses. However, the real relationship between diet calories and weight loss is more complicated.

Although we agree with Guth's statement that diet change "requires ongoing vigilance," sustained dieting efforts do not result in a constant calorie reduction, much less "slow steady weight loss." Rather than achieving a constant reduction in diet calories after the start of weight loss intervention, objective measurements show that calorie intake exponentially increases over time,[2] resulting in a weight loss plateau within 1 year when both intake and expenditure are reduced by approximately 10 kcal per day for every pound of lost weight.[3] Patients report eating the same number of calories after the plateau as they did at the beginning of the intervention during active weight loss,[2] perhaps because they continue to exert a sustained effort in the face of their appetite, which is estimated to increase by approximately 45 kcal per day per pound of lost weight.[4]

The physiological adaptations to weight loss that decrease calorie expenditure[3] and increase appetite[4] require a new rule of thumb relating diet calories to body weight: the 55 kcal per day per pound rule.[5] For example, a patient who initially cuts 500 kcal per day from their diet and sustains a constant effort to adhere to the intervention would be expected to lose only approximately 9 lbs in total (500 kcal/d divided by 55 kcal/d/lb) with no further weight losses after the plateau. This is in contrast to the 3500 kcal rule that fails to account for the known physiological adaptations and therefore predicts a constant reduction of diet calories resulting in steady weight loss without a plateau: approximately 26 lbs after 6 months, 52 lbs after 1 year, and so on. Thus, the 3500 kcal per pound rule overpromises weight loss whereas the 55 kcal per day per pound rule reimagines a dynamic relationship between diet calories and weight loss and presents a more realistic view of the challenges experienced by patients with obesity.

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1. Guth E. Counting calories as an approach to achieve weight control. *JAMA*. 2018;319(3):225-226.

2. Freedhoff Y, Hall KD. Weight loss diet studies: we need help not hype. *Lancet*. 2016;388(10047):849-851.

3. Hall KD, Sacks G, Chandramohan D, et al. Quantification of the effect of energy imbalance on bodyweight. *Lancet*. 2011;378(9793):826-837.

4. Polidori D, Sanghvi A, Seeley RJ, Hall KD. How strongly does appetite counter weight loss? quantification of the feedback control of human energy intake. *Obesity (Silver Spring)*. 2016;24(11):2289-2295.

5. Hall KD, Sanghvi A, Göbel B. Proportional feedback control of energy intake during obesity pharmacotherapy. *Obesity (Silver Spring)*. 2017;25(12):2088-2091.

In Reply Dr Hall and colleagues take issue with the 3500-kcal restriction to lose 1 lb referenced in the Viewpoint. A mathematical model based on laboratory measurements for predicting individual and population weight loss was previously published,[1] in which the example recommends that an individual decrease his or her daily intake from 3000 kcal/d to 1800 kcal/d to lose 44 lbs over 6 months. This clearly would be a laudable achievement. I do not wish to argue with their calculation, but do suggest that asking patients to decrease their daily intake by almost one-third is not a realistic goal.

In clinical practice, patients need basic tools: a simple way to assess their actual intake, an understanding of the effect of their food choices, and motivation to make changes in their diet and other health behaviors. The caloric numbers and anticipated weight loss provide a frame of reference for patients to help them understand how they can lose weight. Weight loss is an ongoing process requiring periodic reassessment. In this context, mathematical models are less useful. Rather, a patient's actual weight loss influences subsequent dietary counseling. A recent study[2] demonstrated an approximately 10 lb weight loss in a year's time that was achieved by having patients reduce their caloric intake by approximately 500 kcal per day. These observations showed that a 500 kcal per day reduction was achievable and could be sustained in the long term. Although participants lost far less than the ideal 1 pound per week, all weight loss is to be celebrated.

In contrast to the somewhat artificial setting in which metabolic studies are performed, weight loss counseling in clinical practice involves human beings going about their daily lives, making an effort to change, who are neither following a rigid experimental protocol nor getting the extensive support usually available in clinical trials. Actual weight loss and weight maintenance remain anchored to patient behavior. The role of the physician is to support, encourage, and assist the patient in this effort as best suited to that individual, a process quite different from mathematical modeling.

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Disclaimer: Dr Guth is the spouse of Edward Livingston, MD, *JAMA* Deputy Editor, who was not involved in the decision to accept this letter for publication.

1. Hall KD, Sacks G, Chandramohan D, et al. Quantification of the effect of energy imbalance on bodyweight. *Lancet*. 2011;378(9793):826-837.

2. Gardner CD, Trepanowski JF, Del Gobbo LC, et al. Effect of low-fat vs low-carbohydrate diet on 12-month weight loss in overweight adults and the association with genotype pattern or insulin secretion: the DIETFITS randomized clinical trial. *JAMA*. 2018;319(7):667-679.

Patient Education on Patellofemoral Pain

To the Editor Patellofemoral pain affects 1 in 14 individuals.[1] We have concerns regarding the JAMA Patient Page on this common problem.[2]

The page was based on an opinion piece from 2007 and lacked consideration or acknowledgment of key research within the last 10 years, including multiple randomized clinical trials, culminating in 5 Cochrane reviews.[3] This research has contributed to understanding and management of patellofemoral pain. Two key questions patients ask are "Why did I develop knee pain?" and "What is my long-term prognosis?" The Patient Page provided factually incorrect answers, suggesting that there is no long-term effect of patellofemoral pain despite current evidence demonstrating that up to 1 in 2 patients continues to experience pain that affects sports participation, quality of life, and general health.[4] Furthermore, the emphasis on the role of shoes in the development and treatment of patellofemoral pain, along with rest and stretching as key interventions, is in contradiction to current evidence and understanding of pain. Up-to-date evidence emphasizes exercise therapy targeting both knee and hip muscle strength,[3,5] along with foot orthoses to relieve pain in the short term.[3] This key information is poorly articulated (exercise) or absent (foot orthoses).

Empowering patients by accurately informing them about their condition and treatment options has the potential to help optimize care. However, patient education materials should be based on current evidence and understanding, developed together with patient needs and preferences.

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1. Smith BE, Selfe J, Thacker D, et al. Incidence and prevalence of patellofemoral pain: a systematic review and meta-analysis. *PLoS One*. 2018;13(1):e0190892.

2. Jin J, Jones E. Patellofemoral pain. *JAMA*. 2018;319(4):418.

3. Crossley KM, van Middelkoop M, Callaghan MJ, Collins NJ, Rathleff MS, Barton CJ. 2016 patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, II: recommended physical interventions (exercise, taping, bracing, foot orthoses and combined interventions). *Br J Sports Med*. 2016;50(14):844-852.

4. Lankhorst NE, van Middelkoop M, Crossley KM, et al. Factors that predict a poor outcome 5-8 years after the diagnosis of patellofemoral pain: a multicentre observational analysis. *Br J Sports Med*. 2016;50(14):881-886.

5. van der Heijden RA, Lankhorst NE, van Linschoten R, Bierma-Zeinstra SMA, van Middelkoop M. Exercise for treating patellofemoral pain syndrome. *Cochrane Database Syst Rev*. 2015;1(1):CD010387.

In Reply Dr Barton and colleagues suggest that our JAMA Patient Page contained outdated information because we cited a background article dating from 2007. This is not true. All of the information presented was up-to-date and consistent with recent clinical evidence as well as our own clinical expertise in patellofemoral pain, an entity for which diagnosis and management has not significantly changed over the past 10 years. As with all JAMA Patient Pages, this article was meant to be a generalized and limited overview of a medical condition, not a comprehensive literature review that specifically cited all recent evidence.

Barton and colleagues state that our Patient Page is "factually incorrect" because it suggested that there are no long-term effects of patellofemoral pain, such as for sports participation, quality of life, and general health. We agree that these are all potential long-term functional effects of patellofemoral pain (although the study cited by Barton and colleagues to support this statement was a poor-quality, survey-based study with 60 patients, representing a 19% response rate). However, our article specifically separated these functional effects from any long-term structural effects on the knee joint, such as arthritis. The authors are physiotherapists and exercise scientists, and patients come to them with a different set of concerns than they do when first presenting to a physician with knee pain. Their focus is on optimizing specific physical therapy modes to improve function and quality of life; our focus for a patient with knee pain is to first rule out structural joint disease. As such, it is vital for patients to understand the difference between the functional components of patellofemoral pain vs structural knee disease.

Barton and colleagues suggest that we did not place enough emphasis on physical therapy, exercise, and foot orthoses as treatments for patellofemoral pain. We disagree, as we specifically stated that "physical therapy is a mainstay of treatment," as it has always been. It is true that foot orthoses were not specifically discussed. Although this could have been included, our concern was that patients may feel empowered to purchase a foot orthosis on their own without proper evaluation. Ultimately, we are in full agreement on the importance of physical therapy as treatment for patellofemoral pain, along with the need for more patient-accessible resources on physical therapy; however, this Patient Page was not meant to serve as a guide for self-directed physical therapy.

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