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Weighing Harm in Therapeutic Decisions of Smear-Negative Pulmonary Tuberculosis

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Purpose. *To relate the intuitive weight of harm by commission and harm by omission in therapeutic decisions for pulmonary tuberculosis, and to compare it with a weight based on probabilities.* ***Methods.*** *Clinicians were asked for an estimation of probabilities related with the outcome of treated and nontreated pulmonary tuberculosis and for the toll of wrong decisions. Three ratios of the weight of forgoing a treatment in false-negative patients against the weight of treating false-positives were calculated. The first was based on intuitive estimations, whereas the second and third were based on calculated, either through intuitive estimations of probabilities or through literature data. The association between experience and the difference between the intuitive and the calculated ratios was assessed.* ***Results.*** *Eighty-one participants from Ecuador, Laos, Nepal, and Rwanda responded. The ratio of intuitive weights was 2.0 (interquartile range [IQR], 1.0–4.0) and the ratio of calculated weights based on intuitive probabilities was 64 (IQR, 25.0–169.6;* $P < 0.001$*). The ratio of calculated weight based on literature probabilities was 30 (IQR, 17.9–59.2). No association (*$R^2 = 0.03$*) was found between experience and accuracy in estimating the weight of errors.* ***Conclusion.*** *The weight of a false negative is more important than the weight of a false positive for therapeutic decisions in pulmonary tuberculosis. The ratio of the intuitively estimated weights was much lower than the calculation based on intuitively estimated influencing factors. Clinicians were accurate in estimating probabilities but failed to incorporate them into therapeutic decisions.* ***Keywords:*** *omission bias; pulmonary tuberculosis; therapeutic decisions; decision threshold; decision theory* ***(Med Decis Making 2009; 29:380–390)***

Pulmonary tuberculosis (Tb) imposes an important toll on developing countries[1]; however, it has been shown that early and optimal treatment, both of smear-positive and smear-negative cases, is a cost-effective strategy for avoiding an important burden of suffering.[2] Clinicians in the front line of clinical care, especially in outpatient clinics and hospital settings, often struggle to find the right moment to start treatment. Because available laboratory methods are not sufficiently sensitive, they feel that patients showing a suggestive pattern of disease but with negative sputum smear or culture deserve a treatment, even if the infection has not been confirmed. On the other hand, most available guidelines recommend a bacteriological confirmation before starting the treatment.

This conflict can be solved by establishing a decision threshold, namely the minimum required probability of disease allowing the start of treatment. This approach considers a compromise between factors related with the treatment (efficacy, risks, and cost), and those related with an untreated disease (mortality, morbidity, and contagiousness in the case of infectious conditions).[3]

Accordingly, in a previous study we formally calculated a decision threshold for pulmonary Tb in a tertiary hospital setting in Rwanda, which yielded a prescriptive figure of 2.8%.[4] This means that in such a setting, a patient with chronic cough and a few more symptoms has reached a sufficiently

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Table 1 Characteristics of Countries

	Ecuador	Laos	Nepal	Rwanda
Total population (thousands)	13,192	5876	25,684	8481.3
Gross domestic product per capita in US$	3580	1720	1320	1270
Income group classification (World Bank)	Lower middle	Low	Low	Low
Tb prevalence per 100,000 people-year	196	318	257	660
Tb mortality per 100,000 people-year	26	25	24	102
New multidrug-resistant Tb %	2.4	2	1.3	1.9
Previously treated multidrug resistant Tb %	24	15	20	8
Tb prevalence in HIV+	0.7	0.2	2	34.5
Cumulative AIDS cases	1559	670	415	22,594

Note: Tb, tuberculosis; HIV+ , human immunodeficiency virus positive; AIDS, acquired immune deficiency syndrome.

high probability to start treatment. Although this is mathematically correct, it could be counterintuitive from the clinician's point of view because, apart from tangible factors related with the disease and the treatment, other subjective factors should be considered when estimating a decision threshold.

Indeed, life-and-death–related decisions are emotionally driven and can differ depending on the perspective of who is making the decision and who the decision will affect.[5] The literature constantly advocates decision making from the patient's perspective; however, the clinician's perspective is also very important and, surprisingly, it has hardly been studied. Eventually clinical decisions are always the responsibility of the clinician and for many diseases the correctness of these decisions could make a difference, not only in individual clinical care but also at the population level. This consideration is more important in low- and middle-income countries because optimal use of scarce resources is a prerequisite.

During training sessions of medical decision making in 3 continents (Asia, Africa, and South America), experienced clinicians relayed innumerable stories where personal feelings played an important role in their decisions. Feelings of regret following a potentially provoked harm due to a medical act were especially apparent. Therefore, in the Rwandese study the weight of harm provoked by treatment was entered into the analysis, showing that the decision threshold considering this subjective factor goes up to 11.9%, 4 times higher than the prescriptive figure.[4]

A similar phenomenon was empirically observed by Ritov, Asch, and colleagues with an example concerning attitudes of parents about whooping cough and flu vaccination of their children. Parents who were informed about the risk of vaccination, the risk of the disease, and the efficacy of the vaccine preferred to avoid vaccination, even though the risk-benefit analysis clearly showed a balance in favor of the vaccine.[6,7] This was called the omission bias, which is the propensity to omit an effective intervention to avoid regretting the possible—but hardly probable—harmful effect of that intervention.

Reasoning biases are important because they influence the estimation of the decision threshold. Ideally, because they are biases, they should not interfere. However, the facts suggest that they are ubiquitous and that an in-depth analysis is necessary to cope with them and to guide caregivers in their estimations of a sound decision threshold.

Considering the above, we wanted to investigate how much regret clinicians put on the possible harm provoked by giving a treatment to somebody who does not have pulmonary Tb compared with the regret of a possible harm provoked by omitting a treatment in somebody who has the disease. We also wanted to assess the influence of mortality and morbidity (related with both disease and treatment) in such regret compared with the weight assigned to a provoked harm. Finally, we substituted probabilities found in the literature for intuitively estimated probabilities to provide an objective standard of comparison.

METHODS

A group of clinicians from countries representative of 3 continents with a high burden of Tb completed a questionnaire. During the preparation phase of the study, the coordinators (JM and JVdE) sent an e-mail request to as many key persons they knew in several low-income countries as possible. The key persons were asked to recruit potential participants and to coordinate the application of the questionnaire. Letters of interest were received from Ecuador in South America, Laos and Nepal in Asia, and Rwanda in Central Africa. The main Tb and human immunodeficiency virus (HIV)-related burdens of these countries for the period of 2001 to 2004, as reported by United

Nations and World Bank, are summarized in Table 1. Recruitment was made on a convenience basis without restrictions in sample size.

A pilot questionnaire was written in French and tested in Rwanda. A Spanish translation was tested in Ecuador. The definitive version was worked out in English and then translated back into Spanish, French, and Lao. Comprehensiveness of the questions and reliability of translations were assured by cross-checking among coauthors, all of them fluent speakers of at least 2 of the 4 languages used in the questionnaire. To complete the questionnaire, all participants convened at a single meeting organized in each country. The form was distributed to every participant and was self-administered during the meeting. Due to the complexity of the questions, 1 of the members of the local research team was available during the sessions to clarify questions when needed. For Lao interviewees, the questionnaire was also projected in their language and script and every question was carefully explained before completing it. Participants who had previous formal training in medical decision making were excluded.

The English version of the questionnaire is shown in the Appendix. The questions explored 2 main issues: i) probabilities related with the disease and the treatment; and ii) values regarding the toll of wrong decisions.

In the probability questions we asked participants to guess at an estimation of mortality and morbidity of nontreated pulmonary Tb and at the risks of mortality and morbidity related with antituberculous treatment. No estimations for costs were asked because Tb treatment is subsidized in most developing countries around the world. Furthermore, the cost of a standard treatment in the international market of generic medicines is below 15 US$ per patient, which gives an extremely low relative cost that hardly influences the results.[4] Contagiousness of the disease was not taken into account because the threshold is intended for uncertain cases, which are, by definition, sputum smear negative and have a low risk of spread.

Questions concerning the toll of wrong decisions were asked for: i) the weight of forgoing a treatment in false negatives; ii) the weight of treating false positives; and iii) the weight given to a death related to a given decision. (See Appendix for detailed questions.)

Based on these data, the following indicators were constructed:

- The ratio of the intuitive weight of false negatives compared with false positives (*IntRatioFNFP*)

$$IntRatioFNFP = Intwfn/Intwfp \tag{1}$$

Where:

Intwfn = Intuitive weight of a false negative (diseased but not treated patient);
Intwfp = Intuitive weight of a false positive (not diseased but treated patient).

Inasmuch as it is not possible to calculate the ratio of the intuitive weight of false negatives against false positives when the intuitive weight for the latter equals 0, we opted to change 0 values of intuitive weights to 0.1. The option to exceed the upper value of 10 was allowed.

- Weight of a false negative

$$WFN = (dis\_mort + dis\_morb^{*} w\_dis\_morb)^{*} regr\_pr\_harm\_om \tag{2}$$

Where:

WFN = Weight of a false negative;
dis_mort = Mortality related with an untreated disease;
dis_morb = Morbidity related with an untreated disease;
w_dis_morb = Weight of morbidity related with an untreated disease, which is the complement of the health status of a person affected by the disease compared with a healthy person of the same age. (See Appendix for the detailed question.)
regr_pr_harm_om = Regret for harm provoked by erroneous omission of the treatment.

- Weight of a false positive

$$WFP = (tr\_mort + tr\_morb^{*} w\_tr\_morb)^{*} regr\_pr\_harm\_tr \tag{3}$$

Where:

WFP = Weight of a false positive;
tr_mort = Mortality due to a severe side effect of the treatment;
tr_morb = Morbidity due to severe side effects of the treatment;
w_tr_morb = Weight of morbidity related due to severe side effects of the treatment;
regr_pr_harm_tr = Regret for harm provoked by the treatment (death in a nondiseased).

Table 2 Literature Data for Probabilities Related with Pulmonary Tuberculosis

	Median of Literature Data (%)	Range of Literature Data (%)	Number of Retrieved Studies
Disease mortality	55	49–66	3
Disease morbidity	19	18–19	3
Treatment morbidity	4.9	1.8–8.6	7
Treatment mortality	0.1	0.08–0.12	2

- The ratio of the calculated weights (*CalRatioFNFP*)

This is the ratio of the weight of false negatives compared with the weight of false positives taking into account influencing factors.

$$CalRatioFNFP = WFN/WFP. \quad (4)$$

A further calculation of the weight of false negatives and false positives was done using literature data for the probabilities of mortality and morbidity associated with disease and treatment. These figures were retrieved in a systematic literature search that was published elsewhere and are detailed in Table 2.[4]

For comparing results among countries, the Kruskal-Wallis statistic test was performed. For comparing results with the different approaches (intuitive, calculated based on intuitive estimations, and calculated based on literature data), the Friedman statistic test was performed. When 2 approaches were compared we performed the Wilcoxon signed-rank test.

The Pearson R^2 test was used to assess the association between years of experience and the difference between the intuitive weight ratio and the calculated weight ratio.

Data input and analysis was performed with SPSS 13.0 for Windows (SPSS Inc., Chicago, IL).

RESULTS

Participants

A total of 81 clinicians from Ecuador, Laos Democratic Republic, Nepal, and Rwanda were interviewed in January 2007. In both Ecuador and Laos 19 (23.5% each) clinicians were recruited, in Nepal 29 (35.8%), and in Rwanda 14 (17.3%). All had current clinical experience in pulmonary Tb.

Participants had a median age of 35 years (interquartile range [IQR], 28.5–46.0) and a median experience of 8 years (IQR, 2.0–19.0). Females were underrepresented with a general female/male ratio of 0.6, except for Laos where 16 females against 3 males participated (Table 3). Most of participants were not specialists: 48 (59.3%). Among those with a specialty, there were 21 (25.9%) internists, 8 (9.9%) mother and children care specialists, and 4 (4.9%) public health officers.

Nine participants did not provide probability data required to calculate the weight of false positives and false negatives or filled in the questionnaire with answers that did not make sense. Hence they were excluded for the analysis of probabilities and values.

Estimated Probabilities

Estimated probabilities were statistically different among countries for the occurrence of treatment side effects and their related conditional probabilities (mortality and morbidity). The difference mainly concerned Lao participants who gave lower estimates for the probability of side effects (Table 4).

Estimated Weights Related with Harm

Participants estimated a similar weight for morbidity related with disease and morbidity related with treatment (the complement of the health status of a person affected by the disease compared with a healthy person of the same age) median (Mdn): 70.0% (IQR, 50.0–90.0%) v. 70.0% (IQR, 42.5–90.0)]. The estimated regret of a death due to omission was rated significantly higher than the regret of a provoked unjustified death [Mdn: 5.0 (IQR, 3.0–6.5) v. 3.0 (IQR, 2.0–5.0); $z = -4.52$, $P < 0.001$]. On the other hand, the latter was also rated significantly higher than a provoked but justified death (related to a treatment in a true positive) [3.0 (IQR, 2.0–5.0) v. 1.0 (IQR, 1.0–2.0); $z = -7.24$, $P < 0.001$]. Except for the weight of morbidity related with a disease and the regret of a provoked but justified death, no significant differences were observed among countries. These differences were mainly accounted for by Lao participants (Table 5).

Weight of False Negatives against False Positives

The median intuitive weight of false negatives was 10 (IQR, 9.0–10.0) and the median intuitive weight of false positives was 4.5 (IQR, 2.0–10.0). Estimations were significantly different among countries; however, this difference was mainly due to the Lao participants who gave a constant value of 10 for the weight of both false negatives and false positives. The other countries gave similar values (Table 6).

Table 3 Participants Data among Countries

		Ecuador	Laos	Nepal	Rwanda	All
	n	**19**	**19**	**29**	**14**	**81**
Age in years	Median	29.0	45.0	32.0	36.5	35.0
	IQR	27.5–39.5	41.5–48.5	27.0–39.0	33.0–42.0	28.5–46.0
Experience in years	Median	2.00	19.00	6.00	9.50	8.0
	IQR	1.3–7.0	13.5–20.5	3.0–12.0	2.0–21.0	2.0–19.0
Sex	Female	7	16	3	5	31
	Male	12	3	26	9	50
	Female/male	0.6	5.3	0.1	0.6	0.6

Note: IQR, interquartile range.

Table 4 Estimated Probabilities among Countries

		Ecuador	Laos	Nepal	Rwanda	All	***P* Value and 95% CI**
	n	**16**	**17**	**27**	**12**	**72**	
Mortality of untreated disease (%)	Median	67.5	80.0	50.0	57.5	60.0	0.195–0.210
	IQR	45.0–80.0	50.0–90	27.5–80.0	50.0–77.5	50–82.5	
Morbidity of untreated disease (%)	Median	30.5	15.0	20.0	20.0	20.0	0.649–0.668
	IQR	14.5–45.0	10.0–45.0	10.0–45.0	15.0–30	10.0–42.5	
Probability of side effects (%)	Median	10.0	3.0	10.0	9.0	9.0	0.010–0.014
	IQR	5.0–20.0	2.0–7.0	4.0–20.0	6.0–12.5	3.0–15.0	
Probability of death if side effects occur (%)	Median	10	2	10	5	5	0.121–0.134
	IQR	5.0–35.0	1.0–10.0	3.5–22.5	1.5–10	2.0–23.8	
Probability of disease if side effects occur (%)	Median	26.5	10	15	10	15	0.052–0.061
	IQR	15.0–35.0	10.0–59.5	5.0–42.5	7.3–10.0	9.6–38.8	
Mortality of side effects (conditional probability) (%) (row 3 * row 4)	Median	1.00	0.30	0.50	0.50	0.50	0.005–0.008
	IQR	0.50–0.25	0.05–0.50	0.30–0.22	0.14–1.38	0.23–2.00	
Morbidity of side effects (conditional probability) (%) (row 3 * row 5)	Median	2.25	0.70	1.40	0.85	1.00	0.047–0.056
	IQR	1.00–6.00	0.20–1.00	0.40–3.05	0.41–1.38	0.41–3.05	

Note: CI, confidence interval; IQR, interquartile range.

Table 5 Estimated Weights and Regret among Countries

		Ecuador	Laos	Nepal	Rwanda	All	***P* Value and 95% CI**
	n	**16**	**17**	**27**	**12**	**72**	
Weight of morbidity related with disease (%)	Median	70.0	97.0	60.0	62.5	70.0	<0.001
	IQR	60.0–90.0	95.0–99.0	47.5–80.0	35.0–70.0	50.0–90.0	
Weight of morbidity related with treatment (%)	Median	65.0	50.0	70.0	55.0	70	0.718–0.735
	IQR	50.0–77.5	22.0–90.0	50.0–90.0	40.0–80.0	42.5–90.0	
Regret provoked but justified death (relative to natural death)	Median	1.0	2.0	1.0	1.0	1.0	0.006–0.010
	IQR	1.0–2.0	2.0–2.0	1.0–2.0	1.0–1.0	1.0–2.0	
Regret provoked but unjustified death (relative to natural death)	Median	3.0	4.0	3.0	2.5	3.0	0.230–0.246
	IQR	2.0–4.5	3.0–5.0	2.0–6.5	2.0–3.0	2.0–5.0	
Regret of death by omission (relative to natural death)	Median	4.5	5.0	5.0	5.0	5.0	0.95–0.95
	IQR	2.0–10.0	4.0–5.0	3.3–9.0	4.5–5.5	3.0–6.5	

Note: CI, confidence interval; IQR, interquartile range.

Table 6 Weights of False Negatives and False Positives among Countries

		Ecuador	Laos	Nepal	Rwanda	All	*P* Value and 95% CI
	n	**16**	**17**	**27**	**12**	**72**	
Intuitive weight of false negatives	Median	10.0	10.0	9.0	9.0	10.0	<0.001
	IQR	10.0–10.0	a	7.5–10.0	8.5–10.0	9.0–10.0	
Intuitive weight of false positives	Median	4.0	10.0	2.0	3.0	4.5	<0.001
	IQR	6.0–8.5	a	1.0–4.0	2.0–4.0	2.0–10.0	
Calculated weight of false negatives (based on intuitive estimations)	Median	3.3	4.0	3.8	3.4	3.7	0.920–0.930
	IQR	1.8–8.7	2.5–5.0	1.7–5.8	2.9–4.0	2.0–5.6	
Calculated weight of false positives (based on intuitive estimations)	Median	0.09	0.03	0.05	0.02	0.05	0.008–0.012
	IQR	0.05–0.26	0.01–0.07	0.03–0.10	0.01–0.05	0.02–0.09	
Calculated weight of false negatives (based on literature probabilities and intuitive weights)	Median	2.9	2.9	3.4	3.2	3.2	0.998–0.999
	IQR	1.5–7.0	2.8–3.7	1.9–6.3	2.8–3.7	2.0–4.8	
Calculated weight of false positives (based on literature probabilities and intuitive weights)	Median	0.10	0.10	0.11	0.07	0.10	0.499–0.519
	IQR	0.07–0.14	0.05–0.13	0.06–0.21	0.05–0.12	0.06–0.14	

Note: CI, confidence interval; IQR, interquartile range.
a. Value is constant.

Five participants (all Nepalese) estimated the weight of false positives at 0.

The median calculated weight of false negatives based on intuitive estimates of probabilities and values was 3.7 (IQR, 2.0–5.6) and the median calculated weight of false positives was 0.05 (IQR, 0.02–0.09). The results for the calculated weight of false negatives were significantly different among countries. Estimates from Lao and Rwandese participants were lower than those yielded from Ecuadorian and Nepalese participants.

In further calculation, taking into account literature data for probabilities related with mortality and morbidity of both disease and treatment, the weight of false negatives was 3.2 (IQR, 2.0–4.8) and the weight of false positives was 0.10 (IQR, 0.06–0.14) (Table 6).

All but 2 participants (both Nepalese) gave higher values for the intuitive weight of false negatives than of false positives. When weights were calculated, either using intuitive estimations or literature data, false negatives consistently exceeded false positives.

The ratio of the intuitively estimated weight for false negatives v. false positives was 32 times lower than those calculations based on intuitively estimated influencing factors, and 15 times lower than the ratio based on literature data (Table 7).

Association between Experience and Ratio Difference

Number of years of experience was plotted against the difference between the intuitive and the calculated ratio of false negative and false positives. No association ($R^2 = 0.028$) was found, suggesting that experience does not increase the accuracy estimating the weight of errors.

Effect of Gender

In a bivariate analysis stratified by country, no significant effect of gender was found for all intuitive estimations ($P > 0.05$ for all estimations).

Open Discussions with Participants

In Laos, an open discussion emerged after completion of questionnaires and therefore did not alter the content of the answers. The reasons participants gave for avoiding false positives were: i) the very important stigma of being declared a Tb patient, leading to isolation, reject from family, sometimes divorce, and so forth; ii) the opportunity cost for patients staying in the hospital and abandoning their income-generating activities, as well as paying transport to get treatment and wasting of time; and iii) the missed diagnosis of the real underlying disease that causes those symptoms.

DISCUSSION

The regret regarding forgoing a treatment in a patient with pulmonary Tb (false negative) is intuitively weighed as twice the regret of treating a nondiseased person (false positive). This means that

Table 7 Ratios of False Negatives against False Positives with Three Different Approaches

		Ecuador	Laos	Nepal	Rwanda	All	Friedman Test *P* Value
	n	**16**	**17**	**27**	**12**	**72**	
Ratio of intuitive weight false negatives/intuitive weight false positives	Median	1.8	1.0	3.3	3.2	2.0	
	IQR	1.2–3.2	1.0–1.0	1.5–8.5	2.8–4.3	1.0–4.0	
Ratio of calculated weight false negatives/calculated weight false positives (based on intuitive estimations)	Median	33.3	102.6	36.5	119.6	64.6	
	IQR	18.1–83.9	57.5–231.6	18.5–122.9	84.6–232.8	25.0–169.6	>0.001
Ratio of calculated weight false negatives/calculated weight false positives (based on literature probabilities and intuitive weights)	Median	29.1	34.5	25.7	42.6	30.0	
	IQR	18.3–69.3	16.4–62.3	19.7–50.6	22.1–65.8	17.9–59.2	

Note: IQR, interquartile range.

participants considered that, for pulmonary Tb, it is worse to omit than to commit. When estimates were based on probabilities, the weight of a false negative became much more important than the weight of a false positive. This effect was also found when data from the literature were considered instead of intuitive probabilities.

Clinicians were accurate in estimating probabilities but failed to incorporate them into therapeutic decisions. Experience did not influence the accuracy of estimates of the weight of errors.

The ratio of false negatives against false positives is not the same as the decision threshold. The former is also known as the Blackstone-like error ratio and the latter is the probabilistic standard of proof. The difference was already explained by Dekay, who warned about the danger of considering the error ratio as a decision threshold.[8] Hence, the purpose of this study was not to estimate a decision threshold for Tb but to explore the influence of omission and commission biases. As stated above, medical decisions can be influenced by emotions. Together with aspects of costs, opportunity costs, national guidelines, and patient's preferences including stigma, a physician's regret of provoking harm because of a medical action plays an important role in the estimation of the decision threshold.[9]

Zikmund-Fisher and others showed that the importance of the omission bias is highly dependent on the perspective of the decision maker.[5] Doctors making decisions for patients are more inclined toward the benefit of an intervention, that is, they are less ''omission biased'' than people making decisions for them. This study was not intended to explore this difference in perspective but rather to learn to what extent clinicians are inclined to omit an intervention to not regret a harm provoked by the treatment.

The study has some weaknesses deserving discussion. There is a lack of homogeneity in age and sex among countries. This could be because selection of participants was made by convenience. The selection put emphasis on the acquaintance of participants with Tb care, rather than on the homogeneity of the sample. It is possible that the distribution of gender reflects the usual demographic pattern of health professionals in these countries, although it is surprising that in Laos most of participants were women. In any case, the bivariate analysis did not find a significant effect of gender stratified by country.

Only pulmonary Tb was considered as a model for the study. This could raise concerns about the generalization of the findings, because Tb is an example of a disease with a low threshold. It is fair to argue and quite possible that for diseases with dangerous and or less efficacious treatments there would be a larger tendency to omit. Nevertheless, the purpose of the study was not to prove that omission is always worse than commission, but to understand the role of weights and probabilities when considering a medical decision.

The large difference between intuitive and calculated weights could be due to a constraint related to a 10-point visual analogue scale not allowing decimal numbers under 1. However, only 5 participants rated harm by omission lower than 1, not affecting our conclusions. We preferred this method because in pilot surveys using open questions, a huge amount of nonsense results were obtained.

It was evident that Lao participants gave different values than the others. Perhaps the most striking difference was in the intuitive weight of false positives, which was much higher (constantly 10) than for the other interviewees, whereas the calculated weight for false positives was not significantly different among countries. One reason might be that in Laos, the national Tb program strictly requires a patient to be smear positive before starting a treatment. The decision to treat a smear-negative patient must be made by a collective of medical doctors, based on X-ray signs and other symptoms. Trial treatments are, in principle, not allowed. Lao participants gave several reasons arguing for their preferences, which are reflected in their intuitive weights. Even if the fact that Laotian participants responded in a somehow different way than other participants could be seen as a weakness, it may also be considered a strength, because it shows the possible variability among countries. Different cultural practices between countries are also possible effects; however, to examine these differences, qualitative methods of analysis are warranted and this was beyond the scope of this study.

The ultimate goal of this study was to examine relevant factors intervening in the decision threshold with pulmonary Tb as an example. The main conclusion is that clinicians are good estimators of baseline probabilities related with treatment and disease, but they fail to integrate them in the estimation of the decision threshold. In the case of pulmonary Tb, this failure could induce an unwanted effect of making errors by omitting the treatment. It has been argued that omission or commission biases should not enter into a rational decision but, as medical decisions often concern matters of life and death, it is not possible to avoid them. Hence the weight of possible omission and commission harm should be considered in the threshold concept.

Analysis of intuitive estimations of the decision threshold has to be promoted. No doctors are willing and few are able to perform formal calculations of the threshold. However, during training sessions a word of caution should be given about the relative influence of all factors, including those emotionally driven. Perhaps the process of promoting reflection about decision making by clinicians could be a way to improve the quality of decisions made and bring rational support to the uncertainty with which clinicians are often confronted.

Finally, the impact of these changes should be tested during training activities as well as during delivery of care. This would yield the most valuable information about the usefulness of the whole threshold approach.

APPENDIX
Questionnaire

Dear Colleagues:

This questionnaire was prepared for a study intending to understand major concepts in medical decision making. It has been applied at the same time in some countries of Asia, Central Africa, and South America.

The obtained results will serve to adapt the training methods in medical decision making. Please follow carefully the instructions and be clear if you make amendments. Thank you for your kind collaboration.

Age: Gender (M or F):
Years of experience since your graduation as doctor:
Specialization (if any):

Suppose a patient with pulmonary tuberculosis who remains untreated, as it was upon a time when specific chemotherapy was not yet discovered. One of the following outcomes can occur: die of tuberculosis, survive with symptoms related with the disease, or spontaneous remission of symptoms (absence of symptoms). According to your experience and knowledge, guess what the probability (frequency) of each of these outcomes is in such a case. Note that the sum must be 100.

(continued)

APPENDIX (continued)

Outcome	**Probability**
Death	%
Survival with life long symptoms	%
Spontaneous remission	%
Total	100 %

Currently a specific treatment is available. In most of the countries a standard schema of 2 months with daily rifampicin, isoniazid, pyrazinamide and ethambutol followed by 4 months of rifampicin and isoniazid is recommended. A patient receiving such a treatment can develop severe side effects, like clinical hepatitis. What is the probability of any such an outcome? Please don't give intervals, try to guess a number.

Standard Treatment	**Probability of Severe Side Effects**
RHZE for 2 months, then RH for 4 months	%

If severe side effects occur the patient can die, but he can also survive either with life-long symptoms related with, e.g., cirrhosis, or without them. Guess what the probability of each of these outcomes is. Note that the sum must be 100.

Outcome	**Probability**
Death	%
Survival with life-long symptoms	%
Remission without symptoms	%
Total	100 %

Somebody surviving with life-long symptoms because he was not treated has an impaired health status, compared with the expected for a healthy person at the same age. For instance, one could say that a tetraplegic person has only 10% of the expected health status compared with a healthy person at the same age. A hemiplegic patient could have 25% of his expected health status. Guess what the percentage of the expected health status is for somebody surviving with symptoms of untreated tuberculosis, which can include ongoing fever, shortness of breath sometimes needing supplementary oxygen to complete common tasks, depression, rejection by relatives, etc.

Percentage of the expected health status for somebody surviving with symptoms because he was not treated for tuberculosis	%

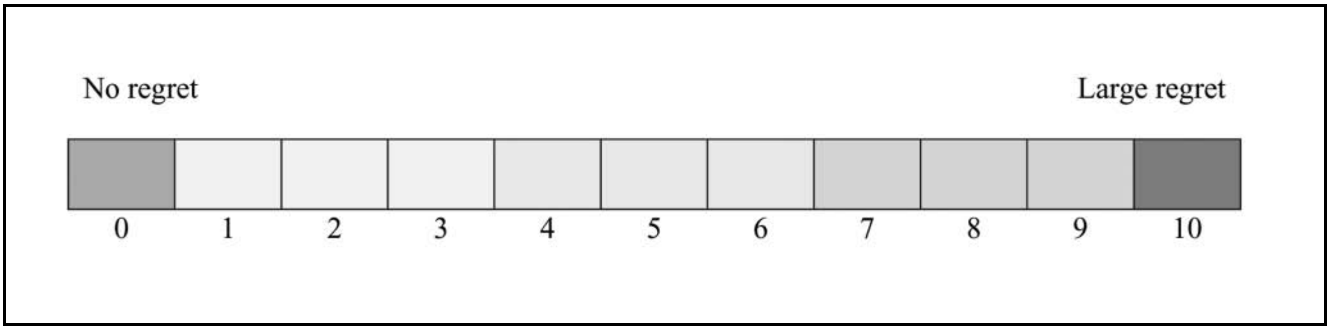
The health status of somebody surviving after drug related severe side effects is also less than the expected, compared with a healthy person at his same age. Guess what the percentage of the expected health status is for somebody with such a condition, which can include cognitive and mobility impairment related with cirrhosis.

Percentage of the expected health status for somebody surviving after drug-related severe side effects	%

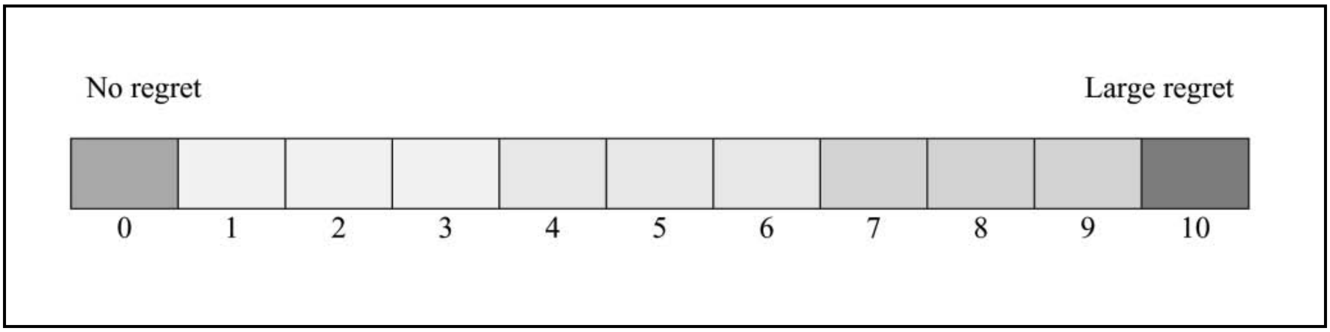
(continued)

APPENDIX (continued)

Now suppose you are in charge of a patient. After exhausting all pertinent and available information, which included three sputum smear examinations for acid-fast bacilli (AFB) which turned out to be negative, you suspect he has pulmonary tuberculosis, but you still are uncertain about the true diagnosis. Among other possibilities, you can err in two ways: treating someone not having tuberculosis, or abstaining from treating somebody actually having the disease. We assume that the cost of drugs is subsidized, so it is not taken into account.



Rate from 0 to 10 the "regret" you would have making the mistake of giving an antituberculous treatment to somebody who does not have pulmonary tuberculosis. (Don't hesitate to surpass 10 if you consider it necessary.)



Now rate from 0 to 10 the "regret" you would have making the mistake of abstaining from treating somebody actually having pulmonary tuberculosis. (Don't hesitate to surpass 10 if you consider it necessary.)

After taking your decision, there is still a very little chance that your patient dies, despite the fact that your decision was based on optimal grounds. Such an outcome could lead to the following reflection.

What is the "weight of regret" we have for being involved in such death? Let's say that a natural death (somebody dying without a specific medical intervention) has a weight equal to "1." What would be the weight of a death resulting of a side effect of a treatment that was prescribed by you? For example, if your answer is "2" it means that you consider a provoked death being 2 times worse than a natural one.

Now give your own rates for the following situations:

1) Weight of a provoked but justified death (a death resulting of a side effect in somebody who had tuberculosis)
2) Weight of a provoked but unjustified death (a death resulting of a side effect in somebody who didn't need the treatment because he/she didn't have tuberculosis)
3) Weight of a death provoked by an erroneous omission of treatment in somebody who had tuberculosis

Thank you very much.

REFERENCES

1. World Health Organisation. Global Tuberculosis Control—Surveillance, Planning, Financing. WHO Report 2005. Geneva: World Health Organisation; 2005.

2. Baltussen R, Floyd K, Dye C. Cost effectiveness analysis of strategies for tuberculosis control in developing countries. BMJ. 2005;331:1364–70.

3. Pauker SG, Kassirer JP. Therapeutic decision making: a cost-benefit analysis. N Engl J Med. 1975;293:229–34.

4. Basinga P, Moreira J, Bisoffi Z, Bisig B, Van den Ende J. Why are clinicians reluctant to treat smear-negative tuberculosis? An inquiry about treatment thresholds in Rwanda. Med Decis Making. 2007;27:53–60.

5. Zikmund-Fisher BJ, Sarr B, Fagerlin A, Ubel PA. A matter of perspective: choosing for others differs from choosing for yourself in making treatment decisions. J Gen Intern Med. 2006;21:618–22.

6. Asch DA, Baron J, Hershey JC, Kunreuther H, Meszaros J, Ritov I, et al. Omission bias and pertussis vaccination. Med Decis Making. 1994;14:118–23.

7. Ritov I, Baron J. Reluctance to vaccinate: omission bias and ambiguity. J Behav Decis Making. 1990;3:263–77.

8. Dekay ML. The difference between Blackstone-like error ratios and the probabilistics standards of proof. Law and Social Inquiry. 1996;21:95–132.

9. Hunink M, Glasziou P, Siegel J, Weeks J, Pliskin J, Elstein AS, et al. Decision Making in Health and Medicine. Integrating Evidence and Values. Cambridge: Cambridge University Press; 2001.