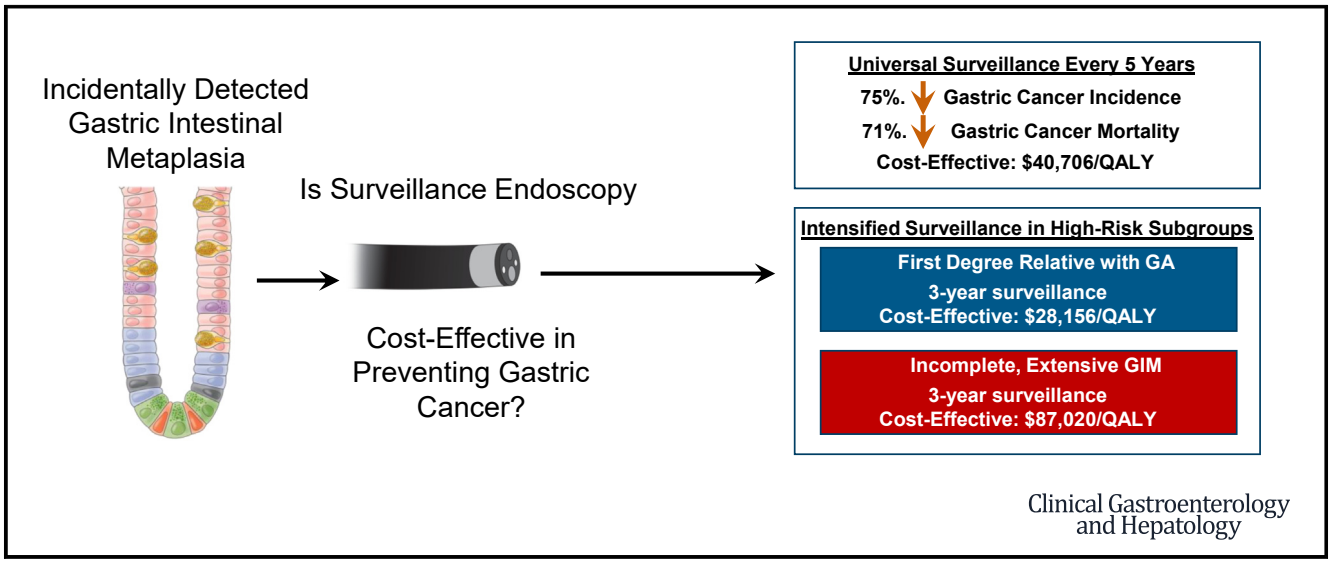
# The Clinical Impact and Cost-Effectiveness of Surveillance of Incidentally Detected Gastric Intestinal Metaplasia: A Microsimulation Analysis

Nikhil R. Thiruvengadam,[1] Shashank Gupta,[2] Seth Buller,[3] Imad Awad,[2] Devika Gandhi,[1] Allison Ibarra,[4] Gonzalo Latorre,[5] Arnoldo Riquelme,[5,6] Michael L. Kochman,[7] Gregory Cote,[8] Shailja C. Shah,[4,9,§] and Monica Saumoy[10,§]

*[1]Division of Gastroenterology and Hepatology, Loma Linda University Health, Loma Linda, California; [2]Department of Medicine, Loma Linda University Health, Loma Linda, California; [3]Loma Linda University School of Medicine, Loma Linda, California; [4]Division of Gastroenterology, University of California San Diego, San Diego, California; [5]Department of Gastroenterology, Faculty of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile; [6]Centro para la Prevención y el Control del Cáncer (CECAN), Santiago, Chile; [7]Division of Gastroenterology and Hepatology, Perelman School of Medicine, Philadelphia, Pennsylvania; [8]Division of Gastroenterology and Hepatology, Oregon Health & Science University, Portland, Oregon; [9]Gastroenterology Section, Veterans Affairs San Diego Healthcare System, San Diego, California; and [10]Center for Digestive Health, Penn Medicine Princeton Medical Center, Plainsboro, New Jersey*




**BACKGROUND & AIMS:** **Gastric intestinal metaplasia (GIM) is associated with a higher risk of noncardia intestinal gastric adenocarcinoma (GA). The aim of this study was to estimate lifetime benefits, complications, and cost-effectiveness of GIM surveillance using esophagogastroduodenoscopy (EGD).**

**METHODS:** **We developed a semi-Markov microsimulation model of patients with incidentally detected GIM, to compare the effectiveness of EGD surveillance with no surveillance at 10-year, 5-year, 3-year, 2-year, and 1-year intervals. We modeled a simulated cohort of 1,000,000 US individuals aged 50 with incidental GIM. Outcome measures were lifetime GA incidence, mortality, number of EGDs, complications, undiscounted life-years gained, and incremental cost-effectiveness ratio with a willingness-to-pay threshold of $100,000/quality-adjusted life-year (QALY).**

[§]Authors share co-senior authorship.

*Abbreviations used in this paper:* EGD, esophagogastroduodenoscopy; GA, gastric adenocarcinoma; GIM, gastric intestinal metaplasia; HP, *Helicobacter pylori*; ICER, incremental cost-effectiveness ratio; LYG, life-years gained; QALY, quality-adjusted life-year; SEER, Surveillance; Epidemiology, and End Results; WTP, willingness to pay.

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**RESULTS:** **In the absence of surveillance, the model simulated 32.0 lifetime GA cases and 23.0 lifetime GA deaths per 1000 individuals with GIM, respectively. Among surveilled individuals, simulated lifetime GA incidence (per 1000) decreased with shorter surveillance intervals (10-year to 1-year, 11.2–6.1) as did GA mortality (7.4–3.6). Compared with no surveillance, all modeled surveillance intervals yielded greater life expectancy (87–190 undiscounted life-years gained per 1000); 5-year surveillance provided the greatest number of life-years gained per EGD performed and was the cost-effective strategy ($40,706/QALY). In individuals with risk factors of family history of GA or anatomically extensive, incomplete-type GIM intensified 3-year surveillance was cost-effective (incremental cost-effectiveness ratio $28,156/QALY and $87,020/QALY, respectively).**

**CONCLUSIONS:** **Using microsimulation modeling, surveillance of incidentally detected GIM every 5 years is associated with reduced GA incidence/mortality and is cost-effective from a health care sector perspective. Real-world studies evaluating the impact of GIM surveillance on GA incidence and mortality in the United States are needed.**

*Keywords:* Gastric Intestinal Metaplasia; Endoscopic Surveillance; Microsimulation Modeling.

Gastric adenocarcinoma (GA) remains a significant cause of cancer-related mortality.[1] In the absence of systematic screening in the United States, GA is most often diagnosed in the symptomatic, advanced stage. Conversely, if diagnosed in the early, asymptomatic stage, resection can be curative with >95% 5-year survival.[2] Chronic infection with *Helicobacter pylori* (HP) is the most common trigger for gastric intestinal metaplasia (GIM) leading to noncardia intestinal-type GA through the Correa cascade.[3]

GIM is associated with a 0.16% annual progression rate to GA.[4] The baseline rate of GIM progression is similar to that of other premalignant changes in the luminal gastrointestinal tract, including nondysplastic Barrett's esophagus, which has an annual progression rate of 0.12%, and low-risk colonic adenomas, both conditions for which endoscopic surveillance are recommended.[5,6] GIM transition rates may be higher or lower depending on additional risk factors, including anatomic extent and histologic type.[7,8] Although race, ethnicity, and birthplace are potential risk factors for GA and for developing GIM, they have not been shown to impact the progression of GIM to GA.[4,7,9]

In the United States, GIM is often diagnosed incidentally on esophagogastroduodenoscopy (EGD). Recently, the American Gastroenterological Association published the first US-based guidelines on GIM management and conditionally recommended against universal surveillance of GIM, given the dearth of studies directly comparing endoscopic surveillance with no surveillance.[10] However, they acknowledged the increased risk of GA in individuals with GIM, particularly if additional risk factors are present, and suggested surveillance every 3–5 years be considered in individuals with GIM and high-risk features.[10] Other international gastroenterology societies recommend endoscopic surveillance every 3 years, depending on additional risk factors.[11,12]

Our objective was to develop a microsimulation model evaluating the benefits and harms of GIM surveillance if incidentally found, at varying yearly intervals, and its cost-effectiveness from a health care sector perspective.

## Methods

We developed a state-transition semi-Markov microsimulation model simulating a base case scenario of no surveillance of GIM (TreeAge Pro 2022 release 2.2; Williamstown, MA). We then superimposed 5 different intervals (10-year, 5-year, 3-year, 2-year, and 1-year) of endoscopic surveillance of GIM starting at age 50 and continuing to age 80.

### *Microsimulation Model*

We developed a natural history module that simulated multiple gastric health states with associated transition pathways to potentially develop GA and different transition probabilities based on HP status (negative, eradicated, persistent infection) with a 1-year cycle length (Figure 1, Supplementary Index S1 and S2). After we calibrated the natural history module, we created a natural history GIM module where all individuals started at different GIM health states depending on GIM histology and anatomic extent (see later). We superimposed surveillance at various intervals with resection of dysplasia/GA. The 2018 Centers for Disease Control and Prevention US Life Tables estimated the age-specific probability of background mortality.[13] Individuals were followed until age 100 or death.

### *Natural History Module Calibration and Validation*

We calibrated the natural history module to the 2010–2016 incidence data and the 5-year stage-specific survival from the Surveillance, Epidemiology, and End Results (SEER) program[14]; and the mean sojourn time of

preclinical (asymptomatic) GA before becoming clinical (symptomatic) GA[15] (Supplementary Index S2). The model was calibrated to fit the GIM to GA weighted annual progression rate in the American Gastroenterological Association technical review (0.16% annually).[7,16,17] We calibrated different progression rates as part of sensitivity analyses. We used a bound-constrained optimization algorithm for the calibration using data from our systematic review to inform sensitivity ranges.[18] We confirmed the internal validity of our model by comparing its output with SEER data[14] and a large-cohort study from the Netherlands (Supplementary Index S3).[16]

### *Incidental Gastric Intestinal Metaplasia Module Development and Validation*

The natural history GIM module with superimposed endoscopic GIM surveillance created the incidental GIM module. We simulated incidental GIM detection by endoscopic biopsies performed for non-GA screening indications. We used baseline probabilities for risk-stratified GIM health states according to histologic subtype, anatomic extent, and HP status based on estimates from the literature (Supplementary Index S2). We modeled that individuals with GIM and biopsy-detected HP would undergo eradication treatment, assuming an 80% eradication rate, which was varied in sensitivity analyses. Individuals would then transition stepwise between health states (Supplementary Index S2). We also modeled the possibility that GIM could regress stepwise to atrophic gastritis, nonatrophic gastritis, and then normal mucosa.[4,8] We externally validated the GIM module by comparing GIM progression with GA against 2 nationwide longitudinal studies (low-GA incidence, Sweden[19]; and high-GA incidence, Colombia[20]) (Supplementary Index S3).

### What You Need to Know

#### Background

Gastric intestinal metaplasia (GIM) is associated with a higher risk of transforming into non-cardia intestinal gastric adenocarcinoma (GA) but current AGA guidelines recommend against surveillance.

#### Findings

Using a microsimulation model from a healthcare sector perspective, we demonstrated that universal 5-year endoscopic surveillance of incidentally identified GIM resulted in reduced GA incidence, GA mortality, and was cost-effective.

#### Implications for patient care

In patients with incidentally identified GIM, 5-year endoscopy surveillance can be considered, while 3-year intervals may be considered in high-risk subpopulations.

### *Surveillance Esophagogastroduodenoscopy*

We modeled GIM surveillance beginning at age 50 and assumed that biopsies were obtained according to the updated Sydney protocol. If individuals had GIM regression (ie, GIM not detected on subsequent endoscopy), then surveillance would cease.

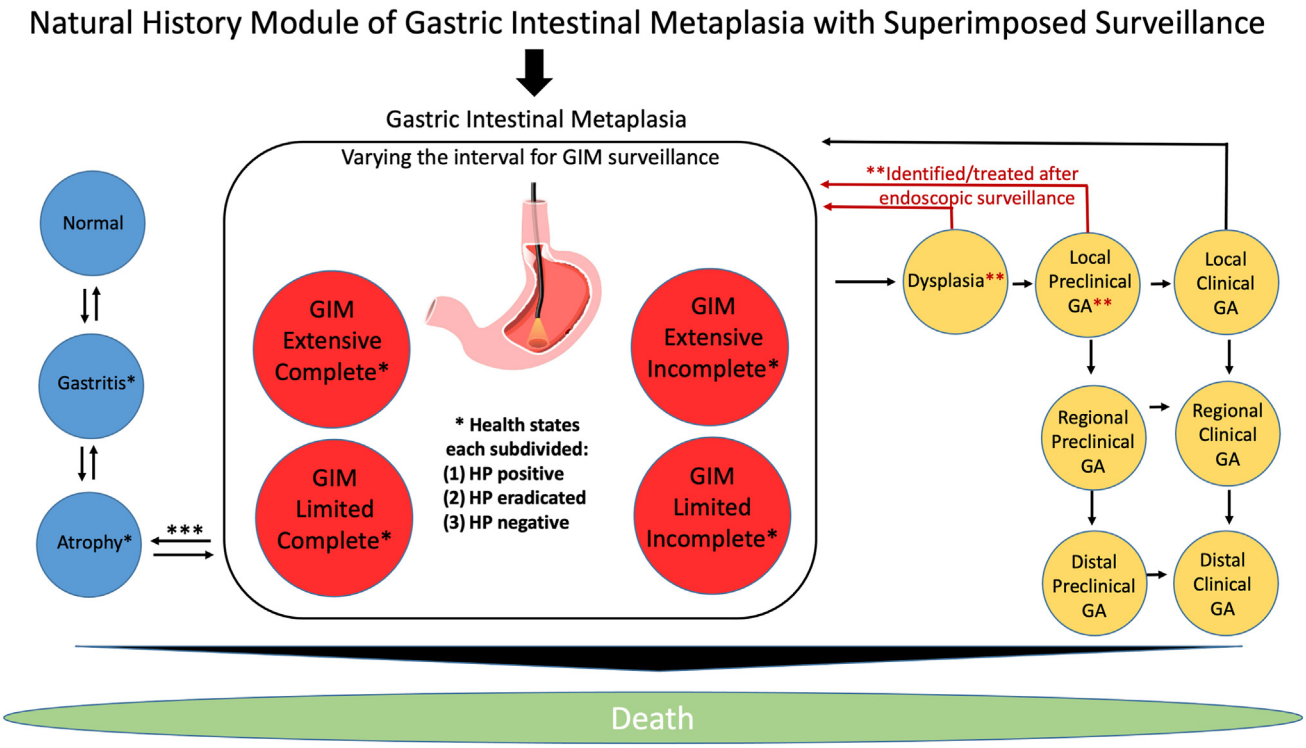


**Figure 1.** Graphical representation of the microsimulation model.

Otherwise, individuals would continue surveillance until age 80.

### Management of Dysplasia and Gastric Adenocarcinoma

Localized GA/dysplasia was resected by endoscopic submucosal dissection or surgery. Lesions could be incompletely resected and remain in that same health state. Following complete resection of dysplasia or localized GA, individuals continued with annual endoscopic surveillance for 5 years and, if there was no recurrence at 5 years, transitioned back to either no surveillance or their assigned GIM surveillance strategy. Individuals with regional/metastatic GA were not eligible for curative resection and received palliative chemotherapy and/or radiation treatment.[21]

### Assumptions

Assumptions were made to simplify the model. First, although transition rates to dysplasia differed based on the types of GIM, once individuals developed dysplasia, the type of GIM did not influence the transition probability to GA. Second, in all individuals, chronic HP infection, either active or eradicated, was assumed to be the initial trigger for GIM. Third, 20% of dysplasia/localized GA would undergo endoscopic submucosal dissection, whereas the remaining underwent surgical resection. Additionally, we assumed perfect adherence to GIM surveillance for the primary analyses, but adherence was varied in sensitivity analyses.

### Model Inputs

Transition probabilities, utilities, and costs were identified from published literature (Supplementary Table 1). Quality-adjusted life-years (QALYs) were used for utilities to describe each state's health-related quality of life. Direct procedure cost estimates were based on the 2021 Medicare estimated national average costs. All costs were updated to December 2021 based on the general consumer price index.

### Analysis/Outcomes

A hypothetical cohort of 1,000,000 50-year-old individuals was simulated from a health care sector perspective over a lifetime horizon. We also looked at a modified societal perspective where we included patient time costs valued at the median US wage of 2021. Undiscounted clinical outcomes included GA incidence and mortality, life-years gained (LYG) from the prevention or delay of GA death accounting for the loss of years from fatal complications, and the number of EGDs and complications. We compared the ratio of LYG with EGDs required when compared with no surveillance for each surveillance strategy to identify the optimal strategy.

Discounted health economic outcomes included cost and QALYs. We included future health costs and disabilities related to other conditions in the model.[22,23] Costs and QALYs were discounted by 3% per year. We reported incremental cost-effectiveness ratios (ICERs; 2021 US dollars per QALY) with a willingness-to-pay (WTP) threshold of $100,000/QALY.

### Gastric Intestinal Metaplasia Surveillance According to Risk Stratification

We modeled the impact of GIM surveillance in individuals with a first-degree relative with gastric cancer and individuals with incomplete-type, anatomically extensive GIM (high-risk) or complete-type, antral-limited GIM (low-risk) by applying published relative risks for GA to the transition probability from GIM to dysplasia. We modeled separate cohorts of 1,000,000 50-year-old individuals for each risk scenario.

### Sensitivity Analyses

We performed sensitivity analyses varying the annual progression rate from GIM to GA from 0.04%–0.24% annually and the sensitivities for EGD for dysplasia (50%–95%) and GA (30%–92%). We applied age-specific adherence rates for colonoscopy to GIM surveillance with EGD. One-way sensitivity analyses were performed using a tornado analysis on all other model inputs.

### Threshold Analyses

We conducted a threshold analysis where we increased the costs for EGD from $10 in the base-case analysis to $10,000 in steps of $10. Next, we conducted a 2-way threshold analysis of both sensitivity for dysplasia and sensitivity for GA at the time of EGD.

### Probabilistic Sensitivity Analysis

We performed a Monte Carlo probabilistic sensitivity analysis for which 10,000 iterations (each with 10,000 individuals) were performed using gamma distributions for cost, beta distributions for transition probabilities and utilities, and log-normal distributions for relative risks.

## Results

### Undiscounted Clinical Outcomes of Universal Gastric Intestinal Metaplasia Surveillance

In the absence of surveillance, the model simulated 32.0 lifetime GA cases and 23.0 lifetime GA deaths per 1000 50-year-old individuals with incidentally detected GIM (Table 1). This estimate was obtained by a calibration of the natural history module to SEER and the GIM

**Table 1.** Detailed Analysis of Outcomes and Cost-Effectiveness of GIM Surveillance Strategies

| Lifetime health outcomes per 1000 patients | No surveillance | Surveillance: different intervals | | | | |
|---|---|---|---|---|---|---|
| | | 10 y | 5 y | 3 y | 2 y | 1 y |
| Gastric adenocarcinoma outcomes | | | | | | |
| GA cases | 32.0 | 11.2 | 7.7 | 6.6 | 6.2 | 6.1 |
| GA deaths | 23.0 | 7.4 | 6.6 | 5.9 | 4.7 | 3.6 |
| Outcomes of surveillance | | | | | | |
| Prevented cancer cases | — | 20.8 | 24.3 | 25.3 | 25.8 | 25.9 |
| Prevented cancer deaths | — | 9.5 | 14.8 | 17.1 | 18.3 | 19.4 |
| EGDs required[a] | 284 | 2545 | 4282 | 6615 | 9593 | 18,173 |
| EGD complications | 0.2 | 15.1 | 28.3 | 42.1 | 57.6 | 107.6 |
| Life-years gained | — | 87 | 155 | 183 | 193 | 190 |
| Cost-effectiveness of surveillance (reported as mean per person) | | | | | | |
| Strategy | No surveillance | 10 y | 5 y | 3 y | 2 y | 1 y |
| Compared with | — | No surveillance | Surveillance every 10 y | Surveillance every 5 y | Surveillance every 3 y | Surveillance every 2 y |
| Cumulative cost[b] (2021 USD) | 225,503 | 227,231 | 228,883 | 231,141 | 234,047 | 242,753 |
| Incremental cost (2021 USD) | — | 1728 | 1652 | 2257 | 2933 | 8679 |
| Effectiveness (QALY) | 16.253 | 16.365 | 16.406 | 16.419 | 16.420 | 16.401 |
| Incremental effectiveness (QALY) | — | 0.113 | 0.041 | 0.013 | 0.001 | -0.019 |
| ICER | — | $15,355/QALY | $40,706/QALY | $170,792/QALY | $5,619,753/QALY | Dominated |

EGD, esophagogastroduodenoscopy; GA, gastric adenocarcinoma; GIM, gastric intestinal metaplasia; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; USD, US dollars.
[a]The total number of EGDs in that individual's lifetime for surveillance, diagnosis, and postoperative surveillance of GA.
[b]The total lifetime costs for medical care related to GA and GIM surveillance and unrelated health care costs are displayed.

to GA annual progression rate of 0.16%, and a modeled overall life expectancy of 26.4 years (because of GA and background mortality). All surveillance intervals were estimated to yield increases in life expectancy (87–190 LYG per 1000) and reductions in lifetime GA cases (20.8–25.9 prevented per 1000) and GA deaths (9.5–19.4 prevented per 1000) while requiring 2545–18173 EGDs per 1000. The simulated lifetime risk of overall EGD complications increased with shorter surveillance intervals (15.1 in 10-year to 107.6 in 1-year surveillance), as did fatal EGD complications (0.24 in 10-year to 1.55 in 1-year) per 1000.

Among all-comers with GIM, as the surveillance interval shortened, the LYG increased, except for 1-year surveillance, which was dominated (Figure 2*A*). Five-year surveillance provided the highest ratio of incremental LYG compared with the incremental number of EGDs required (0.04 LYG/surveillance EGD).

### *Cost-Effectiveness of Universal Surveillance*

Among all-comers with GIM, 5-year surveillance was the cost-effective strategy from a health care sector perspective (ICER $40,706/QALY) (Figure 2*B*). Every surveillance strategy was cost-effective when individually compared with the no-surveillance strategy. Five-year surveillance remained cost-effective from a modified societal perspective (ICER $29,307/QALY; Supplementary Index S4).

### *Gastric Intestinal Metaplasia Surveillance Based on Risk Stratification*

**First-Degree Relative with Gastric Cancer.** Surveillance prevented 67.5–84.5 lifetime GA cases per 1000 and 44.6–65.8 lifetime GA deaths per 1000 with 351–851 LYG per 1000 compared with no surveillance (Supplementary Index S5). Three-year surveillance was cost-effective compared with 5-year surveillance (ICER $28,156/QALY).

**Gastric Intestinal Metaplasia Anatomic-Extent/Histologic-Type.** Among individuals with antral-limited, complete-type GIM, surveillance prevented 11.9–15.0 lifetime GA cases per 1000 and 4.9–10.9 lifetime GA deaths per 1000 with 43–97 LYG per 1000 compared with no surveillance. Five-year surveillance remained the cost-effective strategy compared with 10-year surveillance (ICER $83,747/QALY). By comparison, among individuals with anatomically extensive incomplete-type GIM, surveillance prevented 25.2–30.1 lifetime GA cases and 11.1–21.0 lifetime GA deaths with 157–335 LYG per 1000 persons compared with no surveillance. Three-year surveillance was the cost-effective strategy compared with 5-year surveillance (ICER $87,020/QALY).

### *Sensitivity Analyses*

**Sensitivity Analysis of Annual Progression Rate of Gastric Intestinal Metaplasia to Gastric Adenocarcinoma.** When we varied the annual GIM to GA progression rate

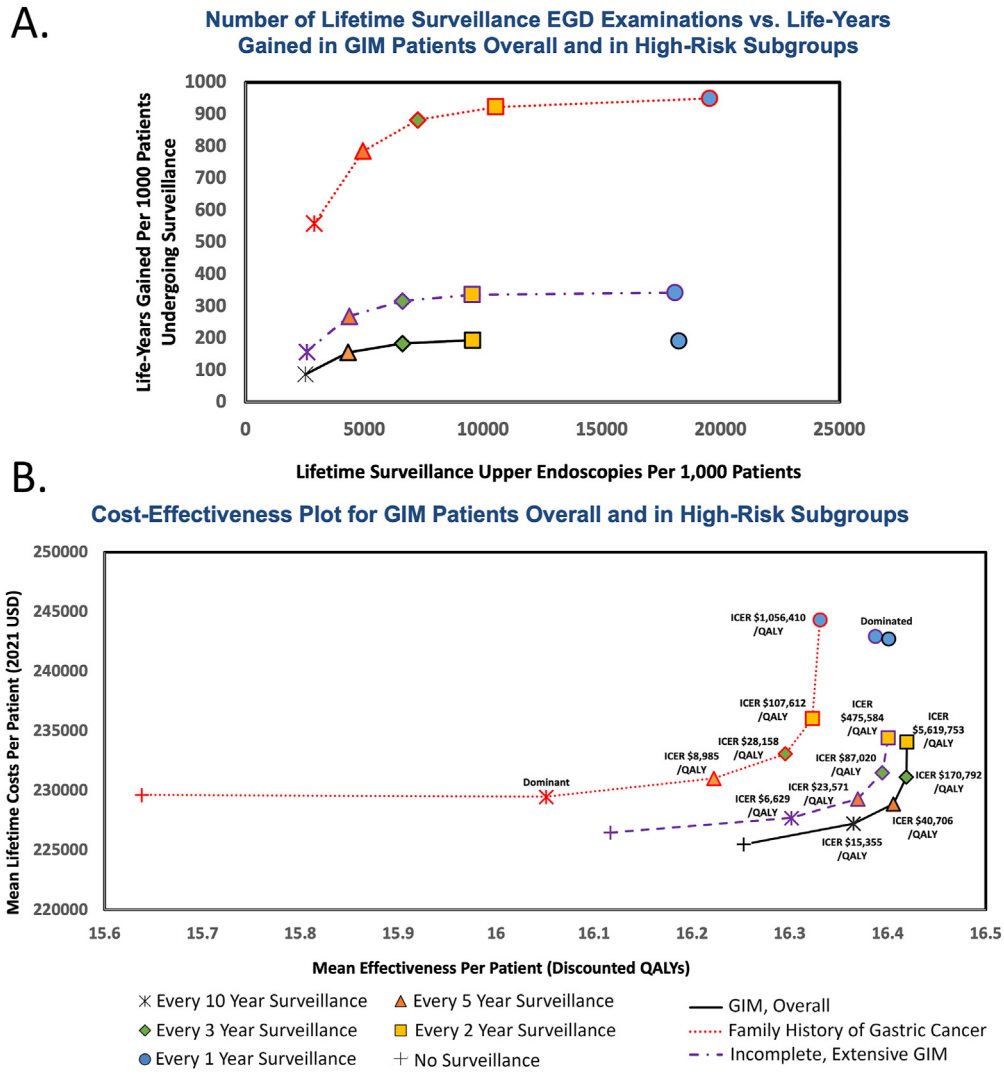


**Figure 2.** (*A*) Undiscounted LYG with each surveillance strategy compared with no surveillance over the number of surveillance upper endoscopies required for patients undergoing surveillance. (*B*) Cost-effectiveness plot comparing universal surveillance and limited surveillance in patients with family history of GA and incomplete, extensive GIM.

from 0.04% to 0.24%, 5-year surveillance was associated with 43–353 LYG per 1000 persons (Figure 3*A*). However, the cost-effective strategy depended on the GIM progression rate. When we modeled a low annual GIM transition probability of 0.04%, the 10-year surveillance strategy was cost-effective (ICER $78,249/QALY; Figure 3*B*). A high annual transition probability of 0.24% resulted in 3-year administration being cost-effective (ICER $83,155/QALY).

**Sensitivity Analysis of Sensitivity Rates for Dysplasia.** When we varied the sensitivity rates for dysplasia, 5-year surveillance was associated with 122–170 LYG per 1000 persons (Supplementary Index S6). The cost-effectiveness of endoscopic surveillance was not sensitive to the sensitivity rate for dysplasia.

**Sensitivity Analysis of Sensitivity Rates for Gastric Adenocarcinoma.** When we varied the sensitivity rates for GA, 5-year surveillance was associated with 131–158 LYG per 1000 persons (Supplementary Index S6). The cost-effectiveness of endoscopic surveillance was not sensitive to the sensitivity rate for GA.

**Sensitivity Analysis Using Age-Specific Adherence Rates.** When we modeled age-specific adherence rates based on screening colonoscopy,[24,25] 5-year surveillance prevented 19.8 lifetime GA cases and 13.7 lifetime GA deaths and was associated with 96 LYG per 1000 persons (Supplementary Index S7). However, when age-specific adherence rates were used, 3-year surveillance was the cost-effective strategy when compared with 5-year surveillance (ICER $45,444/QALY).

**Sensitivity Analysis of Other Model Inputs.** Extensive 1-way sensitivity analyses were performed on all other model inputs and demonstrated that the model was sensitive to the cost of EGD (Supplementary Index S8).

### *Threshold Analysis*

**One-Way Threshold Analysis of Esophagogastroduodenoscopy Cost.** A 1-way threshold analysis identified that if EGD costs less than $3105, 5-year surveillance is cost-effective compared with 10-year surveillance at a WTP of $100,000/QALY (Figure 4*A*). Three-year surveillance was cost-effective compared with 5-year surveillance if EGD costs less than $675 (Figure 4*B*).

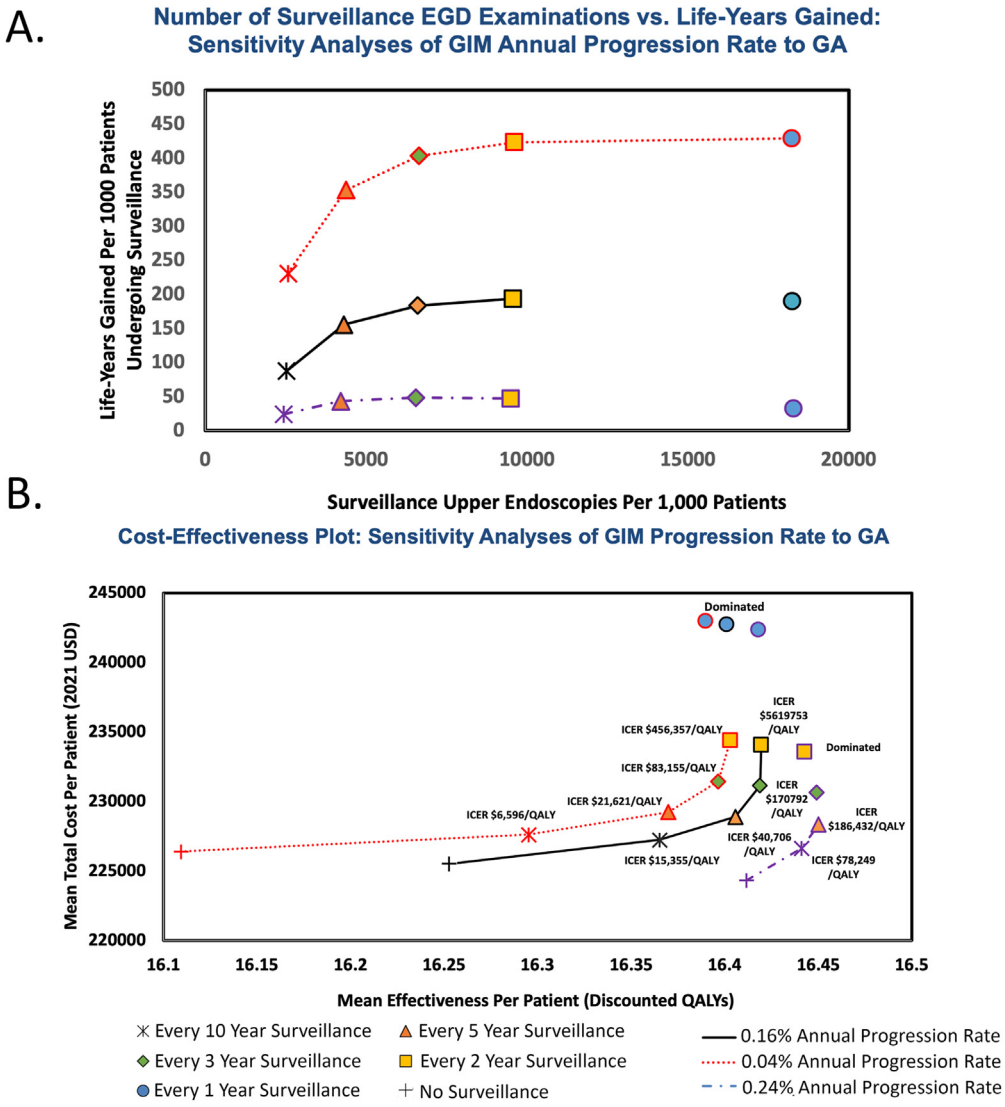


**Figure 3.** (*A*) Sensitivity analyses of the annual progression rate of GIM to GA: evaluating the undiscounted LYG with each surveillance strategy compared with no surveillance over the number of surveillance upper endoscopies required. (*B*) Cost-effectiveness plot comparing universal surveillance and limited surveillance in patients with family history of GA and incomplete, extensive GIM.

**Two-Way Threshold Analyses for the Sensitivity Rate for Dysplasia and Sensitivity Rate for Gastric Adenocarcinoma.** Two-way threshold analyses of the sensitivity rate for dysplasia and the sensitivity rate for GA are shown in Figure 4*C*. They demonstrate that if the sensitivity rate for dysplasia is less than 60% and the sensitivity rate for GA is less than 54%, more intensive 3-year surveillance is cost-effective compared with 5-year surveillance at a WTP of $100,000/QALY.

### *Probabilistic Sensitivity Analyses for Cost-Effectiveness*

For individuals with GIM, 5-year surveillance was the cost-effective strategy in 73.2% of iterations, whereas 3-year surveillance was cost-effective in 17.1% of iterations at a WTP of $100,000/QALY (Figure 5). By contrast, among individuals with a family history of gastric cancer, 3-year surveillance was the cost-effective strategy in 58.8% of iterations, whereas 2-year surveillance was the cost-effective strategy in 37.5% of iterations. Among individuals with anatomically extensive GIM and incomplete-type histology, 3-year surveillance was the cost-effective strategy in 52.6% of iterations. In contrast, among individuals with antral-limited, complete-type histology, 5-year surveillance was the cost-effective strategy in 52.5% of iterations.

## Discussion

Based on a detailed microsimulation model, we demonstrated that 5-year endoscopic surveillance of incidentally detected GIM may be associated with up to 76% lower lifetime GA incidence and 71% lower lifetime GA mortality but required 4282 EGDs with 28.3 complications per 1000 persons with GIM. Among universal surveillance strategies, a 5-year interval provided the most LYG per surveillance EGD and was the cost-effective strategy. More frequent surveillance intervals may be beneficial and cost-effective depending on the presence of additional risk factors for GIM progression to GA.

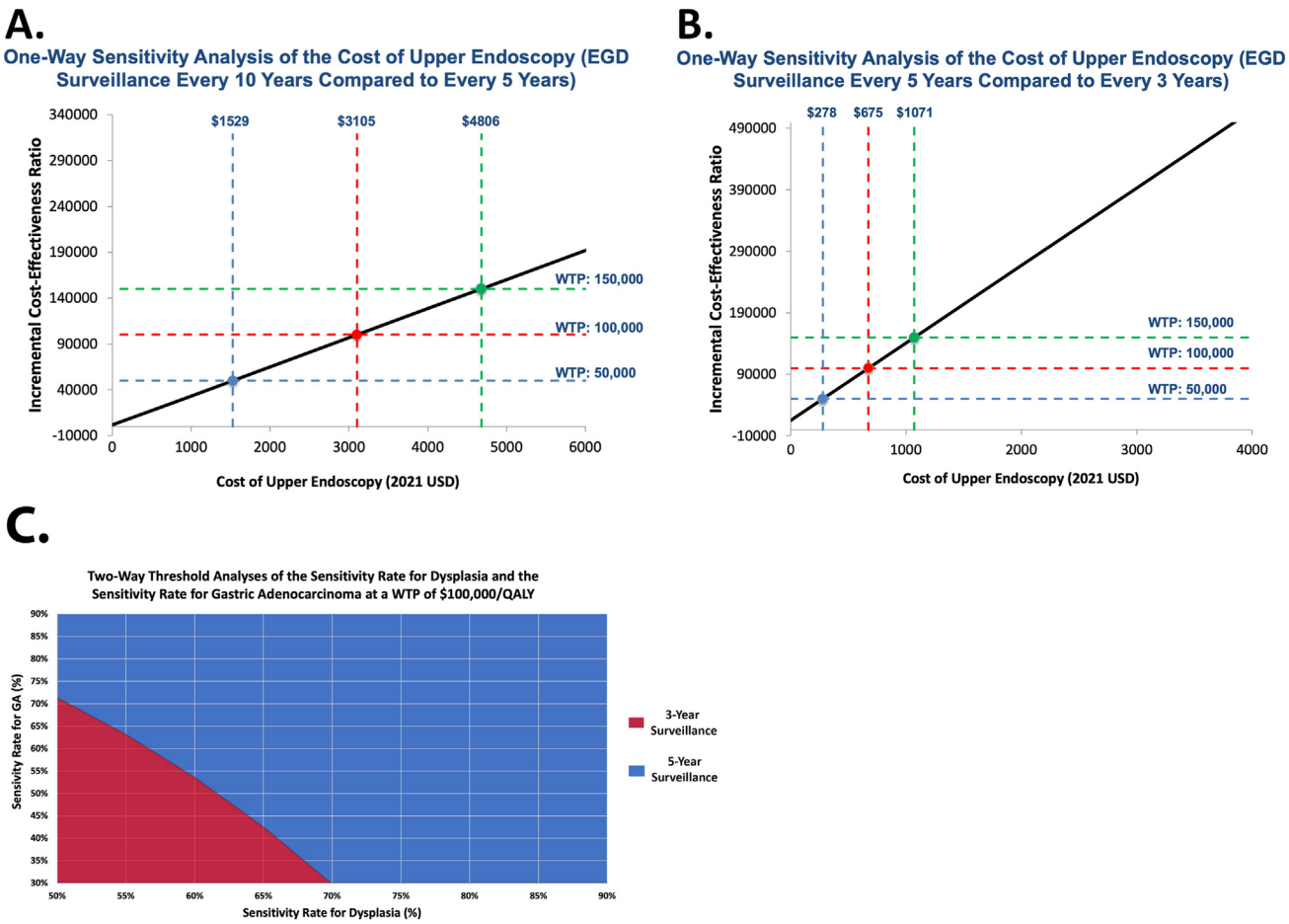


**Figure 4.** (*A*) One-way threshold analysis of cost of EGD (5-year surveillance compared with 10-year). (*B*) One-way threshold analysis of cost of EGD (3-year surveillance compared with 5-year). (*C*) Two-way threshold analysis for the sensitivity rate for dysplasia and sensitivity rate for gastric adenocarcinoma when comparing 3-year with 5-year surveillance.

At least 12 million individuals (ie, 5% of the overall US population) are estimated to have GIM in the United States, with the prevalence significantly higher in immigrants from GA-endemic countries, non-White races, and other groups.[4,7] Current US guidelines recommend against universal GIM surveillance because of the lack of clinical studies comparing the impact of no surveillance versus endoscopic GIM surveillance on GA incidence and mortality.[10] However, our results demonstrated that surveillance of incidentally detected GIM could substantially reduce GA incidence and mortality, especially in patients with additional risk factors for GA. Notably, our findings align with current clinical guidance for GIM surveillance offered by other international gastrointestinal societies,[11,12] which generally recommend 3-year surveillance in individuals with GIM and additional risk factors. Our results follow the DEF paradigm (define, enrich, find) suggested for pancreatic adenocarcinoma surveillance,[26] because once GIM is identified (define a high-risk population), surveillance with more intensive intervals for individuals with risk factors (enrich) is beneficial to identify dysplasia or early GA (find) at stages where endoscopic/surgical resection positively impacts GA incidence and mortality.

The Cancer Moonshot was launched in 2016 with the goal of reducing age-adjusted cancer mortality by 50% by 2030. We demonstrated that 5-year surveillance resulted in 87–190 LYG per 1000 persons compared with no surveillance; when enriched for individual risk factors, such as family history or GIM anatomic-extent and histologic-type, LYG ranged from 351–851 and 157–342, respectively, per 1000 persons compared with no surveillance. In comparison, colorectal cancer screening with colonoscopy yields 286–335 LYG per 1000 people compared with no screening.[27] Biennial mammography for women aged 50–74 years old results in 122 (75–154) LYG per 1000 women screened compared with no screening.[28] Thus, although the present analysis is focused on EGD surveillance for GIM, as opposed to universal GA screening, the LYG for each of the surveillance arms is similar to LYG from colorectal and breast cancer screening, reflecting that we are targeting an enriched, high-risk population.

To our knowledge, this is the first microsimulation model that accounts for the natural history of GIM according to risk factors associated with GIM progression. To further enhance clinical applicability and evaluate real-world performance, our model assumed GIM was diagnosed incidentally, which is the most common

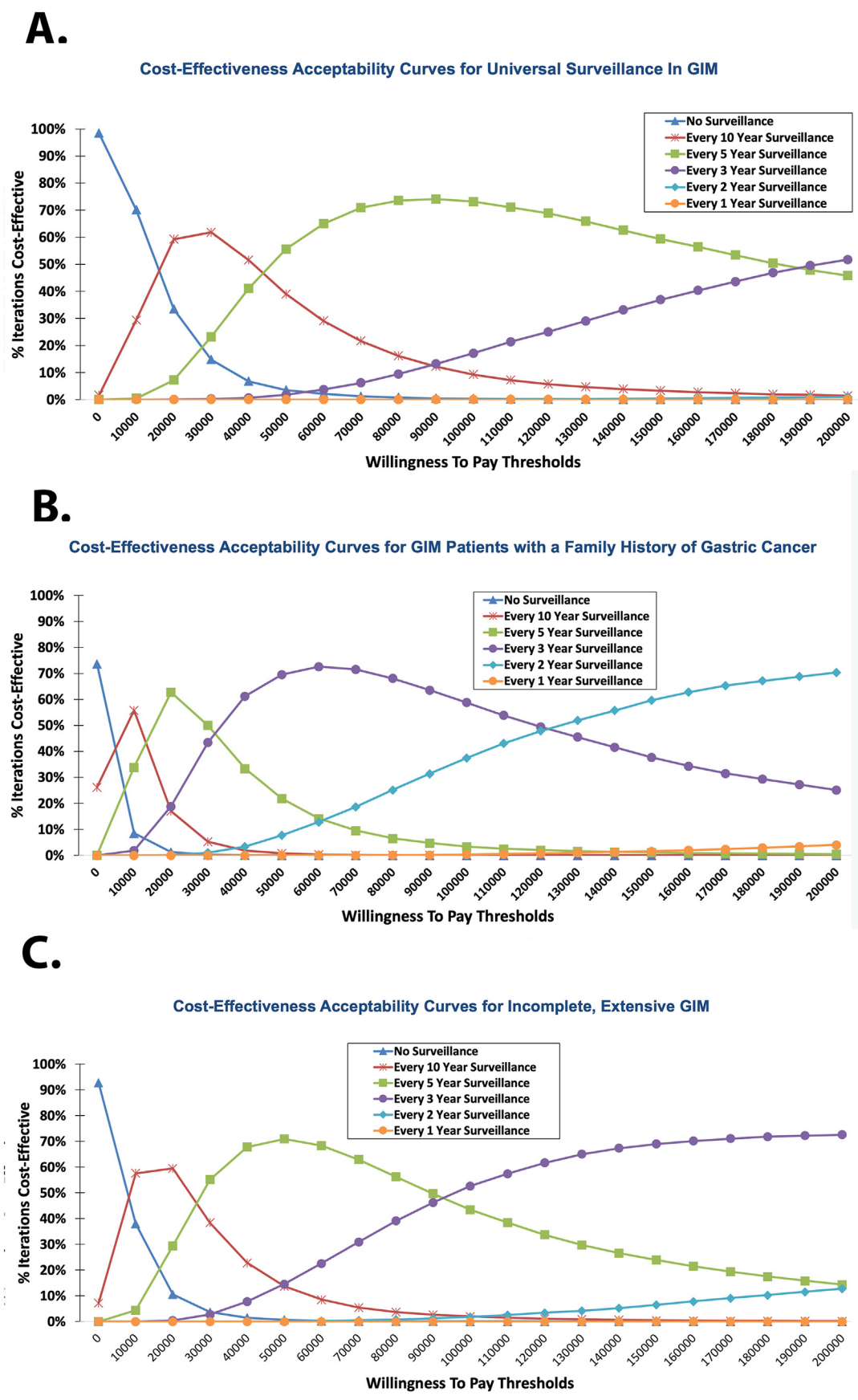


**Figure 5.** Cost-effectiveness acceptability curves using WTPs for each surveillance strategy. (*A*) All individuals with GIM. (*B*) Family history of GA. (*C*) Incomplete, extensive GIM.

scenario in the United States, and also accounted for real-world considerations, including endoscopic miss rate of neoplasia, regression of gastric precancerous changes, less than perfect adherence to EGD, the availability of endoscopic or surgical resection for resectable lesions, and multilevel HP status (negative, successfully eradicated, persistent infection). We intentionally created our model independent of race and ethnicity because there are no compelling data to suggest that once GIM is diagnosed, there is a differential rate of progression based solely on race or ethnicity.[4] Rather, differential progression may relate to factors that correlate with race and ethnicity, such as diet and lifestyle factors.

There are limitations to all microsimulation models that attempt to capture real-world uncertainty. Despite model calibration and validation, our results are still inherently subject to variability and uncertainties in the data inputs and model assumptions. However, extensive 1-way sensitivity analyses were used to determine scenarios where specific strategies were no longer beneficial or cost-effective. Many inputs used to inform the model were not from the United States, given limited epidemiologic studies of GIM previously performed in the United States. But our model was calibrated to reproduce GA incidence in the United States and validated against multiple large nationwide cohort studies[16,19] from countries with similar low-risk for GA. We could only model overall dysplasia because of insufficient data on separate transition probabilities according to dysplasia severity (low vs high); however, because we calibrated an overall progression rate from GIM to GA, our model did not rely on the exact type of dysplasia. Another limitation is that US endoscopists may lack experience in detecting early GA/dysplasia. However, when we modeled low diagnostic sensitivities, surveillance was still associated with lower GA incidence/mortality and was cost-effective. Finally, our cost estimates used Medicare costs without additional anesthesia costs and may not represent actual surveillance costs in different clinical settings.

## Conclusions

Based on a detailed microsimulation model from a health care sector and modified societal perspective, 5-year surveillance of GIM provided the optimal balance of LYG to resource use and was the cost-effective strategy. The surveillance interval can be further optimized according to whether additional risk factors for progression are present. These data are valuable for clinical decision-making related to GIM surveillance, particularly because clinical trials comparing endoscopic strategies are not immediately practical.

## Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2023.05.028.

## References


1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–249.
2. Huang RJ, Epplein M, Hamashima C, et al. An approach to the primary and secondary prevention of gastric cancer in the United States. Clin Gastroenterol Hepatol 2022;20:2218–2228.
3. Correa P, Piazuelo MB. The gastric precancerous cascade. J Dig Dis 2012;13:2–9.
4. Gawron AJ, Shah SC, Altayar O, et al. AGA technical review on gastric intestinal metaplasia: natural history and clinical outcomes. Gastroenterology 2020;158:705–731.
5. Shaheen NJ, Falk GW, Iyer PG, et al. ACG clinical guideline: diagnosis and management of Barrett's esophagus. Am J Gastroenterol 2016;111:30–50.
6. Gupta S, Lieberman D, Anderson JC, et al. Recommendations for follow-up after colonoscopy and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc 2020;91:463–485.
7. Altayar O, Davitkov P, Shah SC, et al. AGA technical review on gastric intestinal metaplasia: epidemiology and risk factors. Gastroenterology 2020;158:732–744.
8. Lee JWJ, Zhu F, Srivastava S, et al. Severity of gastric intestinal metaplasia predicts the risk of gastric cancer: a prospective multicentre cohort study (GCEP). Gut 2022;71:854–863.
9. Tan MC, Jamali T, Nguyen TH, et al. Race/ethnicity and birthplace as risk factors for gastric intestinal metaplasia in a multiethnic United States population. Am J Gastroenterol 2022;117:280–287.
10. Gupta S, Li D, El Serag HB, et al. AGA clinical practice guidelines on management of gastric intestinal metaplasia. Gastroenterology 2020;158:693–702.
11. Banks M, Graham D, Jansen M, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. Gut 2019;68:1545–1575.
12. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy 2019;51:365–388.
13. Arias E, Xu J. United States Life Tables, 2018. Natl Vital Stat Rep 2020;69:1–45.
14. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER Research Data, 17 Registries (excl AK), Nov 2021 Sub (2010-2104) - Linked To County Attributes - Time Dependent (1990-2019) Income/Rurality, 1969-2020 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2022, based on the November 2021 submission.
15. Bae J-M, Shin SY, Kim EH. Mean sojourn time of preclinical gastric cancer in Korean men: a retrospective observational study. J Prev Med Public Health 2014;47:201.
16. de Vries AC, van Grieken NC, Looman CW, et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands. Gastroenterology 2008;134:945–952.
17. den Hollander WJ, Holster IL, den Hoed CM, et al. Surveillance of premalignant gastric lesions: a multicentre prospective cohort study from low incidence regions. Gut 2019;68:585–593.

18. Powell MJ. The BOBYQA algorithm for bound constrained optimization without derivatives. In: Cambridge NA Report NA2009/06, 26. Cambridge: University of Cambridge, 2009.
19. Song H, Ekheden IG, Zheng Z, et al. Incidence of gastric cancer among patients with gastric precancerous lesions: observational cohort study in a low risk Western population. BMJ 2015;351.
20. Piazuelo MB, Bravo LE, Mera RM, et al. The Colombian chemoprevention trial: 20-year follow-up of a cohort of patients with gastric precancerous lesions. Gastroenterology 2021; 160:1106–1117.
21. Ajani JA, D'Amico TA, Bentrem DJ, et al. Gastric cancer, version 2.2022, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2022;20:167–192.
22. Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey. U.S. Department of Health and Human Services, 2021.
23. Hanmer J, Hays RD, Fryback DG. Mode of administration is important in US national estimates of health-related quality of life. Med Care 2007;45:1171–1179.
24. de Moor JS, Cohen RA, Shapiro JA, et al. Colorectal cancer screening in the United States: trends from 2008 to 2015 and variation by health insurance coverage. Prev Med 2018; 112:199–206.
25. Sauer AG, Liu B, Siegel RL, et al. Comparing cancer screening estimates: behavioral risk factor surveillance system and National Health Interview Survey. Prev Med 2018; 106:94–100.
26. Chari ST, Kelly K, Hollingsworth MA, et al. Early detection of sporadic pancreatic cancer: summative review. Pancreas 2015; 44:693–712.
27. Knudsen AB, Rutter CM, Peterse EFP, et al. Colorectal cancer screening: an updated modeling study for the US preventive services task force. JAMA 2021;325:1998–2011.
28. Siu AL, US Preventive Services Task Force. Screening for breast cancer: US Preventive Services Task Force recommendation statement. Ann Intern Med 2016;164:279–296.

**Correspondence**
Address correspondence to: Nikhil R. Thiruvengadam, MD, 11234 Anderson Street, MC 1516, Loma Linda, California 92354. e-mail: NThiruvengadam@llu.edu.

**CRediT Authorship Contributions**

Nikhil Ravi Thiruvengadam, MD (Conceptualization: Lead; Data curation: Lead; Formal analysis: Lead; Investigation: Lead; Writing – original draft: Lead; Writing – review & editing: Supporting)

Shashank Gupta (Data curation: Supporting; Writing – review & editing: Supporting)

Seth Buller (Data curation: Supporting; Formal analysis: Supporting; Writing – review &editing: Supporting)

Imad Awad (Data curation: Supporting; Writing – review & editing: Supporting)

Devika Gandhi (Data curation: Supporting; Formal analysis: Supporting; Writing –review & editing: Supporting)

Allison Ibarra (Data curation: Supporting; Writing – review & editing: Supporting)

Gonzalo Latorre (Data curation: Supporting; Writing – review & editing: Supporting)

Arnoldo Riquelme (Data curation: Supporting; Writing – review & editing: Supporting)

Michael L. Kochman (Conceptualization: Supporting; Data curation: Supporting; Writing –original draft: Supporting)

Gregory Cote (Methodology: Supporting; Writing – original draft: Supporting)

Shailja C. Shah (Data curation: Lead; Formal analysis: Supporting; Writing – original draft: Supporting; Writing – review & editing: Lead)

Monica Saumoy (Conceptualization: Lead; Data curation: Lead; Formal analysis: Lead; Funding acquisition: Lead; Methodology: Lead; Validation: Lead; Writing – original draft: Lead; Writing – review & editing: Supporting)

**Conflicts of interest**

These authors disclose the following: Michael L. Kochman is a consultant for ACI, AGA-Varia, BSC, Dark Canyon Labs, Endiatx, Medtronic, Olympus, and Virgo Systems; and has equity in AGA-Varia, Dark Canyon Labs, Endiatx, EndoSound, and Virgo Systems. Shailja C. Shah serves as an ad hoc consultant and advisor for Phathom Pharmaceuticals and ad hoc consultant for RedHill Biopharma. The remaining authors disclose no conflicts.

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