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Expensive Cancer Drugs: A Comparison between the United States and the United Kingdom

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Context: This article compares the United Kingdom's and the United States' experiences with expensive cancer drugs to illustrate the challenges posed by new, extremely costly, medical technologies.

Methods: This article describes British and American coverage, access, and cost-sharing policies with regard to expensive cancer drugs and then compares the costs of eleven such drugs to British patients, American Medicare beneficiaries, and American patients purchasing the drugs in the retail market. Three questions posed by these comparisons are then examined: First, which system is fairer? In which system are cancer patients better off? Assuming that no system can sustainably provide to everyone at least some expensive cancer drugs for some clinical indications, what challenges does each system face in making these difficult determinations?

Findings: In both the British and American health care systems, not all patients who might benefit from or desire access to expensive cancer drugs have access to them. The popular characterization of the United States, where all cancer drugs are available for all to access as and when needed, and that of the British NHS, where top-down population rationing poses insurmountable obstacles to British patients' access, are far from the reality in both countries.

Conclusions: Key elements of the British system are fairer than the American system, and the British system is better structured to deal with difficult decisions about expensive end-of-life cancer drugs. Both systems face common

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ethical, financial, organizational, and priority-setting challenges in making these decisions.

Keywords: Fairness, access, cancer drugs, affordability, rationing, prioritization, priority setting.

Setting the Scene

Stories in the American media about desperate families taking desperate measures to raise money to pay for expensive medical treatments are, sadly, not uncommon. Indeed, we heard regularly in the 2008 presidential campaign about underinsured or uninsured people who were forced to mortgage their homes, drop out of school to work extra jobs, or rely on the charity of their church or community to secure specialty cancer drugs or other expensive treatments for a loved one. If anything, the frequency of such reports has increased in 2009 as advocates for health care reform bring attention to the additional stress of the current economic crisis on the ability of many Americans to secure expensive medical care (Furlow 2009).

Similarly tragic stories also appeared in 2008 in the British media, albeit with a different twist. Although in practice applied inconsistently, long-standing "rules" that keep public and private treatment separate have meant that patients who "top up" their National Health Service (NHS) care by, for example, purchasing a drug not funded by the NHS on cost-effectiveness grounds are denied the NHS care they would have received had they not bought the drug. Much of the public debate in the United Kingdom has focused on the question of such patients' continued access to NHS services. The top ups controversy has also highlighted the moral and policy challenges posed by cancer drugs that offer limited benefit, but at relatively high cost, to patients with advanced disease. Indeed, the NHS's response to the top ups controversy included a policy commitment to increase its coverage of such high-cost cancer drugs under specified conditions.

In this article, we compare the United Kingdom's and the United States' experience with expensive cancer drugs to illustrate the challenges posed by new and extremely costly medical technologies. There are no fixed criteria for determining when a cancer drug can properly be described as expensive. In this article, we use a threshold cost of treatment

for one year that is 50 percent or greater than the per capita GDP of the United Kingdom or the United States, approximately £22,500 ($36,500) and $47,000, respectively.

We begin by describing the current situation in the United Kingdom, including policy responses to the top ups issue as well as broader questions of accessibility and affordability. We then describe the current situation in the United States. In both cases, we review what is known about access to expensive cancer drugs and how this access is determined and financed. We then consider the implications of these accounts for commonplace assertions about differences between the two countries' access to the latest cancer drugs and their cancer outcomes.

Our assumptions throughout this analysis are, first, that no health care system can provide every medical intervention that offers a prospect of health benefit to everyone, all of the time. Hence, every system must confront the question of how and on what basis to deny potentially beneficial care to some people some of the time. Second, we assume that in any health care system, the wealthy can always circumvent whatever limits or rationing mechanism is in place in order to secure access to technologies that confer (or are perceived to confer) medical benefits, no matter how costly.

Historical Background for the United Kingdom

The United Kingdom's National Health Service (NHS), established in 1948, has always been, and remains, almost wholly funded from a mildly progressive general taxation system, with a global budget set every three years by the government and approved by Parliament. Access to the NHS is universal, free at the point of use (except for some copayments for services such as dentistry), and determined on the basis of medical need. In principle, therefore, the burden of financing the NHS is distributed unequally, with a bias against the rich, whereas the NHS's benefits are distributed equally to those in equal medical need. While the NHS is the main health care provider for the vast majority of the population, there also is a relatively small private health care sector (approximately 10 percent of the market) for which consumption—as in any private market—is determined on the basis of price and income (Tapay and Colombo 2004). Interestingly, the prices of drugs or services in the

private British market are often lower than the list prices in the United States (Reinhardt, Hussey, and Anderson 2004). It is also noteworthy that private care is most commonly delivered by clinicians whose main employer is the NHS but whose NHS contract allows them to practice privately as well.

The creation of the NHS enabled millions of people to gain access to care previously denied because of cost. But difficulties in keeping public and private health care consumption separate arose early on. For example, those who could afford private outpatient consultations were able to jump queues for specialty services but then be treated for free by the NHS as an inpatient. The solution to this perceived inequality in access was that for any particular episode of care, a patient was either wholly private or wholly public. "Mixing and matching" care was seen not only as potentially unfair but also as a state subsidy for private care. In the 1950s, arguments by ministerial and civil servants centered in part on the belief that to do otherwise "would set a dangerous precedent, possibly even undermining the unification of health service and starting the drift towards a two-class service" (Webster 2002, p. 69). There also were worries that without a clear demarcation between public and private care, clinicians could face a conflict of interest between their NHS and their private work. Thus, from the 1950s onward, it has been clear in the United Kingdom that medical care not covered by the NHS, including expensive cancer drugs if licensed for use, could be accessed privately but that services to support such privately obtained care—including, for example, administration of the drug and subsequent monitoring—could not be provided through the NHS.

Before bringing up to date what may seem to Americans as a classic case of denying the individual freedom that NHS types of systems must inevitably impose, we should look at how the NHS grapples with decisions about the access to and pricing of cancer drugs and how it formally—and informally—attempts to balance conflicts between individual choice and benefit and the collective good.

Access to and Pricing of Expensive Cancer Drugs in the United Kingdom

Perhaps surprisingly, the United Kingdom, along with Germany, has Europe's least restrictive pharmaceutical pricing and reimbursement

system. Following the European Union's increasingly centralized licensing process, drugs are launched in the British market at a price set by the manufacturer. It then is up to individual clinicians to make treatment decisions for individual patients, and especially for expensive drugs, it is up to the appointed commissioners who manage the local NHS budgets to pay for drugs at the list (or a lower agreed-on) price. Eventually, almost all cancer drugs become available free through the NHS at the point of service and are paid for by local NHS primary care trusts (PCTs) using taxpayers' money allocated to them by the government for all their local residents' care needs.

In a relatively few instances, for example, for drugs that are likely to have an important clinical impact in a high-priority disease area or that may result in significant savings or costs for the NHS, a central decision is made as to whether they should be made available to NHS patients. Guidance to the NHS in these instances is one of the functions of the National Institute for Health and Clinical Excellence (NICE), established in 1999 to consider the comparative clinical and cost-effectiveness of drugs in order to help the NHS decide which health technologies are good value and should be funded (Pearson and Rawlins 2005).

Central to NICE's decision making is what should be considered cost-effective. In this case, NICE refers to a cost-effectiveness range in which those drugs with an incremental cost-effectiveness ratio of more than £30,000 (~$49,000) per quality-adjusted life year (QALY) are generally considered not to be a worthwhile investment for the NHS, whereas those drugs under £20,000 (~$32,500) per QALY are. Drugs that fall in between require some other justification for acceptance. In practice, however, while the efficiency criterion of cost-effectiveness drives the NICE's decisions, the cutoff between acceptance and rejection is somewhat fuzzier, so arguments specific to the particular circumstances of certain patient groups and drugs also come to bear on decisions (McCabe, Claxton, and Culyer 2008; Rawlins and Culyer 2004).

Since its inception, more than sixty of NICE's decisions (around one-third) have pertained to cancer drugs, and its decisions have increased the use of cancer drugs and reduced the variation in their use (Richards 2006). In nearly half these evaluations, NICE recommended that the NHS pay the full cost of the drug for all patients, including Herceptin (trastuzumab) for early breast cancer and Sutent (sunitinib malate) for late-stage renal cancer, at an annual cost of more than £20,000 per patient. In 46 percent of cases, NICE recommended that the drug be

reimbursed for all licensed indications; in 28 percent of the cases, specific patient groups were identified for whom the NHS should cover the full drug costs; and in 13 percent of the cases, NICE recommended that the NHS should not pay for the drugs (Littlejohns et al. 2009). In 8 percent of the cases, uncertainty about the clinical effects led to a recommendation to adopt the drugs but was conditioned on collecting data from the field to provide the basis for a further review (Chalkidou et al. 2008). For the remaining 5 percent of the cases, industry declined to make a submission to NICE because it felt its product was unlikely to be successfully evaluated (Littlejohns et al. 2009). In this case, NICE could not make a recommendation and so it was left up to the PCTs to make decisions locally, an approach not without problems (Drummond and Mason 2009).

In instances in which patients are told that an expensive cancer drug will not be covered by the NHS, either because NICE has made a restrictive or negative recommendation or because the local Primary Care Trust has determined not to pay for the treatment (in the absence of a NICE recommendation), patients can appeal, and individual PCTs can still decide to cover the drug for them. Approximately 4,000 such individual requests for cancer drugs have been made in England so far. Depending on locality, between 65 and 90 percent of these were approved (Richards 2008). Note, though, that most of the successful appeals were for drugs not evaluated by NICE.

Individual patients can purchase expensive cancer drugs prescribed by a clinician but rejected by the NHS on the private market, often at prices lower than the U.S. list price. The drug is paid for either by private insurance or out of pocket.

In regard to supply, although neither NICE nor the Department of Health (the government department overseeing the NHS) negotiates drug prices, as a monopsonist, the NHS has considerable power over what it pays for drugs—at least in principle—and, by implication, over the drugs' cost-effectiveness. In practice, however, such power is somewhat attenuated, resulting in a tricky balancing act between competing goals: extracting maximum value for the taxpayer and patient versus the need to encourage innovation and to protect a valuable British-based industry. Traditionally, this balance between health and wealth has been achieved through a process conducted by the Pharmaceutical Price Regulation Scheme (PPRS). In effect, the PPRS sets a "fair return" on investment for pharmaceutical companies' drugs purchased by the NHS. Now, however,

new ways of reconciling sometimes competing objectives are being tried. These new ways are part of the recently enacted PPRS reforms and thus are not outside the PPRS but part of it, with NICE playing a greater role. For example, together with support from the pharmaceutical industry, flexible pricing and initiatives designed to improve patients' access to drugs are being introduced, with both measures meant to enhance access while ensuring value. Flexible pricing allows the price of a drug to be increased (or reduced) if evidence of its effectiveness grows (or declines) in practice (or a new indication of higher value is approved), and it always is subject to evaluation by NICE.

Patient access schemes, already piloted by NICE for a number of drugs like Velcade (bortezomib) for multiple myeloma (Garber and McClellan 2007), are meant to facilitate access to new drugs deemed cost-ineffective by NICE either because the benefit they confer is not high enough for their cost (from the NHS's perspective) or because of great uncertainty about their effects in the real world. Through such schemes, the NHS can get a better price deal without affecting the list price (and therefore global prices), and the NHS can encourage or mandate the collection of information on the real-world effectiveness and value of emerging technologies. NICE has used such schemes in a number of cases, especially for those showing little evidence of the comparative clinical or cost-effectiveness of new technologies. In some cases, NICE uses a system to collect evidence that then informs NICE's future (within two to three years) review of the drug's value. If the drug should fail (e.g., Velcade [bortezomib] for multiple myeloma), the manufacturer must bear the risk and reimburse the NHS. In other cases, NICE may set an upper ceiling for number of cycles (e.g., Lucentis [ranibizumab] for macular degeneration) or total cost (e.g., Tarceva [erlotinib] for small-cell lung carcinoma), with the company agreeing to cover any additional doses or cost if the individual clinician judges that the therapy should be continued.

The United Kingdom's Top Ups Controversy

Both flexible value-based pricing and patient access schemes were introduced in part as a response to high-profile cases involving expensive cancer drugs and the top ups controversy regarding NHS coverage for

care for patients going outside the system to purchase drugs or other treatments. The experience of Linda O'Boyle is perhaps the one used most often by those favoring top ups to press for change. Boyle, a sixty-four-year-old from Essex, was diagnosed with bowel cancer in 2006 and received NHS treatment, including chemotherapy, until September 2007. In an effort to prolong her life, she then paid £11,000 for an eight-week course of the drug Erbitux (cetuximab), which was not available in the NHS owing to its lack of cost-effectiveness as determined by a NICE evaluation. Boyle was subsequently denied the NHS care she ordinarily would have received if she had not purchased the drug. She died in March 2008, and her husband and local members of Parliament subsequently campaigned for the government to reconsider the top up rules.

After initially reiterating arguments against top ups—that they would be unfair and would place the NHS in the conflicted position of effectively subsiding treatment it had rejected on the grounds of cost-effectiveness—in the summer of 2008, Alan Johnson, then the secretary of state for health, appointed Professor Mike Richards, the national clinical director for cancer, to review the existing policy.

Richards was asked to take particular account of the importance of "enabling patients to have choice and personal control over their healthcare" but also "the need to uphold the founding principle of the NHS that treatment is based on clinical need, not ability to pay, and to ensure that NHS services are fair to both patients and taxpayers, a founding NHS principle still resonating with the majority of the UK public" (Appleby and Alvarez-Rosete 2005). Some people have interpreted Richards's response to his brief as approving top ups. But a closer reading of his recommendations (and the response from the Department of Health [Department of Health 2008]) suggests that although care that would have ordinarily been provided to a patient would not have been withdrawn if the patient had paid out-of-pocket for a drug, the NHS still would not pay for any care, administration, or monitoring associated with the privately purchased treatment.

Richards also addressed in part what many have seen as a consumer protection issue by recommending additional training programs for clinicians to enhance their skills in discussing treatment options with patients and new ways in which patients could be informed of the risks, benefits, and potential costs of treatments they may consider purchasing.

Finally, the review asked NICE whether it could use more flexible criteria for approving certain drugs, in order to make available drugs

that had failed its cost-effectiveness test. The review also called for investigating ways (such as flexible, value-based pricing and patient access schemes) to reduce pharmaceutical prices to bring excluded drugs within the current cost-effectiveness threshold range. In response to these recommendations, NICE has suggested that for certain patients near the end of life and for certain drugs currently deemed too expensive, it could be more flexible. In effect, NICE formalized the power of its technology appraisal committees to weight the benefits of some treatments for some patients more highly than others, thereby improving those treatments' overall cost-effectiveness. The de facto result of this change is that in the future, some expensive cancer drugs—in particular, drugs to treat small groups of patients with relatively uncommon cancers for whom no other treatment is available—are more likely to be available through the NHS.

Access to and Pricing of Expensive Cancer Drugs in the United States

As in the United Kingdom, in the United States, access to licensed expensive cancer drugs is subject to the willingness of the payer to buy them. Unlike the United Kingdom, which effectively has only one major payer—the NHS—and a small private market, the United States has multiple payers who use different standards and different processes to determine whether expensive cancer drugs should be purchased and reimbursed.

The wide variety of payers in the United States makes it difficult to characterize the access to and financing of expensive cancer drugs for American patients. Purchasing power, state laws and competition, and corporate philosophy and organizational structure all contribute to make up formularies that differentially affect access to cancer care and drugs. In addition, federal- or state-level programs may address specific needs and access issues. For example, the Breast and Cervical Cancer Prevention and Treatment Act of 2000 created a Medicaid waiver that allowed uninsured women who would otherwise be ineligible for Medicaid to gain access to treatment for breast or cervical cancer (CMS 2005a).

More is known about the access to and financing of cancer drugs by Medicare than by most other payers in the United States. Part B of Medicare covers the category of drugs (mostly cancer medications) that

are generally administered in clinical settings. For Medicare enrollees who have purchased Part B coverage (99.2 percent of all Medicare beneficiaries), Medicare is required by law to include cancer drugs that have received what is described as a "medically accepted indication." This instruction is interpreted liberally to include uses approved by the Food and Drug Administration (FDA) as well as drugs reported in peer-reviewed journals and pharmaceutical compendia to have a positive impact (Bach 2009).

The legal situation with regard to Medicare Part D coverage for medications (generally taken orally) purchased from a pharmacy is somewhat less clear but also expansive. The private plans that contract with Medicare to provide Part D benefits are required to cover all cancer drugs that were approved for use in 2006 at the time the program was implemented. Congress has since passed legislation that requires these plans as of 2010 to include all drugs for conditions that are major or life threatening, with cancer drugs cited as a prototypical example (Bach 2009). In addition, Medicare must pay for several drugs and treatments for cancer that have not been approved by the FDA. Some of these treatments, known as "off-label," cost as much as $10,000 a month. Medicare pays for these drugs based on appeals from patients and doctors who see few other possibilities for severely ill patients, as long as these are listed in what are often pharma-funded compendia (Abelson and Pollack 2009).

The addition of pharmaceutical benefits coverage (Part D) to Part B's limited coverage has resulted in payment for drugs for more than 90 percent of the United States' elderly and disabled enrolled in Medicare (Connolly and Marr 2008). But although these beneficiaries thus are now insured for expensive cancer drugs, they still do not have full financial coverage, and their out-of-pocket costs for expensive cancer drugs can still be substantial (see table 1). In the lead-up to passage of the Medicare Prescription Drug, Improvement, and Modernization Act (MMA), the U.S. Congress imposed a $400-billion budget ceiling on the new benefit in response to criticism of the program's huge price tag. In turn, this led to the inclusion of the "donut hole" in Medicare Part D's pharmaceutical benefit rules. That is, patients who have paid the Part D premium must pay an annual $295 deductible, and then Medicare pays 75 percent of their drug costs up to an annual ceiling of $2,700. Beneficiaries pay the full cost until their out-of-pocket expenditures reach $4,350[1] (the donut hole). At that point, catastrophic coverage kicks in, with low copayments for patients—the greater of $2.40 for generics and $6.00 for many other

TABLE 1
Estimated Costs to Patients of Expensive Cancer Drugs

Drug	U.K. National Health Service[a]			U.S. Medicare Part B[b]			U.S. Medicare Part D[c]			U.S. Estimated Retail Price[d]		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
Alimta (pemetrexed disodium); 2 × 500-mg inj/mo[e]	$0	$0	$0	$2,893	$5,787	$11,574	$4,931	$5,820	$7,598	$16,668	$33,336	$66,671
Avastin (bevacizumab); 14 × 4-ml (100 mg) inj/mo[e]	$16,409	$32,817	$65,635	$4,820	$9,640	$19,279	$5,284	$6,608	$9,256	$25,988	$51,975	$103,950
Erbitux (cetuximab) 20 × 100-mg inj/mo[e]	$15,361	$30,723	$61,445	$5,970	$11,940	$23,880	$5,583	$7,206	$10,453	$32,040	$64,080	$128,160
Gleevec (imatinib mesylate); 30 × 400-mg tab/mo	$0	$0	$0	N/A	N/A	N/A	$4,723	$5,404	$6,766	$12,538	$25,076	$50,151
Herceptin (trastuzumab);[e] 2 × 440-mg inj/mo	$0	$0	$0	$3,255	$6,509	$13,019	$5,014	$5,985	$7,929	$17,834	$35,668	$71,336

Continued

TABLE 1—*Continued*

Drug	U.K. National Health Service[a]			U.S. Medicare Part B[b]			U.S. Medicare Part D[c]			U.S. Estimated Retail Price[d]		
	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months	3 months	6 months	12 months
Nexavar (sorafenib tosylate); 112 × 200-mg tab/mo	$7,514	$15,028	$30,055	N/A	N/A	N/A	$4,884	$5,725	$7,408	$20,870	$41,740	$83,480
Revlimid (lenalidomide); 21 × 25-mg cap/mo	$0	$0	$0	N/A	N/A	N/A	$5,153	$6,346	$8,732	$31,502	$63,005	$126,009
Sprycel (dasatinib); 56 × 50-mg tab/mo	$11,751	$23,501	$47,003	N/A	N/A	N/A	$5,039	$6,035	$8,028	$23,326	$46,653	$93,306
Sutent (sunitinib malate); 28 × 50-mg cap/mo[f]	$0	$0	$0	N/A	N/A	N/A	$4,818	$5,678	$7,397	$16,290	$32,580	$65,161
Tarceva (erlotinib); 30 × 150-mg tab/mo	$0	$0	$0	N/A	N/A	N/A	$4,728	$5,413	$6,784	$13,490	$26,980	$53,959

Xeloda (capecitabine);[g] 120 × 500-mg tab/mo	$0	$0	$0	$1,254	$2,508	$5,016	N/A	N/A	N/A	$8,726	$17,451	$34,902

Notes: This table is intended for illustrative purposes only. Exact prices, retail or otherwise, are expected to differ based on location and various other factors. The table assumes one cycle per month for drugs with 21- to 28-day cycles, with the remainder of the calendar month devoted to recovery. In reality, some drugs have back-to-back repeating cycles, which would lead to higher out-of-pocket costs. In addition, while many of these drugs are regularly prescribed for a full year or may be taken for an extended period of time, some would likely be taken for only a few cycles before side effects became unacceptable or the patient died. Expected out-of-pocket costs would be reduced accordingly on a case-by-case basis.

[a]Drugs indicating no out-of-pocket costs to patients are covered under the NHS. Patients may purchase drugs not covered under the NHS, with a prescription, at the nationally agreed-upon British National Formulary prices (BNF 57). Government purchasers, but not individual consumers, may expect volume discounts from list prices. Patients can appeal to their PCT's exception committee against the NICE guidance, as it affects them as individuals. If the appeal is successful, the costs of the drug will be covered. However, appeals of NICE decisions are neither common nor usually successful.

[b]Part B costs are calculated per indicated interval, based on stated dose levels. The reimbursement rate for Medicare Part B is effective from October 1 through December 31, 2009. Part B patients' out-of-pocket costs are equal to 20 percent of the total physician payment. The computation assumes no supplemental coverage.

[c]Medicare Part D rates were estimated using the Medicare Options Compare tool, based on a 65- to 69-year-old in good health, zip code = 21208, using AARP Preferred Rx (a program with one of the highest enrollments). The data were accessed on September 29, 2009.

[d]Prices for Alimta, Avastin, Erbitux, Gleevec, Herceptin, Nexavar, Sprycel, Sutent, Tarceva, Tykerb, Velcade, and Xeloda were found on drugstore.com on September 29, 2009. Prices for Nexavar, Revlimid, and Sprycel were quoted from a Baltimore Walgreens drugstore on September 29, 2009. Some drugs, like Gleevec, were available from both venues. When available, drugstore.com's prices were used, as they were less expensive: about $4,200 on drugstore.com for a month's supply of Gleevec versus $4,500 through Walgreens. But some drugs were comparably priced; for example, on drugstore.com, Tarceva cost $4,497 for a month's supply of 30 pills, and at Walgreens, it cost $4,541. Bulk purchases may enable some discount from the list price. Persons without insurance who buy retail may be eligible for subsidies either through government programs or from the manufacturer directly.

[e]Several drugs are covered under both Part B and Part D. Part B requires that the drug be used as part of a physician's services, versus a normal prescription for treatment, which would be claimed under Part D. A patient would be expected to pay either B or D drug costs (separate from administering/injecting costs), but not both. In addition, cancer drugs covered under Part B, such as Xeloda, may be covered under Part D only when they are for noncancer uses, as indicated by CMS policy: "To the extent that a Part B–covered oral anti-cancer drug has no other medically accepted indication besides cancer treatment, Part D plans should not include these drugs on their formularies because of Part B coverage" (CMS 2005b).

[f]Sutent has a four-week on, two-week off cycle, so prices were estimated accordingly.

[g]Medicare Options Compare did not list information for Xeloda on its tool.

brand-name drugs, or 5 percent of the drug cost—which can be quite large for specialty (Tier 4) drugs (MedPAC 2008). Although the MMA created a set of standard benefits for Part D, private plans competing for consumers under the Medicare Advantage Program have come up with a wide variety of drug classifications, with different tiers of drugs associated with different levels of cost-sharing and deductibles.

Several studies and news reports have documented the burden that the donut hole in the Medicare pharmaceutical creates for cancer patients who do not qualify for low-income subsidies (Berenson 2008; Kaa 2007; Kim 2007; Kolata 2008; Pollack 2009; Schwartz et al. 2009; Ward et al. 2008). Cancer patients can be particularly affected because the high cost per pill may force them into the donut hole as early in the calendar year as February (Kaa 2007), no doubt a problem for individuals on a fixed income. Medicare enrollees with low incomes may be eligible for subsidies and eligibility for Medicaid, which can significantly defray drug costs (9.4 million are enrolled out of 12.5 million eligible) (Summer et al. 2009). But the creation of Part D worsened the financing of treatment for some patients who had been receiving free or subsidized drugs from pharmaceutical companies or special insurance programs. In the most heartrending examples, this meant that some Medicare beneficiaries no longer could receive the oral cancer drugs they previously had been given for free, as they were unable to afford the out-of-pocket costs but earned too much to receive needs-based assistance (Berenson 2008).

Besides stories of hardship, there also is substantial evidence, both statistical and anecdotal, that spending on expensive cancer drugs represents a difficult barrier to care, for younger as well as older cancer patients, both those with no insurance and those with inadequate insurance, who cannot afford to pay what is required, and a serious financial handicap even for those who can (Arozullah et al. 2004; Donelan 2009; Thorpe and Howard 2003; Yabroff, Warren, and Brown 2007). As a recent joint report of the Kaiser Family Foundation and American Cancer Society (ACS) notes (Schwartz et al. 2009), although the majority of cancer patients in the United States under age sixty-five are privately insured, it is impossible to determine how many of these patients face high out-of-pocket health costs.

For insured patients, the percentage of costs that they must pay varies from plan to plan and within plans by type of service. Such

coinsurance requirements are increasingly being applied to so-called Tier 4 or specialty medications, that is, expensive drugs that include a number of biologic treatments for cancer such as Herceptin (trastuzumab) and Avastin (bevacizumab). The most common coinsurance percentage for patients across all types of services in employer-sponsored PPO plans is 20 to 25 percent (Schwartz et al. 2009), and for Tier 4 medications, the estimate ranges from 20 to 33 percent (Lee and Emanuel 2008). Both the drug cost and the physicians' markup to private insurance plans can be substantial. As of 2008, approximately 86 percent of Medicare drug plans and 10 percent of private plans that included drug benefits incorporated Tier 4 coinsurance (Kolata 2008). It is not surprising, then, that news reports suggest that about 12 percent of individuals with advanced cancer—25 percent of those with incomes below $40,000—have not used the care recommended for them by medical professionals because of high cost (Szabo 2008).

Comparison of Access and Cost to Patients in the United States and the United Kingdom

Although the United Kingdom's data are somewhat better, we do not have enough information about either country to determine what percentage of cancer patients with the appropriate clinical indications are treated with expensive cancer drugs, and thus any direct comparison between the two countries on this point is not possible. Table 1 shows the costs of eleven expensive cancer drugs to British patients, to American Medicare beneficiaries, and to American patients with no drug insurance or other financial assistance who therefore must pay the full cost in the U.S. retail market.

Perhaps the most striking contrast between the two countries is that for British cancer patients, the key driver of patient costs is the NHS's coverage decision, whereas for American Medicare beneficiaries, the driver is not coverage but cost-sharing. Specifically, British cancer patients with appropriate diagnoses have no out-of-pocket costs for seven of the eleven drugs in the table. By contrast, for American Medicare beneficiaries with Part B and Part D coverage, every drug carries with it out-of-pocket costs, ranging from about $1,200 to about $24,000, depending on the duration of treatment (three to twelve months) and the

specific drug. Because these patients may well be taking several drugs, their total annual out-of-pocket drug costs are likely to be still higher, although some patients will qualify for financial assistance. At the same time, British patients receive no support from the NHS for four of the eleven cancer drugs, whereas between Parts B and D, Medicare covers all eleven.

It is not possible to estimate how many people in the United Kingdom pay the full cost of expensive cancer drugs not covered by the NHS (or go without). As already noted, about 10 percent of the British population has private health insurance that frequently includes coverage of expensive therapies, and patients without private insurance can appeal a negative NHS ruling, often successfully.

It also is not possible to estimate how many U.S. patients pay the full cost of expensive cancer drugs entirely out-of-pocket (or go without). Some of the estimated 47 million to 50 million Americans without health insurance would qualify for some sort of hardship assistance if they needed treatment with an expensive cancer drug. At the same time, some insured Americans have such limited coverage that they themselves would likely have to pay most, if not all, the costs of an expensive cancer drug. As table 1 notes, these costs range from about $8,700 to $32,000 for a three-month supply, and when twelve months of treatment is indicated, these costs can soar to more than $100,000. The out-of-pocket retail costs to British patients for expensive cancer drugs not covered by the NHS also are substantial, although they are lower than for the same drugs in the United States. For example, the cost to a patient paying out-of-pocket for a three-month supply of Avastin in the United Kingdom would be about $16,400, compared with about $26,000 in the United States.

Note that more than half the U.S. population is not represented in the table, including, significantly, those with employer-sponsored health insurance (ESI), covering more than 50 percent of the population, and those with private/non-group-health insurance (approximately 5 percent of the population). Information comparable to that for the NHS and Medicare regarding the coverage of expensive cancer drugs and related out-of-pocket costs for both ESI and individual plans is not available. Although we can safely assume that few ESI and individual plans will pay the full cost of the drugs listed in the table, little information about coverage specific to particular drugs is publicly available. Moreover, estimating the actual costs to patients would require information about

many elements of any particular plan, including copayments, coinsurance, and lifetime and annual caps. As noted earlier, at least 10 percent of private plans treat many expensive cancer drugs as Tier 4 drugs, resulting in significant out-of-pocket expenses for patients. In addition, at least 14 percent of nonelderly adults are estimated to be "underinsured"; that is, their insurance coverage does not cover the full cost of their health care needs. Many, if not most, underinsured Americans would face substantial personal financial costs if they tried to access expensive cancer drugs.

Differences and Converging Trends

Despite profound limitations in available data, it is clear that the often-depicted contrast between the United States, where all cancer drugs are supposedly available for all when needed, and the British NHS, where top-down population-level rationing decisions supposedly pose insurmountable obstacles to access for UK patients, is far from the complex reality in both countries. The bottom line is that in the British and American systems alike, all expensive cancer drugs are not accessible to all cancer patients. This fact is consistent with our basic assertion that no health care system (private or public, fragmented or unified) can provide every potentially effective medical intervention to everyone, all of the time, and it raises three basic questions. First, which system is fairer? Second, in which system are cancer patients better off? Third, assuming that at least some expensive cancer drugs for some clinical indications are medical interventions that no system can sustainably provide to everyone, what challenges does each system face in making the necessary but difficult determinations?

Fairness

Whether the practices and policies that determine access to expensive cancer drugs are ethically defensible depends on several features of the health care system, including, most notably, questions of substantive and procedural fairness. Numerous substantive criteria have been suggested for making judgments about fairness in regard to health care access and priority setting, including considerations of health utility and

cost-effectiveness (Gold 1996; Gold, Sofaer, and Siegelberg 2007; Ubel 2001; Waters 2000), unjust inequalities and systematic disadvantage (Powers and Faden 2006), need (Atkinson 1983; Brock 2002; Mooney 1987; Veatch 1999), and fair equality of opportunity (Daniels 2008). There is disagreement about how these considerations relate to one another and what prominence each should be given in specific policy contexts. At the same time, however, to be ethically acceptable, inequalities in access or in accompanying financial burdens must be defensible by appeal to these or other morally relevant, substantive considerations. For example, insofar as allocating all medical care solely by ability to pay cannot be defended by any ethically relevant consideration, conditioning access to (or the rationing of) all medical care by income or wealth is ethically unacceptable.

Substantive considerations also are important to questions of procedural fairness. Whether the process for making decisions about coverage and costs is fair depends heavily on giving people who are affected by these decisions the ethically relevant reasons that stand behind them. Also important to the fairness of the process is a meaningful opportunity for effective appeal, as well as transparency and consistency in implementing the decision criteria (Daniels 2008; Daniels and Sabin 2008).

In discussions about the ethics of health care systems, it has become cliché to say that the United States rations people and that the United Kingdom rations treatments. Although an oversimplification, in the case of expensive cancer drugs the cliché is not inapt. In the United Kingdom, all residents of England and Wales[2] with appropriate medical indications have an NHS entitlement to some expensive cancer drugs, such as Herceptin (trastuzumab) for early and advanced breast cancer and Alimta (pemetrexed) for mesothelioma, because these drugs have been approved by NICE. Other cancer drugs, such as Avastin (bevacizumab) and Erbitux (cetuximab) for metastatic colorectal cancer, that have been determined by NICE to have poor value, are available only to patients who can afford to pay privately, either through private insurance or, most often, out-of-pocket, or to those who receive an exception from their local primary care trust commissioners, following a request for funding by their clinicians. As for drugs not yet evaluated by NICE but approved for sale within the United Kingdom, the current national guidance is that it is up to local commissioners to decide whether to fund treatment.

The substantive criteria by which NICE and local commissioners make judgments about availability of expensive cancer drugs are publicly known and debated. These criteria reflect and are rooted in a system that was explicitly created to guarantee comprehensive medical care to all, thereby eliminating or minimizing inequity of access to care based on what were judged to be morally irrelevant factors such as income or geography. In practice, although access to expensive cancer drugs is not completely uniform throughout England and Wales because of variations in decision making by clinicians and local PCTs, NICE's evaluations and the universal NHS entitlement that accompanies a favorable NICE appraisal, have substantially decreased geographic variation (Department of Health 2009b).[3]

The processes used by NICE to make national coverage decisions about expensive cancer drugs also are well known and publicly debated. This is less true, however, of local and individual coverage decisions made by PCTs, owing to the variation in decision-making practices. In all cases, cancer patients who are denied treatment can appeal, and as noted earlier, if the appeal is against a PCT's decision, it is likely to be successful.

While cancer patients and families affected by an unfavorable NICE recommendation or PCT judgment may well feel that such outcomes are indefensible, from the population perspective that NICE and PCTs are entrusted with assuming, the substantive commitments of the system on which these judgments are based, in which securing universal comprehensive coverage is privileged over access to cancer drugs judged to have poor value, are plausibly ethically defensible. Moreover, despite the problems with the transparency of decision-making practices, particularly at the PCT level, the processes used to implement those commitments can plausibly be defended as, at very least, more fair than not.

By contrast, it is difficult to support similar claims for the United States. Unlike their English counterparts, American cancer patients do not share a common, universal entitlement to expensive cancer drugs, or to any drug for that matter. Whether they receive treatments like Xeloda (capecitabine) for colon cancer or Alimta (pemetrexed disodium) may be entirely contingent on whether they have health insurance that includes drug coverage that extends to these expensive treatments, whether they have the resources to pay the difference between the drug benefit and the costs of the drug, and whether they can afford to pay for the drugs

on their own. While these and most other cancer drugs are completely free to British cancer patients, it is likely that few American cancer patients have free access to expensive cancer drugs when needed. Most American cancer patients, regardless of their insurance status, must pay out-of-pocket for at least some of the cost of their cancer drugs. For some of these patients, access imposes substantial financial hardships, and in other cases, these drugs are completely out of financial reach.

Against this backdrop, it is difficult to defend the American situation with regard to expensive cancer drugs on substantive moral grounds. As best as we can determine, in the United States, the primary factors responsible for disparities in access to cancer drugs, and their related financial burdens, are having excellent health insurance and substantial personal financial resources. Unless these factors themselves are morally relevant considerations, such disparities are not distinguishable by any ethically defensible differences between those cancer patients who secure access without threatening the financial security of their families and those who do not.

Insofar as Medicare coverage and cost-sharing decisions about expensive cancer drugs are controlled by Congress, the fairness of these decisions depends in part on views about democratic legitimacy and entitlement determinations. In the American private insurance sector, it is difficult to characterize as fair the process by which coverage and cost-sharing decisions about expensive cancer drugs are made. The substantive criteria and mechanisms used to make these determinations are often neither publicly known nor debated. Although private insurance companies have appeals procedures, anecdotal evidence suggests that these appeals are frequently unsuccessful (Alltucker 2008; Miller 1998; Tyler 2008). Patients sometimes resort to litigation, but this, too, often fails to reverse a coverage decision in time for a seriously ill cancer patient.

Benefit for Cancer Patients

In addition to concerns about the fairness of the distribution of benefits and burdens to individuals in the British and American health care systems is the question of under which system cancer patients are better off. What it might mean for cancer patients to be better off is itself an open issue, in part because people differentially value the chance

to extend life, however limited, and they differentially disvalue the related burdens of treatment. If we assume that most cancer patients want expensive cancer drugs, even when they offer minimal medical benefit and can cause significant side effects, then we might assume that patients are better off in the country where a higher proportion is actually treated with these drugs. We do not have enough information about either country, however, to determine what percentage of cancer patients receive expensive cancer drugs (or the value they attach to any extra health gain they might receive), and so we cannot compare the two countries on this point. Alternatively, we might argue that patients are better off when they have guaranteed access to expensive cancer drugs and thus are able to make their own decisions about treatment trade-offs without regard to financial burdens or concerns. Here again, the data are limited. It is not possible to conclude whether, for all expensive cancer drugs, cancer patients in the United Kingdom have more or less choice than cancer patients in the United States, particularly given the paucity of information about choice for American cancer patients who do not qualify for Medicare.

Clinical outcomes such as survival and mortality rates provide alternative indicators of benefit. Although for most cancers, the gap has been narrowing between the two countries, survival rates in the United States are better than in the United Kingdom (Coleman et al. 2008; OECD 2009). But it is doubtful that access to expensive cancer drugs plays any significant role in explaining this disparity. While there are differences in the speed with which new cancer drugs are made available in the United States and the United Kingdom (Bosanquet et al. 2008), these differences do not appear to be the sole or even the primary cause of differential cancer survival rates in the two countries, as some people contend. For example, the Karolinska report published in the *Annals of Oncology* in 2007 attributes British survival rates to the "low and slow" adoption of drugs but was heavily criticized for relying on poor data and inappropriate methodology. The report attempted to explain low survival for patients diagnosed ten years ago in terms of "low usage or expenditure on cancer drugs today" (Coleman 2007, p. 1433). In the case of England, low breast cancer survival has been attributed to late diagnosis and the underuse of radiotherapy rather than the low usage of expensive anticancer drugs (Gatta et al. 2000; Sant et al. 2003). Indeed, England's recent cancer strategies pathway program, which appears to be improving cancer survival in that country, is having noteworthy success

with determinants of cancer outcomes other than expensive treatments, such as radiotherapy and screening and diagnosis programs (Rachet et al. 2009).

If American cancer patients are more likely than British cancer patients to secure expensive cancer drugs, or if they have access to the newest expensive treatments sooner, there is another, potentially more fundamental reason why any such differences are not likely to affect the two countries' differences in cancer survival or mortality rates. Many expensive cancer drugs do not add enough survival time to enough people to significantly affect overall cancer mortality rates.

Common Challenges in Making Difficult Determinations about Expensive Cancer Drugs

In the United Kingdom, the newly framed NHS Constitution reiterates the 1948 promise that the NHS will provide a "comprehensive service" to patients. It also, for the first time, explicitly states that what constitutes comprehensiveness is subject to constraints. In particular, patients have "a right to drugs and treatments that have been recommended by NICE for use in the NHS, if your doctor says they are clinically appropriate for you" (Department of Health 2009a). For treatments for which no NICE guidance exists, local NHS decisions on funding should be made "rationally following a proper consideration of the evidence." Furthermore, even if a doctor considers a nonfunded treatment to be clinically appropriate, the constitution states only that patients have a right to an explanation of the decision not to fund.

By contrast, in the United States, health insurance is not universal; there are many payers and thus decision makers regarding coverage; there is no national structure for determining either the clinical or the cost-effectiveness of expensive cancer drugs; there is little public acceptance of the need to limit the purchasing of and access to health care treatments; and there is continued resistance to the prospect of centralized, public-sector decision making about health care (Morone 1992). As Lee and Emanuel point out, the current American structure cannot distinguish between Avastin (bevacizumab), which slows the progression of breast cancer but does not appear to improve survival, and Herceptin (trastuzumab), which can achieve a cure rate of between 4 and 6 percent. In many health plans, both drugs are treated as Tier 4 medications, with

the same coinsurance rates and thus the same financial barriers to access (Lee and Emanuel 2008). By contrast, Avastin is not available through the NHS but Herceptin is, precisely because of this documented difference in health benefit. Thus it would seem that the United Kingdom is organizationally, structurally, culturally, and politically better suited than the United States to make decisions about which cancer drugs should be made available to all clinically relevant cancer patients.

In general, this observation seems correct. The intent in the United Kingdom is that what the NHS provides will be driven by what it considers to be cost-effective; if an expensive cancer drug does not meet that test, it will not be funded. While this intent establishes the backdrop for a consistent and arguably equitable approach across the NHS, as the debate about top ups—and in particular NICE's response to the Richards's review—revealed, what is and is not cost-effective is not merely a technical decision but requires judgments to be made about the value of life and about the role of competing or additional criteria that might be applied to decisions to fund treatments. Moreover, there are more similarities, and more common challenges, between the two countries than might appear to be the case.

As the national response to both Richards's review of top ups and NICE's guidance on end-of-life treatments (NICE 2008) illustrate, national policymaking plays a much greater role with respect to these difficult decisions in the United Kingdom than in the United States. As we have discussed, however, decisions and judgments concerning access also are made at local levels. Only about 1.5 percent of the total NHS budget (and about 10 percent of the drug budget) is attributable to positive national—NICE—decisions to adopt new technologies. As already noted, only positive (access-enhancing) NICE guidance is mandatory (in requiring that the needed funding be made available), whereas restrictive recommendations can be challenged and overturned by PCTs and prescribing clinicians on a case-by-case basis. Similarly, in the public programs in the United States, national-level decisions are made by Medicare (national coverage determinations), and state-level decisions are made by Medicaid. As is the case in England, such central decisions do not cover all services. For the majority of cases, Medicare delegates the purchasing decisions to the fiscal intermediaries that actually pay the bills. Once again, local providers and individual clinicians and their patients play a crucial role in deciding the final course of treatment, which also is true in the private-sector insurance market.

Finally, the top ups debate illustrates just how difficult it is in any system to work through the ethical and political challenges that surround the emotionally difficult question of what should be provided to cancer patients who are gravely ill and at the end of their medical ropes. While some expensive cancer drugs are not targeted to patient groups of this description, those that are, like Erbitux (cetuximab) sought by Linda O'Boyle for her end-stage bowel cancer, may offer the prospect of extending life by only weeks and months. Moreover, such drugs can be accompanied by severe side effects and the real possibility that life will be foreshortened rather than extended. Indeed, a recent national inquiry in the United Kingdom into chemotherapy near the end of life showed that in 27 percent of cases, systemic anticancer treatment actually caused or hastened death (Mort et al. 2008). These sobering findings return us to the difficult question of what it would mean for cancer patients to be better off. As much if not more than in any clinical context, the tragic trade-offs involved in the treatment decisions facing gravely ill cancer patients engage deeply held and deeply personal values. They also evoke different responses from the public about how moral values like compassion and respect for those at the end of life should be balanced against obligations to others in less dire circumstances who are more likely to benefit clinically from medical services (Kasemsup et al. 2008; NICE 2006; Nord 1993, 2005; Ubel, Arnold, and Caplan 1993).

Nowhere are these trade-offs more difficult than with regard to expensive cancer drugs. On the one hand, even the United Kingdom, with its successful track record of making difficult coverage decisions, is adjusting its practices in response to end-of-life cancer drugs. Oregon's Health Plan Plus, the only state Medicaid program with an explicit waiver permitting such trade-off considerations, is in the process of revising its coverage guidance with regard to end-of-life cancer drugs, prompted in part by a case in which a patient was denied coverage for Tarceva (erlotinib) (Associated Press 2008). On the other hand, no health care system can sustain the costs of universal access to all expensive cancer drugs. A recent estimate projects that if all 550,000 patients who die of cancer each year in the United States were treated with a drug that extended their lives by one year, at a cost extrapolated from the price tag of $80,000 for the 1.2 months of additional survival attributed to Erbitux (cetuximab), approximately $440 billion would be spent each year—but without curing anyone (Fojo and Grady 2009).

Regardless of what social judgments are ultimately reached about which cancer drugs should be made available for all, both the British and U.S. systems need, at minimum, to gather the best possible data about the impact of these drugs and alternative management options on the lives and well-being of patients and make this information easily accessible. Without such information, the difficult decisions facing patients and their families and physicians can be made even more wrenching. These decisions may be choices from a menu of available services provided by the NHS in the United Kingdom or from a public or private insurer in the United States. In both systems, it is likely that some expensive cancer drugs, particularly those that neither change survival nor clearly improve quality of life, will remain or become largely or exclusively available through out-of-pocket payment only, in which case helping patients and their families understand what is at stake in pursuing such drugs is ethically paramount.

Conclusion

At least with regard to expensive cancer drugs, a common depiction of the differences between the United States and the United Kingdom, in which American patients have easy access to the most expensive treatments in the world, whereas British patients face major obstacles in access because of top-down rationing controls, is overblown (Donaldson and Ruta 2005; Feachem et al. 2002). While we do not have available the data to directly compare access in both countries, it is clear that expensive cancer drugs are not available to some cancer patients in both the United States and the United Kingdom. Although key elements of the British system are fairer than the American system and the British system is better structured to deal explicitly with difficult decisions about very expensive end-of-life cancer drugs, both systems face common ethical and organizational challenges in making these decisions.

Endnotes

1. Since the establishment of the Part D benefit, approximately 6.4 million low-income people who are elderly or disabled ("dual eligibles") have been moved from Medicaid into the Medicare drug benefit program. Although state governments can legally negotiate prices for drugs with the pharmaceutical companies, Medicare is prevented by law from negotiating prices under its Part D program. As a result, Medicare drug prices are approximately 30 percent higher than

state-level Medicaid prices. However, this difference is paid by the Medicare program and not by the individual beneficiaries (Wilson 2009).

2. NICE recommendations apply to England and Wales only, although Scotland also operates a NICE-type review system (which tends to reach similar decisions), and Northern Ireland's NHS has recently started to accept NICE's recommendations.
3. For example, as a result of NICE guidance, the use of cancer drugs increased overall uptake by almost 50 percent and reduced variation from threefold to eightfold to twofold to threefold across England and Wales, compared with a comparable basket of cancer drugs not evaluated by NICE (Department of Health 2009b).

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