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# Cost-Effectiveness of Regular Surveillance Versus Endoscopy at Need for Patients With Barrett's Esophagus: Economic Evaluation Alongside the Barrett's Oesophagus Surveillance Study (BOSS) Randomized Controlled Trial

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**BACKGROUND & AIMS:** The Barrett's Oesophagus Surveillance Study (BOSS) was the first randomized study of surveillance. This study reports the costs and quality of life outcomes from the BOSS trial and models the outcomes and cost-effectiveness of surveillance beyond the follow-up period of the BOSS study. This trial showed similar stages and rates of esophageal cancer in both arms, but the regular surveillance arm did identify more high-grade dysplasia after a median of 12.8 years follow-up. **METHODS:** We used a decision tree model based on results from BOSS to conduct a cost-effectiveness analysis of costs and quality-adjusted life years (QALYs). A Markov model was used to extrapolate costs and outcomes over a further 10 years after the trial had ended, representing a 22.8-year time horizon. The proportion with high-grade dysplasia and QALYs was derived from the randomized trial. **RESULTS:** The total costs associated with 2-yearly surveillance was $5309 vs $3182 in the at-need arm. Total QALYs in the 2-yearly endoscopy arm were 8.647 compared with 8.629 in the at-need arm. Compared with at-need endoscopy, 2-yearly surveillance costs $115,563/QALY gained. In the sensitivity analyses around assumptions on the proportion of high-grade dysplasia that is undetected in the at-need endoscopy arm, surveillance had an incremental cost effectiveness ratio of $94,513/QALY for the best-case and $146,272/QALY for the worst-case scenario. **CONCLUSION:** Barrett's esophagus surveillance every 2 to 3 years is unlikely to be a cost-effective strategy. Guidelines should take this into account when deciding surveillance intervals

*Keywords:* Quality-Adjusted Life Years; High-Grade Dysplasia; Esophageal Adenocarcinoma; Markov Model; Cost-effectiveness Acceptability Curve.

Most guidelines in the developed world recommend surveillance of Barrett's esophagus (BE) every 3 to 5 years.[1–3] The rationale for guidelines is that BE is a major risk factor for esophageal adenocarcinoma (EAC), which has a high mortality when detected symptomatically. Patients with BE have a much greater risk of developing EAC compared with the general population,[4] and screening BE can detect dysplasia before EAC develops, when it is amenable to ablation or endoscopic mucosal resection.[5] Even if EAC has already developed, regular surveillance may detect the cancer early when surgery can result in a substantially higher survival.[6] The risk of progression to cancer in BE is low,[7] so the question is whether surveillance is cost-effective given the ever-increasing cost of treating gastrointestinal disease and the need to use scarce resources wisely.

Most health economic models suggest BE surveillance is cost-effective,[8–11] although there are exceptions.[12,13] The main reason for discrepancies in assessments of cost-effectiveness of BE surveillance are differing assumptions around risk of progression to cancer and the effectiveness of surveillance.[13] These inputs to the models rely on observational data. The rise in large electronic databases allows for more accurate determination of the annual risk of progression, which most agree is $<0.4\%$ per year.[14] The effectiveness of surveillance, however, is uncertain because observational studies tend to overestimate due to confounding and bias.[15]

We conducted the first long-term randomized controlled trial (RCT) assessing surveillance vs at-need endoscopy with

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***Abbreviations used in this paper:*** **BE, Barrett's esophagus; BOSS, Barrett's Oesophagus Surveillance Study; EAC, esophageal adenocarcinoma; EQ-5D-3L, EuroQoL 5-Dimension 3-Level; HGD, high-grade dysplasia; LGD, low-grade dysplasia; QALYs, quality-adjusted life years; RCT, randomized controlled trial; WTP, willingness-to-pay.**



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**WHAT YOU NEED TO KNOW**

BACKGROUND AND CONTEXT

Surveillance for Barrett's esophagus is recommended every 3 to 5 years. A randomized trial showed there was no difference in the incidence of esophageal adenocarcinoma or the stage detected between regular surveillance or at-need endoscopy.

NEW FINDINGS

A modeling exercise was conducted to determine whether surveillance would be cost-effective over a further 10 years of follow-up. There was a modest gain in quality of life, but this was not cost-effective.

LIMITATIONS

Although data from the randomized trial were mainly used, literature sources were used for some assumptions. The trial did have significant contamination that would bias results toward the null.

CLINICAL RESEARCH RELEVANCE

These data suggest surveillance every 2 to 3 years is not cost-effective, and future guidelines need to take this into account when recommending surveillance intervals for Barrett's esophagus.

BASIC RESEARCH RELEVANCE

Further work needs to be done on animal models and biomarkers to better risk stratify those who need more frequent vs less frequent surveillance because the current strategy is unlikely to be cost-effective.

follow-up for 10 to 15 years, the Barrett's Oesophagus Surveillance Study (BOSS trial).[16] This trial reported no difference in all-cause or EAC mortality.[17] There was a difference in high-grade dysplasia (HGD) detected, with more patients having this detected in the regular surveillance arm compared with the "at-need" arm of the trial. It is possible that ablation of HGD would result in lower EAC rates in the surveillance arm beyond the 10- to 15-year follow-up of the trial and that this could result in the surveillance strategy being cost-effective over a longer time horizon.

Additionally, although the difference in overall stage of cancers detected in the 2 arms was not significant, there was a trend toward a higher number of T1a cancers in the surveillance arm. This trial also has the advantage that it determined the quality-adjusted life years (QALYs) of individuals in various states from nondysplastic BE to HGD and EAC.

The RCT showed no difference in EAC rates or stage between the surveillance and at-need arm. The at-need arm had fewer endoscopies, and therefore, over the medial 12.8 years of the trial, the surveillance arm had greater costs with the same outcome. Cost minimization would suggest at need would be the cheaper option; however, a post hoc analysis to evaluate the detection of dysplasia found 114 of 1733 (7%) in the surveillance group compared with 48 of 1719 (3%) in the at-need group had low-grade dysplasia (LGD) as the most advanced grade of dysplasia detected during the trial. Similarly, 47 of 1733 (3%) in the surveillance group compared with 19 of 1719 (1%) in the at-need group had HGD as the most advanced grade of dysplasia detected during the trial. It is possible that if we had evaluated patients for longer, we would have found a lower incidence of EAC in the surveillance group due to ablation of HGD. We have therefore modeled the RCT data going beyond the duration of the trial to evaluate whether BE surveillance is likely to be cost-effective.

## Methods

The methods and results of the BOSS RCT have been reported elsewhere.[16,17] Briefly, patients aged >18 years with at least 1 cm of BE with no HGD were randomized to surveillance endoscopy every 2 years or endoscopy only if they developed symptoms such as dysphagia, weight loss, or worsening upper gastrointestinal symptoms. QALYs were measured using the EuroQoL 5-Dimension 3-Level (EQ-5D-3L) questionnaire[18] every 2 years until the end of the trial. Follow-up was at least 10 years. The main outcome was all cause mortality, and secondary outcomes included cancer-specific mortality, stage of EAC, and frequency of endoscopy.

The trial randomized 1733 patients to endoscopy every 2 years and 1719 to at-need endoscopy, with a mean follow-up of 12.8 years for the primary end point. There was no difference in all-cause mortality (19.2% in the surveillance arm and 20.7% in the at-need arm) or EAC mortality (7% in the surveillance arm and 5% in the at-need arm). As expected, the difference in endoscopy rates between the groups was significant: 93% of the surveillance arm had at least 1 endoscopy compared with 59% in the surveillance arm

### *Model Development*

We conducted a cost-effectiveness analysis using a decision tree model, comparing costs and QALYs associated with 2-yearly surveillance vs endoscopy at need. The decision tree represents the progression of BE to LGD, more severe disease (HGD and EAC), and associated costs and QALYs, over the BOSS 10-year time horizon, in both arms (because all participants in the BOSS trial had at least 10 years of follow-up). The long-term cost and QALYs associated with detected HGD and EAC were calculated using a Markov-type decision analytic model that extrapolates costs and outcomes associated with the detection and treatment of HGD and EAC over the following 10 years after the trial was completed.

The model draws on the difference between arms in the number of HGDs and EACs detected within the 10 years of the BOSS trial, exploring whether early detection of HGD and EAC prevents progression to advanced-stage cancer and leads to significant differences in costs and quality of life. The analysis was conducted from a United Kingdom National Health Service and Personal Social Service perspective. We have calculated EQ-5D utility values associated to each state (LGD, HGD, EAC) from the BOSS trial. Participants with HGD completed the EQ-5D in the trial before being aware of the diagnosis and before any treatment, and the QALY for this group was slightly lower than those with nondysplastic BE. We used this value in the model, even if the participant was not aware of the diagnosis, to mirror results of the trial as much as possible but modeling them a further 10 years.

In line with National Institute for Health and Care Excellence guidance, costs and benefits are discounted at 3.5% per year.[19] Costs are based on the 2021/2022 price level or adjusted accordingly using national indices. Costs were translated from Great British pounds to United States dollars using the purchasing power parity (PPP) conversion factor.[20] The decision tree and the Markov model were developed using Microsoft Excel. A Health Economics Analysis Plan (HEAP) was developed and is available upon request. Parameters distributions were chosen following standard guidance.[21]

## Decision Tree

The BOSS decision tree (Figure 1) is structured with 2-yearly endoscopy and endoscopy at need as the 2 competing strategies in the management of patients with BE. The model

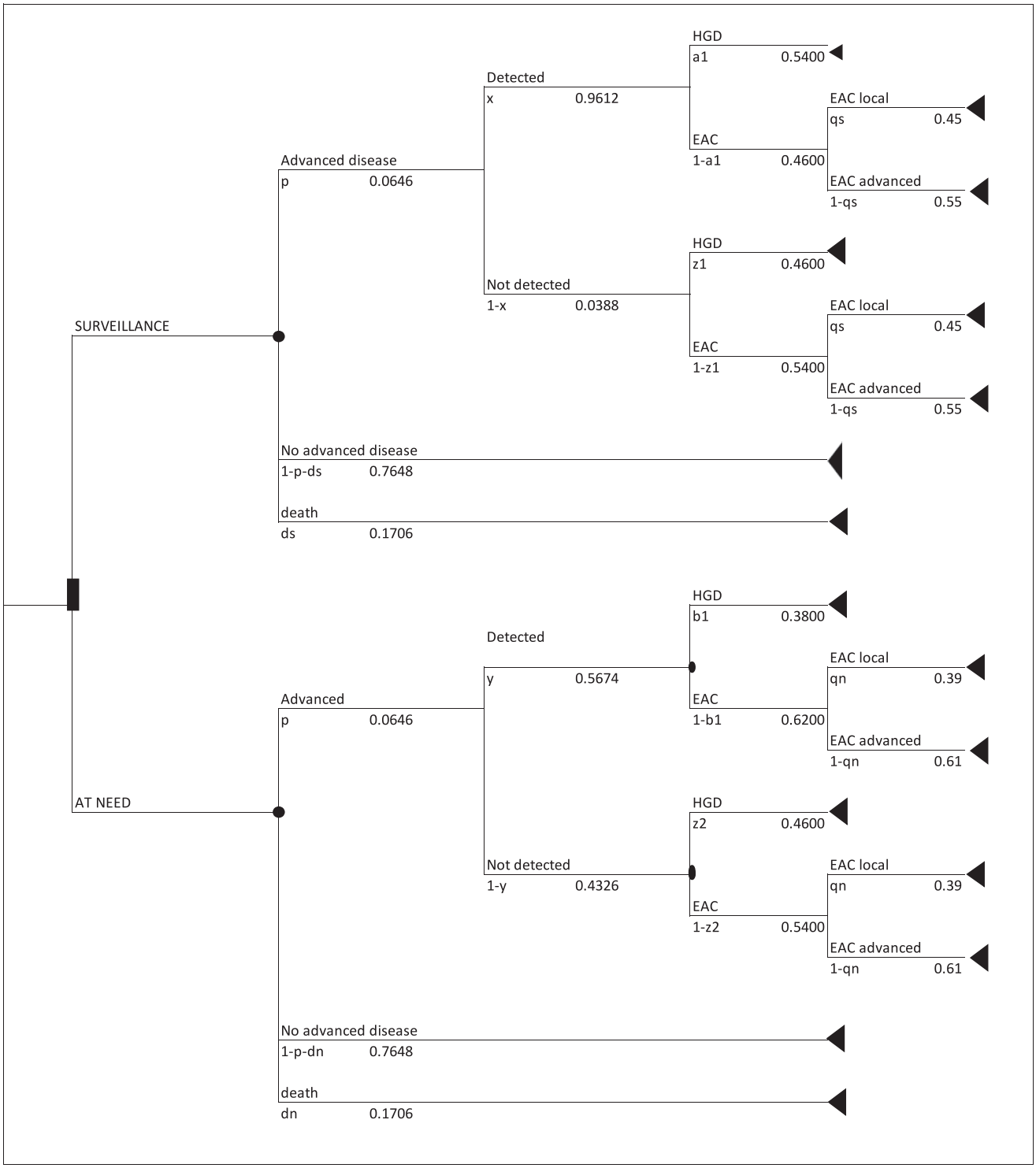


**Figure 1.** BOSS decision tree. Decision tree of 2-yearly surveillance endoscopy (*upper branch*) and endoscopy at need (*lower branch*) for patients with BE. No advanced disease indicates metaplasia (M) or LGD. (See Table 1 for probabilities.)

represents the progression of BOSS patients within the trial period (ie, patients with BE diagnosis, with an average age of 63 years), with results taken from the BOSS study. At the end of the 10 years, patients can be categorized as having developed an advanced disease state (HGD or EAC), no disease (metaplasia or LGD), or died.

The 2 main branches on the left of the tree represent the trial arms, whereas the branches on the right side represent the events associated with the progression of BE. All branches in the tree are assigned a probability value, and each stage of BE progression is associated with QALYs and costs. Expected costs and QALYs are calculated as weighted averages of pathway probabilities and cost and QALY.

Table 1 summarizes the probability parameters used in the decision tree and the assumptions made. Patients are randomized to surveillance or the at-need arm with equal probability. We assume that the population prevalence of HGD and EAC, *p*, by the end of the trial period, is equal to the prevalence detected in the surveillance arm. We assumed that 95% of EAC during the trial would be detected by endoscopy[22] (those in the at-need arm were offered an exit endoscopy) and so used the prevalence of EAC from trial data.

We used the death probability at 10 years estimated from the Kaplan-Meier analysis in the BOSS trial to model the death rate in the surveillance and at-need arm ($d_s$ and $d_n$). Considering the BOSS trial result showing no significant difference in survival between arms, we assume these are equal. The *x* and *y* represent the proportion of detected advanced diseases (HGD+EAC) in the surveillance and in the at-need arm, respectively, over the expected number of events.

The proportion of HGD over the total of detected and undetected EAC + HGD is indicated with parameters $a_1$ and $z_1$ (surveillance arm) and $b_1$ and $z_2$ (at-need arm), with their complement representing the proportion of EAC. Specifically, $b_1$ has been calculated as the number of HGD over the total number of HGD and EAC detected in at-need arm. We assume that $z_1$ (proportion of undetected HGD) equals the proportion of HGD over the total HGD + EAC detected in the surveillance arm. We assume that the value of $z_2$ is the midpoint between $a_1$ and $b_1$ and use $a_1$ and $b_1$ in a sensitivity analysis. The proportion of local cancers has been calculated from the BOSS trial and indicated with parameters $q_s$ (surveillance arm) and $q_n$ (at-need arm).

A table with the number of events (metaplasia, LGD, HGD, EAC) by trial arm as well details on calculations of the model parameters are included in Supplementary Table 1 and Supplementary Table 2. Costs and QALYs associated with detection, treatment, and progression of the HGD and EAC states have been estimated using a Markov decision analytic model, as described in the following section. Results are expressed as an incremental cost-effectiveness ratio which is the difference in cost divided by the difference in outcomes between the 2-yearly surveillance strategy and the at-need scenario.

## Markov Model

The Markov model (Figure 2) projects progression of HGD and early EAC into treatment, advanced EAC, early EAC treatment, and associated mortality, quality-adjusted life expectancy, and costs. The model simulates a cohort of patients after 10 years in the BOSS trial (aged 73 at the beginning of the model) and includes 5 mutually exclusive states (HGD; successful endoscopic treatment for HGD; EAC local; successful treatment for EAC local, EAC advanced) and death (an absorbing state). All members of the cohort start in HGD or EAC local stage. With each cycle of the model, patients have an annual probability of remaining in the same state or moving to another state.

Health-related quality of life associated with HGD and EAC states was measured within the trial using EQ-5D-3L. Information about quality of life was collected at baseline for all, at endoscopy for all (unless the endoscopy is only 3 months from the previous endoscopy), and then every 2 years for

**Table 1.** Probabilities Used in the Barrett's Oesophagus Surveillance Study Decision Tree

| Parameter | Description | Value | Source and assumptions |
|---|---|---|---|
| Probabilities | | | |
| p | Prevalence (HGD + EAC in BE population) | 0.06 | BOSS trial—assume prevalence is EAC+HGD in surveillance arm + 5% missed events |
| x | Probability (detection HGD + EAC surveillance arm) | 0.96 | Number of cases detected: HGD + EAC, BOSS trial (surveillance arm) |
| y | Probability (detection HGD + EAC at-need arm) | 0.57 | Number of cases detected: HGD + EAC, BOSS trial (at-need arm) |
| $a_1$ | Probability (HGD\| detection surveillance arm) | 0.54 | Calculations from BOSS trial |
| $1-a_1$ | Probability (EAC\| Detection SURVEILLANCE ARM) | 0.46 | Calculations from BOSS trial |
| $z_1$ | Probability (HGD\| no detection) | 0.46 | Assume midpoint between $a_1$ and $b_1$. Assume it's the same between arms |
| $1-z_1$ | Probability (EAC\| no Detection) | 0.54 | Assume midpoint between $a_1$ and $b_1$. Assume it's the same between arms |
| $b_1$ | Probability (HGD\| Detection at-need arm) | 0.38 | Calculations from BOSS trial |
| $1-b_1$ | Probability (EAC\| Detection at-need arm) | 0.62 | Calculations from BOSS trial |
| $d_s$ | Probability of death in the surveillance arm | 0.17 | Calculations from BOSS trial |
| $d_n$ | Probability of death in the at-need arm | 0.17 | Calculations from BOSS trial |
| $q_s$ | Proportion of EAC local/total EAC, surveillance arm | 0.45 | Calculations from BOSS trial |
| $1-q_s$ | Proportion of EAC advanced/total EAC, surveillance arm | 0.55 | Calculations from BOSS trial |
| $q_n$ | Proportion of EAC local/total EAC, at-need arm | 0.39 | Calculations from BOSS trial |
| $1-q_n$ | Proportion of EAC advanced/total EAC, at-need arm | 0.61 | Calculations from BOSS trial |

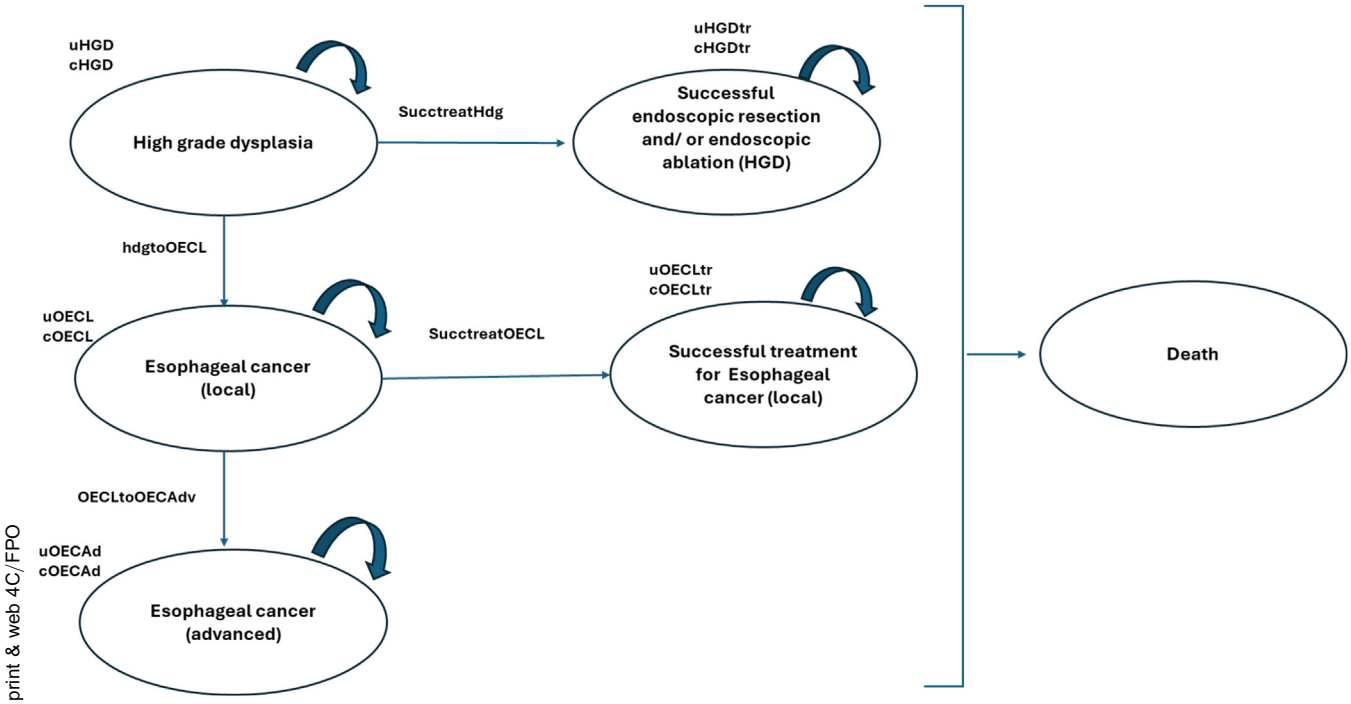




**Figure 2.** Markov model. cHDG: cost, HDG; cHDGtr: cost, endoscopic treatment for HDG; cOECAd: cost, esophageal adenocarcinoma (advanced); cOECL: cost, esophageal adenocarcinoma (local); cOECLtr: cost, treatment for esophageal adenocarcinoma (local); OECLtoOECAdv: transition probability, esophageal adenocarcinoma (local) to esophageal adenocarcinoma (advanced); SucctreatHdg: transition probability, successful HDG treatment; SucctreatOECL: transition probability, successful treatment for esophageal adenocarcinoma (local); uHDG: utility, HDG; uHDGtr: utility, endoscopic treatment for HDG; uOECAd: utility, esophageal adenocarcinoma (advanced); uOECL: utility, esophageal adenocarcinoma (local); uOECLtr: utility, treatment for esophageal adenocarcinoma (local).

those in the at-need arm if they did not have an endoscopy. Health-related quality of life associated with HGD and local EAC was estimated from the BOSS trial, adjusting by trial arm, age, and sex. The utility associated with HGD successful treatment, as well as the utility associated with EAC advanced, were estimated from secondary literature, because it was not possible to obtain reliable estimates from the BOSS trial data.

The cost of endoscopy, as well as the annual health service cost associated with each of the disease states, was obtained from the National Health Service reference costs[23] and the National Institute for Health and Care Excellence guidelines for EAC and incorporated within the model. Further details on cost calculations and sources are provided in the Supplementary Material and Supplementary Table 3.

In consideration of the low number of events detected in the BOSS trial, estimating transition probabilities between HGD and EAC states using the BOSS trial data was not possible. Annual transition probabilities were thus estimated from secondary literature. The survival probabilities associated with HGD resection/ablation were estimated using the national life-tables by the Office for National Statistics in United Kingdom and corrected by the additional mortality associated with BE.[24] The mortality rate associated with EAC was estimated from the BOSS trial. Because we did not find any difference between the arms in overall survival or cancer-related survival,[17] we used the same mortality in both scenarios. Table 2 lists the model parameters.[9,23–27]

### *Sensitivity Analysis*

We performed a deterministic sensitivity analyses to assess the robustness of results to the value of $z_1$ (ie, proportion of undetected HGD in both arms). With $z_1$ unknown, we assume this is equal to the midpoint between $a_1$ and $b_1$ and relax this assumption (using $a_1$ and $b_1$) in a sensitivity analysis.

In addition to the scenario analysis, a probabilistic sensitivity analysis was conducted to account for the uncertainty around the model parameters. A Monte Carlo simulation was run 1000 times to generate random values for each of the input parameters. The uncertainty around the incremental cost-effectiveness pair has been represented in the cost-effectiveness plane. Cost-effectiveness acceptability curves have been shown as well, to represent the probability that 2-yearly surveillance is cost-effective compared with surveillance at need at different willingness-to-pay (WTP) thresholds.

## Results

Table 3 summarizes the cost-effectiveness results for the base-case analysis. The total cost associated with 2-yearly surveillance was $5309 vs $3182 in the at-need arm. As expected, 2-yearly surveillance is more expensive than the at-need arm ($1894), in consideration of the difference in the number of endoscopies undertaken in the 2 arms (3.5 surveillance arm; 1.8 at-need arm). Total QALYs in the 2-yearly endoscopy arm were 8.647 compared with 8.629 in

**Table 2.** Markov Model Parameters

| Parameter | Mean | SE | Reference |
|---|---|---|---|
| Transition probabilities | | | |
| Successful HGD ablation/resection | 0.88 | 0.172 | [9] |
| Successful EAC local treatment | 0.87 | 0.1 | [25] |
| Transition HGD to EAC local | 0.06 | 0.008 | [26] |
| Transition EAC local to EAC advanced | 0.14 | 0.05 | [27] |
| Increased mortality from BE | 1.21 | 95% CI 1.14–1.30 | [23] |
| Increased mortality from EAC (advanced) | 4.4 | 1.19 | BOSS RCT |
| Utilities | | | |
| HGD | 0.76 | 0.03 | BOSS RCT |
| EAC local | 0.74 | 0.04 | BOSS RCT |
| EAC advanced | 0.675 | 0.032 | [27] |
| HGD/EAC local treatment (year 1) | 0.55 | 0.002 | [27] |
| HGD/EAC local treatment (year 2–20) | 0.74 | 0.03 | BOSS RCT |
| Cost ($) | | | |
| HGD | 0 | 0 | |
| HGD treatment year 1 | 11,075 | 1439.8 | NHS reference costs, NICE[23] |
| HGD treatment year 2–6 | 1332 | 173.2 | NHS reference costs, NICE[23] |
| HGD treatment year 7–20 | 0 | 0 | NHS reference costs, NICE[23] |
| EAC local | 0 | 0 | NHS reference costs, NICE[23] |
| EAC local treatment year 1 | 40,607 | 5279 | NHS reference costs, NICE[23] |
| EAC local treatment year 2 | 10,652 | 1385 | NHS reference costs, NICE[23] |
| EAC local treatment year 3–20 | 1332 | 173.2 | NHS reference costs, NICE[23] |
| EAC advanced | 11,697 | 1520 | NHS reference costs, NICE[23] |
| Discount rate | | | |
| Discount rate cost | 0.035 | | |
| Discount rate QALY | 0.035 | | |

NHS, National Health Service; NICE, National Institute for Health and Care Excellence; SE, standard error.

the at-need arm, resulting in a small QALYs gain of 0.018. The intermediate outcomes of EAC cases and EAC deaths in both arms are given in Supplementary Table 4. Compared with at-need endoscopy, 2-yearly surveillance costs $115,563/QALY gained, thus being unlikely to be cost-effective. Indeed, the cost-effectiveness acceptability curve in the base-case analysis (Supplementary Figures 1 and 2), shows the likelihood of 2-yearly surveillance being cost-effective equal to 22% and 52% for a WTP of $50,000 and $100,000 WTP threshold values, respectively.

### *Sensitivity Analysis*

Table 4 gives the results related to the sensitivity analysis around the differences in the proportion of HGD detected in the surveillance and at-need arms. In the scenario analysis, we change the assumption that $z_1$ (ie, the proportion of undetected HGD) is equal to the midpoint between $a_1$ (proportion of detected HGD in surveillance arm) and $b_1$ (proportion of detected HGD in at-need arm). Assuming $z_1$ equal to $b_1$ (scenario 1), the total cost associated with 2-yearly surveillance was $5315 vs $3251 in the

**Table 3.** Incremental Costs and Incremental Quality-Adjusted Life Years for the Base-Case Analysis

| Base-case scenario | Costs | Incremental | 95% bootstrapped CI | |
|---|---|---|---|---|
| Biennial surveillance | 5,309 | 2,128 | 1235 | 3021 |
| Surveillance at need | 3,182 | | | |
| | QALY | Incremental | 95% bootstrapped CI | |
| Biennial surveillance | 8.647 | 0.018 | −0.010 | 0.060 |
| Surveillance at need | 8.629 | | | |
| ICER | 115,563 | | 33,563 | dominated |

CI, confidence interval; ICER, incremental cost-effectiveness ratio.

**Table 4.** Incremental Costs and Incremental Quality-Adjusted Life Years for the Sensitivity Scenarios

| Sensitivity analysis I ($z_1 = 0.38$) | Costs | Incremental | 95% bootstrapped CI | |
|---|---|---|---|---|
| Biennial surveillance | 5315 | 2065 | 1125 | 3141 |
| Surveillance at need | 3251 | | | |
| | QALY | Incremental | 95% bootstrapped CI | |
| Biennial surveillance | 8.647 | 0.022 | −0.007 | 0.055 |
| Surveillance at need | 8.625 | | | |
| ICER | 94,513 | | 37,298 | Dominated |
| | Costs | Incremental | 95% bootstrapped CI | |
| Biennial surveillance | 5,304 | 2,190 | 1141 | 3162 |
| Surveillance at need | 3,113 | | | |
| | QALY | Incremental | 95% bootstrapped CI | |
| Biennial surveillance | 8.647 | 0.015 | −0.010 | 0.056 |
| Surveillance at need | 8.632 | | | |
| ICER | 146,272 | | 34,103 | Dominated |

CI, confidence interval; ICER, incremental cost-effectiveness ratio.

at-need arm. Total QALYs in the 2-yearly endoscopy arm were 8.647 compared with 8.625 in the at-need arm, resulting in a small QALY gain of 0.022. Setting $z_1$ equal to $a_1$ (scenario 2), the total cost associated with 2-yearly surveillance was $5304 vs $3113 in the at-need arm. Total QALYs in the 2-yearly endoscopy arm were 8.647 compared with 8.632 in the at-need arm, resulting in a small QALY gain of 0.015. Compared with at-need endoscopy, 2-yearly surveillance costs $94,513/QALY (scenario 1—best case) and $146,272/QALY (scenario 2—worst case). The cost-effectiveness acceptability curves for the best and worst case are given in Supplementary Figures 3 to 6. Supplementary Figure 7 provides information on which variables lead to most uncertainty in the model.

## Discussion

This is the first health economic model of Barrett's surveillance based on large-scale RCT data with long-term follow-up. The RCT showed no difference in overall survival or EAC mortality between 2-yearly surveillance and no surveillance with endoscopy only offered at need for symptoms. Given the outcomes were the same between the groups, that the more intensive surveillance arm would not be cost-effective is not surprising. However, HGD was detected twice as often in the surveillance arm, and 10 to 15 years of follow-up may not have been sufficient to capture all the benefit of surveillance. We therefore modeled this and found surveillance was still not likely to be cost-effective after a further 10 years of follow-up, even with optimistic assumptions around the benefit of detecting and treating HGD.

The RCT offered endoscopy every 2 years, whereas most guidelines suggest surveillance every 3 to 5 years.[1–3] It could be argued that the trial did not reflect the frequency of surveillance currently recommended. However, the average surveillance interval in the trial was 3 years, and this is what was costed, so this does reflect existing practice. Future guidelines may find this information useful when formulating new surveillance recommendations. The bottom line is that EAC deaths are relatively uncommon,[7] surveillance is imperfect at preventing these rare events,[17] and most patients will die of unrelated causes.[28] Given this, the cost of more intensive surveillance does not seem justified.

These data have other implications. There is interest in case finding and screening everyone with heartburn over a certain age threshold or focusing on men, or both, to increase the yield.[29] This may not be cost-effective if done by endoscopy, but new less-invasive approaches have reasonable accuracy to detect BE and may be cost-effective.[30] If surveillance of BE is of uncertain cost-effectiveness, then screening to detect new cases is even less likely to be economically sensible.

This study has several strengths. Many of the transition probabilities are based on randomized trial data and extrapolation to a further 10 years is more likely to be accurate than previous models. We have also used trial-based QALYs data so quality of life gains can be more accurately estimated.

However, there are several weaknesses. The trial was conducted in the United Kingdom, and cost-effectiveness calculations may not apply to other countries. The cost of endoscopy is higher in the United States, so costs are likely to be higher with no additional benefit than observed in this study. We assumed no one had surveillance for the extra 10 years of modeling and looked at the benefit of treating HGD detected in the first 10 to 15 years. It could be argued that we

should model continued surveillance and at-need endoscopy for the extra 10 years in the 2 groups. However, the trial did not show any benefit for those who did not have EAC or HGD at baseline, so this is will not show any benefit for those without these conditions having surveillance for an extra 10 years but will add extra cost. As such, our approach is weighted in favor of surveillance, and yet, the model found this was not likely to be cost-effective.

We also did not evaluate subgroups such as those with extensive BE and men. We did not do this because the randomized trial showed no difference in outcome in these high-risk subgroups. We did have QALY measurements for participants of the trial, but this was completed infrequently in the last few years of the trial related to coronavirus disease 2019, and we do not have robust longer-term data on QALYs. This could diverge in either direction, with patients being made anxious at the approach of their endoscopy and waiting for biopsy results (and anxiety continuing with a LGD diagnosis) or reassured when results are negative.

QALYs early in the trial were the same in both groups, so the most likely scenario is that there is little difference. EAC events are also rare, so 95% confidence intervals around transition probabilities are wide. We also did not model different surveillance intervals because we wanted to adhere as close as possible to the trial data. The trial did have significant contamination, with many of the at-need endoscopy arm having some endoscopy that would bias results toward the null.

Ablation strategies[31] and advanced imaging techniques[5] are improving. Currently, whether they will improve HGD and EAC detection and management is uncertain, but this could alter cost-benefit in the future.

Finally, we did not formally validate our model against other cohorts because we were modeling our randomized trial data to evaluate whether regular surveillance could be cost-effective if we hypothetically monitored participants for another 10 years. That the randomized trial may not be reflective of the general population could be argued, but we believe this is unlikely because the rates of EAC seen in the trial were similar to those seen in population-based studies.[32,33]

Our model suggests that the cost of surveillance is high and the benefit is modest, even when considering more long-term benefits of treating HGD. Future guidelines should consider this when formulating surveillance recommendations.

## Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2025.04.026.

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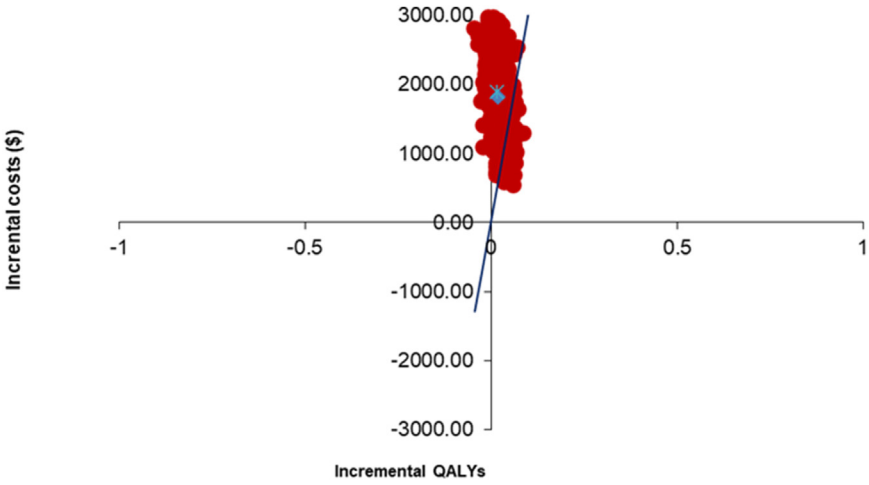
## Supplementary Material

Supplementary Table 1 shows the number of patients diagnosed with metaplasia, LDG, HGD, and EAC in the BOSS full data set. Because there are multiple diagnoses (ie, multiple endoscopies over time) per patient, we keep the most severe diagnosis at first occurrence.

Assuming an underlying prevalence of EAC+HGD is equal to 6.5%, the rate of detection of EAC+HGD is 96% in the surveillance arm and 57% in the at-need arm. When considering HGD and EAC separately, 2-year surveillance is detecting 96% of HGD and 96% of EAC, compared with endoscopy at need (77% EAC and 40% HGD) (Supplementary Table 2).

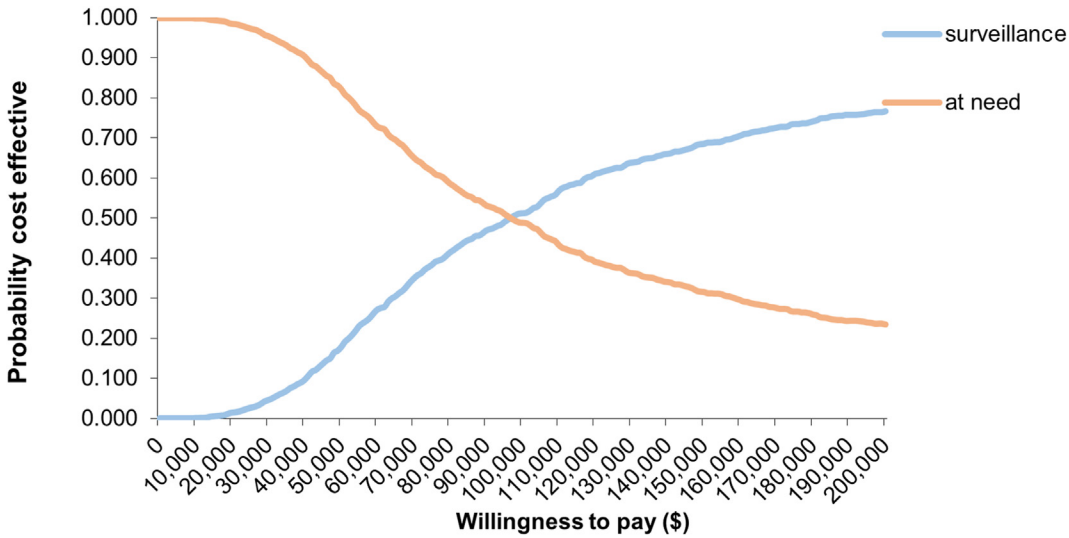
Following standard guidelines, we assumed that patients with HGD will have endoscopies approximately every 3 months for 12 months while having treatment (usually 3–4 treatment endoscopies with radiofrequency ablation/endoscopic mucosal resection), then stay on more frequent surveillance (6 months), then every 12 months for the next 5 years. Patients with early EAC (endoscopically treatable) would follow the same pattern as HGD above. Patients with later cancer needing surgery or palliative treatment would not have regular endoscopy afterward. Patients with advanced cancer may receive chemotherapy if they have metastatic disease or sometimes chemotherapy and radiotherapy if local disease but not fit for surgery. Supplementary Table 3 lists the unit costs, values, and sources of treatments for HGD, local EAC, and advanced EAC.

The final cost associated with HGD treatment and local EAC treatment states in the Markov model has been calculated as a weighted average, using information on the proportion of patients receiving each treatment (or a combination of treatments), retrieved from United Kingdom cancer registry data (UK Cancer data 2018-2020, https://www.cancerdata.nhs.uk/getdataout/data).

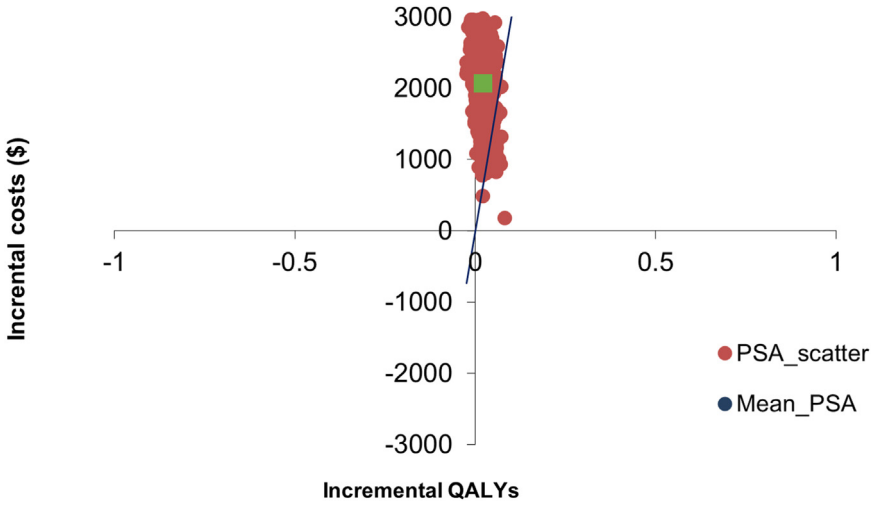



**Supplementary Figure 1.** Cost-effectiveness plane, base-case analysis.



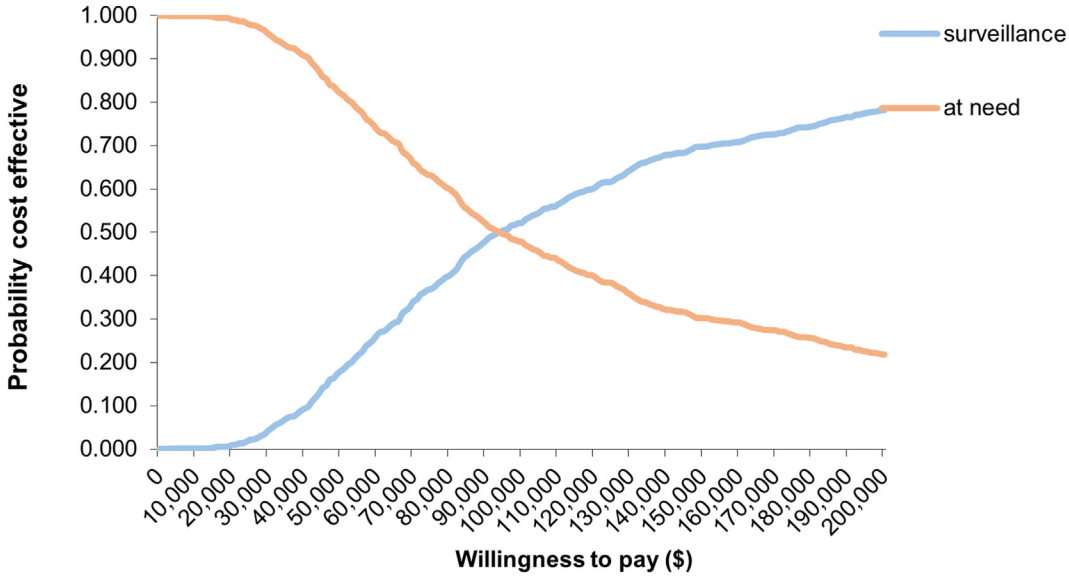



**Supplementary Figure 2.** Cost-effectiveness acceptability curve, base-case analysis.




**Supplementary Figure 3.** Cost-effectiveness plane, sensitivity analysis, and proportion of undetected HGD, $z_1 = 0.38$. PSA, probabilistic sensitivity analysis.

web 4C/FPO

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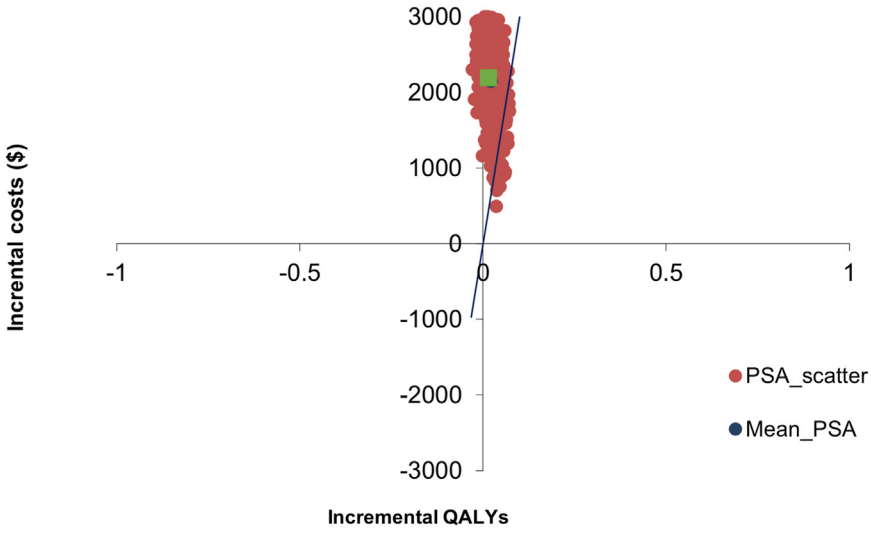
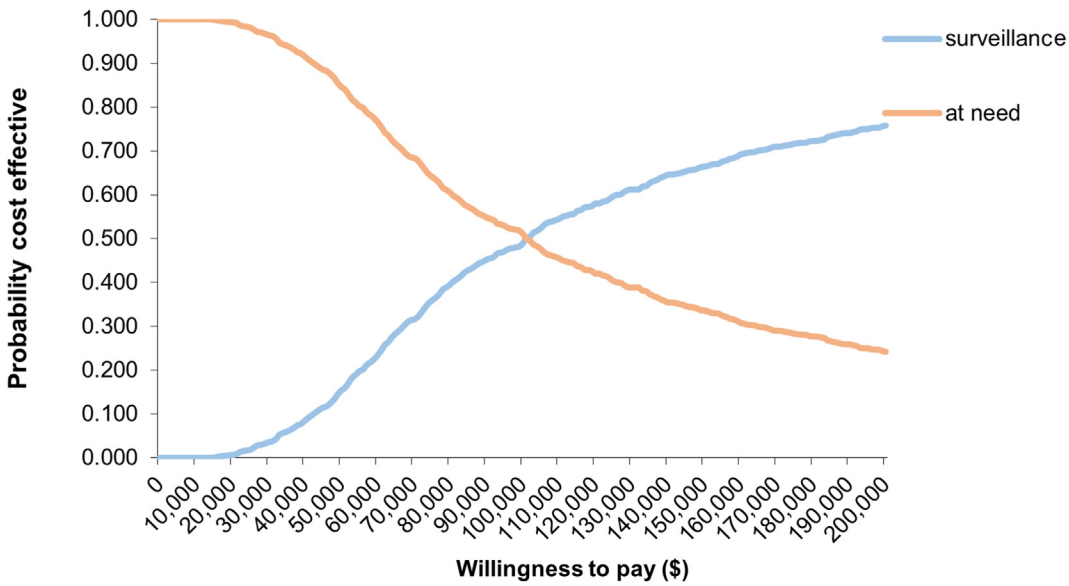
**Supplementary Figure 4.** Cost-effectiveness acceptability curve, sensitivity analysis, and proportion of undetected HGD, $z_1 = 0.38$.



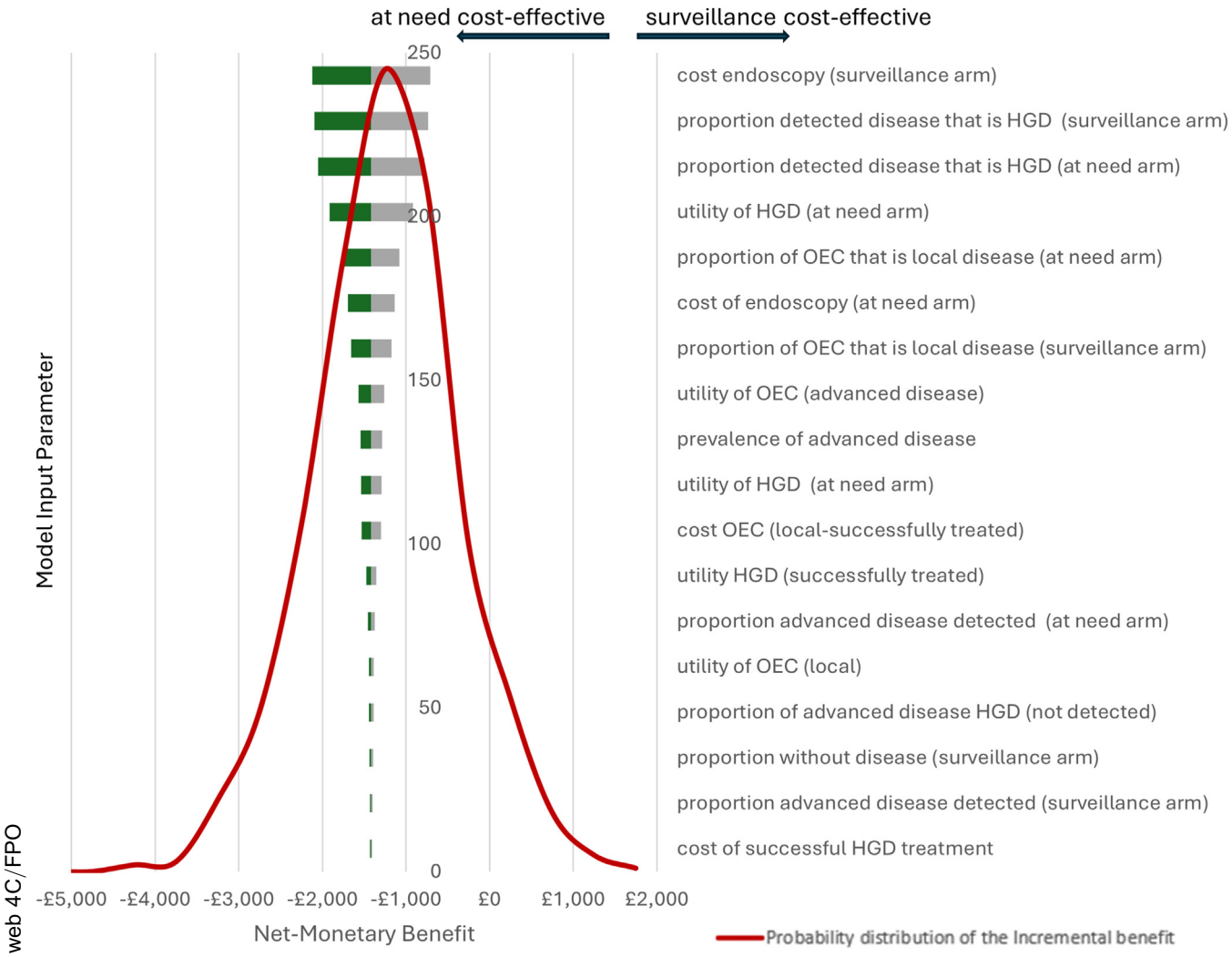

**Supplementary Figure 5.** Cost-effectiveness plane, sensitivity analysis, and proportion of undetected HGD, $z_1 = 0.54$. PSA, probabilistic sensitivity analysis.








**Supplementary Figure 6.** Cost-effectiveness acceptability curve, sensitivity analysis, and proportion of undetected HGD, $z_1 = 0.54$.




**Supplementary Figure 7.** Tornado plot of variables contributing to the uncertainty in the model. The plot visually represents how changes in each variable influence cost-effectiveness in the model, with the bars in order of magnitude of their influence. OEC, (o)esophageal adenocarcinoma.

**Supplementary Table 1.** Number of Patients Diagnosed With Metaplasia, Low-Grade Dysplasia, High-Grade Dysplasia, and Esophageal Adenocarcinoma

| Disease stage | Treatment arm (Surveillance) | Control arm (At need) | Total |
|---|---|---|---|
| Metaplasia | 1212 | 650 | 1862 |
| LGD | 114 | 48 | 162 |
| HGD | 47 | 19 | 66 |
| EAC | 40 | 31 | 71 |
| Total | 1413 | 748 | 2161 |

NOTE. The number of events was calculated considering the most severe diagnosis at first occurrence.

**Supplementary Table 2.** Rate of Detection of High-Grade Dysplasia and Esophageal Adenocarcinoma by Trial Arm

| | Expected vs detected HGD + EAC | | Prevalence of HGD+EAC, % | Expected HGD+EAC in 10 years, n | Parameters x and y |
|---|---|---|---|---|---|
| | Patient recruited | Deaths | | | HGD+EAC detected, % |
| Surveillance | 1733 | 333 | 6.5 | 91 | 96 |
| At need | 1719 | 356 | 6.5 | 88 | 57 |
| | Expected vs detected HGD | | | | |
| | | | Prevalence HGD, % | | |
| Surveillance | 1733 | 333 | 3.5 | 49 | 96 |
| At need | 1719 | 356 | 3.5 | 48 | 40 |
| | | | Prevalence EAC, % | | |
| Surveillance | 1733 | 333 | 3.0 | 42 | 96 |
| At need | 1719 | 356 | 3.0 | 41 | 77 |

**Supplementary Table 3.** Unit Costs Values and Sources of Treatments for High-Grade Dysplasia, Local Esophageal Adenocarcinoma, and Advanced Esophageal Adenocarcinoma

| Treatment | Unit cost ($) | Source and assumptions |
|---|---|---|
| Chemotherapy | 5348 | NICE Guideline - Oesophago-gastric cancer: assessment and management in adults, https://www.nice.org.uk/guidance/ng83/evidence/appendix-i-pdf-170036297748. Table 5 (average of 4 available treatment). Assume 4 cycles/year. |
| Radiotherapy | 9012 | Preparation for Complex Conformal Radiotherapy SC51Z £982 + Deliver a Fraction of Complex Treatment on a Megavoltage Machine SC23Z £212 (assume 23 number of fractions) |
| Surgery | 2583 | Very complex, esophageal, stomach or duodenum procedure, 19 years and over (FZ80), weighted average, NHS reference costs |
| Other palliative care | 14,222 | NHS reference costs, Endoscopic Insertion of Luminal Stent into Gastrointestinal Tract with CC Score 7+ FE10A |
| Endoscopy | 1332.307692 | NHS Reference Costs 2020–21 FE21Z Diagnostic Endoscopic Upper Gastrointestinal Tract Procedures with Biopsy, 19 years and over—Total |
| HGD treatment | 5746 | National tariff workbook 22/23 code; FE21Z, FE02C, FE02C, FE22Z, 106 |

NHS, National Health Service; NICE, National Institute for Health and Care Excellence.

**Supplementary Table 4.** Intermediate Outcomes, Trial, and Follow-up

| | EAC cases in trial | Deaths with EAC in trial | Total EAC cases (trial + modeling and extra 10 years) | Deaths with EAC (trial + modeling and extra 10 years) | Life-years total | QALY total |
|---|---|---|---|---|---|---|
| Biennial | 40 | 20 | 47 | 30 | 11.19 | 8.65 |
| At need | 31 | 15 | 49 | 43 | 11.17 | 8.63 |