Supporting Information

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SI Text

A. Proof of Eq. 2

The right-hand side of Eq. **1** is additively separable in x. Hence, the optimal δ may be obtained by solving the subproblem

$$\max_{[\delta_S(x),\delta_{T0}(x),\delta_{T1}(x,p),\delta_{T1}(x,n)]\in[0,1]^4} [1-\delta_S(x)][1-\delta_{T0}(x)]E[y(0,A)|\, x] + [1-\delta_S(x)]\delta_{T0}(x)E[y(0,B)|\, x] + \sum_{r\in\{p,n\}} f(r\mid x)\{\delta_S(x)[1-\delta_{T1}(x,r)]E[y(1,\ A)|x,r] + \delta_S(x)\delta_{T1}(x,r)E[y(1,B)|\, x,r]\} \quad \textbf{[S1]}$$

separately for each $x \in X$.

Eq. **S1** may be solved in two steps. First, hold $\delta_S(x)$ fixed and maximize Eq. **S1** with respect to $[\delta_{T0}(x), \delta_{T1}(x, p), \delta_{T1}(x, n)]$. This yields Eqs. **2B–2D**. Insertion of the maximizing allocations into Eq. **S1** yields the concentrated maximization problem

$$\max_{\delta_S(x)\in[0,1]} [1-\delta_S(x)][\max\{E[y(0,A)|\, x], E[y(0,B)|\, x]\}] + \delta_S(x)\sum f(r\mid x)\sum_{r\in\{p,n\}}[\max\{E[y(1,A)|\, x,r], E[y(1,B)|\, x,r]\}]. \quad \textbf{[S2]}$$

This yields Eq. **2A**.

B. Proofs of Eqs. 5–8

First, consider E[y(0, A)|x]. The law of iterated expectations gives the decomposition

$$E[y(0,A)|x] = E[y(0,A)|x,z=1]P(z=1|x) + E[y(0,A)|x,z=0]P(z=0|x), \quad \textbf{[S3]}$$

where $P(z = 1|x)$ is the fraction of the study population that was tested. The evidence reveals E[y(0, A) |x, z = 0], P(z = 1|x), and P(z = 0|x). It does not reveal E[y(0, A) |x, z = 1]. When outcomes are bounded and scaled to lie in the unit interval, E[y(0, A)|x, z = 1] takes an unknown value in the unit interval. Hence, the identification region for E[y(0, A) |x] is given in Eq. **5**.

Analogous reasoning yields the identification regions for f(r = n|x) and f(r = p|x). Consider the former. A decomposition analogous to Eq. **S3** gives

$$f(r=n|x) = f(r=n|x,z=1)P(z=1|x) + f(r=n|x,z=0)P(z=0|x). \quad \textbf{[S4]}$$

The evidence reveals the test results of the tested members of the study population but not the untested ones. Hence, the identification region for f(r = n|x) is given in Eq. **8A**.

The derivations for E[y(1, A) |x, n] and E[y(1, B) |x, p] are more complex because these mean responses condition on a person's test result, which is observed only when the person is tested. I focus on E[y(1, A) |x, n]. The derivation for E[y(1, B) |x, p] is analogous.

A decomposition analogous to Eq. **S3** gives

$$E[y(1,A)|x,n] = E[y(1,A)|x,n,z=1]P(z=1|x,n) + E[y(1,A)|x,n,z=0]P(z=0|x,n). \quad \textbf{[S5]}$$

The evidence reveals E[y(1, A) |x, n, z = 1] but not E[y(1, A) |x, n, z = 0]. So far the derivation parallels those given earlier.

What makes this case differ is that the evidence is only partially informative about P(z|x, n). To see what the evidence does reveal, use Bayes' Theorem to write

$$P(z=1|x,r=n) = \frac{f(r=n|x,z=1)P(z=1|x)}{f(r=n|x,z=1)P(z=1|x) + f(r=n|x,z=0)P(z=0|x)} \quad \textbf{[S6A]}$$

$$P(z=0|x,r=n) = \frac{f(r=n|x,z=0)P(z=0|x)}{f(r=n|x,z=1)P(z=1|x) + f(r=n|x,z=0)P(z=0|x)}. \quad \textbf{[S6B]}$$

Of the quantities on the right-hand side of Eqs. **S6A** and **S6B**, the evidence reveals f(r = n |x, z = 1), P(z = 1 |x), and P(z = 0 |x) but it is uninformative about f(r = n |x, z = 0). The identification region for E[y(1, A) |x, n] is obtained by inserting the expressions on the right-hand side of Eqs. **S6A** and **S6B** into Eq. **S5** and letting the two unknown quantities E[y(1, A) |x, n, z = 0] and f(r = n |x, z = 0) jointly range over the unit square. The result is Eq. **6**.

C. Dominance with Observation of Aggressive Treatment with Positive Testing as Standard Practice

Partial knowledge may suffice to conclude that an allocation is dominated. To illustrate, consider the setting in *Identification of Response to Testing and Treatment When ATPT Is Standard Practice*, where the evidence is generated by the aggressive treatment with positive testing (ATPT) practice. Suppose one thinks it credible to assume that testing is random and that the test result is a monotone instrumental variable (MIV). These assumptions in the presence of some configurations of the evidence imply that aggressive treatment dominates active surveillance regardless of the test result. However, the same assumptions in the presence of other evidence yield no conclusion about the better treatment option.

To see this, recall that the assumption of random testing reveals E[y(1, A)|x, n] and E[y(1, B)|x, p], which equal E[y(1, A) |x, n, z = 1] and E[y(1, B) |x, p, z = 1] by Eqs. **9B** and **9C**, respectively. Asserting Eq. **10** for (s, t) = (1, A) implies that E[y(1, A) |x, p] ≤ E[y(1, A) |x, n], whereas asserting it for (s, t) = (1, B) implies that E[y(1, B) |x, n] ≥ E[y(1, B) |x, p].

Suppose the evidence shows that patients with positive test results, who receive aggressive treatment, fare better on average than those with negative results, who receive active surveillance; that is, E[y(1, B) |x, p, z = 1] > E[y(1, A) |x, n, z = 1]. Then E[y(1, B) |x, p] > E[y(1, A) |x, p] and E[y(1, B) |x, n] > E[y(1, A) |x, n]. Thus, aggressive treatment of tested persons is better than active surveillance regardless of the test result.

On the other hand, no conclusion holds if E[y(1, B) |x, p, z = 1] ≤ E[y(1, A) |x, n, z = 1]. Then the evidence and assumptions imply that both E[y(1, B) |x, p] and E[y(1, A) |x, p] are no larger than E[y(1, A) |x, n] but they yield no ordering of E[y(1, B) |x, p] and E[y(1, A) |x, p] relative to one another. Similarly, they yield no ordering of E[y(1, B) |x, n] and E[y(1, A) |x, n] relative to one another.

Whatever the evidence may be, combining it with the maintained assumptions does not reveal whether the clinician should order a diagnostic test. Nor does it reveal whether aggressive treatment is better than active surveillance when patients are untested. Optimization in these respects requires knowledge of E[y(0, B) |x]. The evidence and assumptions in the illustration are uninformative about this quantity.

D. Some Decision Criteria

There is no optimal choice among undominated actions, but decision theorists have not wanted to abandon the idea of optimization. So they have proposed various ways of transforming the unknown welfare function into a function of actions alone, which can be optimized. One idea averages the welfare function over the elements of the state space and maximizes the resulting function. This yields maximization of expected welfare. Another seeks an action that, in some sense, works uniformly well over all elements of the state space. This yields the maximin and minimax-regret criteria. These criteria yield different prescriptions for decision making, each of which may be described as "reasonable" but none as "optimal." I discuss these criteria in the context of the welfare function in Eq. **1**.

Maximization of Expected Welfare. A clinician maximizing expected welfare places a probability distribution, say π, on the state space. He then chooses an allocation that maximizes expected welfare. Thus, the criterion is

$$\max_{\delta\in\Delta}\int W(\delta,\gamma)d\pi, \quad \textbf{[S7]}$$

where Δ is the set of undominated allocations.

The solution to Eq. **S7** depends on the distribution π placed on Γ. Thus, maximization of expected welfare is not a single decision criterion but rather a collection of criteria. Decision theorists recommend that π should express the decision maker's personal beliefs about where γ lies within Γ. Hence, π is called a subjective probability distribution.

Subjective expected welfare takes a relatively simple form if π makes $f_\gamma(r)$ statistically independent of $E_\gamma[y(1, A)|r, x]$ and $E_\gamma[y(1, B)|r, x]$ that is, if the decision maker's beliefs about f(r|x) would not change given knowledge of E[y(1, A)|r, x] and E[y(1, B)|r, x]. Then

$$\begin{aligned}\int W(\delta,\gamma)d\pi = \sum_{x\in X} P(x)\big[[1-\delta_S(x)][1-\delta_{T0}(x)]E_\pi[y(0,A)|x]\\ +[1-\delta_S(x)]\delta_{T0}(x)E_\pi[y(0,B)|x]\\ +\sum_{r\in\{p,n\}} f_\pi(r|x)\{\delta_S(x)[1-\delta_{T1}(x,r)]E_\pi[y(1,A)|x,r]\\ +\delta_S(x)\delta_{T1}(x,r)E_\pi[y(1,B)|x,r]\}\big].\end{aligned} \quad \textbf{[S8]}$$

Here $E_\pi[y(0, A)|x] = \int E_\gamma[y(0, A)|x]d\pi$ denotes the subjective mean of $E_\gamma[y(0, A) |x]$ and the other quantities subscripted by π are defined analogously. The right-hand side of Eq. **S8** is the welfare that allocation δ would yield if the actual values of {E[y (0, t) |x], E[y (1, t) |x, r], f(r|x), t ∈ {A, B}, r ∈ {n, p}} were {E_π[y (0, t) |x], E_π[y (1, t) |x, r], f_π(r|x), t ∈ {A, B}, r ∈ {n, p}}. Thus, a clinician maximizing subjective expected welfare chooses the allocation that would be optimal if each unknown quantity were to equal its subjective mean.

Maximin Criterion. In the absence of a subjective distribution, a decision maker must cope with ambiguity. I discuss the two most prominent suggestions in the literature, the maximin and minimax-regret criteria.

A clinician using the maximin criterion chooses an action that maximizes the minimum welfare that might possibly occur. Heuristically, this criterion operationalizes the medical exhortation to "do no harm" by choosing an action that minimizes potential harm. Formally, for each allocation δ, consider the minimum feasible value of W(δ, γ), that is, $\min_{\gamma\in\Gamma}$ W(δ, γ). A maximin rule chooses an allocation that solves the optimization problem

$$\max_{\delta\in\Delta}\min_{\gamma\in\Gamma} W(\delta,\gamma). \quad \textbf{[S9]}$$

The minimum welfare expression $\min_{\gamma\in\Gamma}$ W(δ, γ) takes a relatively simple form in some special cases. Suppose that the clinician knows the distribution f(r|x) of test results, perhaps from a randomized trial of testing. Also suppose that the state space is such that it is feasible for all of the unknown mean responses {E[y(0, t) |x], E[y(1, t) |x, r], t ∈ {A, B}, r ∈ {n, p}} to simultaneously take their lowest possible values. Then

$$\begin{aligned}\min_{\gamma\in\Gamma} W(\delta,\gamma) = \sum_{x\in X} p(x)\big[[1-\delta_S(x)][1-\delta_{T0}(x)]E_L[y(0,A)|x]\\ +[1-\delta_S(x)]\delta_{T0}(x)E_L[y(0,B)|x]\\ +\sum_{r\in\{p,n\}} f(r|x)\{\delta_S(x)[1-\delta_{T1}(x,r)]E_L[y(1,A)|x,r]\\ +\delta_S(x)\delta_{T1}(x,r)E_L[y(1,B)|x,r]\}\big].\end{aligned} \quad \textbf{[S10]}$$

Here E_L[y(0, A) |x] denotes the lowest possible value of E_γ[y(0, A) |x] and the other quantities subscripted by L are defined analogously. The right-hand side of Eq. **S10** is the welfare that allocation δ would yield if the actual values of {E[y(0, t) |x], E[y (1, t) |x, r], t ∈ {A, B}, r ∈ {n, p}} were {E_L[y(0, t) |x], E_L[y (1, t) |x, r], t ∈ {A, B}, r ∈ {n, p}}. Thus, when Eq. **S10** holds, a clinician maximizing minimum welfare chooses the allocation that would be optimal if each unknown mean response were to equal its lowest possible value.

Minimax-Regret Criterion. A clinician using the minimax-regret criterion chooses an allocation that minimizes the maximum loss to welfare that can possibly result from not knowing the welfare function. A minimax-regret allocation solves the problem

$$\min_{\delta\in\Delta}\max_{\gamma\in\Gamma}\left[\max_{d\in\Delta} W(d,\gamma) - W(\delta,\gamma)\right]. \quad \textbf{[S11]}$$

Here $\max_{d\in\Delta}$ W(d, γ) − W(δ, γ) is the regret of allocation δ in state of nature γ, that is, the welfare loss associated with choice of δ relative to an action that maximizes welfare in state γ. The actual state is unknown, so one evaluates δ by its maximum regret over all states and selects an action that minimizes maximum regret.

The maximin and minimax-regret criteria are sometimes confused with one another. Comparison of Eqs. **S9** and **S11** shows that they are generally distinct. Whereas the maximin criterion considers only the worst outcome that an action may yield, minimax regret considers both best and worst outcomes. The two criteria coincide only in special cases. In particular, they coincide if $\max_{d\in\Delta}$ W(d, γ) is constant for all $\gamma \in \Gamma$. Then minimax regret reduces to maximin.

Maximization of expected welfare is equivalent to minimization of expected regret as opposed to maximum regret. The usual description of the expected welfare criterion is $\max_{\delta\in\Delta} E_\pi[W(\delta, \gamma)]$. The expected regret of allocation δ is $E_\pi[\max_{d\in\Delta} W(d, \gamma) - W(\delta, \gamma)] = E_\pi[\max_{d\in\Delta} W(d, \gamma)] - E_\pi[W(\delta, \gamma)]$. The first term on the right-hand side does not vary with action δ. Hence, minimization of expected regret is equivalent to maximization of expected welfare.

Maximum regret is a more complex mathematical expression than is expected or minimum welfare. Hence, determination of the minimax-regret allocation may be more difficult than determination of the allocations that maximize expected or minimum welfare. However, an intriguing finding emerges when the testing decision is predetermined and the only task is to choose between treatments A and B.

In this context, ref. 1 shows that the minimax-regret criterion balances the maximum losses in welfare from making two types of errors in patient care. A type A error occurs when treatment A is chosen but is actually inferior to B, and a type B error occurs when B is chosen but is inferior to A. Balancing the potential welfare losses minimizes maximum regret. The result turns out to be a fractional treatment allocation, one that assigns positive fractions of patients to both treatments.

Put another way, a clinician who uses the minimax-regret criterion to cope with ambiguity diversifies treatment. Diversification is a common recommendation in financial planning, when an investor has to allocate an endowment among multiple investments and is unsure which investment will yield the highest return. Manski (1) shows that diversification may also be appealing to a clinician or other planner who treats a population of persons and does not know the optimal treatment.

1. Manski C (2009) Diversified treatment under ambiguity. *Int Econ Rev* 50:1013–1041.