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SCIENTIFIC INVESTIGATIONS

Decision Modeling in Sleep Apnea: The Critical Roles of Pretest Probability, Cost of Untreated Obstructive Sleep Apnea, and Time Horizon

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Study Objectives: Obstructive sleep apnea (OSA) is associated with increased morbidity and mortality, and treatment with positive airway pressure (PAP) is cost-effective. However, the optimal diagnostic strategy remains a subject of debate. Prior modeling studies have not consistently supported the widely held assumption that home sleep testing (HST) is cost-effective.

Methods: We modeled four strategies: (1) treat no one; (2) treat everyone empirically; (3) treat those testing positive during in-laboratory polysomnography (PSG) via in-laboratory titration; and (4) treat those testing positive during HST with auto-PAP. The population was assumed to lack independent reasons for in-laboratory PSG (such as insomnia, periodic limb movements in sleep, complex apnea). We considered the third-party payer perspective, via both standard (quality-adjusted) and pure cost methods.

Results: The preferred strategy depended on three key factors: pretest probability of OSA, cost of untreated OSA, and time horizon. At low prevalence and low cost of untreated OSA, the treat no one strategy was favored, whereas empiric treatment was favored for high prevalence and high cost of untreated OSA. In-laboratory backup for failures in the at-home strategy increased the preference for the at-home strategy. Without laboratory backup in the at-home arm, the in-laboratory strategy was increasingly preferred at longer time horizons.

Conclusion: Using a model framework that captures a broad range of clinical possibilities, the optimal diagnostic approach to uncomplicated OSA depends on pretest probability, cost of untreated OSA, and time horizon. Estimating each of these critical factors remains a challenge warranting further investigation.

Keywords: cost, effectiveness, home sleep test, obstructive sleep apnea, PSG

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INTRODUCTION

Obstructive sleep apnea (OSA) affects 5% to 15% of adults, with epidemiological estimates suggesting that up to 80% of cases remain undiagnosed.[1] Untreated OSA leads to negative health and performance consequences in proportion with severity, including daytime sleepiness,[2] motor vehicle accidents,[3] and cardiovascular morbidity and mortality.[4] In the United States, untreated OSA incurs annual costs estimated in the tens of billions of dollars.[5] Positive airway pressure (PAP) therapy for OSA is cost-effective and has both subjective and objective medical benefits.[6] Various studies have demonstrated cost-effectiveness using different assumptions, time horizons, and outcomes, such as quality-of-life benefit in moderate to severe OSA,[7] benefit for vascular outcomes and mortality in severe OSA cases,[8] and benefit for quality of life and motor vehicle accident in moderate to severe cases.[9]

In-laboratory polysomnography (PSG) is considered the gold standard for diagnosing OSA,[10] but it has certain potential drawbacks such as labor intensity, cost, and unfamiliar environment. The growing interest and availability of home sleep testing (HST) kits has led to ongoing debate about optimal utilization of these options.[11–13] HST may be an appropriate alternative for certain patients, and published guidelines from the American Academy of Sleep Medicine (AASM) define such appropriateness based on existing evidence.[14,15] These guidelines require, among other criteria, a high pretest probability (> 80%) of at least moderate OSA (apnea-hypopnea index [AHI] ≥ 15), reflecting the concept that HST is meant to confirm high-suspicion cases by raising the posttest probability to > 95%. However, the guidelines do not specify how one can arrive at this high pretest probability. Estimating the pretest probability is not straightforward and may be influenced as much by medical comorbidities as it is by classic OSA symptoms.[16]

It is often assumed that HST kits are cost-effective solutions for OSA management. One reason for widespread acceptance of this idea is the fact that they are much less expensive than a laboratory PSG for the step of diagnostic testing. However, many factors affect the broader question of cost-effectiveness

BRIEF SUMMARY

Current Knowledge/Study Rationale: Home Sleep Testing (HST) kits are assumed to be a cost-effective strategy for obstructive sleep apnea (OSA). However, economic models have not consistently supported this assumption.

Study Impact: Our model, designed to generalize across a variety of clinical circumstances, shows that multiple factors impact the relative cost-effectiveness of in-laboratory versus at-home strategies for OSA. Pretest probability of OSA, cost of untreated OSA, and the time horizon of the model were all critical determinants of the optimal strategy.

that always reaches beyond the time point of diagnostic testing. Even when restricted to straightforward OSA cases, the diagnostic accuracy of HST kits is inferior to PSG, which results in downstream burdens of false negative and false positive results as a trade-off to the reduced cost of the kits. The two published cost-benefit models that did not consider long-term consequences of missed diagnoses (false negatives) concluded that HST was less costly than in-laboratory PSG.[17,18] This is not surprising given the short time horizon considered (i.e., the diagnostic testing alone) and failure to consider downstream consequences of false positives and false negatives. Because the clinically relevant consequences of untreated OSA are encountered on a chronic time horizon, conclusions regarding cost-effectiveness from short-time horizon models are questionable. To illustrate the fallacy, if one disregards the downstream consequences of missed diagnoses, then a strategy of doing no testing at all would erroneously be considered "cost-effective" compared to PSG or HST.

By contrast, several recent cost-effectiveness models that do in fact consider downstream consequences have challenged the view that HST is cost-effective.[19–21] Although they share the common goal of addressing the balance of cost and accuracy over longer time horizons, these studies employed distinct model assumptions, treatment strategies, parameter values, and outcomes. They also assumed a fairly high pretest probability of OSA (50% to 85%), which is in the range of the recommendations of the AASM guidelines for using HST (80% pretest probability of AHI > 15). Whether these model studies can generalize across practice settings, which may include lower pretest probability cases, or lack of routine laboratory PSG backup for negative HST results, remains uncertain. In addition, the extent to which clinical practice and/or insurance standards follows AASM guidelines has not been well studied. For example, whether in-laboratory PSG is performed for every negative HST result, which is explicitly recommended by the AASM, remains unknown. Regarding the question of pretest probability of OSA, the largest cohort of adult HST findings was recently published,[22] the results of which indicate that HST usage extends well below the published pretest probability requirements in the AASM guidelines[23].

The current study uses decision models to address some of the uncertainties in this area and yield broadly relevant conclusions. We consider two types of modeling, from a third-party payer perspective: cost-effectiveness (which incorporates a quality of life measure) and a pure-cost approach (which does not include quality of life). Within each of these frameworks, we consider a wide range of pretest probabilities, the presence or absence of in-laboratory backup for the at-home strategy, short- and long-term horizons, and a range of costs associated with untreated OSA.

METHODS

We used Tree Age Pro 2014 software (Williamstown, MA) to evaluate a decision model for the evaluation of health-economic strategies for the diagnosis and treatment of OSA. We performed the modeling in two ways, both of which focus on costs. Cost-effectiveness involves assumptions about quality of life or utility of outcome states, to form a ratio of costs to effectiveness (cost-benefit usually refers to monetized effectiveness instead of units referring to quality of life). Pure-cost models do not consider quality of life, but instead consider only the expenses (in this case, the third- party payer perspective) to compare management strategies.

Model Overview

Our model considers four strategies for approaching OSA: no testing and no treatment (No-Rx); treat all patients empirically without testing (Rx-All); in-laboratory PSG followed by treatment of those testing positive; and at-home strategy (HST for diagnosis, and home autoPAP to treat those testing positive). In the at-home group, we compared two strategies that reflect potential differences in practice: whether or not in-laboratory PSG is pursued for negative HST results. In addition, in our model, in-laboratory PAP titration is performed as a backup if home autoPAP trial is not successful. Both the in-laboratory and at-home arms of the model include an opportunity to re-test if initial testing was negative. OSA positive in-laboratory PSGs have a chance of meeting split-night criteria (testing and continuous positive airway pressure [CPAP] titration in one night) or to have a full diagnostic night followed by a second CPAP titration night in the laboratory on a second night (assumed to be 50%). False-positive results are possible, and in those cases, the probability of accepting PAP therapy is reduced.

Assumptions and Parameters

We assumed the patients undergoing testing are adults free of comorbid sleep disorders such as insomnia and periodic limb movements of sleep (PLMS), which are considered independent indications for in-laboratory PSG and can potentially compromise the accuracy of HST devices. Treated OSA patients and those without OSA are assumed to have a quality of life value = 1. Untreated OSA was given a lower utility value of 0.8. We do not specify whether the reduced utility of untreated OSA is a manifestation of sleepiness or other subjective complaints such as reduced attention or cognition; precisely defining this has been challenging.[24] Instead, the model is intentionally general such that the utility reduction can be conceptualized most broadly, which allows individualized application to any patient.

Costs were considered from a third-party payer perspective. **Table 1** contains the baseline costs, utilities, and parameters used in our model. We assumed that both at-home and in-laboratory strategies have equal probabilities of patients accepting PAP treatment following a positive test for OSA, and that empiric trial of CPAP does not differ in terms of adherence after diagnostic testing.[25–27] Similarly, false-positive cases who initially accept treatment have a reduced probability of adherence compared to true-positive cases. We assumed that patients treated with CPAP incur the costs of therapy (with a base case value of $1,000, between that proposed by Pietzsch et al.[19] and by Deutsch et al.[20]). We considered time horizons between 1- and 10-y after diagnostic testing.

The model makes several simplifying assumptions in its structure. We replace time-dependent rates of CPAP adherence with time-independent probability of acceptance. We make no

Table 1—Model parameters.

Parameter	Value (range)	Reference
Pretest probability OSA (prevOSA)	0–100%	–
Cost untreated OSA (cOSA)	$0–5,000	–
Sensitivity HST	0.91	Pietzsch 2011
Specificity HST	0.83	Pietzsch 2011
Sensitivity PSG	0.93	Pietzsch 2011
Specificity PSG	0.97	Pietzsch 2011
Cost CPAP/y	$1,000	Pietzsch 2011, Deutsch 2006
Cost APAP trial	$200	Pietzsch 2011, Deutsch 2006
Cost PSG	$800	Pietzsch 2011, Deutsch 2006
Cost HST	$200	Pietzsch 2011, Deutsch 2006
Utility untreated OSA	0.8	Schmidlin 2010
Pr(accept APAP trial)	0.9	Estimated
Pr(accept CPAP titration)	0.9	Estimated
Pr(accept PAP treatment after APAP trial)	0.7	Sawyer 2011
Pr(accept PAP treatment after CPAP titration)	0.7	Sawyer 2011
Pr(accept PAP treatment after split night)	0.7	Sawyer 2011
Pr(meet split night criteria on diagnostic PSG)	0.5	Estimated
Pr(lab PSG after negative HST)	0 or 0.9	Estimated
Pr(repeat lab PSG after negative laboratory PSG)	0.01	Estimated
Adjustment for accept CPAP if false pos ("a")	0.5	Skomro 2007

APAP, auto-positive airway pressure; CPAP, continuous positive airway pressure; HST, home sleep testing; OSA, obstructive sleep apnea; PAP, positive airway pressure; PSG, polysomnography.

assumptions about how the pretest probability of OSA is determined. Clinicians may use a combination of symptoms, signs, and medical history, as have been formalized in scales such as the "STOP-Bang" or other tools.[28,29] This intentionally allows the model to generalize across practice patterns, where any method could be utilized to predict the OSA probability before testing. We recognize that establishing the pretest probability remains challenging.[16,30] Simplifying assumptions were also utilized for costs, to achieve the dual aims of interpretability and broad clinical applicability. For example, while other models have considered the acute and ongoing costs associated with important risks such as heart attack, stroke, and motor vehicle accidents using Markov methods,[19] we make no assumptions about how the costs of untreated OSA are determined. This has the advantage of flexibility in application of the framework, and it respects the fact that untreated OSA may have different health implications depending on the clinical context. Although the possibility that costs of untreated OSA are time dependent (there are likely higher costs with advancing age and increasing cardiovascular risk), this can be accounted for in our sensitivity analysis by testing a range of annual costs of untreated OSA.

RESULTS

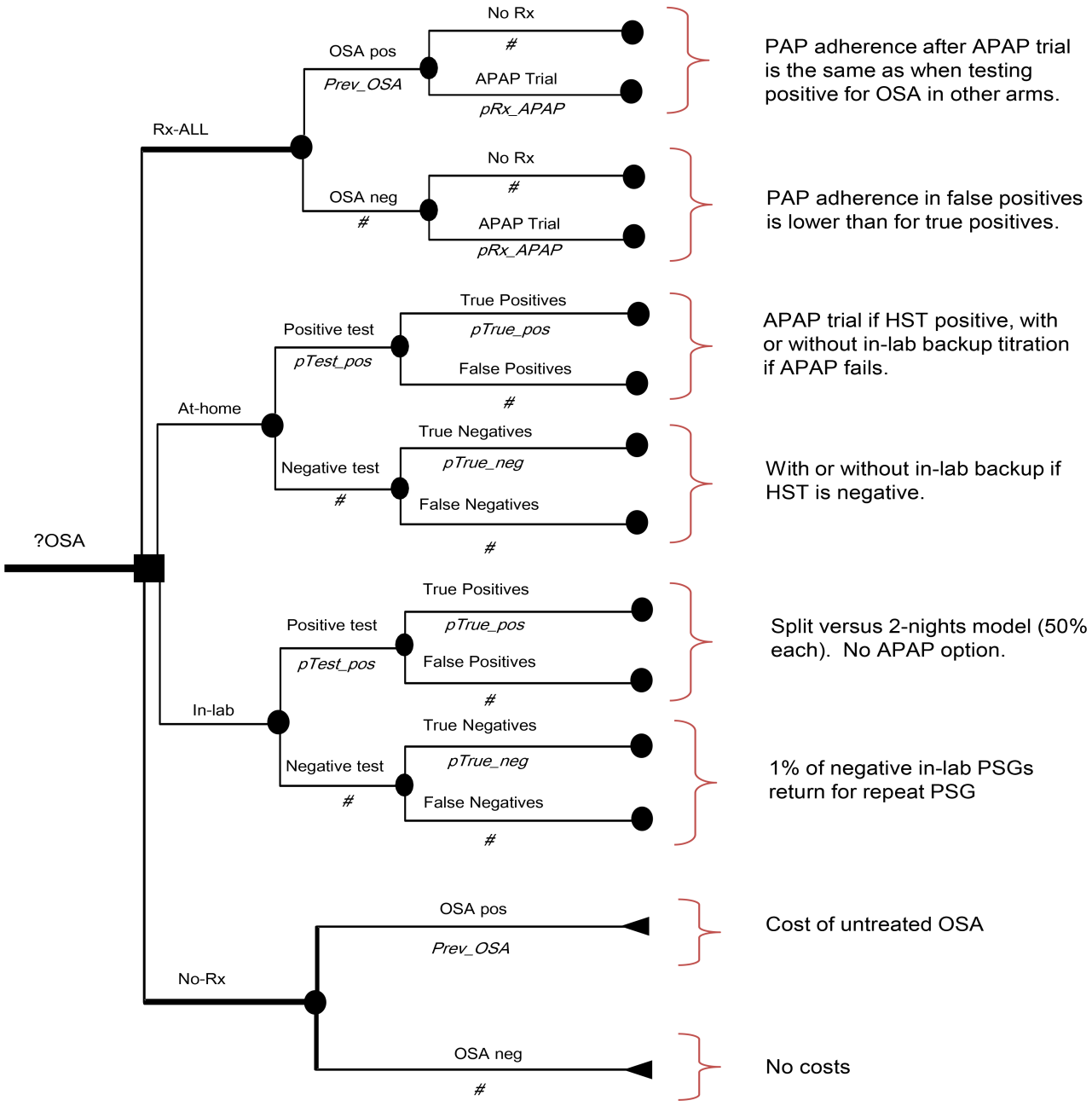
Figure 1 illustrates the main model structure. The model compares four approaches: (1) no testing or treatment for anyone ("No-Rx"); (2) empiric treatment for everyone, without testing ("Rx-All"); (3) at-home approach using HST for diagnosis and autoPAP for therapy (also see **Figure S1**, supplemental material); (4) in-laboratory PSG approach for the diagnostic and titration steps. We performed a separate analysis to compare the consequences of whether or not in-laboratory backup was used in the at-home arm for negative HST results and failed autoPAP trials.

We first considered the setting in which the at-home strategy does not have a backup of in-laboratory PSG for diagnosis or for titration (**Figure 2**). In other words, the at-home strategy has only HST and autoPAP available. This strategy represents one end of the spectrum of clinical practice in regards to how negative HST findings are handled. The other end of the spectrum (next paragraphs) allows failed steps of the at-home arm to have in-laboratory backup (which is in accordance with AASM guidelines). Within this at-home strategy, we separately examined the cost-only approach (ignoring utility values; **Figure 2A**), and a cost-effectiveness approach (incorporating a utility discount for untreated OSA; **Figure 2B**), across a range of time horizons. This enabled three-way sensitivity analysis across prevalence of OSA (prevOSA), cost of untreated OSA (cOSA), and time horizon (years).

As expected, when cost is the only consideration, the No-Rx approach is favored when either the cOSA is low or when the prevOSA is low (**Figure 2A**). Also as expected, when the cOSA is high and the prevOSA is high, the empiric Rx-All approach is favored. As the time horizon is advanced, the preference of the at-home approach is increased. Eventually, by 10-y, the in-laboratory approach becomes increasingly favored over the No-Rx and Rx-All approaches.

To illustrate how to interpret these two-way sensitivity analysis plots, consider a circumstance in which the prevOSA value is 20%,

Figure 1—Model basic structure.

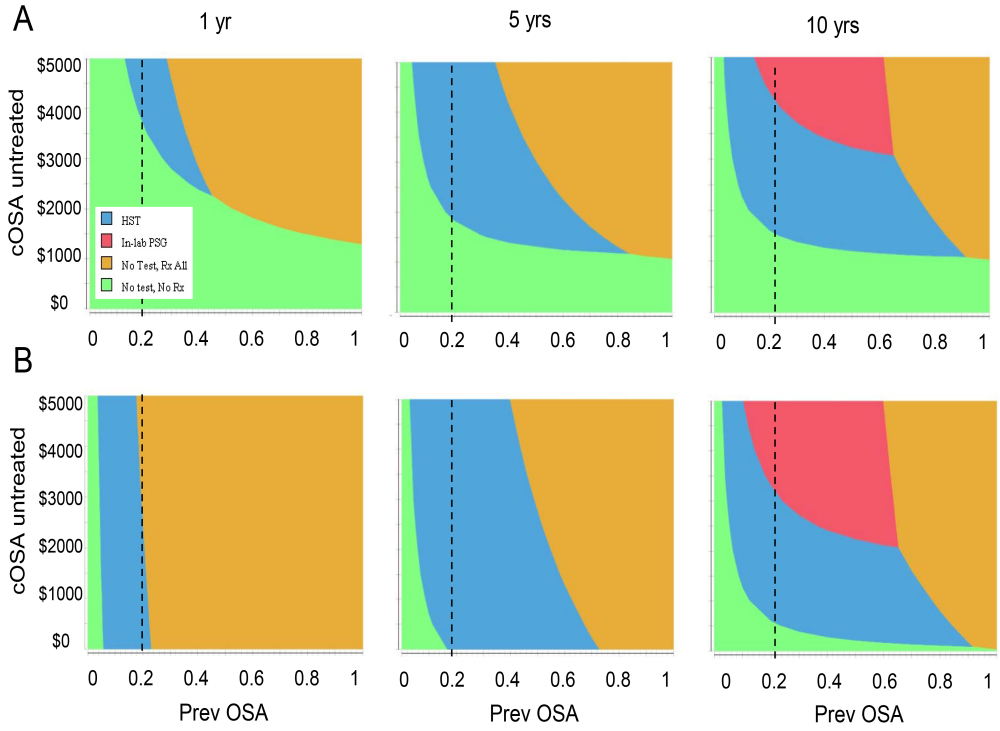


The model contains four strategies, emerging as branches from the original decision node (square). Each subsequent branch is determined by a probability (circle nodes), and its complement (#). In the branches associated with positive airway pressure (PAP) therapy (first three), the probability of accepting PAP therapy is lower in the false-positive settings. In branches involving a diagnostic step (middle two), the probability of false-positive and false-negative results depends on the pretest probability of OSA ("prev_OSA"). Terminal nodes are given by triangles. For simplicity, the subsequent branches of the strategies involving PAP therapy are described in bracketed text.

somewhat higher than present in the general adult population. Depending on the individual's predicted annual cost of untreated OSA, and the time horizon in question, the preferred strategy differs: for example, do-nothing is favored in some settings (**Figure 2A**, left panel, when cOSA is below ~$3,000), whereas in-laboratory PSG strategy is favored in others (**Figure 2A** and **2B**, 10-y time horizon, when cOSA is above $3,000–4,000).

For comparison, the same three-way sensitivity analyses were performed using a cost-effectiveness approach and assuming untreated OSA has reduced utility of 0.8 (**Figure 2B**). In this case, the No-Rx arm is markedly reduced and the Rx-All arm is favored. Again, over advancing time horizons, the at-home testing arm preference increases, and after a decade, in-laboratory testing becomes cost-effective.

Figure 2—Three-way sensitivity analysis, assuming the at-home strategy has no laboratory backup option.



In each panel, the prevalence of OSA is considered over the range of 0–1 probability (Prev_OSA; X-axes), and the cost of untreated OSA is considered over a range of $0–5,000 (cOSA; Y-axes). The vertical dashed line illustrates a prevalence of 20%, for visual comparison of favored strategies at that level. The three columns indicate different time horizons (1, 5, or 10 y). The top **(A)** and bottom **(B)** rows indicate whether the quality of life associated with untreated OSA (uOSA) is 1 or 0.8, respectively. The key shown in the top left graph applies to all panels. The X and Y axes are the same in all panels.

We next considered the same model, but allowing for in-laboratory backup of negative HST results and failed auto-PAP trials in the at-home arm (**Figure 3**). As expected, when cost is the only consideration, the No-Rx approach is favored when either the cOSA is low or when the prevOSA is low (**Figure 3A**). Also as expected, when the cOSA is high and the prevOSA is high, the Rx-All approach is favored. These findings are similar to those shown in **Figure 2A**. As the time horizon is advanced, there is a large increase in preference for the at-home arm, mainly at the expense of the Rx-All arm. The in-laboratory arm is only preferred in a small region at the border between No-Rx and the at-home arm in the 5- and 10-y models.

The same three-way sensitivity analyses were performed assuming untreated OSA has reduced utility of 0.8 (**Figure 3B**). In this case, the No-Rx arm is again markedly reduced, and the at-home arm is more favored. With longer time horizons, small increases in preference for the at-home arm occur, and again, as in **Figure 3A**, eventually the in-laboratory strategy enters. To illustrate how to interpret this set of two-way sensitivity analysis plots, we can again consider the prevOSA value of 20%, and observe that the optimal strategy depending on cOSA and time horizon.

Tables 2 and **3** summarize the net monetary benefit (NMB) associated with the four base cases, based on combinations of pretest probability of OSA (high versus low) and cost of untreated OSA (high versus low), at 5- and 10-y time horizons. The willingness to pay (WTP) is set at $50,000 per quality-adjusted life-year (QALY), and we assumed a pure-cost perspective (that is, uOSA = 1). NMB is calculated as the WTP per QALY minus cost per QALY (reported as an annual average). For example, if the cost per QALY were $5,000, the NMB would be $45,000 ($50,000–$5,000). The preferred strategy (mapping to the appropriate locations in **Figures 2** and **3**) are given as well.

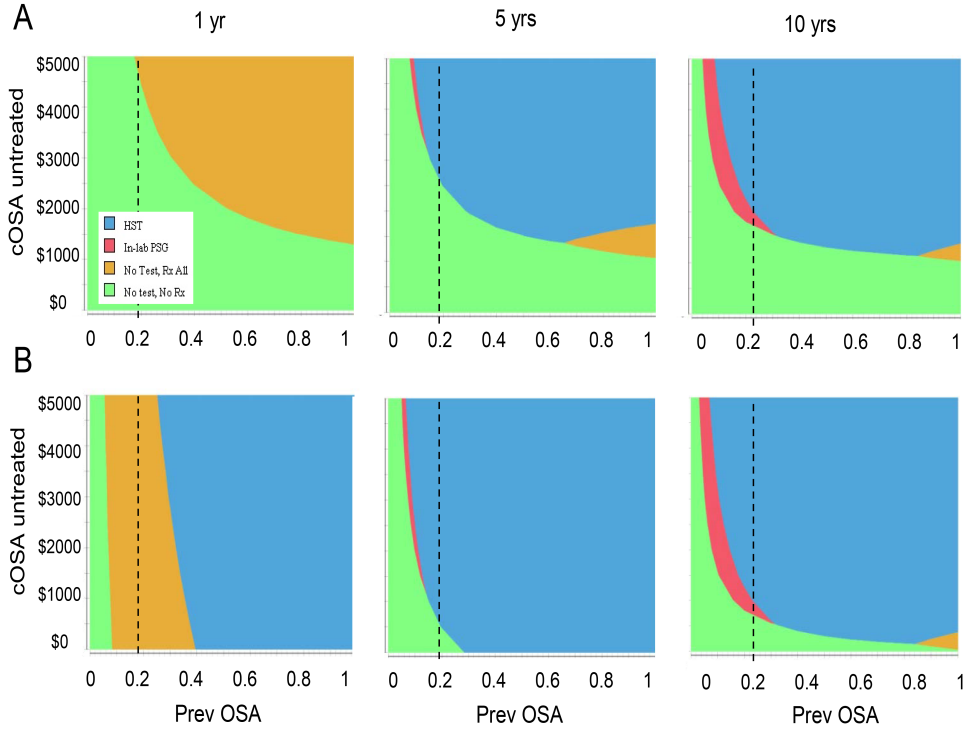
DISCUSSION

We used decision analysis to compare four strategies for OSA diagnosis and PAP treatment: No-Rx, Rx-All, in-laboratory pathway, and at-home pathway (with and without laboratory backup option in the at-home pathway strategy). We found that the optimal strategy depended on several key features: cost of untreated OSA, pretest probability of OSA, the time horizon under consideration, whether in-laboratory backup was employed in the at-home arm, and whether cost was the sole outcome (versus a combination of cost and quality of life). The results offer a framework for determining optimal diagnostic utilization that is flexible to patient-specific information, broadly applicable across clinical settings, and offers insights into variability among existing cost-effectiveness publications in this field.

Comparison with AASM Guidelines

The AASM and its leadership have issued two publications that specify the standard of care in regards to the use of HST to

Figure 3—Three-way sensitivity analysis, assuming in-laboratory backup is available for failed diagnostic and treatment steps in the at-home strategy.



In each panel, the prevalence of OSA is considered over the range of 0–1 probability (Prev_OSA; X-axes), and the cost of untreated OSA is considered over a range of $0–5,000 (cOSA; Y-axes). The vertical dashed line illustrates a prevalence of 20%, for visual comparison of favored strategies at that level. The three columns indicate different time horizons (1, 5, or 10 y). The top **(A)** and bottom **(B)** rows indicate whether the quality of life associated with untreated OSA (uOSA) is 1 or 0.8, respectively. The key shown in the top left graph applies to all panels. The X and Y axes are the same in all panels.

diagnose OSA. For example, assuming no contraindications to HST exist (such as comorbid sleep disorders or certain medical disorders), the AASM practice parameters[15] and technology review[14] specify a high pretest probability of at least moderate OSA (AHI > 15) is required to qualify for HST. This approach reflects the intention that HST kits are meant to confirm high-suspicion cases, and specifically not for general screening. The technology review defines "high" probability as 80%, stipulating that the diagnosis of OSA should require a posttest probability of 95% and assuming that the positive likelihood ratio for an HST device would be at least 5. However, the guidelines do not currently specify how to achieve that pretest probability.

The AASM guidelines do not comment on the time horizon or the costs associated with untreated OSA. These two factors however must play a major role in cost-effectiveness estimations of any model of OSA management and are particularly relevant from the payer perspective. To the extent that patients and providers must consider insurance regulations in decision making, the results suggest that utilization recommendations should consider more than pretest probability and severity. This is particularly important because the pretest probability itself is challenging to determine.[30] The model results indicate that the preferred strategy is strongly influenced by the pretest probability. Thus, the pretest probability aspect of the guidelines is important conceptually, especially in light of recent data that suggest that HST is being used across a broader range of pretest probability and severity than recommended by the AASM.[22,23]

The concept of pretest probability, and uncertainty therein, directly affects the practice of following up negative HST results with in-laboratory confirmation (as recommended by the AASM). In-laboratory backup for negative HST results, in the context of the AASM guidelines, is meant to capture false-negative cases that are most concerning when HST is restricted to high-probability cases. If the at-home strategy with in-laboratory backup is considered across a range of pretest probability of OSA (**Figure 3**), our results indicate that this strategy becomes favored strongly over the in-laboratory arm. This is because having a two-step process yields overall greater accuracy than either one can yield alone. Although this improvement occurs at greater incurred diagnostic costs, the overall approach is still within the WTP cost of $50,000.[31]

Regarding the use of in-laboratory backup across lower pretest probability cases, it is worth noting that interpretation of HST results is less straightforward than when HST is restricted to high probability cases. In general, according to Bayes theorem, for any test administered in a low pretest probability setting, most positive results will be false and most negative results will be true. This logic would imply that only positive HST findings in low pretest populations should be confirmed in-laboratory, whereas negative results would not require this (i.e., the opposite of the high pretest probability setting). However, HST

Table 2—Comparison of net monetary benefit across four base cases (assuming no in-laboratory backup).

Base Cases	Years	prevOSA	cOSA ($)	NMB ($)	C/E Branch
			Low prev, high cost		
1	5	15%	2,500	48,291.80	At-home
	10	15%	2,500	46,834.17	At-home
			Low prev, low cost		
2	5	15%	500	49,625.00	No-Rx
	10	15%	500	49,250.00	No-Rx
			High prev, high cost		
3	5	75%	2,500	43,595.00	Rx-All
	10	75%	2,500	37,370.00	Rx-All
			High prev, low cost		
4	5	75%	500	48,125.00	No-Rx
	10	75%	500	46,250.00	No-Rx

C/E, cost-effective branch favored; cOSA, cost of untreated OSA; HST, home sleep test; NMB, net monetary benefit (NMB = WTP − cost per QALY); prevOSA, prevalence of OSA; WTP, willingness to pay.

Table 3—Comparison of net monetary benefit across four base cases (assuming in-laboratory backup is available).

Base Cases	Years	prevOSA	cOSA ($)	NMB ($)	C/E Branch
			Low prev, high cost		
1	5	15%	2,500	48,125.00	No-Rx
	10	15%	2,500	46,668.62	In-lab
			Low prev, low cost		
2	5	15%	500	49,625.00	No-Rx
	10	15%	500	49,250.00	No-Rx
			High prev, high cost		
3	5	75%	2,500	44,139.09	At-home
	10	75%	2,500	39,050.79	At-home
			High prev, low cost		
4	5	75%	500	48,125.00	No-Rx
	10	75%	500	46,250.00	No-Rx

C/E, cost-effective branch favored; cOSA, cost of untreated OSA; HST, home sleep test; NMB, net monetary benefit (NMB = WTP − cost per QALY); prevOSA, prevalence of OSA; WTP, willingness to pay.

tends to underestimate the AHI, especially in mild cases.[14] Thus, to the extent that low pretest probability cases would be enriched for mild AHI values, there is a risk in principle of both false-positive (by Bayes' theorem) and false-negative (by virtue of AHI underestimation) results when HST is used, against AASM guidelines, in low pretest probability settings.

Finally, it is worth mentioning that the AASM guidelines do not recommend empiric treatment. Several studies have reported the use of empiric PAP therapy in those with high pretest probability.[25,26] However, using compliance with CPAP as a marker for the presence of OSA in these studies had weak sensitivity and specificity. The inclusion of this option of empiric PAP in our model answers the question: which combinations of OSA pretest probability and cost of untreated OSA would justify empiric treatment? It is interesting to note that the AASM guidelines suggest that 95% certainty of OSA as a goal of diagnostic inquiry, whereas our results suggest that, at least from a cost-effectiveness perspective, lower levels of certainty might not be unreasonable. Future studies are needed to elucidate the settings in which this approach might be considered in practice.

Comparison with Prior Decision Analysis Findings

Table 4 summarizes the prior work in this area. Several studies using modeling or actual clinical data considered only the "acute" time horizon, that is, the relative costs of diagnostic testing.[17,18,32] These studies concluded that home testing is cost-effective, despite the lack of consideration for downstream consequences required to contextualize the concept of cost-effectiveness in chronic diseases such as OSA. Our results confirm the expected relationship of time horizon with any cost-effectiveness balance: the longer the time frame, the more weight is placed on missing the diagnosis, that is, the cumulative effect of untreated OSA. This effect is paralleled by the accumulated costs associated with OSA treatment. The importance of time horizon is demonstrated in our results shown in the 1-y sensitivity plots, which were often quite different from later time points that favored more testing. Had we modeled a

Table 4—Summary of cost and decision models regarding obstructive sleep apnea diagnosis and management.

Reference	Population	Strategies	Time Frame	Comments
Reuvini 2001	70% prevalence	• In-lab, HST, attended HST	n/a	Focused on process costs, similar between PSG and HST
I.C.E.R. 2013	50% prevalence	• In-lab, HST, screen then PSG	n/a	Assume no failed HST, no PSG after negative HST, and no consequence for dx errors
Masa 2013	90% prevalence (clinical trial data)	• In-lab, HST, and HST only for high probability cases	n/a	Focused on process costs; HST only favored when limited to high probability cases
Teferra 2014	49% prevalence (actual clinic data)	• HST vs screen then HST	n/a	Screening to stratify HST use, with PSG backup for negative or low-risk cases, is favored
Chervin 1999	At least moderate OSA, older men, 85% prevalence	• In-lab (2-night) • HST, then lab CPAP if positive • No testing	5 y	PSG assumed to be 100% accurate. HST sensitivity and specificity both 95%.
Deutsch 2006	At least moderate OSA, male, 85% prevalence	• Full night PSG • Split-night PSG • HST, APAP	5 y	Quality of life reduced in OSA, but no downstream costs were considered.
Pietzsch 2011	At least moderate OSA, male, 50% prevalence	• Full night PSG • Split night PSG • At-home • No testing • Empiric CPAP	10 y; Lifetime	Specific events modeled (car accident, stroke, heart attack)

APAP, auto-positive airway pressure; CPAP, continuous positive airway pressure; HST, home sleep testing; I.C.E.R., The Institute for Clinical and Economic Review; OSA, obstructive sleep apnea; PSG, polysomnography.

time frame restricted to the night of testing, the No-Rx path would always be preferred, underlining the critical importance of time frame in any conceptualization of cost-effectiveness regarding a chronic disorder.

Prior work that utilized longer time horizons and incorporated adverse health consequences of untreated OSA differed in terms of which kinds of costs were considered and how the costs and quality of life of untreated OSA were considered. The most comprehensive model considered both acute and chronic costs and quality of life from heart attack, stroke, and motor vehicle accidents.[19] That model also considered No-Rx and Rx-All strategies, which were generally not favored in their sensitivity analysis. In addition to other structural differences from one another and from the current study, the references in **Table 4** each assumed a fairly high pretest probability of OSA (50% to 80%). Our model was intentionally general regarding certain costs, such as grouping all of untreated OSA into one cost value, specifically to allow broad generalization.

It is worth noting that other treatment modalities have different compliance determinants versus CPAP, such as dental appliance therapy, or do not require compliance at all, such as certain kinds of surgical therapy. Decision modeling suggests that CPAP is more cost-effective than dental appliance therapy[6] and dental appliance therapy is more cost-effective than no therapy.[33] Other modeling suggests that hypoglossal nerve stimulation compared to no therapy[34] and palate surgery compared to CPAP[35] may also be cost-effective in certain clinical settings.

Bayes' Theorem: The Importance of Pretest Probability

Bayes' theorem formalizes the idea that test results must be interpreted in the context of the pretest probability. The AASM practice parameters for HST emphasize that HST be reserved for high pretest probability OSA cases (80% chance of AHI > 15). Interestingly, reaching such a high pretest probability is more difficult than one might expect. For example, the sensitivity and specificity of expert clinical impression are each reported to be < 70%.[30] Considering the best-validated clinical screen, the "STOP-Bang" tool, and assuming a pretest probability of OSA in the general adult population of 10%, a positive screen yields a posttest probability of only 15% (sensitivity 93%, specificity 43%, for AHI > 15).

In general, when the pretest probability is low, false-positive risk is the main concern, whereas false-negative risk is greatest when the pretest probability is high. However, with HST, false-negative results can also occur at low pretest probability of OSA, because the kits tend to underestimate the AHI.[14] We did not model this eventuality explicitly, but rather included an adjustment term that assumed patients who with false-positive results would be less likely to accept CPAP treatment. The effect of false-positive results on overutilization of CPAP treatment remains uncertain.

Clinical Implications and Resource Utilization

PAP therapy for OSA is widely considered to be cost-effective, especially for those with at least moderate severity disease as defined by AHI > 15.[6] This is due in part to the increased costs and reduced QALY associated with untreated OSA. The costs of untreated OSA are diverse and include: increased clinical resource utilization (hospitalizations, physician visits, and medication), medical morbidity (heart disease, stroke, hypertension), and motor vehicle accidents, as well as indirect costs such as absenteeism and presenteeism.[5] Estimating the costs is

challenging because modeling often assumes a single perspective, such as the third-party payer (as in this study), although the employer cost perspective includes such factors as absenteeism and presenteeism, which may be more challenging to quantify than medical outcomes. In order to maximize the generalizability of our model, we collapsed the cost of OSA into a single value that can represent any cost consideration. As such, we varied the cost of untreated OSA in sensitivity analysis to span published data using a broad range. For example, Kapur et al.[4] reported that the health care costs incurred by OSA patients was $1,300 more per year before versus after initiating OSA therapy.[4] This strategy of a purposefully general concept of cost reflects the reality that individual patients may have different risks (and associated costs) of untreated OSA.

The time horizon is a critical variable as the costs of treatment as well as morbidities that may be low probability per year accumulate over time with important implications for cost-benefit balancing. Restricting analysis to inappropriately short time frames fails to capture the implications of misdiagnosis. In the case of OSA testing, the trade-off is that the less expensive HST kits have lower accuracy compared to in-laboratory PSG, even when HST use is restricted to populations in which contraindications are absent.[14] As described previously, when there is no consequence associated with reduced accuracy, the cheaper path will always be preferred.

It is worth mentioning that including a reduced utility of untreated OSA has a similar impact on the model as increasing the costs of untreated OSA. However, this quality factor is not easily translated into the perspective of payers faced with tangible financial pressures. Our model allows the composite variable of cOSA to capture the concept of reduced utility in that some of that reduction can in principle translate into a financial cost (for example, when sleepiness results in an accident).

Limitations and Future Directions

Our model does not consider factors that independently suggest the need for in-laboratory PSG, such as parasomnia, insomnia, narcolepsy, periodic limb movements, and complex apnea. Thus, like previous literature in this area, our model cannot account for all patient circumstances to predict the correct pathway. Accounting for such co-morbidities would be expected to favor in-laboratory pathways. For example, insomnia may be comorbid in a substantial portion of OSA patients,[36] which may have implications for PAP therapy adherence as well as for the accuracy of HST. Specifically, HST devices mainly utilize time in bed, rather than total sleep time, as the denominator for calculating event indices, leading to underestimation in proportion to the degree of objective insomnia present. It is also worth noting that only a subset of HST devices report body position, and in those cases validation data for the position sensor are sparse.[14] We and others have shown that body position is more important than sleep stage in regard to the potential for misclassification of OSA severity,[37] and positional OSA may predict response to position therapy and other non-PAP therapies,[38] and thus is of interest to clinical care in OSA. Including considerations such as these would likely favor in-laboratory PSG from a cost-benefit standpoint. Finally, certain features remain difficult to quantify in practice, beyond the pretest probability challenge. For example, the time horizon could refer to the probability that a patient remains with a given insurer, or it could refer to life expectancy. The cost of untreated OSA, likewise, will depend on likely complicated models of comorbidities, medical resource utilization prior to OSA diagnosis, and the extent to which OSA is linked to costs for an individual patient. Further investigation is warranted to inform each of the variables that we identified as important, in order to better address the utilization dilemmas in this field.

ABBREVIATIONS

AASM, American Academy of Sleep Medicine
AHI, apnea-hypopnea index
cOSA, cost of untreated OSA
CPAP, continuous positive airway pressure
HST, home sleep testing
OSA, obstructive sleep apnea
NMB, net monetary benefit
PAP, positive airway pressure
PLMS, periodic limb movements of sleep
prevOSA, prevalence of OSA
PSG, polysomnography
QALY, quality-adjusted life-year
Rx, treat
uOSA, utility of untreated OSA
WTP, willingness to pay

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