Cost Sharing in Insurance Coverage for Precision Medicine[*]

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Introduction

Many medicines (and other treatments) work well for some otherwise apparently similar patients but not others. One of the factors known to determine effectiveness of a treatment is the genetic makeup of the patient or the disease. While physicians for centuries have honed the skill of determining which patients are good candidates for which treatments, the advent of "precision medicine" adds a tool in the form of a genetic test to predict effectiveness (or its absence) in a treatment regimen. The main advantage of such a test is avoiding the cost, side effects, and false hope for those for whom the treatment is unlikely to work, while at the same time reassuring those willing to go through the treatment that they will ultimately benefit. The promise is that testing may both lower total spending (on the specific treatment whose effectiveness can now be predicted) and improve health outcomes by avoiding specific treatment side effects for those for whom it would have been ineffective. But is cost reduction and outcome improvements a reason for generous insurance coverage of tests? More specifically, what is the optimal pattern of insurance coverage for tests and related treatments?

Some insurance coverage is now near universal in the United States but insurance does not fully cover everything a physician or patient might think useful. Coverage is incomplete, with sometimes substantial patient cost sharing (as high deductibles, coinsurance, or copayments), both to avoid insurer administrative cost, and to inhibit inefficient stimulation to low or no-value use. Coverage may also wholly exclude some products and services judged experimental or overpriced. In this paper, I will outline some intentionally simple theoretical models of the ideal role of insurance in such settings with

testing and the specific treatment where effectiveness is predicted by the test. I will then contrast those theoretical prescriptions with what appears to be current practice in public and private insurance coverage.

Coverage of the specific treatment will not usually be a major issue, though proportional cost sharing of specialty drugs can add up, and high deductibles usually apply to all tests and treatments. However coverage of testing will be an interesting question, in part because some testing is still experimental, some insurances do not cover purely diagnostic tests at all, and many insurances deductibles (including the most popular plans on exchanges) will leave tests of those not yet involved with expensive care uncovered. Coverage decisions involve both the binary decision whether to cover a test and/or treatment at all (presumably in part as a function of evidence on cost effectiveness), and the continuous question of what level of positive cost sharing to impose, given that there is to be some coverage some of the time. The pricing of tests, the alternatives to testing, and the effect of testing on the pricing of treatment will all be important.

An Important digression.

We will explore in detail later in the paper the pricing of test and treatment when either or both markets are not competitive (as opposed to resulting in P=MC). However, we should note here that it is very likely that the price of the treatment, especially if it is a drug treatment under patent protection and/or FDA exclusion, is likely to exceed marginal cost by a wide margin. This means that if we use price rather than marginal cost in the benchmark model, we are much more likely to find the test is "efficiency" improving from an insurer or

consumer perspective because it helps to avoid a treatment which, in addition to possible side effects, carries a very high *price* offset. However, this saving is not true saving from a societal welfare perspective because (at least in the short run and without more complexity) the financial benefit from spending on precision medicine to the insurer or the patient substantially overstates the benefit to society since the avoided price is well above the value of the resources saved. We will tussle with the issue of whether the buyer perspective on "costs" or the societal perspective defines optimality toward the end of the paper, but it is important here to note that pricing of drugs above marginal cost can engender a significant overuse of precision medicines and precision medicine tests even for treatments with small side effects, while overpricing of proprietary genetic tests can lead to underuse.

Heterogeneity

In the general theory of optimal coinsurance, the key determinant of the level of cost sharing, if it is to take on a value between zero and one, is the shape of distribution of marginal benefits (otherwise known as the demand curve). If patients are identical, with identical marginal benefits from care at any quantity of care and identical disutility from side effects of testing (so there are perfectly horizontal demand curves for testing and treatment for everyone at risk), and if the population at risk can be defined and limited precisely, we either get optimal coverage being 100% or zero (Pauly, 2015). We will first treat that case, equivalently one of a representative person or a world of identicals, before introducing heterogeneity.

One possibility is that there are indicators that can be detected by patient or physician

which help to predict what the test result would be. Indicators might be family history, presentation of symptoms, uninsurable costs, or other information. Depending on the level of these indicators, the expected net benefit of the test plus treatment could be high or low—there could be an array of values of net benefits (before considering the cost of testing). The distribution of this array could take many forms, from highly variable (elastic) to near uniform (inelastic). If insurers or other external planners could also obtain complete information about these levels, the test would still ideally be free of out of pocket cost for those with favorable values, would be conditional on those values, and so would not be covered at all for those with less favorable values.

Then one need for cost sharing greater than zero but less than one would arise if the third party could not obtain this information accurately—if physicians or patients would neglect to mention or lie about these indicators, permitting someone with expected benefits less than cost to go on to test and/or treatment. This information asymmetry would then create moral hazard, and positive cost sharing could in principle lead low expected benefit patients to select out of the test plus treatment regimen (Finkelstein 2014) The role of cost sharing (as in the classic case) would be to persuade those with low net benefits to self- select out of the opportunity for testing when it has benefits worth less than the cost. However, here we assume that the insurer is provided by physicians with all the clinical information they know, while patients retain private information on the value they place on health outcomes (e.g., as measured by QALYs).

With that assumption, it is variation in the monetary value attached to expected outcomes that can generate negatively sloped demand curves. These are known by the

patient-consumer, but not by the insurer. (Ideally, the physician as perfect agent should know them too). The conventional Quality Adjusted Life Years (QALY) measure already assumes away differences across subjects in the value of length of life (from successful treatment) versus quality of life (from treatment side effects), but there is considerable reason to believe that the monetary valuation of a QALY varies across people, based on both income and tastes. It is this variation that will be our primary focus as a rationale for optimal insurance to contain partial cost sharing.

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The cases just discussed furnish the primary and most consequential reason for "interior" cost sharing of tests or treatments in precision medicine, but there are some other possible rationales. If the cost of either test or treatment is very low, the administrative expense of paying claims may not justify the benefit of a tiny reduction in risk. If the plan has standard coinsurance rates that it applies across the board to categories of clinical services in the interest of administrative simplicity, it may choose to apply them rather than make coverage even more complex than it really is. We also abstract at this point from the problems raised by Filipova-Neumann and Hoy (2014) that a test may change subsequent incentives to engage in preventive behaviors (like monitoring through other tests), but we will consider this later. If patients underestimate the benefits of tests or treatment, there may be a case for value based cost sharing (Pauly and Blavin 2008)

Situations and solutions.

While positive cost sharing can improve efficiency by reducing moral hazard in the heterogeneous- hidden information case, the extent to which it will do so depends on how

responsive demand is to such charges. The classic optimal insurance proposition is that, the more responsive is use to insurance coverage, the higher the ideal level of cost sharing. We will show that this proposition still applies to genetic and genomic testing, but it is more complicated than usual.

This proposition becomes more complex because of interrelated demands such as we have here— design needs to take into account both price responsiveness of demand for tests and price responsiveness of demand for treatment. But one baseline finding is that if neither testing nor treatment responded to cost sharing and the package has net benefit greater than the threshold value, there would be no point in modest cost sharing—just make care free. Later we will see what empirical evidence we have on this question.

Insurance and pricing.

Often the seller of test or treatment has patent protection or other source of market exclusivity and is inclined to charge the monopoly price (which of course can much exceed marginal cost). What are the issues in optimal insurance design when either or both markets are not competitive?

There are three possible (non-competitive) situations here with respect to IP protection: (1) both test and treatment are patented; (2) testing is competitive but treatment is monopolized; (3) testing is monopolized but treatment is competitive. In case (1) there is also the issue of whether the same firm holds both patients.

If either the test or the treatment is monopolized alone, the equilibrium total price will be the same, since the monopoly rent can be collected at either stage of the production process, ignoring game theory issues. Adding monopoly control of one component when the firm already controls the other component will not add to profits since the monopoly price can only be collected once. If the firms are separate, the outcome is ambiguous and depends on bargaining.

The profit maximizing combination price for test and treatment when sold by a single firm is thus different from that if the two monopoly firms are separate. Compared to the absence of a test, the price of a treatment will increase when the test becomes available because its marginal effectiveness will increase. For example, if there is a 50-50 chance the treatment will work but the test picks out the half of the population where it will work, the treatment price will at least double (Pauly 2009). This increase in markup will also increase the bias in favor of testing as noted above. There will also be an addition to the total cost to reflect the ability to avoid side effects of useless treatment for those who test negative. Compared to the price of a single firm monopolizing both test and treatment, the price under bilateral monopoly will be higher unless the seller of the treatment subsidizes the price of the test.

How do these pricing considerations feed back into the design of cost sharing in insurance, especially if prices sometimes vary?

The most important consideration here is the proof by Gaynor, Haas-Wilson, and Vogt (2000) that consumers cannot be made better off by monopoly pricing of insured

services if insurance markets are competitive. While prices higher than marginal cost will discourage the use of care under a given level of proportional coinsurance, competitive firms will set coinsurance rates with competitive pricing that always make consumers better off than under "ideal" coinsurance with monopoly pricing (and higher benefit payouts). As a general conclusion, the dollar amount of cost sharing will be higher under monopoly and may discourage both test and treatment, even with constant proportional coinsurance. We cannot predict the direction of the coinsurance percentage because the higher financial risk may cause it to fall just as the higher price may cause it to rise.

The other issue is whether monopoly pricing may make the entire therapeutic approach not cost effective from an insurer perspective (who must pay the price charged, not the marginal cost). The answer seems clearly affirmative and it is unclear if there is an obvious work-around this overpricing.

Adverse selection.

Regulation now forbids insurers from charging different premiums for the same nominal coverage except on the basis of age and location. Hence the ability of secret test results to contribute to adverse selection is severely constrained especially by ex post risk transfers. But there is nothing to prevent variation in coverage if there is interaction between test results and the amount or form of treatment.

The insurer will most want to retain for treatment patients whose test results suggest easy cases for high value treatment—for example, the future regimen will be unusually short, cheap, and effective. However, there will usually not be an opportunity to switch coverage

between test and treatment. If there is, the prediction from the usual selection model is that the insurer will set higher coinsurance to attract the better risk if the risk transfers are imperfect. But we do not believe this will be a serious issue.

Current Patterns of Prices and Coverage for Genetic Tests and Related Treatments

There is considerable variation across clinical conditions and types of insurance coverage - both the gross prices paid for genetic tests and genetic counseling, and for the prices of treatments whose selection depends on test results. In this discussion, I will focus primarily on tests and treatments for cancer, but will also comment on some broader patterns.

Pricing of genetic tests have usually been dropping as the technology for genetic tests has become quicker and more accurate. The price of a test obviously depends both on what genetic variation is being explored and how extensive a description of the genome in terms of genetic variants is sought. Simpler genetic tests can now be obtained for as little as $200-500 for common tests targeted at common parts of the genome up into thousands of dollars for tests for all variants and all modifications ("med tech language").

In addition to tests per se, often genetic counseling is either required or useful. The cost of counseling has not been falling and generally exceeds $200 for a single test for a single treatment. The prices of treatments also vary greatly, depending on type and payer. For cancer, generally a treatment whose selection and use might be determined to be a test is in the (wide) range of $50,000 to $500,000, although some oral (non-insured) treatments sell for less depending on patents and FDA exclusions. The more restrictive intellectual property protection and the fewer close substitutes available, the higher the price.

Both the maximum reimbursed and the willingness to restrict use varies across insurers. Private sector insurers have the ability both to negotiate the prices for tests, counseling, and treatments, and to refuse to cover except on favorable terms. Some Medicaid managed care carriers also have this process. Traditional Medicare, in contrast, cannot negotiate prices for Part D drugs, can only set administrative prices for Part B drugs, and is required to cover all FDA approved drugs when they are clinically appropriate. It has somewhat more flexibility in coverage of genetic tests, and different carriers, as we shall show, seem to have different policies as to which they will cover and how. Part D (oral drugs) are subject to Part D cost sharing. Part B specialty drugs in medicine can be subject to coinsurance (and in Medicare Advantage plans as well), usually at 20-30% if it is required. Most beneficiaries buy Medigap coverage to offset patient cost sharing.

Private insurers usually cover genetic tests under the same cost sharing provisions (deductibles and coinsurance) as they apply to other tests. Thus cost sharing can vary across carriers and across employer customers within insurers. If genetic tests are designated clinical laboratory tests, they must be covered in full, but this does not cover tests used for a screening or prevention.

There is some consistency in coverage patterns. The ACA requires zero coinsurance for BRAC tests (two genes only) for women with breast cancer for testing and counseling. The more common genetic tests (e.g., for Lynch Syndrome in colon cancer) are generally covered, though cost sharing may still vary based on overall cost sharing provisions in a policy. More rare and more experimental tests are subject to enormous variation, from full coverage (e.g., as first of a trial) to no coverage at all for a test deemed experimental by the insurers. Beyond

these obvious cases, there has been considerable variation in coverage of testing across insurers and over time.

There have been a few surveys of insurers asking about their testing coverage policy. Results generally show that in the 2000-2010 decade, coverage generally became more available for tests that entered routine clinical use. A survey in 2013 by Graf et al found that 77% of large insurers indicated coverage of at least one genetic test. A 2016 review sponsored by the Commonwealth Fund of tests for women found 15% (of 109 insurers) excluded coverage of genetic tests not required by law. We examined more recent data on coverage (Table 1) and found similar patterns of coverage in principle for tests accepted as clinically useful. As indicated, there all large insurers (except for Medicare) cover genetic testing in general. But as the table shows, coverage for specific tests is irregular. In addition websites tell us that the amount of cost sharing varies with policy cost sharing provisions (deductibles and coinsurance) which themselves vary widely; for this reason they do not give an average amount of cost sharing. We explored some large claims data bases but the frequency of genetic tests is so low that it was not efficient to gather cost sharing information from that source. Over time, as more genetic tests have been clinically linked to therapy with specific drugs, Medicare coverage has become more extensive (Medicare.gov, 2016). There is apparently still some variation across carriers, but most carriers now follow the "Palmetto" list of approved genetic and genomic tests. Medicaid coverage is more variable across state programs, with explicit coverage specification often not publically accessible.

The ACA required that BRCA-1 and BRCA-2 tests and counseling be covered in full, but that is virtually the only regulatory regularity (Kaiser Foundation, 2015). Clinical opinion affects

coverage dramatically; if a large number of physicians want to run a test it will end up being covered.

Insurers explain their determination of coverage by appeal to the concept of "medical necessity." One large insurer (CIGNA, 2017) defines "medical necessity" in the context of genetic tests as having three requirements:

1) The test is FDA approved and/or performed in a CLIA-approved lab.

2) The test is medically necessary for the diagnoses indicate

3) Results of the test will directly impact clinical decisionmaking

However, different insurers have different interpretations of these criteria (especially the second one). In some cases, as in the case of testing for BRCA, there is "a clear algorithm for whether or not to test {for BRCA mutations}," and sometimes testing is required by the FDA for use of a treatment, but in other cases pathways and protocols are unclear.

Pricing of genetic tests have usually been dropping as the technology for genetic tests has become quicker and more accurate. The price of a test obviously depends both on what genetic variation is being explored and how extensive a description of the genome in terms of genetic variants is sought. Simpler genetic tests can now be obtained for as little as $200-500 for common tests targeted at common parts of the genome, up into thousands of dollars for tests for all variants and all modifications. Interestingly, as genetic test prices have fallen, the willingness of insurers to cover them has risen—an example yet again of the vacuity of the concept of medical necessity (Ho, 2017). In addition to tests per se, often genetic counseling is

either required or useful. The price of counseling has not been falling. Some insurers require genetic counseling before approving testing or treatment (CIGNA, 2017)

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When the level of coverage is mentioned on private insurer websites, it is linked to the overall pattern of cost sharing for diagnostic tests in the insurance policy, whatever that might be. Those levels of coinsurance vary fairly widely over a range from zero to 30% coinsurance, but expenses also are subject to deductibles (eg, in a high deductible health plan). Even less is known about the coverage of genetic counseling (except for BRAC for breast and ovarian

cancers where coverage with no cost sharing for those judged to be at elevated risk is required by law). Some insurers require counseling before a genetic test will be approved using managerial limits rather than cost sharing to constrain testing of lower clinical value.

There is no information on the demand elasticity for genetic tests or counseling. The demand elasticity for cancer treatment has been estimated to be in the range of -0.01 to about -0.2. The demand elasticity for drugs in general is said to range from 0.2 to 0.6. Coinsurance for specialized cancer drugs is common in Medicare Advantage and part B plans unless the person has purchased Medigap insurance. Clinicians also provide examples of patients who declined genetic tests that were not well-covered.

The patterns of coverage of specialty drugs, already noted to involve percentage coinsurance and high out-of-pocket costs relative to income for those receiving multiple treatments with experimental agent appears, to have little stated economic rationale. Insurers explain its purpose is to "save money" but if it does not affect use its only result is to expose patients to financial risk, sometimes substantial.

Estimates of demand elasticity for specialty drugs also cover the range from 0.01 to 0.2 – a wide range but one consistent with low demand elasticity (as deductibles or copayments). The theory of optimal coinsurance suggest strongly that in such cases, high cost sharing is not optimal. Explanations of insurer behavior in imposing high cost sharing in a desire for higher profits or lower premiums are quite unsatisfactory, because such provisions make insurance unattractive thus reduce demand. Higher cost sharing may be a risk selection device, required precisely to discourage cancer patients from enrolling because their higher risk is not

adequately offset by risk adjustment payments. The inefficiencies from well known selection in Medigap insurance may also play a role in offsetting the effects of Medicare cost sharing, and diminishing any cost containment effects of Medicare cost sharing in curtailing moral hazard.

Relationship to our Analysis

Our theoretical analysis generally supports the view that current coverage of both tests and treatment is too low.

The ultimate argument in favor of coverage with lower cost sharing for tests and treatment, in either sector, must be based on cost and effectiveness results. If the treatment, and therefore coverage of them, can be shown to generate high net value, employees can ensure profits by offsetting better benefits and Medicare and Medicaid can enhance social value in a way that can be demonstrated to taxpayers as a preferred goal to cost containment per se. The empirical work needed to document demand elasticity and marginal clinical effectiveness relative to cost of precision medicine remains to be done, as does analysis of the pricing choices in the face of government induced distortions through the patient system and FDA grants of exclusivity. But these goals can in principle be accomplished and result in some lives saved for moderate spending.

Table 1

Website Coverage Information: 30 Large Private Insurers*

	Genetic Testing	Genetic Counseling	BRCA 12	Oncotype Dx	Lynch syndrome
Covered	30	26	27	25	24

Not covered	0	0	0	2	0
Not mentioned	0	4	3	3	6

*Enrollment ≥ 2 million persons

Some Simple Theory

We now provide a brief sketch of the theoretical possibilities for cost and health outcomes with and without genetic testing being possible. This discussion will characterize situations in which the use of testing is or is not undertaken in and efficient end-state outcome. It will also describe the potential changes in patient behavior from a setting when no testing is available. Many scenarios are possible in theory, but some of them will be ruled out for institutional reasons. For example, in many situations FDA regulations rule out the use of a drug treatment unless testing is first done.

Notation and description:

π = probability of being in high risk population

p = probability of genetic mutation, given a person is high risk

Let:

B = voluntary increase in marginal benefits from successful treatment

$$=\frac{(\Delta QALYS)(VQALY)}{\Delta T}$$

Commented [MP2]: move this up; it is the denominator of the fraction above

(uniform)

(If p = illness probability conditional on genetic defect and treatment is 100% effective, this is p(-QALYS))

L = side effects of treatment $-\frac{(\Delta QALYS)(VQALY)}{\Delta T}$

Commented [MP3]: extend line under VQALY

$P_t = C_t$ = price or marginal cost of specific treatment

$P_g = C_g$ = price or marginal cost of genetic test plus counseling

C_f =marginal cost of treatment for future illness for patient with positive result (present discounted value)

Before the test exists, two behaviors are possible (in the world of identicals):

Case A

(1) $p(B+C_f) - L > P_t \rightarrow$ cover treatment and expect all to be treated

Case B

(2) $p(B+C_f) - L < P_t \rightarrow$ do not cover treatment and expect none to be treated

When the test becomes available, the marginal conditions are:

Cover test and treatment if

(3) $p(B+C_f - L) > P_g + pP_t$

and

(4) $(1-p)\ P_t+L > P_g$

In case A, if (4) holds, condition (3) will hold as well. Since the treatment is chosen even when there is a "cost" of treating and causing side effects for those who do not test positive, it must be optimal to treat if it becomes optimal to test, that is, if the avoided cost and side effects for those who do not test positive are greater than the price of the test.

In case B, it is optimal to cover test and treatment if conditions (3) and (4) hold. But now condition (4) may hold (given treatment, it is optimal to test) but condition (3) may not. This can either happen because the treatment does not provide net benefit for those who test positive or the treatment does provide net benefit but that benefit is not large enough to cover the cost of the test.

What is the impact of availability of the test on treatment volume and total cost? In case A, treatment volume falls as the test winnows out those who do not test positive and otherwise would incur treatment cost. Total cost will fall if the expected cost savings from not treating those who do not test positive exceeds the cost of the test, but costs need not fall even if treatment volume falls if the value of avoided side effects is large and that test is expensive.

Treatment volume rises in case of risks in Case B if the two conditions hold, because the test avoids the unnecessary disutility and treatment cost for those who would not benefit and that will clear the way for those who would benefit to use the treatment. However, if either of the marginal conditions does not hold (the treatment is not worth it to those who test positive or the test costs more than the avoided adverse consequences for those who would not test

positive), then the availability of the test will not affect the optimal outcome: it should still be no treatment along with no testing.

In these cases, what should be the optimal level of insurance coverage?

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1) If (a) testing provides more benefits (in terms of avoided cost of treatment and the value of avoided side effects of treatment) than its price and (b) the combination of testing and treatment provide more benefits (in terms of net QALYs gained and avoided future treatment cost) than the sum of the price of testing and the expected price of treating those who test positive, then both testing and treatment should be fully covered. Those for whom the expected side effects of treatment (e.g., prophylactic colectomy) outweigh the benefits will not opt for testing and treatment even at a zero user price.
2) Treatment should be fully covered but not testing If condition (a) does not hold but the benefits from treatment in terms of expected net QALYs gained from treating all— expected value of QALYs gained from treatment plus avoided future treatment costs from those who would have tested positive minus QALYs lost from side effect of treating all — is greater than the price of treatment.

   If both (a) and (b) do not hold, neither test nor treatment should be covered.

Going From Homogeneity to Heterogeneity

If consumers differ in the values they place on QALYs but, based on are identical in terms of expected clinical outcomes and financial risk aversion, there can be variation in the cost effectiveness of treatment and testing, or treatment alone, around a mean measure of net

benefits per person (Value of net QALYs gained minus incremental spending on treatment and testing). The cost effectiveness ratio for alternative strategies combined with the shape of the distribution of these values will determine whether there should be insurance with partial cost sharing. In what follows we provide both some illustrative hypothetical examples of different possible scenarios and insurance coverages and then discuss ideal insurance coverage from some examples of genomic testing to determine the effectiveness of treatment. To focus on the effect of testing, we assume that insurance coverage of the specific and expected future treatments I either 100% or zero, and consider positive cost sharing for testing and counseling. We first present two polar case examples of the cost impact of that availability (Tables 2 and 3).

These two numerical examples indicate that the potential for genetic testing to lower cost depends on the frequency in the population at risk of the condition the test will detect. If the condition is rare but takeup of the treatment is high, the test will reduce costs because it will eliminate expensive treatment of no benefit. Conversely, if the condition is common but the takeup of the treatment is low (because of fear of side effects), testing may lower cost if the alternative to treatment is costly future care. In these dominance cases, full coverage of testing will be optimal. In both cases testing will be cost reducing if the price of testing is low relative to the (net-of-future-costs) price of treatment. But there can be cases in which testing adds to cost yet improves outcomes. Then the issue is the magnitude of the improvement in outcomes (net of any side effects) and the value attached to that improvement. These are the situations in which cost effectiveness analysis is relevant as well as the threshold value attached to health outcomes. If it is high, full coverage for testing may be optimal, and if it varies across the population at risk partial cost sharing will be ideal.

Next, to estimate the net change in utility from raising cost sharing from zero to some positive number (such as 0.3) we need to calculate two effects of the change. One effect is that consumers are exposed to greater financial risk because their out of pocket payment now becomes positive. The value of that out-of-pocket payment for this high risk population is the volume of tests (compared to zero cost sharing) times the out of pocket percentage. The risk premium that comes from the risk of incurring part of the cost of the test is some proportion of this amount. One way to approximate that additional willingness to pay to avoid the risk of having to pay the designated amount out of pocket is to observe the marginal loading on insurance at which many are willing to buy coverage. We assume that the marginal insurance buyer purchases individual insurance with a loading of 33%.

The other component is the marginal reduction in the welfare cost of moral hazard associated with this change in insurance coverage. In terms of Figure 1, where the demand curve is the (net) marginal value of testing, it is the rectangle ABCD plus the triangle DCE, which (in the case of 0.3) coinsurance equals [0.7 (net change in expected cost) (change in volume) + ½(0.3) (Net change in cost) (change in volume)].

In terms of the numerical example where there was a positive change in total cost from testing, the calculations are as follows:

Note that the net marginal benefit curve from test and treat includes any disutility of treatment.

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Figure 1

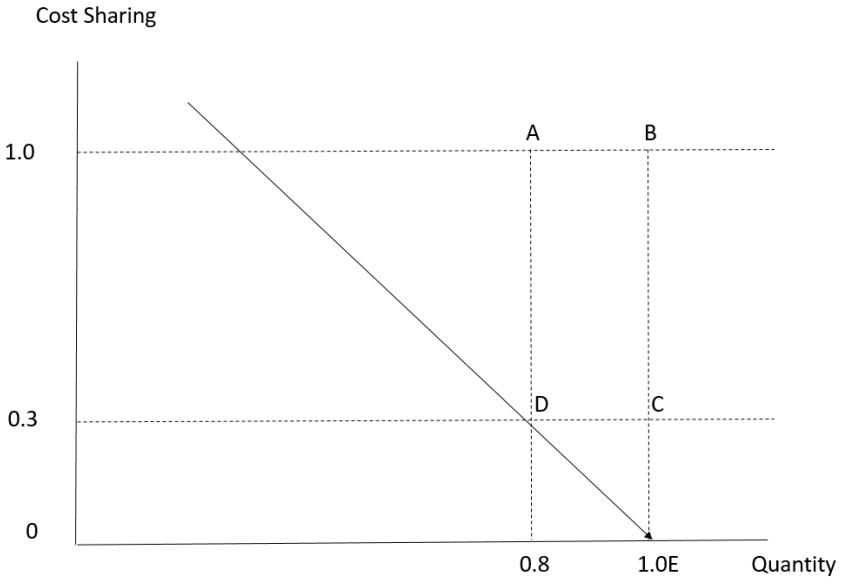

Cost Sharing
1.0
0.3
0
A
B
D
C
0.8
1.0E
Quantity

Table 2

EXAMPLE 1: RARE CONDITION

so

Probability test is positive: 0.1

Cost of specific treatment conditional on positive test: $50,000

Present discounted value of future treatment costs without treatment: $10,000.

Case A: **Treat all**

Total cost/person (in $ thousands): 50-(0.1) (10)=49

Case B: **Treat none**

Total cost/person: (0.1) (10) = 1

Test and treat

Total cost/person: 4+(0.1) (50-10) = 8

Incremental costs: TT vs. Treat all: -41

Incremental costs: TT vs Treat none: +7

QALYS added per person:

Treat all: 0.9 (L)

Implications for efficiency and insurance coverage

If initial state is treat all, do testing since it is a dominant strategy: lower cost and the same outcome unless there is disutility to treatment. Insurance coverage of testing should be 100% if treatment is cost effective.

If initial state is treat none, efficient strategy depends on the value of net benefit from treatment compared to

Table 3

EXAMPLE 2: COMMON CONDITION

Change probability test is positive to 0.95

Then cost of treating all (40.5) is less than cost of test and treat (42); gain from testing only if disutility of treating those who would have tested negative is larger than $1500. There is a much larger incremental cost compared to treating none but a larger gain in outcomes: ICER is unaffected.

CALCULATIONS FOR EXAMPLE 2, COMMON CONDITION

Price of test: $4000

Probability test is positive: 0.95

Cost of specific treatment conditional on a positive test: $50,000

Present discounted value of future treatment costs without specific treatment: $10,000

Case A: treat all

Total cost per person: 50-(0.95)(10)= 40.5

Case B: treat none

Total cost/person: (0.95) (10) = 9.5

Test and treat:

Total cost per person: 4+ (0.95)(50-10)=42

HYPOTHETICAL EXAMPLE OF INCREMENTAL COST WITH TESTING AND DETERMINATION OF WELFARE COST AND RISK PREMIUM OF PARTIAL COST SHARING.

EFFECT OF COST SHARING AT 30% OF TEST AND 0% OF TREATMENTS (VS. TREAT ALL)

ASSUME THAT COST SHARING REDUCES QUANTITY OF TESTING BY 20%, RISK PREMIUM IS 33% OF OUT OF POCKET COST, PROBABILITY OF POSITIVE TEST IS 0.95, DEFAULT OPTION WITHOUT TEST IS TREAT ALL.

COMPUTING OPTIMAL INSURANCE COVERAGE: NARRATIVE

INITIAL STATE: FULL COVERAGE OF TEST AND TREATMENT (IF USED).

I. Cost sharing when alternative is treat all:

MWC=(0.7(4-(0.05(50))(0.2) + 0.5((0.3) (4-(0.05) (50)) (0.2)=210+45=255

RP= .3 (.8) (4)(.33) =320

This implies that cost sharing of 30% is only a little higher than optimal.

II. In the treat none case the reason for no treatment is the FDA rule, not the valuation of the treatment. If the treatment and any future treatments are fully insured, probably the optimal insurance for the test is no coverage, so as to impose some limit on the use of expensive treatments of low value to some consumers.

One key issue is whether patients' demand for testing—which reflects the value of avoiding side effects—is based on correct information or is correctly advised by physicians. If not then the optimal level of coinsurance may be different from that in the classic analysis. If patients undervalue benefits there may be a case for lower coinsurance as a value based benefit, and

conversely if they overvalue benefits. There have been some surveys of consumer willingness to pay for genetic testing but they primarily explore the correlates of willingness to pay, rather than whether or not it affects the true value of testing in avoiding side effects (if the alternative is to treat all) or as a gateway to treatment with positive net benefits.

Some Current Examples of Genetic Testing and Treatment

The data on test and treatment cost and outcomes for three prominent examples of the use of genomic testing is displayed in Table 4. Here we discuss what is known about those cases and speculate about what it implies for insurance coverage.

Table 4

Test/Treatment	BRCA – Prophylactic surgery	BRCA – Tamoxifen Prophylaxis	PDL1+ – Keytruda vs.	KRAS test – Erbitux + FOLFIRI v. FOLFIRI Alone	KRAS test – Erbitux + FOLFIRI v. Avastin + FOLFIRI
Price of test and counseling ($)	2933	2933 (81211+81213 + 230 counseling))	790	247	1467
Price of specific treatment for those who test positive	15925 (2006 price)	623 (5y)	82201	105216	300018
Avoided future costs for those who test positive and have treatment	3601 per BRCA positive (no mammograms) 9742 (avoided	1396 per testee (avoided cancer costs)	N/A	N/A	N/A

	cancer costs for BRCA+)				
Proportion testing positive	0.25*	0.25*	0.255	0.67	0.67
Total spending per person with testing and treatment	12389	16910	36031	83668	283489
Total spending per person with treatment only	10023	14546	35241	83014	282022
Total spending per person with no testing or treatment (usual care)	16686	16686	19168	37939	245485
Gain in QALYs with avoiding illness	N/A - Cost Saving	0.30/testee	1.05	0.51	0.5
Loss In QALYs from side effects of treatment	N/A - Cost Saving	?	?	?	?
Comparator (test all or test none)	Test none, cancer costs as normal	Test None, costs from mammograms and cancer	Test none; Chemotherapy for all	Test none; FOLFIRI for all	Test none; FOLFIRI + Avastin for all
Change in total cost from test and treatment relative to comparator	4297 saved per patient	224 increase per patient	3140704804; 16863/patient	1302899556; 45729/patient	1082813102; 38004/patient
Cost-effectiveness ratio if change is positive	N/A	737/QALY	62982/QALY	133827/QALY	113445/QALY

*- indicates risk of testing positive for testing high risk patients (<1% of total population)

BRCA 1/2: Women who test positive for a particular set of genes (BRCA-1 and BRCA-2) are much more likely than average to develop breast and ovarian cancer at an early age and to die from cancer. The medical costs incurred by a designated high risk population (definitions vary but include those with breast cancer at an early age and those with first degree relatives who contracted breast cancer at an early age) have been studied under the alternative scenario of no genetic testing versus genetic testing and then prophylactic surgery if the test is positive. Testing and counseling of the high risk population has been recommended (with a "B" recommendation) by the US Preventive Services Task Force and and consequently all insurers are currently required to cover both testing and counseling for this population. The alternative to surgery is a plan of more frequent mammograms and preventive cancer chemotherapy such as taxitol.

In what follows we assume that the alternative to testing and a treatment with large negative side effect is no treatment and no testing. We assume that surgery has negative effects on short term and long term quality of life, but avoids future lifetime costs for this type of cancer.

Looking only at medical care costs, studies have compared the cost of testing and counseling all members of the population and the cost of surgery for those with positive findings with the future costs for screening for, biopsing, and future surgery and treatment for these cancers. The cost offset in terms of the present discounted value of related future medical costs is larger than the cost of testing and treatment. Unless a high value is attached to reduction in quality of life from surgery, the net change in QALY is usually estimated to be

positive.

Hence, compared to no testing and no treatment, use of genetic testing followed by prophylactic surgery for positive test results is a dominant strategy. It saves money and leads to outcomes which are better. It follows that testing and treatment should be fully covered by insurance to protect against the risk of becoming at high risk for this condition. Cost effectiveness has not been determined if a non-surgical alternative is chosen after a positive test, but cost reduction is unlikely in this case. It would be difficult to condition insurance coverage for testing on followup with preventive surgery.

*Erbitux and testing for metastatic colon cancer.*The FDA current approves Erbitux (cetucimab) for treatment of colon cancer following a test to determine whether the person's genetic makeup has an abnormality or is "wild type" with no abnormality. Erbitux is only effective for wild type genetic profiles, and about 2/3 of those with colon cancer have this profile. Though one might suppose that a strategy of universal treatment might be reasonable, the FDA currently recommends Erbitux only after testing and a finding of no genetic defects. The alternative to testing and treatment with Erbitux is a colectomy (surgical removal of the colon) or more frequent colonoscopies.

Studies find that, compared to a strategy of treating everyone at high risk with Erbitux without testing, testing and then Erbitux treating based on test results is cost reducing. However, compared with usual care (no testing, no Erbitux) , testing and then treating with Erbitux adds to total cost but improves health outcomes. If FDA guidelines are followed, it is the second case that is more relevant.

Because testing is a mandatory gateway to Erbitux treatment, we can consider cost sharing for testing as effectively an increase in cost sharing for treatment with probability p. There is no benefit to those who test negative. The average $/QALY for Erbitux is $62,982

Keytruda and testing for non-small-cell lung cancer. Keytruda is a new and expensive drug that has shown efficacy against non-small-cell lung cancer and other tumors. In the NSCLC case, the drug is effective only if the patient tests positive for PD-L1 and negative for the genes EGFR and ALK., In some cases the drug is used if EGFR and ALK inhibitors have failed as has platinum based chemotherapy.

About 80% of NSCLC patients would pass both of the genetic screens just described. The test and counseling to determine the status of a patient costs about $1000. Compared to a strategy of no testing and no treatment, there is a positive cost and positive health benefits from adding both testing and Keytruda. There has been no analysis of the costs and benefits from testing if all NSCLC patients were using Keytruda. Hence the case is similar to Erbitux but with a more expensive test and treatment. The net incremental cost per QALY added is $167,000 at a discounted price for Keytruda.

This ratio would often be regarded as above the threshold for efficient use of the testing and treatment program, but if there is variation across consumer around the mean ratio because of variation in the values attached to increments in health or side effects there may still be demand for and optimal provision of coverage for the combination for those with high values. However, mandatory coverage by private insurance is not warranted nor is universal coverage for all Medicare beneficiaries. Medigap insurance will also not cover costs of care that

is experimental or not deemed medically necessary.

The FDA requirement for testing before treatment effectively rules out the "treat all/ no test" option for consumers, so the value of testing per se is irrelevant. Private insurers may or may not choose to cover the Keytruda program, without or without additional conditions or restrictions. Medicare coverage is uncertain; if Medicare determines that testing for Keytruda responsiveness is not medically necessary, coverage is unlikely to be provided by private insurers. One response of Medicare when clinical evidence is not conclusive (as in the case of genetic testing to predict responsiveness to warfarin) is to limit coverage to those participating in clinical trials of effectiveness, so called "coverage with evidence determination." Private insurers generally restrict their coverage until the clinical evidence is generated.

Optimal coinsurance when no treatment is the alternative to testing and treatment. In both the cases of Erbitux and Keytruda, If there is variation in the value attached to net QALYs added by test and treatment (additional years of survival minus reduction in quality of life due to treatment side effects), there will be a demand curve for test-treatment combination that will be affected by any cost sharing for the test. In effect, cost sharing on either test or treatment raises the user price of the combination package. The distribution of these values determines the response to test cost sharing. It is possible that the key assumption behind the QALY measure is violated—for example, if the person attaches no value to a few more months of survival but wants to avoid the side effects of an aggressive treatment—but in that case there will be no demand for testing even a zero price and no value to insurance coverage of either test or treatment.

The relevant price here is, as before, the price of the test plus p times the price of treatment- any cost offset from avoided illness. The latter savings can be "taken off the top" so the percentage cost sharing depends on whether we analyzed the gross price or the price net of cost offsets; cost sharing as a proportion of net cost will be larger than cost sharing as a proportion of gross price.

Summary. These cases show some of the practical range of considerations that would govern specification of insurance coverage for testing and treatment. In the case of BRCA testing leading to prophylactic surgery, the evidence that total cost is reduced by testing while the health levels of those who opt for testing and this treatment is improved implies that coverage should be complete for both testing and treatment. In the two examples where testing is required for treatment but one has a higher cost effectiveness ratio than the other, the ideal pattern of insurance depends on the extent and form of variation in values attached to health improvements. If it is small, and if the threshold value for the great majority of the population is equal to or greater than $100,000 (say), then coverage should be nearly complete for Erbitux but lower for Keytruda. If there are few people with values per QALY above the mean value for Keytruda, it may be (second best) efficient to have high cost sharing for testing and, if feasible, for treatment. If health plans can sort consumers by their personal values of health improvements, plans with full coverage of testing and treatment for Erbitux should be more common than plans with full coverage for Keytruda.

Conclusion

Our review of coverage for genetic testing reveals a trend toward a more general acceptance of such tests as having clinical utility and therefore in principle appropriate candidates for insurance coverage. There is still a reluctance to cover tests deemed experimental, and relatively high bars for the evidence that can make coverage routine—though in most cases the coverage usually follows rather than facilitates clinical practice.

Genetic testing to determine the effectiveness of treatment is still relatively new though growing rapidly. There does seem to be a common cycle in which three trends compete. Evidence for and use of a test gets better over time, the price of the test falls over time, but insurance coverage (though present) imposes higher cost sharing. In principle cost effectiveness studies could provide the basis for determining those tests so efficient that coverage should be 100%, but this determination may vary across consumers depending on their willingness to pay for health outcomes and avoiding side effects of treatment. So coverage may become broader but shallower.

The other conflicting influence is that, as test prices fall, insurance coverage one way or another becomes less of an issue (but usually defaults to coverage once a deductible is met), while new but initially expensive tests appear that do impose a financial burden but with dubious evidence for their effectiveness or cost effectiveness are generally not covered. Thus there is likely to be continued debate on how insurance should deal with both the testing and treatment associated with personalized medicine.

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Appendix A

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