SCIENTIFIC CONTRIBUTION

Precision medicine and the fragmentation of solidarity (and justice)

Leonard M. Fleck

Accepted: 4 January 2022 / Published online: 10 January 2022
© The Author(s), under exclusive licence to Springer Nature B.V. 2022

Abstract
Solidarity is a fundamental social value in many European countries, though its precise practical and theoretical meaning is disputed. In a health care context, I agree with European writers who take solidarity normatively to mean roughly equal access to effective health care for all. That is, solidarity includes a sense of justice. Given that, I will argue that precision medicine represents a potential weakening of solidarity, albeit not a unique weakening. Precision medicine includes 150 targeted cancer therapies (mostly for metastatic cancer), all of which are extraordinarily expensive. Our critical question: Must a commitment to solidarity as defined mean that all these targeted cancer therapies should be guaranteed to all within each country in the European Union, no matter the cost, no matter the degree of effectiveness? Such a commitment would imply that cancer was ethically special, rightfully commandeering unlimited resources. That in itself would undermine solidarity. I offer multiple examples of how current and future dissemination of these targeted cancer drugs threaten a commitment to solidarity. An alternative is to fund more cancer prevention efforts. However, that too proves a threat to solidarity. Solidarity, with or without a sense of justice, is too abstract a notion to address these challenges. Further, we need to accept that we can only hope to achieve “rough justice” and “supple solidarity.” The precise practical meaning of these notions needs to be worked out through a fair and inclusive process of rational democratic deliberation, which is the real and practical foundation of just solidarity.

Keywords Solidarity · Justice · Rational democratic deliberation · Precision medicine · Cost control · Immunotherapies

Introduction
Solidarity is a fundamental social value in many European countries, though the precise practical and theoretical meaning of this term is open to dispute.1 Our concern is with the application of the concept of solidarity to health care. Hence, our first task will be to critically assess various meanings attached to solidarity. Solidarity is often used in a descriptive mode. However, a dominant feature of health care today, whether in the US or the EU, is that it is too costly. No society, whether for political or economic reasons, can afford to provide to all its members anything and everything medicine might offer, no matter the cost, no matter how meagre the benefit (Wilking et al. 2017; Aggarwal and Sullivan 2014).2 This implies the need for health care rationing and priority-setting. The emergence of precision medicine, primarily for the benefit of metastatic cancer patients, significantly exacerbates this problem of health care cost control (Vokinger

1 See (Buyx and Prainsack 2018), especially Chapter three “What is Solidarity?”. This volume is a very thorough discussion of solidarity in the context of health care, though in a more descriptive mode, less so in a normative mode. See also Meulen (2018), who offers a useful history of the emergence of the concept of solidarity in the opening chapter, followed by an analysis of the concept and its relation to the concept of justice, concluding with some emerging challenges to solidarity, especially in the Netherlands. Though Meulen focuses on the Netherlands, the challenges will be similar across the EU (as discussed below). For other analyses and applications of the concept of solidarity in health care, see (Danis, 2018; Schindler et al, 2018; Gheaus, 2017; Butler, 2012; Wilking et al., 2017; Groot et al. 2020; Davies and Savulescu, 2019; Reichlin, 2011; Gould, 2018; Biller-Adorno and Zeltner 2015; West-Oram, 2018; Derpmann, 2018).

2 Four factors contribute the most to the problem of escalating health care costs in both the US and the EU: (1) costly emerging medical technologies with varying degrees of effectiveness, (2) a growing aging population, (3) an increasing burden of chronic illness related to both the aging population and emerging medical technologies, and (4) enhanced patient expectations related to the promises of those emerging medical technologies. See Aggarwal et al., (2014) and Janus and Minvielle, (2017).
et al. 2020). In addition, it threatens to fragment solidarity in practice, not simply because of associated costs, but because of the way in which precision medicine fragments the population of metastatic cancer patients and gives preeminence to the treatment of cancer, as opposed to many other life-threatening medical conditions. How can health care solidarity be sustained in these circumstances?

Answering this last question requires a normative understanding of solidarity. However, the prevailing understandings of solidarity are too abstract and too vague to be adequately responsive to this very complex challenge. Consequently, I argue that a normatively useful understanding of solidarity must include a conception of health care justice. However, multiple conceptions of justice are part of our ethical armamentarium. They too can contribute to the fragmentation of solidarity. Consequently, I ultimately argue that carefully constructed, fair, inclusive processes of rational democratic deliberation are necessary both to articulate just limits on health care spending (fair and affordable precision medicine) and to specify the shared commitments that will constitute solidarity in practice so far as access to the fruits of precision medicine is concerned.

**Health care solidarity: what might it mean?**

Appeals to solidarity have been used in a number of social and political contexts over the past two centuries to build, for example, coalitions of workers to fight for their rights and better wages. The message to workers was, “We are all in this together; we are all oppressed by the capitalist owners of these factories.” This is a descriptive and practical use of the concept of solidarity intended to build political strength through the creation of a political identity. However, our focus will be on the concept of solidarity in a health care context. This is much more of a challenge because health care itself, and what we call health care needs, are extremely complex and heterogeneous. Marx could appeal to “workers of the world” to unite for their common good. It is much harder to concoct a convincing appeal to “patients of the world” in the hopes of uniting for a common good.

The good of cardiac patients is seen in practical terms as being very different from the good of cancer patients or renal patients or patients with a variety of disabilities, and so on. If health care resources were unlimited, these differences would make no practical difference. But health care resources are limited by the willingness of taxpayers to raise taxes or to pay higher health insurance premiums “for the benefit of others” (as perceived by payers in very good health).

In a health care context, the concept of solidarity will capture a number of related notions. Saltman (2015), citing Bayertz (1999), includes in the notion of solidarity “reciprocity (asymmetrical for the needy); social cohesion; altruism and fellowship; citizenship duties; universal brotherhood; political and/or social justice.” All these notions have a virtuous quality about them. They are readily endorsed by any reasonable person living in a community where all are vulnerable to the various misfortunes of life. If my house is struck by lightening and burns to the ground, I can count on others in my community to help me rebuild. And I would do the same for them. This is a simple example of reciprocity. However, things are more complicated in the world of health care, in part because of the complexity of health care itself, in part because of the insurance mechanism, whether public or private.

What does a commitment to reciprocity mean when millions in the EU are afflicted with chronic degenerative conditions (sometimes lifelong) that effectively undermine their ability to reciprocate? Prior to 1990 (to pick a somewhat arbitrary date), health care costs were largely socially affordable in the EU. It did not matter that some individuals had minimal ability to reciprocate by helping to meet the health care needs (and related costs) of others. What mattered was that everyone was vulnerable to serious health needs, sometimes life-threatening, but treatable at significant expense. All were in this together. Beyond 1990 many more expensive, emerging medical technologies began to proliferate. They were a potential threat to reciprocity (and solidarity) because it was not as if these technologies were emerging more or less uniformly across a broad range of diseases and other health infirmities. Some would benefit; others would not. Further, it was not as if these technologies were emerging randomly; these technologies came to be as a direct result of deliberate public and private investment in specific health needs and research (not with a commitment

---

3 Vokinger et al. (2020) write: “The prices of drugs for cancer have been shown to increase even when evidence emerges that the drug might be less effective than initially believed” (at 664). The headline from a commentary in the journal *Cell* captures the problem precisely: “How much longer will we put up with $100,000 cancer drugs?” (Workman et al., 2017). In 2017 there were about 70 such cancer drugs; in 2021 there were at least 150 with FDA approval. Literally hundreds of journal articles in the past three years have raised alarms regarding the cost of these drugs as part of the precision medicine initiative. Little else is comparable in the way of socio-economic concern for any class of drugs outside cancer. This is a primary reason why these drugs represent a focused threat to health care solidarity and health care justice.

4 The vast majority of workers will be workers for their entire life. In contrast, patients tend to be patients episodically, often with different medical needs at different times. That fact by itself makes it difficult to create a persistent identity among patients for the pursuit of a common good.
to reciprocity and solidarity). Still, the effects over the past thirty years might have been a relatively minor erosion in overall commitment to reciprocity and solidarity with regard to health care if it were not for the emergence of these very expensive, marginally beneficial targeted therapies at the heart of precision medicine.

Rapid increases in health care costs have generated demands for controlling those costs. It is easy to imagine everyone endorsing greater efficiency and eliminating wasteful care. That can be seen as reinforcing solidarity. We are all better off getting health care more efficiently. More problematic has been the emerging rhetoric around personal responsibility for health, especially when failure in that regard results in very high health care costs for the rest of society. The argument is that individuals who fail to take responsibility for their health (smoking, poor diets, lack of exercise, medical non-compliance) are exhibiting indifference to the reciprocal aspects of solidarity (Davies and Savulescu 2019). They are consuming health care resources which they would not have needed if they had been more attentive to protecting their own health. This, it is argued, is irresponsible and incompatible with a genuine commitment to reciprocity. It is a clear gap in solidarity that only grows wider as treatment costs develop metastatic cancers that are very expensive to treat. For example, patients who struggle with substance abuse, with the explanation that they simply chose not to be altruistic in that regard? That seems intuitively incoherent and arbitrary.

Saltman and Bayertz also link citizenship duties and universal brotherhood to some understandings of solidarity. However, those linkages fail to address the question of what the scope of those citizenship duties might be so far as assured access to needed health care is concerned. The same is true with regard to the notion of universal brotherhood. If extremely expensive life-saving or life-prolonging medical technologies consistently yielded cures or greatly improved length and quality of life, it would be clear that a society committed to solidarity owed that to all its citizens who had those needs, even if there were overall concerns about controlling health care costs. However, all of that is contrary to fact. There are persistent and growing concerns about controlling health care costs throughout the EU, and those costs are largely driven by very costly emerging life-prolonging medical technologies that often yield only marginal gains in life expectancy and quality of life, far out of proportion to those costs. Precision medicine is a prime example of this challenge.

The vast majority of metastatic cancer patients achieve only marginal gains in life expectancy at very great social expense. That would suggest that such patients should be denied access to these therapies at social expense, though

5 “This article argues that health care systems that are grounded in solidarity have the right to penalize some users who are responsible for their poor health” (Davies and Savulescu, 2019, at 133).
6 Meulen (2018) calls attention to the demand in the Netherlands for more personal responsibility regarding health maintenance as a cost control measure. He quotes one Minister of Health Care saying, “Nobody has the right to an unhealthy lifestyle” (at 133). Meulen also cites survey research in the Netherlands supporting the view that people with an unhealthy lifestyle should be forced to pay higher insurance premiums (at 134). No doubt smokers and sunworshippers who develop metastatic cancers that are very expensive to treat would be among the irresponsible imposing these costs on the responsible. This is a clear gap in solidarity that only grows wider as treatment costs become greater.
7 Segall (2010), for example, who is a luck egalitarian, will argue that those who are irresponsible with their health, and impose those costs on others, have no just claim to having their health needs met. Nevertheless, he adds, compassion requires that society meets those needs, at least for basic health care. In a society committed to solidarity, that reduces those individuals to second-class citizens because they will have clear limits to socially funded health care while all others will have more comprehensive access to socially funded health care.
8 “Confronted with the growing number of new therapies entering the market at high prices, many OECD countries have raised concerns about their ability to reconcile access to oncology treatments with spending efficiency and sustainability. Expenditure on oncology medicines has steadily increased over time, not only due to higher launch prices, but also to steady increases in the number of patients being treated (a combination of rising prevalence, new treatment options, and increasing duration of treatment)” (OECD Health Division 2020, at 9).
(as we discuss below) some number of patients generally not identifiable before the fact do gain extra years of life from these drugs. These patients are referred to as “super responders.” However, if such patients could be identified reliably before the fact, and if they alone had socially funded access to these drugs, that would entail an obvious risk of fragmentation to solidarity. Alternatively, an unlimited commitment could be made to funding any and all somewhat effective therapies for these metastatic cancer patients. However, that too would risk the fragmentation of social solidarity, unless social funding were extended to all patients faced with chronic degenerative illness for anything medicine could offer that would forestall death. That would mean giving up to a large extent the goal of health care cost control, which would yield yet another threat to social solidarity. At this point, Saltman and Bayertz call attention to the role of social justice as integral to social solidarity.

Saltman (2015, at 1–2) writes, “To some, solidarity means that every individual regardless of income or social standing has the same services delivered by the same health care providers and with the same clinical outcome.” For others, Saltman observes that solidarity is about shared financial sacrifice that included some understanding of fairness regarding degree of sacrifice. However, what those understandings of solidarity do not specify is the precise content of health services that will be assured to all as part of that commitment to solidarity. These latter uses of the concept are intended to be taken normatively. Consequently, Saltman and Bayertz agree with other writers who will see some conception of health care justice as being intimately linked to solidarity. Habermas (1990), for example, sees justice and solidarity as two sides of the same coin, a notion endorsed by Meulen (2015) as well. The thought is that a commitment to solidarity by itself is too vague to have significant normative force. Solidarity implies a commitment to a common purpose. In the case of health care, the common purpose would be to prevent premature death and to restore health when individuals have suffered as a result of disease or accident. That can mean roughly equal access to effective health care for all. In other words, if a particular costly drug for multiple sclerosis is an approved treatment for that disease, then all patients with that disease will have access to that drug at social expense (assuming no medical contraindications). This undergirds the expectation of universal coverage. In addition, it can also include commitment to the idea that higher income groups will pay more health care costs than lower income groups (using a progressive tax mechanism), and lower health risk groups will help pay the costs of higher health risk groups. However, I will still argue that precision medicine represents a threat to this societal commitment to this last normative understanding of solidarity.

**Precision medicine and the need to control costs**

Precision medicine today (2021) includes more than one hundred and fifty targeted cancer therapies or immunotherapies (almost exclusively for advanced and metastatic cancer). The “target” of these therapies are certain genetic features of a cancer, mutations that are responsible for “driving” that cancer and causing it to spread and multiply. These targeted therapies generally have prices of €50,000 to €75,000 annually or for a course of treatment. These prices might be justified if they saved many lives, but the sad fact is that for the vast majority of patients gains in life expectancy will be measurable in months, not years. Cure is not a reasonable expectation. One form of immunotherapy, CAR T-cell therapy (for various leukemias), has front-end costs of $475,000, and at least 30% of these patients will not survive a year. There are 1.3 million cancer deaths each year in the EU. Here is our critical question: Must a commitment to solidarity mean that all these targeted cancer therapies and immunotherapies are included as part of a benefit package guaranteed to all in each EU country, no matter what the cost, no matter what degree of effectiveness? If not, how is solidarity preserved when some metastatic cancer patients are denied access to the only drugs that might yield some gain in life expectancy?

I argue that health care cost control is essential to preserving solidarity. We can see the reason for this if we simply look at practice in the United States. In 2020 total health care...

---

9 Carrabregu (2016) calls attention to Bayertz (1999) suggesting that solidarity ought to be understood as a supererogatory commitment. That would effectively eliminate the moral challenges posed by precision medicine and other very high-cost life-prolonging medical technologies because social financing of all these interventions would be entirely optional, i.e., non-obligatory. However, that eviscerates almost entirely the normative force of solidarity for purposes of governing the ethically defensible distribution of very costly life-prolonging technologies.

10 These numbers are roughly half what the costs of these targeted therapies are in the US. This is primarily the result of EU countries being able to bargain as a whole with pharmaceutical companies for extensive discounts (Vokinger et al. 2020). However, the authors emphasize that these cancer drugs will be leading contributors to health care cost escalation in both the US and the EU. They write, “The prices of drugs for cancer have been shown to increase even when evidence emerges that the drug might be less effective than initially believed” (at 664).

11 In all of Europe in 2018 there were 1.93 million cancer deaths, and 3.91 million new cases of cancer diagnosed. What is significant is that Europe has only 9% of the world’s population but 25% of the total world burden of cancer. See Ferlay et al. (2018).
expenditures in the US were about $4.0 trillion, or 18% of our Gross Domestic Product [GDP], compared to 1960 when total expenditures were $26 billion [roughly $224 billion in 2020$], or 5.2% of GDP (Keehan et al. 2020). European countries today are generally spending 8–12% of GDP on health care. Roughly half of that $4.0 trillion in the US represents public spending, i.e., Medicare for the elderly, state Medicaid programs for the poor. The other 50% is largely paid through private, employer-based insurance or out of pocket.

Employers see their profits at risk because of rapidly escalating health care costs, largely related to costly advancing medical technologies, such as these targeted cancer therapies. Consequently, employers use a variety of techniques to control the costs of health insurance for which they have assumed responsibility. Most of those techniques involve shifting more health care costs and health insurance costs to their employees, either by requiring employees to pay a larger portion of the insurance premium, or by reducing the scope of covered services. Employers also achieve some degree of cost control in relation to these targeted cancer therapies (and other very high cost medical interventions) through (1) very high co-pays required to access these therapies, or (2) these therapies are simply removed from a basic comprehensive benefit package and left to the purchase of supplemental private insurance paid by individuals, or (3) cancers related to poor health behaviors (smoking and lung cancer) may be excluded from coverage.

What should be clear is that all of these mechanisms used in the US would certainly be destructive of solidarity if adopted in a European context and if “solidarity” is understood to include something like “equal access to needed and effective health care without financial barriers.” What is common to all these mechanisms is that access to needed and effective health care is dependent upon the financial status of individuals. Individuals in the lower half of the economic spectrum who are faced with very high health care costs will simply forego that care and accept the consequences for their health of doing so, including premature death. This can be accurately described as “self-rationing,” which has the desirable effect from an employer’s perspective of freeing them from blame or responsibility for the “unfortunate” health outcomes that then befall their employees.

European readers might believe that patients who are covered by public programs in the United States would be spared these economically motivated risks to health that are common in the private sector. However, taxpayers (mostly healthy individuals) pressure state and federal legislators to control costs in the Medicare and Medicaid programs. Consequently, coverage of health services for the poor uninsured (variously defined by each state) will vary considerably from state to state, depending upon the willingness of legislators to raise taxes to fund the Medicare program. The Medicare program used to be described as “national health insurance for the elderly”. However, over the past decade Medicare has become increasingly privatized through individual ability to purchase a variety of Medicare Advantage policies with various mixes of coverage and costs to individuals at the time of medical need (Miller 2020). This was a deliberate choice by Congress with the intent of reducing health care costs to Medicare and shifting more of the responsibility for absorbing those costs to Medicare recipients or the private insurers promoting Medicare Advantage policies. European countries could choose to make comparable choices in order to control the costs associated with these targeted cancer therapies (and other very high cost life-prolonging medical technologies) but such choices would surely represent the fragmentation of solidarity, as I argue below.

**Solidarity: the challenge of limited resources**

The basic ethical problem we address can be captured in these two questions: (1) What does it mean to be a just and caring society when that society has limited resources to meet unlimited health care needs? (2) What does it mean to be a society committed to solidarity as a fundamental social value when that society has limited resources to meet virtually unlimited health care needs? Resources are limited by what taxpayers are willing to pay to assure everyone with specific health needs to have those needs met effectively. Resources for health care are also limited by the legitimate demands for resources required by a broad range of other social needs. Health care needs are virtually unlimited because, as Daniel Callahan (1990) has argued, what we regard as morally compelling health needs are tied directly to emerging medical technologies. In other words, there was no “need” (in an ethically relevant sense) for these targeted cancer therapies until these targeted cancer therapies were invented. Finally, we must ask whether cancer is somehow morally special, such that it justifiably commands unlimited resources while all other health care needs are subject to cost constraints. This has recently been referred to as “oncosexual exceptionality,” and is regarded as being ethically problematic (Salcher-Konrad and Naci 2020; Fu et al. 2021).

---

12 I remind my EU readers that employers in the US have no legal obligation to provide health insurance to their employees. It is entirely voluntary, largely dependent upon the affordability of that benefit from an employer’s perspective.

13 Weyco, an insurance benefits administrator in Michigan, required all its employees who were smokers to quit smoking within a year or be fired. The company did random testing to enforce this rule. The no-smoking ban covered off-hours as well, not just working hours (Peters 2005).
Precision medicine as a threat to solidarity

Why does precision medicine represent a threat to solidarity? The first reason would be the extraordinarily high cost of the interventions that are covered by the rubric of precision medicine. The second reason would be the very large number of patients with metastatic cancer who would be eligible for these interventions annually. The third reason would be the very marginal gains in life expectancy that are the result for the vast majority of these patients. These are the very broad reasons; more specific reasons are discussed below. Before turning to those reasons, some medical and scientific background regarding metastatic cancer and the distinctive features of precision medicine will be useful.

If a cancer is diagnosed at stage one or two, 80% of those patients will survive at least ten years. Ordinarily, we might think of those patients as being ‘cured’. However, most medical researchers are reluctant to use that term, preferring instead ‘long term remission’. This reflects the fact that so much is not understood regarding the origins, evolution, complexity, and recurrence of cancer. For many diseases, medicine can identify a specific initiating event in an individual, i.e., infection with a virus of some sort. In other cases, such as heart disease, monitoring cholesterol levels and blood pressure, allow careful disease management and tracking. Neither of these options generally apply to cancer.

Precision medicine and the wiliness of cancer

Recent research suggests that a cancer might get established with the dysregulation of one or more tumor suppressor genes. TP53 is the most common of those tumor suppressor genes. TP53 is responsible for repairing genes that might have become mutated, or, alternatively, initiating cell death in those cells with mutated genes to prevent the development of a cancer. TP53 itself is highly mutated in ~50% of all cancers and minimally functional in the rest of cancers. Certain mutations of TP53 result in its acquiring oncogenic properties, i.e., actually promoting the spread of a cancer instead of destroying cancer cells. However, unlike viral infections whose initiation can usually be identified quickly, it might be fifteen years after TP53 mutation before there is detectable clinical evidence of a cancer. This is one of many insidious aspects of cancer that makes early identification, control and cure difficult to impossible. Another insidious element is the genetic heterogeneity of cancer, especially metastatic cancer. Cancer cells tend to be genetically unstable, which means that successive generations of cancer cells become more and more mutated. What this means in practice is that a particular tumor might have multiple drivers of that cancer within that tumor. Also, tumors throughout the body will often have multiple drivers, some of which will be genetically different from the driver of the original tumor. The consequence of this genetic diversity is cancer drug ‘resistance’.

As noted above, targeted cancer drugs are aimed at stopping the functioning of specific drivers of tumors. For example, tyrosine kinase inhibitors [TKIs] block specific enzymes that send growth signals within cells. TKIs will be used to treat several types of cancer. Non-small cell lung cancer would be one good example. Erlotinib is a TKI that inhibits the epidermal growth factor receptor [EGFR] when mutated and driving the growth of a cancer. This drug works well in preventing disease progression for as long as ten to fourteen months. However, because these tumors are constantly acquiring new mutations (sometimes in response to the drug itself), resistance develops, typically in the form of a T790M mutation. Osimertinib, a next generation TKI, can then be given, though resistance to it will develop as well, primarily as a result of a C797S mutation in exon 20. Very recently (August, 2021), research was reported on the drug quercetin, another TKI, which will attack non-small-cell lung cancers with that C797S mutation (Huang et al. 2021). Why should this medical scenario be a threat to solidarity?

---

14 Roughly 50% of metastatic cancer patients today would be medically eligible to receive either some targeted therapy or some immunotherapy. That fraction will continue to grow with each new cancer therapy.

15 See Prasad (2017a, b); Leighl et al. (2021). Leighl et al. write, “Across Europe, there are large variation in access to novel cancer medicines, with less developed countries in Eastern Europe reporting the greatest limitations” (at e2). Also, “Currently, cancer drug pricing does nor correlate with value or clinical benefit” (at e1).

16 Prostate cancer would be the obvious exception, where PSA levels are monitored for disease progression.

17 See Zhou et al. (2019); also, Mantovani et al. (2019). Both these articles precisely capture the paradox of p53, namely, that it is designed to prevent cancer but (once mutated) promotes the spread of cancer.

18 The ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium (2020). “On average, cancer genomes contained 4–5 driver mutations when combining coding and non-coding genomic elements; however, in around 5% of cases no drivers were identified, suggesting that cancer driver discovery is not yet complete.” This was an enormous piece of research that did whole genome sequencing of 2778 tumors across 38 cancer types. This allowed researchers to reconstruct the evolutionary history of each of those tumors, “revealing that driver mutations can precede diagnosis by several years to decades.” Current research suggests there might be 140 genetically distinct drivers of cancer.
Solidarity and targeted cancer therapies

As noted already, roughly 1.3 million patients in the EU die of cancer each year. These targeted cancer therapies have costs in excess of €75,000 or more per patient per year. If any of these patients have a solidarity right to one of these drugs, then they would all seem to have that right (assuming no medical contraindications). To give those 1.3 million metastatic cancer patients an extra year of life would cost €98 billion. At present, we have a targeted cancer drug or immunotherapy for the genetically specific cancer of 50% of all those patients, though the ultimate goal of medical research is 100%. The goal is actually much more ambitious than that, as our discussion above of TKIs makes clear. If one drug fails after a year to halt cancer progression because of resistance, then we want to provide another drug that is responsive to the new genetic driver of that cancer, thereby gaining another year, and a year after that, and another year after that. In other words, cancer may not be curable, but maybe it can become a managed chronic disease, as has happened with HIV. HIV+ patients have gained as much as thirty extra years of life from the three- and four-drug combinations used to manage the virus as it mutates.

In the case of metastatic cancer, let us consider a more modest scenario of five-year survival with drugs costing €75,000 per year. Five cohorts of future metastatic cancer patients would add almost €500 billion annually to health care costs in the EU, which would not be the total cost of cancer care. This huge figure just represents the cost of these drugs, not the cost of genetically analyzing tumors or managing side effects, and so on. A cost increase of this size for one disease either squeezes out whatever is judged to be lower priority care for some other diseases, or it requires a very substantial increase in taxes, or it requires some form of rationing access to these drugs, i.e., trying to articulate and discriminate among high-value cancer care and low-value cancer care. For example, would individuals with early stage dementia or moderate dementia and metastatic cancer not be offered these targeted cancer drugs? Would offering these drugs in these circumstances be regarded as low-value (solidarity optional) care? Roughly 20–30% of patients with non-small cell lung cancer will have mutations in KRAS genes that are driving that cancer. In a review article, Parums (2014) notes that “KRAS mutations are associated with a decreased response to EGFR TKIs and with a worse prognosis” (at 515). It is not that the TKIs are completely ineffective. The median gain in overall survival might be four weeks. Is that gain insufficient to justify the cost of these TKIs? May these drugs then be denied to these patients with KRAS mutations? All these considerations suggest potential cracks in solidarity.

Why precisely would there be cracks in solidarity? Patients with metastatic cancer can accept the fact that at this time there is no targeted therapy for their cancer with this specific driver of their cancer. This is just bad luck and does not undermine solidarity. In the KRAS mutation example, the four weeks is a median gain in overall survival. Where is the tail on that curve? That tail might be six months out, or one year out. The number of patients represented by that tail will be very small. It is easy to imagine a metastatic cancer patient with that KRAS mutation wanting that small chance of being in the tail. Denying that patient that option will feel like a denial of solidarity. Saying to that patient that everyone who has that cancer with that driver mutation will be denied that TKI at social expense, thereby honoring some form of fairness, will not speak to the solidarity issue. From the perspective of that patient, everyone in that diagnostic category will have been removed from solidarity with other cancer patients. Further, our hypothetical patient might argue that patients with his cancer but a different driver mutation for which a drug promises a nine-month median gain in overall survival will have that drug paid for socially. However, patients at the very low end of that median figure might only gain two months of additional life, or even less. They are embraced in solidarity, which will seem unjust to our hypothetical patient. The obvious response from a societal representative is to say we simply do not know before the fact who will be at either end of that tail. However, as discussed below, much research is ongoing, seeking prognostic and predictive biomarkers. If future research uncovered biomarkers predicting poor response to a targeted therapy, i.e., less than two months gain in overall survival for specific patients (though predicted median gain in overall survival for the entire cohort would be nine months), and if that knowledge were used to deny these poor responding patients that targeted therapy, that would look like another crack in solidarity. Allowing such patients to purchase access to these drugs at their own expense, or even with a 50% social subsidy, would only make the cracks worse. Further, why would the ‘poor responder line’ be drawn at two months overall survival gain rather than three months or four months? There are many more potential cracks.

Cracks in solidarity

Another new class of drugs is called checkpoint inhibitors. They are a form of immunotherapy. Ordinarily we would expect the immune system to attack cancer cells because they are ‘not us.’ That is, they should be recognized as

---

19 There are reasons why exercising that right would be irrational. If for some biological reason in an individual patient that drug would do no good at all, or if it could be known before the fact that it would do more harm than benefit, that patient would have no right to that drug. If anything, denying a patient a targeted therapy with these considerations in mind would reinforce solidarity, not undermine it.
something foreign in our bodies. When our bodies are subject to a serious viral infection, the immune system attacks in force. That attack would itself cause damage if it were not ‘checked’ once the alien microbes had been destroyed. Cancer cells use that checkpoint strategy to trick the immune system into believing nothing was awry. Checkpoint inhibitors, such as pembrolizumab and nivolumab, block the checkpoints [PD-1 or PD-L1] and allow the immune system to recognize and kill the cancer cells. Unfortunately, only a small percentage of patients (~ 20%) will derive significant benefit from these drugs (Grisham 2017), though half of these cancer patients would be medically eligible for these drugs. Cost is again relevant. Generally, these drugs will cost €80,000 [$156,000] per year or for a course of treatment. Melanoma and non-small-cell lung cancer are the cancers most often treated with these drugs, though at least 15 major cancers would be treated with these drugs (National Cancer Institute 2019).

Recent research suggests that patients who derive the most benefit, more than an extra year of life, are patients whose tumors have the most mutations, which seems to make the tumors more visible to the immune system and these drugs (Klemperner et al. 2020). Here we have another challenge to solidarity. Is it acceptable, from a solidarity perspective, to deny patients with melanoma or lung cancer access to these drugs at social expense because their tumors do not have ‘enough’ mutations? In other words, these drugs would be unlikely to yield much in the way of benefit. This is what Callahan has characterized as the ‘ragged edge’ problem (Callahan 1990, chap. 2). Where should the line be drawn that identifies enough mutations in a tumor that these drugs are more likely to yield substantial benefit? It would be easy to draw that line if below it there were no chance of benefit (and only the risk of toxic side effects), while above the line would be substantial benefit. Instead, the reality is a continuum, which means wherever the line is drawn some individuals would be denied some degree of medical benefit that they may have wanted. Is that outcome something congruent with a certain understanding of solidarity? The very costly alternative is to provide these drugs to everyone with melanoma or lung cancer (or any other cancer for which a checkpoint inhibitor would be appropriate), though this would be largely wasteful in as much as 80% of those cases. This would be a very high price to pay, ethically and economically, to preserve a specific sense of solidarity (perhaps a very strict egalitarian sense of solidarity).

More recently, much research has focused on using combinations of checkpoint inhibitors, sometimes with one of the targeted cancer therapies. This would be as first-line treatment instead of the current chemotherapy regimen. The first thing to be noted is that this substantially increases cost, roughly £125,000 ($256,000) per year or per course of treatment. There are corresponding gains in medical benefit. For example, in the case of metastatic non-small cell lung cancer, a combination of nivolumab and ipilimumab will yield progression free survival for one year of 42%, if there are more than ten mutations per megabase, though median progression free survival will be 7.2 months. If total mutational burden is less than 10 mutations per megabase with this drug combination, then median progression free survival will be 3.2 months. The point to emphasize is that this latter figure is not one week. It might well be significant to patients in this latter category who have no other life-prolonging options. Also, we are talking about a median, which means half the patients will do better than 3.2 months, some very much better. For the sake of overall cost control, does a commitment to solidarity permit not treating patients with this very expensive drug combination if their mutational burden is less than 10 mutations per megabase? This looks like another potential fracture in solidarity.

The trial that generated the data above was the Checkmate 227 trial. Another statistic worth noting from that trial is the following: Among all the patients in the trial median survival was 17.1 months with the nivolumab plus ipilimumab combination and 14.9 months with chemotherapy (Hellman et al. 2019). The median net gain in survival was 2.2 months, which would come at a very high price for that limited gain (~ $400,000 vs. ~ $30,000). Should a commitment to solidarity require paying that price from limited social resources? Alternatively, should a 30% co-pay be required from patients who wanted the nivolumab-ipilimumab combination while the chemotherapeutic regimen would be wholly paid from social resources? This would mean the relatively wealthy could afford the checkpoint combination. This would address the need for cost control, though this could readily be seen as eroding solidarity (in the moderate egalitarian sense endorsed by Saltman and Bayertz). The problem is this: It is one thing for two patients to have metastatic melanoma, only one of whom has a genetic mutation in their cancer that can be attacked by some specific targeted therapy. The other patient might feel badly but they would not feel as if they had been treated unjustly. From a precision medicine perspective, it is as if these patients had two different diseases, only one of which had a relevant therapy. This does not corrode solidarity. In the scenario above, however, all those patients have the “same disease,” and we are treating the financially well off with a somewhat more effective therapy while relegating the financially less well off to a less effective therapy. This will have a corrosive effect on solidarity, especially if we are mindful of the fact that the financially less well off will be helping to finance through their taxes that 70% of the cost of the combination therapy.
**Is solidarity affordable?**

Probably the most expensive cancer therapy in practice today is CAR T-cell immunotherapy. This therapy involves extracting a patient’s T-cells, re-engineering them so that they can more effectively attack one or another blood cancer through targeting specific proteins on the surface of cancer cells, then injecting them back into a patient. In the United States, the front-end cost of this therapy is $475,000. In addition, more than half of these patients will experience a side effect known as cytokine release syndrome (with a range from somewhat serious to very serious), which will require a lengthy ICU stay for recovery and add more than $200,000 to the overall cost of the procedure if more serious (Santomasso et al. 2019). In the US ~70,000 individuals with leukemia or lymphoma would be potential recipients of CAR T-cell therapy (if all were fully insured and if the technical capacity to meet that volume were available). In the EU that number would be ~120,000 individuals. Depending upon specific medical circumstances, 30%+ of adult patients offered CAR T-cell therapy will not survive a year. The remainder may gain two to four years of life expectancy, at which point the T-cells will often be exhausted. Research is going on to develop a version of this therapy that can be used to treat tumors in solid organs (Greens 2019). If such research were successful, that would dramatically increase the number of individuals who would be candidates for this therapy. Consider now the solidarity-rupturing questions that are associated with this therapy.

Considerable research is occurring with regard to all these immunotherapies and targeted therapies to identify predictive biomarkers aimed at making "more appropriate" use of these therapies (Bairi et al. 2019). First question: Should such research be funded when the goal is to find biomarkers that will identify patients who have a 90% chance of not surviving a year after CAR T-cell therapy? Second question: If such research is successful, should it be used to deny patients access to CAR T-cell therapy at social expense, assuming a 90% likelihood they will not survive a year? What needs to be kept in mind is that this is the proverbial "last chance" therapy; there are no other therapeutic options for such patients. What also needs to be kept in mind is the question of whether cost-effectiveness is a relevant consideration. Do such considerations necessarily corrupt solidarity? The implication of cost-effectiveness is that two patients might have the same cancer requiring the same targeted therapy with different predictable outcomes, such that from a social point of view one of those patients might be twice as expensive from a cost-effectiveness perspective as the other, even though the same volume of dollars or euros might be spent in both cases. If a patient survives (and is predicted to survive) only six months with CAR T-cell therapy, then from a cost-effectiveness perspective, those six months cost $950,000 per life-year gained (at least), while another patient receiving that same therapy and surviving three years would have a cost of $150,000 per life-year gained. Alternatively, is there some limit to what should be spent reasonably to protect solidarity?

Next question: Researchers are now exploring whether patients who fail CAR T-cell therapy the first time should be offered the option of trying it again. The conclusion from one small study is that the results of a second infusion are not as good as the first infusion (Keown 2019). The solidarity implications of this conclusion can be taken in a couple different ways. If the judgment was that individuals who were predicted to fail CAR T-cell therapy in less than a year still had to be offered the therapy at social expense (because appeals to cost-effectiveness were a threat to solidarity), then that logic would require offering a second chance at CAR T-cell therapy. In addition, if individuals failed CAR T-cell therapy after three or four years, then this same logic would require offering all of them another round of CAR T-cell therapy. It would be unlikely that they would gain another three or four years, but a two-year gain would be significant. If these conclusions are accepted, then it would seem the implicit message would be that cost does not matter when metastatic cancer patients have no other life-prolonging options. This would demonstrate an unwavering commitment to protecting solidarity…among cancer patients. However, this is really a very awkward conclusion. It represents tribal solidarity. This is hardly the sense of solidarity that most advocates for solidarity have in mind.

**Is tribal solidarity good enough?**

If cost is irrelevant for metastatic cancer patients when only one life-prolonging therapy is available to them, then non-tribal solidarity will require providing comparable life-prolonging therapies to patients with end-stage heart disease, or liver disease, or lung disease, or multiple sclerosis, and so on. We can take the logic of this position one step further. What we have described in this last sentence is one very large, very inclusive tribe of individuals who are terminally ill but for whom something can be done to prolong their lives. This is a tribe that few of us are enthusiastic to join, especially if we have a chronic degenerative condition that will ultimately result in death. What we would much prefer, if cure of our condition is just not medically possible in a predictable future, is that the slope of decline be ameliorated and prolonged as much as possible by anything medicine might offer us. Also, if we are paying taxes to pay for extremely costly life-prolonging technologies for individuals with very late-stage illness, in effect saying cost does not matter, then we might well expect that cost should not matter with regard to our medical needs as well. What, we might ask rhetorically, is the moral logic that would...
dictate penuriousness with respect to the use of therapeutic resources in the earlier stages of a chronic degenerative illness, so that we could speed along to those final stages when unrestrained spending would be the rule? For example, the current cost of fourteen drugs that would slow the decline of multiple sclerosis will range from $67,000 per year to $92,000 per year (Huff 2018). This is a lot less than the front-end costs of CAR T-cell therapy. However, patients can be on these drugs for two or three decades, yielding an aggregated cost per patient of two to three million dollars over the course of a lifetime. In the United States there are about one million people living with multiple sclerosis. How should this be thought about from the perspective of solidarity? Can there be a cost-conscious form of solidarity that does not yield fragmented or tribal solidarity?

Another recent example is a drug called tafamidis. It would be used to treat a very specific form of heart failure called transthyretin amyloidosis. Roughly 100,000 to 150,000 patients in the US have this version of heart failure. The cost of this drug is $225,000 per patient per year (Court 2019). This is a drug, like the MS drugs, that could be taken for several years. One of the medical oddities associated with this drug is that only 4% of patients with this condition are correctly identified as having this condition in current medical circumstances because their symptoms are not distinctive enough to be recognized by most cardiologists. Consequently, they are simply identified as heart failure patients, and they are treated with relatively inexpensive drugs. This raises a provocative question for countries committed to solidarity. Should all patients now identified generically as heart failure patients undergo more sophisticated diagnostic testing to identify correctly those with this very specific version of heart failure, potentially adding $20 billion per year to the cost of treating these patients? Powerful economic considerations for health care cost control would likely speak against such an effort. Would solidarity considerations make such an effort ethically obligatory? Recall that a small percentage of these patients would already be correctly diagnosed by a few astute clinicians who now would know of this drug. Would solidarity be best preserved if this drug were not offered to any of these patients? This sounds like a plausible option. However, in the arena of targeted cancer therapies and immunotherapies, all manner of genetic testing is being done to identify patients whose tumors have specific genetic mutations likely to elicit a beneficial response with some novel drug. This information is not being hidden from these patients. Why should such information be withheld from cardiac patients who would stand to benefit from tafamidis?

The challenges to solidarity, cost control, and precision medicine might be manageable if these last two examples were the only two examples of concern. However, the list of emerging, very costly, life-prolonging medical technologies is growing rapidly. For patients with cystic fibrosis there is now Trikafta®, a drug that partially corrects for the genetic deficiency that results in cystic fibrosis. The cost of that drug is $310,000 per patient per year. This is another drug that could be taken for several decades with per patient lifetime costs in the millions of dollars or euros. There is also Zolgensma® for spinal muscular atrophy at a one-time cost of $2.12 million per patient. There are enzyme replacement therapies for patients with either Pompe disease or Gaucher’s disease, each of which has costs of $300,000 per patient per year. The cost of dialysis in the United States is $91,000 per patient per year, currently for 570,000 patients, who can gain seven to ten extra years of life, sometimes more. The implied argument from these statistics is that if we are willing as a society to pay these costs now for all these other patients, how could we justify refusing to pay the costs associated with the cancer therapies under the rubric of precision medicine, especially in countries that embrace solidarity as a fundamental social value?

Someone might argue that all the therapies listed above are very effective, resulting in additional years or decades of life. In contrast, for a large majority of metastatic cancer patients the targeted therapies are marginally effective at best, and only somewhat more effective for most of the rest of those patients. However, defenders of these targeted therapies will point out that the social costs for many of these other patients are in the millions of dollars for lifetime costs, whereas the costs for these cancer patients might be $100,000. Also, it might cost $150,000 to give a metastatic cancer patient an extra year of life while these other patients are getting many years of life for $300,000 or more per extra year of life. That, the argument goes, does not appear congruent with a commitment to solidarity. However, someone might then argue that perfect solidarity is a utopian illusion; we just have to accept some moderate deviations from solidarity, given the complexity of medical needs and costs.

This last point generates the obvious follow-up question: How should we (a society committed to solidarity) decide which deviations from solidarity are acceptable? What should be the relevant criteria? For example, women who are HER-2+ for breast cancer are typically treated with the targeted therapy, trastuzumab. If they are judged to be at low risk of recurrence, then that therapy will go on for a year. However, some recent research has shown that a nine-week course of this therapy is almost as good as a year-long course of therapy. To be precise, at the five-year mark disease-free survival was 87.5% for the one-year group and 85.4% for the nine-week group (Nixon et al. 2018). The advantage of the shorter course is reduced risks of toxicity and a savings to a public funder of about $60,000 per patient. As a cost control measure,
should all women in these circumstances simply receive the nine-week course of therapy? Is this only a minor deviation from solidarity that all should accept as reasonable? After all, the absolute difference is only 2%. However, we should note that it was a five-year study. What is unknown is whether at the ten-year mark a much wider survival gap might emerge, perhaps a difference of thirty or forty percentage points. The likelihood is that outcome will never be known, especially if a policy decision needs to be made at five years based on this research. How should that be assessed from the perspective of a commitment to solidarity?

**Precision medicine or precision prevention: whither solidarity?**

Another challenge to solidarity comes from advocates for a much stronger effort to prevent cancer in the first place, or else to identify and treat it as early as possible. On the face of it, such efforts seem eminently reasonable and affordable. One such advocate for this strategy is Azra Raza, who is a physician/cancer researcher who recently authored a book, *The First Cell and the Human Costs of Pursuing Cancer to the Last*. Her research for the past twenty years has been about myelodysplastic syndromes and acute myeloid leukemia. The sub-title of her book makes clear her point of view. She regards all the resources spent on metastatic cancer, all the targeted therapies and immunotherapies, to be a huge waste of resources. She wants all those resources redirected with solidarity that all should accept as reasonable?

Raza sees blood tests for circulating cell-free DNA, so-called liquid biopsies, as the key to identifying cancer in its earliest stages. It was after the publication of her book that a company called GRAIL announced they had developed such a test that could detect 20 different cancers and their likely tissue of origin with 99% specificity. Sensitivity, however, varied with the specific type of cancer and the stage at which that cancer was detected. More precisely, sensitivity for Stage I was 32%; 76% for Stage II; 85% for Stage III; 93% for Stage IV (Baldwin 2019). In early 2021 Grail announced a new liquid biopsy test capable of detecting fifty different cancers from a single blood draw (Reno 2021). The cost of this test is $950.

A first question for consideration would be who should have access to these tests. A second question would be who would pay for these tests. Relative to drugs that cost $100,000 or more for a course of treatment, this sounds like an astounding bargain at $950. However, given the lifetime risk for cancer for anyone in the US or the EU is 40% (American Cancer Society 2020), that would suggest that 200 million adults in the US or 370 million adults in the EU would be potential users of this test. That translates into an annual cost in the US of $190 billion and $350 billion in the EU. Why would all these people want to have such a test every year? The short answer is that it is non-invasive; it could catch a cancer very early when theoretically treatable; the cost would be socially absorbed; it would eliminate cancer anxiety. Furthermore, some cancers, such as ovarian and pancreatic cancers, tend to present with symptoms only in very late stages when a terminal prognosis is nearly certain. Where does a commitment to solidarity fit regarding this discussion of cancer prevention?

Recall that Raza judges that the money we are spending on treating late stage metastatic cancer is a waste. She wants that money to be used instead to pay for something like the GRAIL liquid biopsy test (known as Galleri). As noted already, in the US, about 1.7 million individuals are diagnosed with some form of cancer annually. That represents less than 1% of the adult population who would be candidates for this liquid biopsy. That means that 99% + of these individuals would derive no benefit (other than psychological assurance) from the test each year, and more than half of those individuals will never have cancer. Raza’s critics will see that as a waste of resources, likely arguing that a much more targeted approach is necessary. Furthermore, if all the resources needed for this preventive effort come from withdrawing of funds from these targeted cancer therapies and immunotherapies, that means these metastatic cancer patients will die ‘prematurely’. For a majority of these cases, individuals would be denied extra months of life, perhaps a year of life, which they might well desperately want. Others, however, the strong responders, would lose extra years of life for the sake of saving the ‘statistical lives’ of unnamed and unnamable others. This will strike many as being incongruent with solidarity, certainly if we accept Bayertz’, Saltman’s and Habermas’ understanding of solidarity. The core of the problem is that patients with late stage metastatic cancer are identifiable individuals. They have names and faces; they are visibly suffering and facing death, knowing today that these therapies exist that might postpone death for them.

---

20 If nothing else, Raza should be ethically commended for requiring that resources to support broad liquid biopsy testing must come from resources currently used to treat cancer, as opposed to heart disease, or lung disease, or some other non-cancerous health need. That may be seen as being congruent with a commitment to health care justice. Potential cancer patients should not be appropriating resources now allocated for actual heart disease to meet the needs of (anxious) potential cancer patients. The relation to solidarity is less clear. Statistically, 25% of those potential cancer patients will have life-threatening heart disease sometime in their life.
A substantial debate has been ongoing regarding the question of whether statistical lives in this sort of situation should be weighed just as heavily, morally speaking, as the identifiable lives of patients burdened with disease (Faust and Menzel 2012; Cohen et al. 2015). This is not a debate that can be addressed in this essay. However, it is a debate that is integral to our understanding of solidarity. We might imagine seeking a compromise of some sort. More specifically, liquid biopsies should only be available at social expense for individuals in various high-risk categories. Individuals with a strong family history of cancer would be one obvious category. More challenging would be individuals who had an elevated risk of cancer associated with their DNA, as known through whole genome sequencing. This is another place where the ragged edge problem would emerge with a vengeance, again as a significant threat to solidarity.

I cannot think of any cancer related to our DNA that is 100% penetrant. Instead, the much more common reality is that an individual could be told that whole genome sequencing indicated that their lifetime risk for cancer ‘X’ was 20% (using a polygenic risk score), while the lifetime risk for any random individual for that same cancer might be 10%. Should we conclude from those statistics that the individual with that 20% lifetime risk should have access at social expense to the GRAIL liquid biopsy? However, what do we say, as solidarity supporters, to the individual with that 10% lifetime risk? Are they not eligible for an annual liquid biopsy at social expense? They will point out that it will still be the case that one out of every ten individuals with that 10% risk for cancer ‘X’ will in fact be diagnosed with that cancer. Further, some of those individuals will be diagnosed too late; their cancer will be advanced and incurable. How can such an outcome be congruent with a commitment to solidarity? What if that lifetime risk of cancer ‘X’ is 5% or 3%? Is that clearly the point at which denial of access to that liquid biopsy annually at social expense is justly denied? That is the ragged edge. What is a reasonable response to that challenge from the perspective of solidarity?

The scenario suggested here is in reality too simplistic. For the vast majority of us, the likelihood is that we might be vulnerable to several different cancers. For almost all of them the lifetime risk might be in the low single digits. However, we can imagine there might be one that poses a lifetime risk of 15%. Should we then conclude that solidarity would require annual access at social expense to that liquid biopsy test? The vast majority of cancers (90%) are not a simple result of mutations somewhere in our DNA; environmental factors are often key contributors to the initiation of a cancer, such as radiation exposure (natural or artificial), chemical exposure, smoking, excess alcohol consumption, and many other known or suspected factors. Individuals might have some control over some of these factors but very little control over others. How should such factors be considered in determining whether any particular individual, or class of individuals, should have access to this liquid biopsy test at social expense?

### Solidarity, justice, and rational democratic deliberation

Solidarity is a fundamental social value that ought to be nourished and cultivated. It undergirds a commitment to universal health care access in many European countries. However, as I have argued in this essay, precision medicine and the growing dissemination of very costly, marginally beneficial targeted cancer therapies, threaten to fragment solidarity. The rapid rise in the cost of cancer care threatens the adequacy of resources needed to address many other serious health care problems. Within cancer itself we can see the potential emergence of competing cancer tribes, defined by genetic features of their cancers and the drugs used to treat those cancers. The basic problem is that the concept of solidarity does not have the conceptual resources within

---

21 This is a commitment that often gets qualified in subtle ways in a number of European countries. In Austria, for example, Grossmann et al., (2020) write, “In the inpatient sector, reimbursement decisions on (often costly) drugs are made by the regional hospital corporations. These fragmented decision-making processes can lead to unequal access between the nine Austrian federal states or even among hospital corporations.” The same is true in the Nordic countries. “This is the case in Nordic countries. For example, local or regional administrations may have variable capacity—both administrative, technical and financial—to respond to the pressures that cancer medicines pose to their systems” (OECD Health Division 2020, at 58). To be clear, coverage of various targeted therapies may have been approved at the national level, thereby honoring a commitment to national solidarity. But the practical application of that commitment below the national level might be quite variable, thereby creating inequities within the country. Are those serious inequities, given the largely marginal benefits associated with most of these targeted therapies? Maybe not, though for a small percentage of patients who might have gained extra years of life if they had had access to a non-covered targeted therapy that loss would be significant (though no one would know who they were). A number of European countries permit the purchase of private health insurance, atop or instead of some national plan. In Switzerland the purchase of heavily regulated private insurance is mandatory with a limit on health care costs of 10% of income. Individuals may purchase private insurance for services not mandated by the government. CAR T-cell therapy was approved for funding in 2020. The Dutch have been moving in the direction of a more privatized health financing arrangement. A reasonably comprehensive plan is guaranteed to everyone but the well-off can purchase additional insurance for costly health interventions not covered in the basic plan (Meulen 2018). If health costs must be controlled, then Meulen argues the package guaranteed to all may be thinned, thereby encouraging the purchase of more supplementary insurance, or, alternatively, co-pays for more expensive interventions with likely marginal benefits can be required within the national plan for everyone. This would likely result in some fragmentation of solidarity (Meulen 2018, at 135–36).
itself to address the fracturing tendencies inherent in the medical and economic aspects of precision medicine. The concept of solidarity is simply too abstract a notion.

In another essay I have argued that the concept of solidarity must be qualified by a pluralistic conception of health care justice (Fleck 2015). We need to articulate a conception of just solidarity. To be clear, a well-articulated conception of just solidarity will still not be able to completely address the ethical challenges being created by the emergence of precision medicine. The contemporary world of medicine, economics and health care politics is simply too complex. Relevant considerations of justice (egalitarian, utilitarian, libertarian, prioritarian, sufficentarian, luck egalitarian) are likewise too complex for pure rational resolution. The philosopher John Rawls (1993, at 54–58) refers to this as the ‘burdens of judgment.’ What this notion means is that at the practical level of resource allocation within health care we may be able to do no better than hope to achieve ‘rough justice’ and ‘supple solidarity.’ The need for tradeoffs is inescapable. We cannot afford to do everything that is medically possible, most especially when life is at stake and a patient is faced with a terminal prognosis (as in the case of metastatic cancer).

The ‘we’ I have been referring to is all of us. Multiple fundamental social values are relevant to making allocation and rationing decisions within any health care system.22 A reasonable balance must be achieved among them that is integral to protecting a commitment to solidarity, what Rawls (1993, at 8–11) refers to as a ‘reflective equilibrium’. There is no perfect balancing among these values. Most often several possible balancings will be ‘just enough’ and ‘protective enough’ of a commitment to just solidarity. However, we cannot simply stop there. We need to make specific choices that are reasonably fair and affordable. We all need to be participants in the processes of rational democratic deliberation through which such balancing can be articulated and legitimated.

Let me offer a very succinct picture of what a rational democratic deliberative process might look like. We will use the example of metastatic colorectal cancer treated with the checkpoint inhibitor, pembrolizumab. Recall that tumor mutational burden (TMB) has proven to be a good predictive biomarker for prolonged therapeutic effectiveness (greater overall survival) (Klempner et al. 2020). It seems the more mutations in the tumors, the stronger the response from pembrolizumab (or other checkpoint inhibitors). This will be especially true with a TMB greater than 35 mutations/Mb. If that number drops to 25 mutations/Mb, the degree of effectiveness will decrease significantly, but not to zero. This is the ragged edge problem. The deliberative process could endorse a rationing protocol as being “just enough” that would not fund from public resources pembrolizumab for a colorectal cancer below that TMB of 35 mutations/ Mb because cost-control judgments had to be made somewhere. That would reduce to some degree the survival benefit for patients whose colorectal cancer was below that TMB mark. Some deliberators might object to sacrificing those extra months of life “for the sake of money.” Some deliberators might argue that this checkpoint inhibitor ought to be provided to any patient who might benefit to any degree with a TMB that would predict some likelihood of some benefit. In other words, they would bypass the “ragged edge” problem by refusing to draw any bright line “in this case.”

Another deliberator could ask what it was about “this case” that would justify not drawing a bright line that would save resources. Unless such a rationale were forthcoming, the implication of endorsing this view is that no bright line would be drawn in the case of any targeted therapy or immunotherapy that promised any degree of benefit with regard to prolonging survival. To be clear, there would be nothing intrinsically unjust about paying for everything under the rubric of precision medicine that yielded any degree of medical benefit. However, another deliberator could reasonably ask whether the same would be true in every other area of medicine when individuals were faced with a terminal prognosis and some very expensive intervention could yield some marginal benefit. If that were the practice, this would have drastic economic and ethical consequences either for other non-life-threatening medical needs or for some range of non-medical social needs. From the perspective of Rawls’ notion of wide reflective equilibrium, the outcome would be unjust and disruptive of solidarity. No justice-relevant compelling reasons can be given for providing unlimited resources either to cancer care or medical therapies for patients with a terminal prognosis. Moreover, it would be socially imprudent to endorse such targeted largesse, given the scope and diversity of health care needs in the population as a whole. It would also be imprudent for each and every individual to endorse such limited largesse, given that in the real world the vast majority of us are behind a health care veil of ignorance.23

---

22 In one scoping review Paulden et al. (2015) identified nineteen such factors that would be relevant to making “value-based” decisions regarding these targeted therapies or other very expensive orphan drugs.

23 An anonymous referee pointed out two issues needing some additional commentary in this paragraph. First, early critics of Rawls contended that behind the veil of ignorance everyone thought the same way. Hence, one rational thinker was all that was needed to get the correct principles of justice. Rawls addressed that challenge is his later work when he called attention to the “burdens of judgment” and the fact of “reasonable pluralism.” These are the social and political facts that warrant an appeal to rational democratic deliberation. Very often, in matters of health care justice, there may be no one right answer. There may be several reasonable, ethically equiva-
The practical, justice-relevant implication of this attenuated democratic dialogue is that bright lines (even with a little wiggle) must be drawn through the deliberative process rather than allowing very arbitrary and very wide ragged edges to determine resource allocation decisions in cases such as our TMB case above. That sort of arbitrariness would certainly undercut solidarity. Agreeing to create these bright lines does result in “rough justice” because we know some marginal gains in life expectancy will be sacrificed, and sometimes those foregone gains will be more than marginal. Further, those sacrificed gains are attached to patients who command our empathy because they are very visible. However, those empathic sentiments must not be allowed to distort the just allocation of resources for the needs of other patients who will necessarily be invisible.

Rawls invokes the notion of a ‘veil of ignorance’ to assure impartiality in choosing principles of justice. Critics often deride the unreality of that notion. However, the veil of ignorance is perfectly real and relevant when it comes to the deliberative process that I have in mind for addressing the problem of health care rationing, whether narrowly in the context of precision medicine or more broadly. For the vast majority of us at any point in our lives we are entirely ignorant of the health-related disorders with which we might be afflicted. That provides a suitable environment for rational, objective, impartial thinking about specific health care rationing problems. Further, even if I have an early-stage serious cancer (or know that I am at greater risk for some cancer than the average person), and might be initially biased toward more funding for cancer-related health care interventions that most would regard as not being very cost-effective, I can be reminded through the deliberative process that I am still vulnerable to many other threats to my life and my health other than cancer problems. I would also be reminded through the deliberative process that there are many other people to whom I am emotionally connected who are at risk for a broad array of health problems, some of which would be life-threatening. Consequently, I would want to make with my fellow deliberators the fairest and most prudent choices possible, given that we have only limited resources and virtually unlimited health care needs. Put another way, the deliberative process need not degenerate into competing interest groups or health care tribes. Instead, we are all capable of recognizing that we are largely incapable of taking complete responsibility for meeting our health care needs; we all need to take responsibility for each other, given the uncertainty and complexity of future possible health needs.24

In conclusion, given a society committed to accepting a reasonable pluralism, it will rarely be the case for any particular rationing problem that there will be one “most just” choice that all reasonable persons would recognize. The more common situation will involve several possible choices that might all be regarded as being ‘just enough’ or non-ideally just (along with other possibilities that would not be ‘just enough’). The goal of the deliberative process would be to legitimate a choice that would be ‘just enough’ and ‘not reasonably rejectable’ by those who might have favored a different option. This is how a just solidarity is constructed in a diverse society for purposes of addressing the ethical ambiguity created by precision medicine.

To be clear, precision medicine is not a unique threat to solidarity and health care justice. The broader threat is represented by various life-prolonging technologies that are extraordinarily expensive and generally yield only marginal benefits for a substantial majority of patients. Unchecked expenditures for these technologies and these patients threaten the just allocation of health care resources elsewhere in the health care system. If solidarity and health care justice are nothing more than abstract idealizations, that threat cannot be abated. To counter that threat, the normative force of solidarity and health care justice must be institutionalized and concretized through fair and inclusive processes of rational democratic deliberation, as briefly illustrated above. Precision medicine is in many respects the scientific quintessence of the healing arts, but it is also the worst instantiation of the technological imperative run amok, generating “wicked” ethical problems that threaten the integrity and justness of the healing arts.25

---

Footnote 23 (continued)

lent options, but only one of which can ultimately be chosen as the governing policy. Second, the reviewer noted that in the paragraph I seemed to offer a resolution “unexpectedly quickly and cursorily.” In a true deliberative process addressing a complex problem of health care justice, that sort of result will not happen. It would take a long book chapter to capture all that dialogue. The reader should regard what I have written as a sort of executive summary.

Footnote 24 I (Fleck 2009) have worked out in this volume in a much more detailed fashion what a process of democratic deliberation ought to look like that is fair, reasonable, legitimate, and inclusive. In this essay I could provide only the briefest synopsis. More recently (Fleck 2022), I have addressed the complexity of the problems of distributive justice in relation to precision medicine, specifically, targeted metastatic cancer therapies.

Footnote 25 I wish to express my deepest thanks to a very patient anonymous referee who has taken the time to offer helpful suggestions on several drafts of this essay. I believe this essay is much improved as a result of those patient efforts. I need to offer one further comment. The notion of rational democratic deliberation might seem to be at this point in time a hopeless utopian delusion, given the irrational resistance in both Europe and the United States to the public health requirements for vaccination against Covid-19. I would just add that the creation and maintenance of our liberal democratic institutions and public reason has been a three-hundred-year struggle which will need to continue with the sustained efforts of dedicated democratic citizens in solidarity.
Declarations

Conflict of interest The authors declare that they have no conflict of interest.

References

Aggarwal, A., O. Ginsburg, and T. Fojo. 2014. Cancer economics, policy and politics: what informs the debate? Perspectives from the EU, Canada, and US. *Journal of Cancer Policy* 2: 1–11.

Aggarwal, A., and R. Sullivan. 2014. Affordability of cancer care in the United Kingdom—is it time to introduce user charges? *Journal of Cancer Policy* 2: 31–39.

American Cancer Society. 2020. Lifetime risk of developing or dying from cancer. https://www.cancer.org/cancer/cancer-basics/lifetime-probability-of-developing-or-dying-from-cancer.html Accessed 11 April 2021.

Bairi, K., A.G. Atanasov, M. Amrani, and S. Afqir. 2019. The arrival of predictive biomarkers for monitoring therapy response to natural compounds in cancer drug discovery. *Biomedicine and Pharmacotherapy* 109: 2492–2498.

Baldwin, K. 2019. New technologies offer the possibility of identifying cancer from a single blood draw. *American Society of Clinical Oncology*. https://www.asco.org/about-asco/press-center/news-releases/new-technologies-offer-possibility-identifying-cancer-single. Accessed 5 October 2021.

Biller-Andorno, N., and T. Zeltner. 2015. Individual responsibility and community solidarity—the Swiss health care system. *New England Journal of Medicine* 373: 2193–2197.

Bayertz, K. 1999. Four uses of ‘solidarity.’ In *Solidarity: philosophical studies in contemporary culture*, ed. K. Bayertz, 3–28. Amsterdam: Kluwer Academic Publishers.

Butler, S.A. 2012. A dialectic of cooperation and competition: Solidarity and universal health care provision. *Bioethics* 26: 351–360.

Buyx, A., and B. Prainsack. 2018. *Solidarity in biomedicine and beyond*. Cambridge, England: Cambridge University Press.

Callahan, D. 1990. *What kind of life: The limits of medical progress*. New York: Simon and Schuster.

Cancer Research UK. 2015. Cancer survival rates three times higher with early diagnosis. *Guardian*. https://www.theguardian.com/society/2015/aug/10/cancer-survival-rates-higher-earlier-diagnosis. Accessed 5 October 2021.

Carrabregu, G. 2016. Habermas on solidarity: An immanent critique. * Constellations* 23: 507–522.

Cohen, G., N. Daniels, and N. Eyal, eds. 2015. *Identified Versus Statistical Lives: An Interdisciplinary Perspective*. New York: Oxford University Press.

Court, E. 2019. Doctors who helped develop heart drug now balk at $225,000-a-year price. *Bloomberg Law*. https://news.bloomberglaw.com/health-law-and-business/doctors-who-guided-pfizer-drugs-research-balk-at-225-000-price. Accessed 5 October 2021.

Danis, M. 2018. Floating all boats: Promoting solidarity to advance social justice. *American Journal of Bioethics* 18 (10): 15–17.

Davies, B., and J. Savulescu. 2019. Solidarity and responsibility in health care. *Public Health Ethics* 12: 133–144.

Derpmann, S. 2018. Union’s inspiration: Universal health care and the essential partiality of Solidarity. *Bioethics* 32: 569–576.

Eurostat Statistics Explained. 2017. https://www.ec.europa.eu/eurostat/statistics-explained/index.php/Cancer_statistics. Accessed 5 October 2021.

Faust, H., and P. Menzel, eds. 2012. *Prevention vs. treatment: What’s the right balance?* New York: Oxford University Press.

Ferlay, J., M. Colombet, I. Soerjomataram, et al. 2018. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. *European Journal of Cancer* 103: 356–387.

Fleck, L.M. 2015. Just solidarity: the key to fair health care rationing. *Diametros* no. 43 (March): 44–54. https://doi.org/10.13153/diam.43.2015.713.

Fleck, L.M. 2022. *Distributive justice and precision medicine: ‘Wicked’ problems for democratic deliberation*. New York: Oxford University Press.

Fleck, L.M. 2009. *Just caring: Health care rationing and democratic deliberation*. New York: Oxford University Press.

Fu, M., H. Naci, C.M. Booth, et al. 2021. Real-world use of and spending on new oral targeted cancer drugs in the US, 2011–2018. *JAMA Internal Medicine* 181 (12): 1596–1604.

Gheaus, A. 2017. Solidarity, justice and unconditional access to healthcare. *Journal of Medical Ethics* 43: 177–181.

Gould, C. 2018. Solidarity and the problem of structural injustice in health care. *Bioethics* 32: 541–552.

Grens, K. 2019. The next frontier of CAR T-Cell therapy: solid tumors, *The Scientist*. https://www.the-scientist.com/features/the-next-frontier-of-car-t-cell-therapy-solid-tumors-65612. Accessed 5 October 2021.

Grisham, J. 2017. Why do immune checkpoint inhibitors work for only some people with cancer? *On Cancer*. Memorial Sloan Kettering Cancer Center. https://www.mskcc.org/blog/why-do-immune-checkpoint-inhibitors-only-work-some-people Accessed 5 October 2021.

Groot, C.A., R. Heine, M. Krol, and J. Verweij, 2020. Unequal access to newly registered cancer drugs leads to potential loss of life-years in Europe. *Cancers* 12: 2313. https://doi.org/10.3390/cancers12082313.

Grossmann, N., M. Robausch, W. Willenbacher, et al. 2020. “Magnitude of clinical benefit” of solid tumor drugs and their real-world application in the Austrian health care setting. *Journal of Cancer Policy*. https://doi.org/10.1016/j.jcpo.2020.100235.

Habermas, J. 1990. Justice and solidarity: on the discussion concerning stage 6. In *The moral domain: Essays in the ongoing discussion between philosophy and the social sciences*, ed. Thomas E. Wren, 224–251. Cambridge, MA: MIT Press.

Hellman, M.D.L., R.B. Caro, Paz-Ares, et al. 2019. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. *New England Journal of Medicine* 381: 2030–2031.

Huang, K., T. Wang, C. Chen, et al. 2021. Growth suppression in lung cancer cells harboring EGFR-C797S mutation by quercetin. *Biomolecules* 11: 1271. https://doi.org/10.3390/biom11091271.

Huff, C. 2018. MS drugs: Expensive, often lifelong, and not cost effective, *Managed Care Magazine*. https://www.managedcaremag.com/archives/2018/10/ms-drugs-expensive-often-lifelong-and-not-cost-effective. Accessed 5 October 2021.

ICGC/TCGA Pan-Cancer Analysis of Whole Genomes Consortium. 2020. Pan-cancer analysis of whole genomes. *Nature* 578 (7799): 704–714.

Janus, K., and E. Minvielle. 2017. Rethinking health care delivery: What European and United States health care systems can learn from one another. *Health Affairs*. https://doi.org/10.1377/hblog20171214.835155.

Keehan, S.P., G.A. Cuckler, J.A. Poisal, et al. 2020. National health expenditure projections, 2019–2028: Expected rebound in prices drives rising spending growth. *Health Affairs* 39: 704–714.

Keown, S. 2019. Try, try again: can a 2nd dose of CAR T-cells succeed when the first fails? *Hutch News Stories*. https://www.fredhutch.org/en/news/center-news/2019/12/repeat-dose-car-t-cells.html. Accessed 5 October 2021.
Klempner, S., D. Fabrizio, S. Bane, et al. 2020. Tumor Mutational burden as a predictive biomarker for response to immune checkpoint inhibitors: A review of current evidence. *The Oncologist* 25: e147–e159.

Leighl, N.B., S. Nirmalakumar, D.A. Ezeife, and B. Gyawali. 2021. An arm and a leg: The rising costs of cancer drugs and impact on access. ASCO Educational Book. https://doi.org/10.1200/EDBK_100028.

Mantovani, F., L. Collavin, and G. del Sal. 2019. Mutant p53 as a guardian of the cancer cell. *Cell Death and Differentiation* 26: 199–212.

Meulen, R.T. 2018. Solidarity and justice in health and social care. Cambridge England: Cambridge University Press.

Miller M. 2020. Medicare’s Private Option is Gaining Popularity, and Critics. *New York Times* (2/23). https://www.nytimes.com/2020/02/21/business/medicare-advantage-retirement.html?action=click&module=News&pgtype=Homepage. Accessed 5 October 2021.

National Cancer Institute. 2019. Immune checkpoint inhibitors. https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/checkpoint-inhibitors. Accessed 15 May 2021.

Nixon, N.A., M.B. Hannouf, and S. Verma. 2018. A review of the value of human epidermal growth factor receptor 2 (HER2)-targeted therapies in breast cancer. *European Journal of Cancer* 89: 72–81.

OECD Health Division. 2020. Addressing Challenges in Access to Oncology Medicines. https://ec.europa.eu/health/sites/default/files/policies/docs/access_ontologymedicines_rep_web_en.pdf. Accessed 15 May 2021.

Parums, D.V. 2014. Current status of targeted therapy in non-small cell lung cancer. *Drugs of Today* 50: 503–525.

Paulden, M., T. Staﬁniski, D. Menon, and C. McCabe. 2015. Value-based reimbursement decisions for orphan drugs: A scoping review and decision framework. *PharmacoEconomics* 33: 255–269.

Peters, J.W. 2005. Company’s smoking ban means off-hours too. *New York Times*. https://www.nytimes.com/2005/02/08/business/companys-smoking-ban-means-offhours-too.html. Accessed 16 May 2021.

Prasad, V. 2017a. Overestimating the beneﬁts of cancer drugs. *JAMA Oncology* 3: 1737–1738.

Prasad, V. 2017b. Do cancer drugs improve survival or quality of life? *BMJ* 359: j4528. https://doi.org/10.1136/bmj.j4528.

Rawls, John. 1993. *Political liberalism*. New York: Columbia University Press.

Raza, A. 2019. The first cell and the human costs of pursuing cancer to the last. New York: Basic Books.

Reichlin, M. 2011. The role of solidarity in social responsibility for health. *Medicine, Health Care, and Philosophy* 14: 365–370.

Reno, J. 2021. This new test can detect 50 types of cancer from a single blood draw. Healthline. https://www.healthline.com/health-news/this-new-test-can-detect-50-types-of-cancer-from-a-single-blood-draw. Accessed 15 May 2021.

Salcher-Konrad, M., and H. Naci. 2020. Unintended consequences of coverage laws targeting cancer drugs. *Journal of Law, Medicine, and Ethics* 48: 552–554.

Saltman, R.B. 2015. Health sector solidarity: A core European value but with broadly varying content. *Israel Journal of Health Policy Research* 4: 5.

Santomasso, B., C. Bachier, J. Westin, et al. 2019. The other side of CAR T-Cell therapy: Cytokine release syndrome, neurologic toxicity, and financial burden’. ASCO Educational Book 39: 433–444. https://doi.org/10.1200/EDBK_238691.

Schindler, M., M. Danis, S.D. Goold, et al. 2018. Solidarity and cost management: Swiss’ citizens’ reasons for priorities regarding health insurance coverage. *Health Expectations* 21: 858–869.

Segall, S. 2010. *Health, luck, and justice*. Princeton, NJ: Princeton University Press.

Vokinger, K.N., T.J. Hwang, T. Grischott, et al. 2020. Prices and clinical benefit of cancer drugs in the USA and Europe: A cost-benefit analysis. *Lancet Oncology* 21: 664–670.

West-Oram, P. 2018. Solidarity as a national health care strategy. *Bioethics* 32: 577–584.

Wilking, N., G. Lopes, K. Meier, et al. 2017. Can we continue to afford access to cancer treatment? *European Oncology &amp; Haematology* 13 (2): 114–119.

Workman, P., G.F. Draetta, J.H.M. Schellens, and R. Bernards. 2017. How much longer will we put up with $100,000 cancer drugs? *Cell* 168: 579–583.

Zhou, X.Q., and H.Lu. Hao. 2019. Mutant p53 in cancer therapy— the barrier or the path. *Journal of Molecular Cell Biology* 11: 293–305.

**Publisher’s Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.