

Projected Benefit and Cost-Effectiveness of Offering a Choice of Blood-Based Screening Versus Existing Screening Tests for Colorectal Cancer in Two Real-World Settings

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¹Freenome Holdings Inc., South San Francisco, CA, US; ²Stanford University School of Medicine, Stanford, CA, US; ³VA New York Harbor Health Care System, New York, NY, US; ⁴NYU Langone Health, New York, NY, US

^aAffiliation at the time the study and/or analyses were conducted

INTRODUCTION

- Screening for colorectal cancer (CRC) reduces CRC-associated incidence and mortality¹ and is recommended for average-risk adults starting at age 45 years^{2,3}
- Recent CRC screening statistics reveal that only 59% of eligible individuals are up to date, which is well below the US nationwide goal of 80%¹⁴
- Emerging blood-based tests for CRC detection, free from some of the drawbacks associated with existing tests, such as bowel preparation, sedation, and stool-handling, could potentially improve screening rates⁵⁻⁹
- However, there is concern that replacing existing tests with blood tests could adversely impact health outcomes and costs due to the lower sensitivity of current blood tests for advanced precursor lesions¹⁰⁻¹²
- Two recent studies in patients who previously declined screening found that offering a choice between blood-based screening vs existing screening options (colonoscopy or stool testing) increased overall adherence, with limited replacement of existing screening^{8,9}

OBJECTIVE

- To estimate the long-term clinical and economic impact of adherence patterns observed for CRC screening with blood-based tests vs existing tests in two real-world studies

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISNET)¹³ model was replicated, validated, and then used to evaluate the observed mix of screening patterns across the studies' control and intervention arms
- The assumed performance for blood testing was 74% CRC sensitivity and 90% specificity (Table 1), satisfying the minimum US coverage criteria as defined by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma sensitivity was conservatively assumed
- Assumed costs were based on CMS reimbursement rates, using stool-DNA (sDNA) costs as a proxy for blood-based tests
- Outcomes assessed were deaths averted, projected life-years gained (LYG), and incremental cost/quality-adjusted life-years (QALY) for offering the choice of blood testing

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Blood test ^a (CMS minimal requirements)
Specificity	-	0.97	0.90
Sensitivity for non-AA ^b	0.75-0.85	0.07	0.10
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

^bThe model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

Model inputs for screening patterns

- Assumed adherence to colonoscopy every 10 years, annual fecal immunochemical test (FIT), and triennial blood testing were based on observed utilization in Liang et al.⁸ and Coronado et al.⁹ (Table 2)
- In both studies, a significantly higher proportion of participants underwent screening in the intervention arm (OR 1.96, $P=0.04$; and, OR 3.08, $P<0.001$), which offered blood-based testing as a screening option, compared with the control arm, which did not offer blood-based testing^{8,9}
- Colonoscopy and FIT utilization were similar between study arms in both studies
- In the model, adherence to screening was assumed to remain at observed levels

Table 2. CRC screening patterns

Patients screened, n (%)	Liang et al., 2023 ^a			Coronado et al., 2024 ^b		
	Control ^a n=178	Intervention ^b n=181	OR (P value) ^c	Usual care ^a n=1003	Intervention ^b n=181	OR (P value) ^c
Colonoscopy	2 (1.1%)	4 (2.2%)	1.99 (0.68)	15 (1.5%)	12 (1.2%)	0.80 (0.70)
Fecal testing	15 (8.4%)	18 (9.9%)	1.20 (0.72)	115 (11.5%)	99 (9.9%)	0.85 (0.28)
Blood testing	- (0%)	9 (5.0%)	-	- (0%)	204 (20.4%)	-
Total	17 (9.6%)	31 (17.1%)	1.96 (0.04)	130 (13.0%)	315 (31.5%) ^d	3.08 (<0.001)

^aDid not include blood-based testing as a screening option.

^bIncluded blood-based testing as a screening option.

^cFisher's exact test.

^dCoronado et al. reported n=305 screened with intervention (OR 2.94), but test-specific numbers and visual data from the study suggest n=315 (OR 3.08).
CRC, colorectal cancer; OR, odds ratio.

Model inputs for adherence patterns for follow-up colonoscopy

- In both Liang et al. and Coronado et al., 50% of the individuals who had a positive blood test result completed a follow-up colonoscopy, while the follow-up rate for fecal tests ranged from 0% to 70%^{8,10} (Table 3)
- As differences were not statistically significant, we assumed a rounded follow-up rate of 50% for both blood and fecal testing based on the overall average of 51.4%
- To account for uncertainty, higher reported rates in literature, and potential future improvements, we also evaluated scenarios with 75% and 100% follow-up

Table 3. Adherence pattern for follow-up colonoscopy

Patients, n (%)	Liang et al., 2023 ^a			Coronado et al., 2024 ^b		
	Fecal testing	Blood testing	P value ^a	Fecal testing	Blood testing	P value ^a
Screened	33	9		214	204	
Positive	3	2		10	22	
Followed up ^b	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.^{2,3}

RESULTS

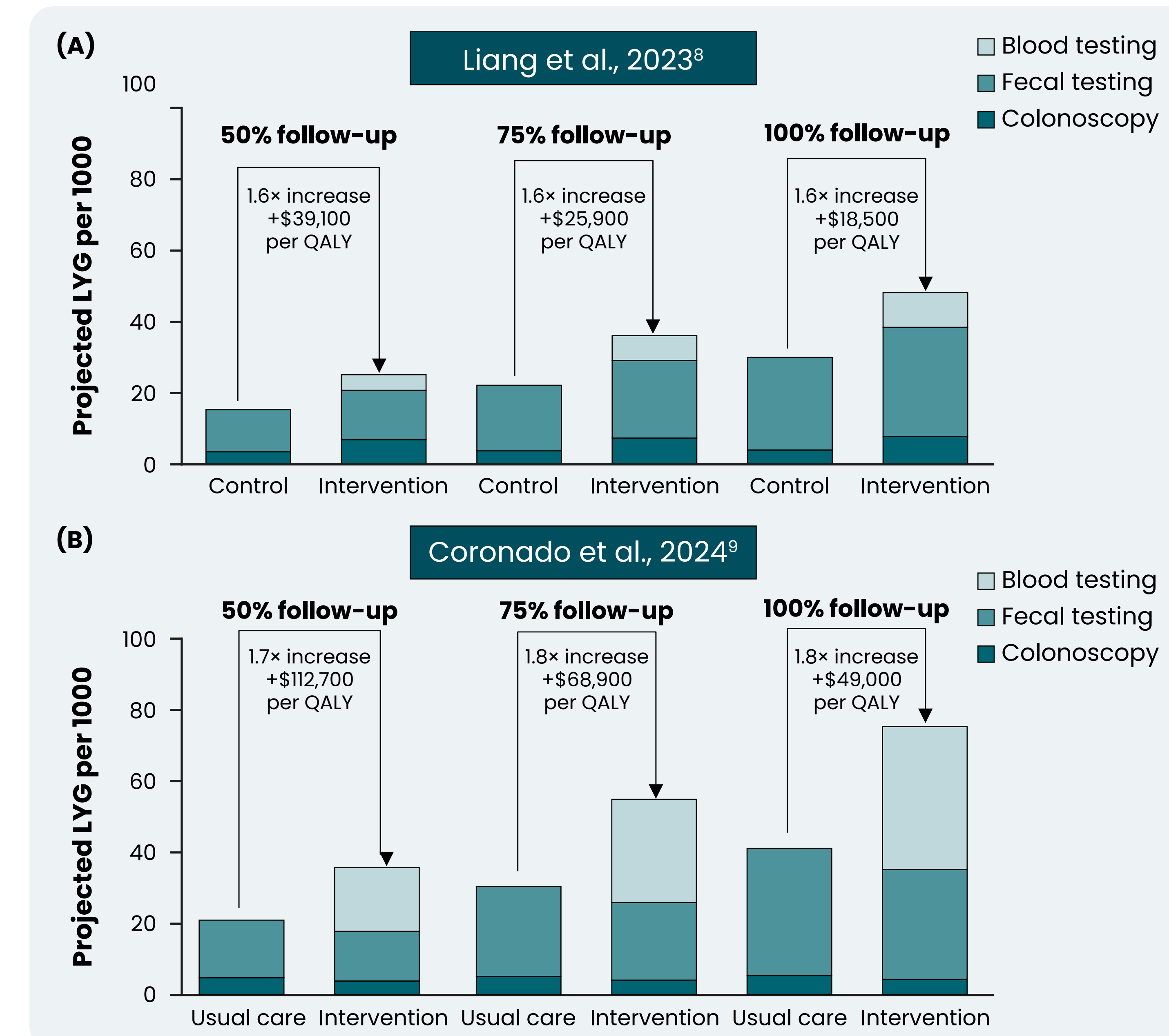
Projected clinical and cost-effectiveness of blood-based testing using observed adherence patterns for screening and follow-up colonoscopy

- With 50% assumed adherence to colonoscopy follow-up and with observed screening patterns from Liang et al., offering blood testing in addition to existing tests was projected to result in 1.6 additional CRC deaths averted per 1000 persons, and to increase the LYG by 1.6 times, at a cost of \$39,100/QALY gained (Figure 1A)
- With observed screening patterns from Coronado et al., offering blood-based screening resulted in 2.9 projected CRC deaths averted per 1000 persons, and increased the LYG by 1.7 times, at a cost of \$112,700/QALY (Figure 1B)

Projected clinical and cost-effectiveness of blood-based testing with higher assumed adherence to follow-up colonoscopy

- With assumed follow-up adherence of 75% and 100% and observed screening patterns from Liang et al., offering blood-based screening resulted in a steady increase in LYG per 1000 persons at a cost of \$25,900/QALY and \$18,500/QALY, respectively (Figure 1A)
- At 75% and 100% assumed follow-up adherence and observed screening patterns from Coronado et al., offering blood-based testing resulted in a steady increase in LYG per 1000 persons at a cost of \$68,900/QALY and \$49,000/QALY, respectively (Figure 1B)

Figure 1. Projected benefit and cost-effectiveness of blood-based testing by adherence pattern for follow-up colonoscopy



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LYG, life-years gained; QALY, quality-adjusted life-years.

KEY FINDINGS AND CONCLUSIONS

- Trial data and modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may substantially improve outcomes at an acceptable cost
- Adequate follow-up of positive screening results with colonoscopy is essential, especially when blood testing replaces some of the existing screening, such as observed in Coronado et al.⁹
- Our analysis extrapolated observed test utilization patterns from studies with a single screening round in patients who previously declined standard screening
- More research is needed to understand the impact of first-line blood testing and longitudinal adherence on projected benefits and cost-effectiveness

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Acknowledgments

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Disclosures

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- Emerging blood-based tests for CRC detection, free from some of the drawbacks associated with existing tests, such as bowel preparation, sedation, and stool-handling, could potentially improve screening rates⁵⁻⁹
- However, there is concern that replacing existing tests with blood tests could adversely impact health outcomes and costs due to the lower sensitivity of current blood tests for advanced precursor lesions¹⁰⁻¹²
- Two recent studies in patients who previously declined screening found that offering a choice between blood-based screening vs existing screening options (colonoscopy or stool testing) increased overall adherence, with limited replacement of existing screening^{8,9}

OBJECTIVE

- To estimate the long-term clinical and economic impact of a choice between blood-based screening vs existing screening options (colonoscopy or stool testing) in patients who previously declined screening

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISNET) model was replicated, validated, and then used to evaluate the impact of different screening patterns across the studies' control and intervention arms
- The assumed performance for blood testing was 74% CRC sensitivity and 97% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based tests set by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma (AA) sensitivity was conservatively assumed
- Assumed costs were based on CMS reimbursement rates, using existing screening costs as a proxy for blood-based tests
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering a choice between blood-based screening vs existing screening options

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Colonoscopy sensitivity for AA ^a
Specificity	-	0.97	-
Sensitivity for non-AA ^b	0.75-0.85	0.07	-
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

^bThe model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

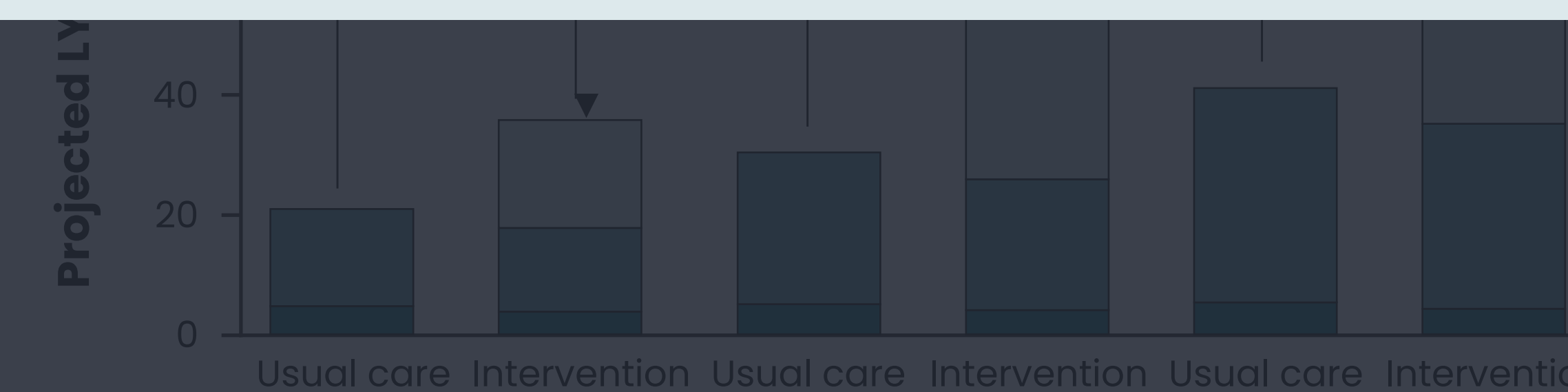
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- Two recent studies in patients who previously declined screening found that offering a choice between blood-based screening vs existing screening options (colonoscopy or stool testing) increased overall adherence, with limited replacement of existing screening^{8,9}

Screened	33	9	214	204		
Positive	3	2	10	22		
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LY, life-years gained; QALY, quality-adjusted life-years.

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RGSM: employee, Freenome Holdings Inc. AP: employee, Freenome Holdings Inc., with equity. LB: former employee, Freenome Holdings Inc., with equity. NMG: former employee, Freenome Holdings Inc. PSL: research support, Epigenomics, Freenome Holdings Inc., participation in advisory board. Guardant Health, Natara.

RESULTS AND CONCLUSIONS

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Modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost

Offering a choice between blood-based screening vs existing screening options (colonoscopy or stool testing) increased overall adherence, with limited replacement of existing screening

Isolated observed test utilization patterns from the screening round in patients who previously declined screening

Need to understand the impact of first-line blood-based screening on adherence on projected benefits and costs

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- Screening for colorectal cancer (CRC) reduces CRC-associated mortality¹ and is recommended for average-risk adults starting at age 50².
- Recent CRC screening statistics reveal that only 59% of eligible adults are screened, which is well below the US nationwide goal of 80%^{1,4}.
- Emerging blood-based tests for CRC detection, free from some of the burdens associated with existing tests, such as bowel preparation, sedation, and discomfort, could potentially improve screening rates⁵⁻⁹.
- However, there is concern that replacing existing tests with blood-based tests could impact health outcomes and costs due to the lower sensitivity of blood-based tests for advanced precursor lesions¹⁰⁻¹².
- Two recent studies in patients who previously declined screening (one comparing a choice between blood-based screening vs existing screening [blood-based or stool testing] increased overall adherence, with limited impact on screening^{8,9}).

OBJECTIVE

- To estimate the long-term clinical and economic impact of adherence patterns observed for CRC screening with blood-based tests vs existing tests in two real-world studies

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of different screening patterns across the studies' control and intervention arms.
- The assumed performance for blood testing was 74% CRC sensitivity and 95% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based screening set by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma sensitivity was conservatively assumed.
- Assumed costs were based on CMS reimbursement rates, using existing test costs as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering blood testing.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)
Specificity	0.95	0.97
Sensitivity for non-AA ^a	0.75-0.85	0.07
Sensitivity for AA	0.95	0.22
Sensitivity for CRC	0.95	0.74

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The model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

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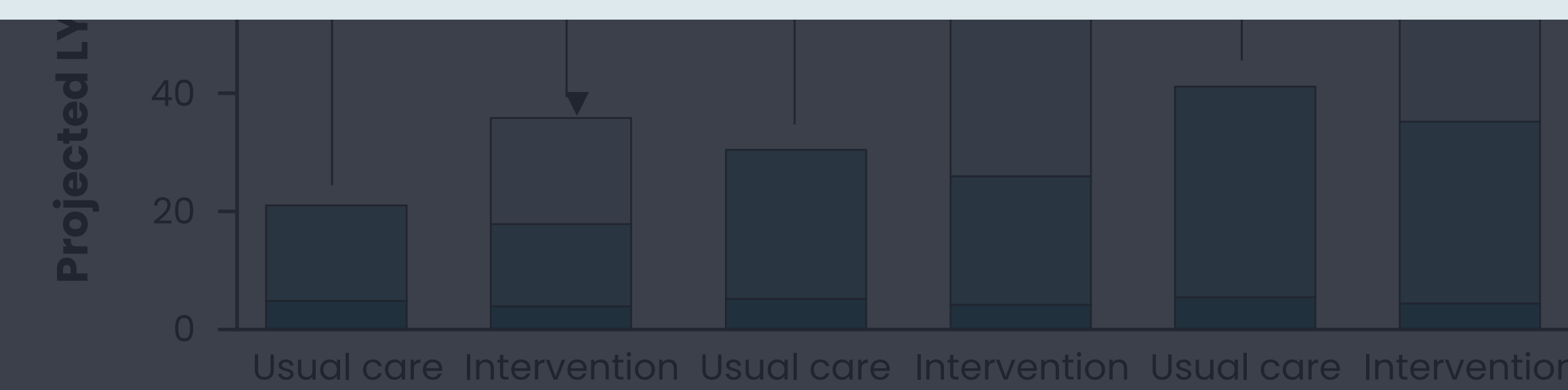
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	Usual care	Intervention	Usual care	Intervention	Usual care	Intervention
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Positive	3	2	10	22		
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



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RESULTS AND CONCLUSIONS

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Modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost.

Comparison of positive screening results with colonoscopy is likely when blood testing replaces some of the existing tests observed in Coronado et al.⁹

Isolated observed test utilization patterns from the screening round in patients who previously declined screening.

Need to understand the impact of first-line blood-based screening on adherence on projected benefits and costs.

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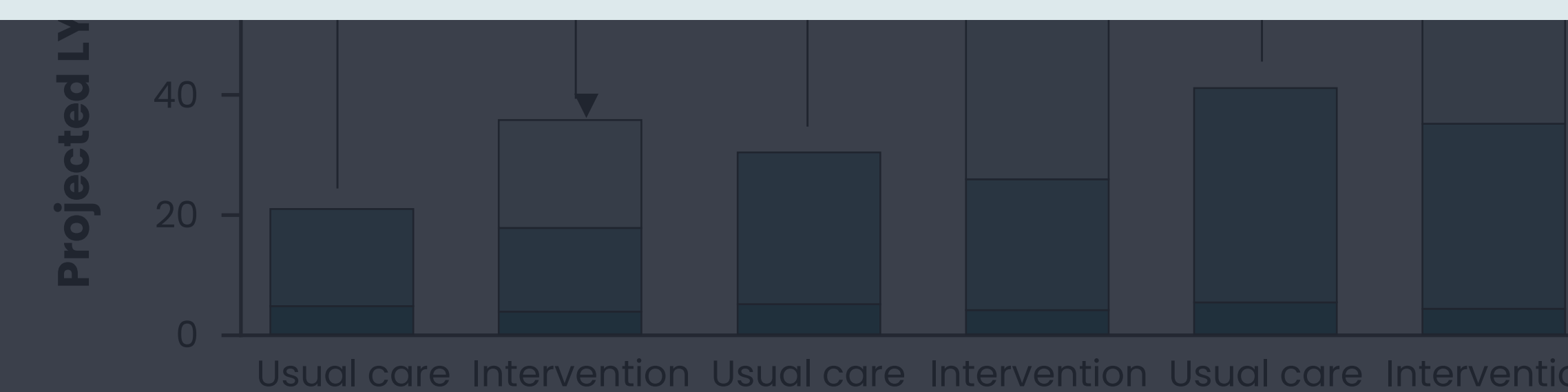
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	Screened	Positive	Followed up ^a
Usual care	33	3	0 (0%)
Intervention	9	2	1 (50%)
Usual care	214	10	0.40
Intervention	204	22	7 (70%)
Usual care			11 (50%)
Intervention			0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



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Offering a choice between blood-based screening vs existing screening tests increased adherence, with limited reported impact on outcomes when blood testing replaces some of the existing tests observed in Coronado et al.⁵

Isolated observed test utilization patterns from the screening round in patients who previously declined screening.

We needed to understand the impact of first-line blood-based screening on adherence on projected benefits and costs.

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Disclosures were provided by Iyshwarya Balasubramanian, PhD (Healthcare Consultancy Freenome Holdings, Inc. This study was sponsored by Freenome Holdings, Inc.

Projected Benefit and Cost-Effectiveness of Offering a Choice of Blood-Based Screening Versus Existing Screening Tests for Colorectal Cancer in Two Real-World Settings

Reinier G.S. Meester,^{1,2} Andy Piscitello,¹ Lance Baldo,^{1a} Noelle M. Griffin,^{1a} Peter S. Liang^{3,4}

¹Freenome Holdings Inc., South San Francisco, CA, US; ²Stanford University School of Medicine, Stanford, CA, US; ³VA New York Harbor Health Care System, New York, NY, US; ⁴NYU Langone Health, New York, NY, US

^aAffiliation at the time the study and/or analyses were conducted

INTRODUCTION

- Screening for colorectal cancer (CRC) reduces CRC-associated mortality¹ and is recommended for average-risk adults starting at age 45².
- Recent CRC screening statistics reveal that only 59% of eligible adults are screened, which is well below the US nationwide goal of 80%¹⁴.
- Emerging blood-based tests for CRC detection, free from some of the barriers associated with existing tests, such as bowel preparation, sedation, and cost, could potentially improve screening rates⁵⁻⁹.
- However, there is concern that replacing existing tests with blood-based tests could impact health outcomes and costs due to the lower sensitivity of blood-based tests for advanced precursor lesions¹⁰⁻¹².
- Two recent studies in patients who previously declined screening (one comparing a choice between blood-based screening vs existing screening or stool testing) increased overall adherence, with limited impact on outcomes^{3,8}.

OBJECTIVE

- To estimate the long-term clinical and economic impact of offering a choice of blood-based screening vs existing screening tests, based on observed for CRC screening with blood-based tests vs existing screening tests.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of offering a choice of blood-based screening vs existing screening patterns across the studies' control and intervention groups.
- The assumed performance for blood testing was 74% CRC sensitivity and 90% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based tests outlined by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma (AA) sensitivity was conservatively assumed.
- Assumed costs were based on CMS reimbursement rates, using existing test costs as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering a choice of blood-based screening vs existing screening tests.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Blood test ^a (CMS minimal requirements)
Specificity	-	0.97	0.90
Sensitivity for non-AA ^b	0.75-0.85	0.07	0.10
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

^bThe model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

MODEL ASSUMPTIONS

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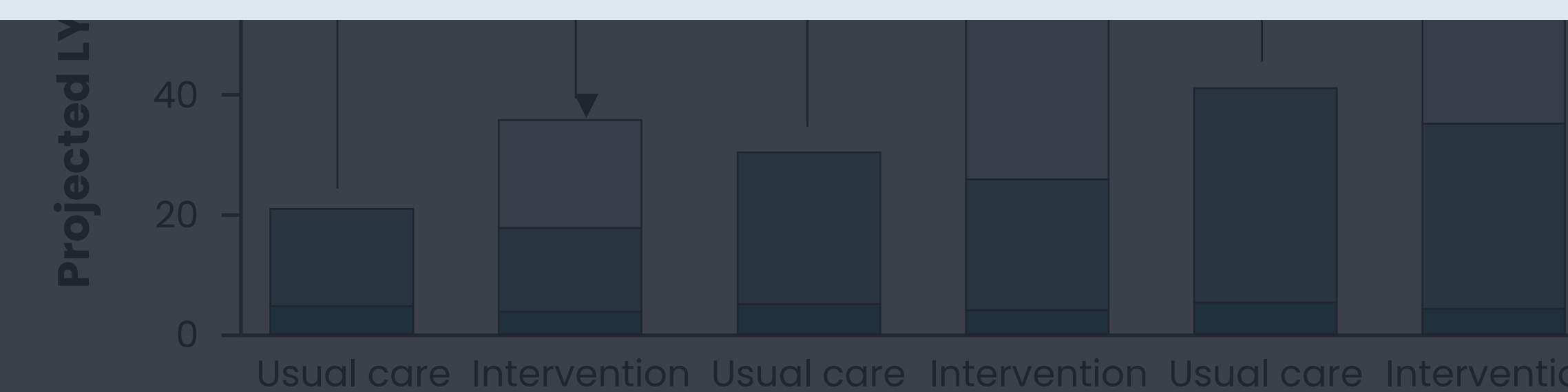
Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

Screened	33	9	214	204		
Positive	3	2	10	22		
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LY, life-years gained; QALY, quality-adjusted life-years.

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RESULTS AND CONCLUSIONS

Modeling suggest that offering patients a choice of blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost.

Offering a choice of positive screening results with colonoscopy is likely when blood testing replaces some of the existing screening tests observed in Coronado et al.⁸

Isolated observed test utilization patterns from the screening round in patients who previously declined screening.

We needed to understand the impact of first-line blood-based screening on adherence on projected benefits and costs.

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OBJECTIVE

- To estimate the long-term clinical and economic impact of offering a choice of screening patterns across the studies' control and intervention arms, compared with existing screening patterns.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of offering a choice of screening patterns across the studies' control and intervention arms, compared with existing screening patterns.
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- Assumed costs were based on CMS reimbursement rates, using existing test costs as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering a choice of screening patterns.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	OR
Specificity	-	0.97	-
Sensitivity for non-AA ^a	0.75-0.85	0.07	-
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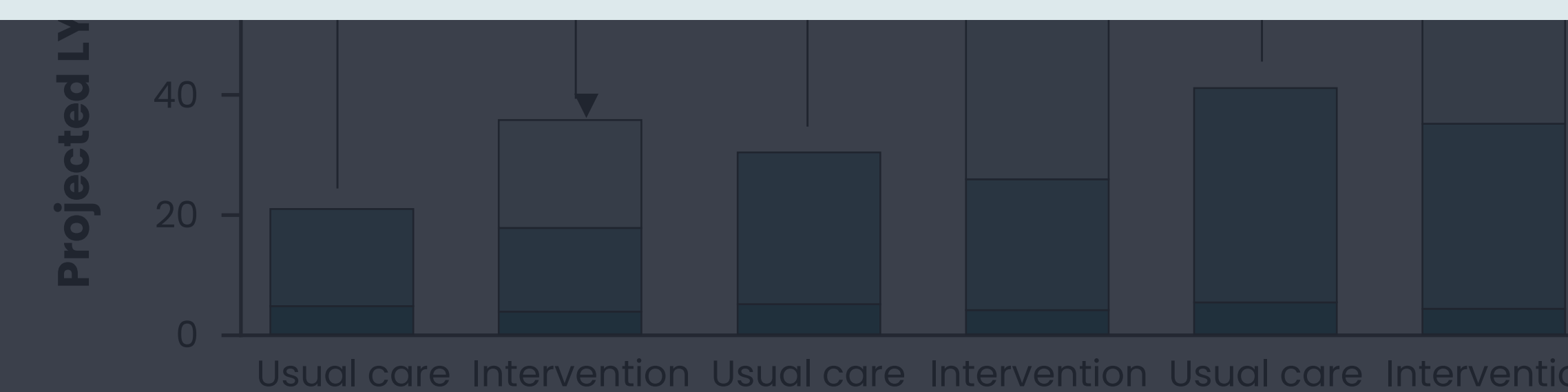
Model inputs for screening patterns

- Assumed adherence to colonoscopy every 10 years, annual fecal immunochemical test (FIT), and triennial blood testing were based on observed utilization in Liang et al.⁸ and Coronado et al.⁹ (Table 2)
- In both studies, a significantly higher proportion of participants underwent screening in the intervention arm (OR 1.96, $P=.04$; and, OR 3.08, $P<.001$), which offered blood-based testing as a screening option, compared with the control arm, which did not offer blood-based testing^{8,9}
- Colonoscopy and FIT utilization were similar between study arms in both studies
- In the model, adherence to screening was assumed to remain at observed levels

	Study 1 (Liang et al.)	Study 2 (Coronado et al.)	OR
Screened	33	9	214
Positive	3	2	10
Followed up ^a	0 (0%)	1 (50%)	0.40
	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LYG, life-years gained; QALY, quality-adjusted life-years.

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DISCUSSION AND CONCLUSIONS

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Modeling suggest that offering patients a choice of blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost.

Offering a choice of positive screening results with colonoscopy is likely when blood testing replaces some of the existing tests observed in Coronado et al.⁹

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Need to understand the impact of first-line blood-based testing on adherence on projected benefits and costs.

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- Emerging blood-based tests for CRC detection, free from some of the barriers associated with existing tests, such as bowel preparation, sedation, and discomfort, could potentially improve screening rates⁵⁻⁹.
- However, there is concern that replacing existing tests with blood-based tests could impact health outcomes and costs due to the lower sensitivity of blood-based tests to detect advanced precursor lesions¹⁰⁻¹².
- Two recent studies in patients who previously declined screening (one comparing a choice between blood-based screening vs existing screening or stool testing) increased overall adherence, with limited reported impact on screening¹³.

OBJECTIVE

- To estimate the long-term clinical and economic impact of a choice between blood-based screening vs existing screening tests in patients who previously declined screening.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of different screening patterns across the studies' control and intervention groups.
- The assumed performance for blood testing was 74% CRC sensitivity and 97% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based testing set by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma (AA) sensitivity was conservatively assumed.
- Assumed costs were based on CMS reimbursement rates, using existing test costs as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering blood testing.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	OR (95% CI)
Specificity	-	0.97	-
Sensitivity for non-AA ^a	0.75-0.85	0.07	-
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

^bThe model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

MODEL ASSUMPTIONS

Table 2. CRC screening patterns

Patients screened, n (%)	Liang et al., 2023 ^b			Coronado et al., 2024 ⁹		
	Control ^a n=178	Intervention ^b n=181	OR (P value ^c)	Usual care ^a n=1003	Intervention ^b n=181	OR (P value ^c)
Colonoscopy	2 (1.1%)	4 (2.2%)	1.99 (0.68)	15 (1.5%)	12 (1.2%)	0.80 (0.70)
Fecal testing	15 (8.4%)	18 (9.9%)	1.20 (0.72)	115 (11.5%)	99 (9.9%)	0.85 (0.28)
Blood testing	- (0%)	9 (5.0%)	-	- (0%)	204 (20.4%)	-
Total	17 (9.6%)	31 (17.1%)	1.96 (0.04)	130 (13.0%)	315 (31.5%) ^d	3.08 (<0.001)

^aDid not include blood-based testing as a screening option.

^bIncluded blood-based testing as a screening option.

^cFisher's exact test.

^dCoronado et al. reported n=305 screened with intervention (OR 2.94), but test-specific numbers and visual data from the study suggest n=315 (OR 3.08).

CRC, colorectal cancer; OR, odds ratio.

Screened	33	9	0.40	214	204	0.95
Positive	3	2	0.45	10	22	0.45
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵

RESULTS AND CONCLUSIONS

Modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost.

Offering a choice of positive screening results with colonoscopy is likely when blood testing replaces some of the existing tests observed in Coronado et al.⁹

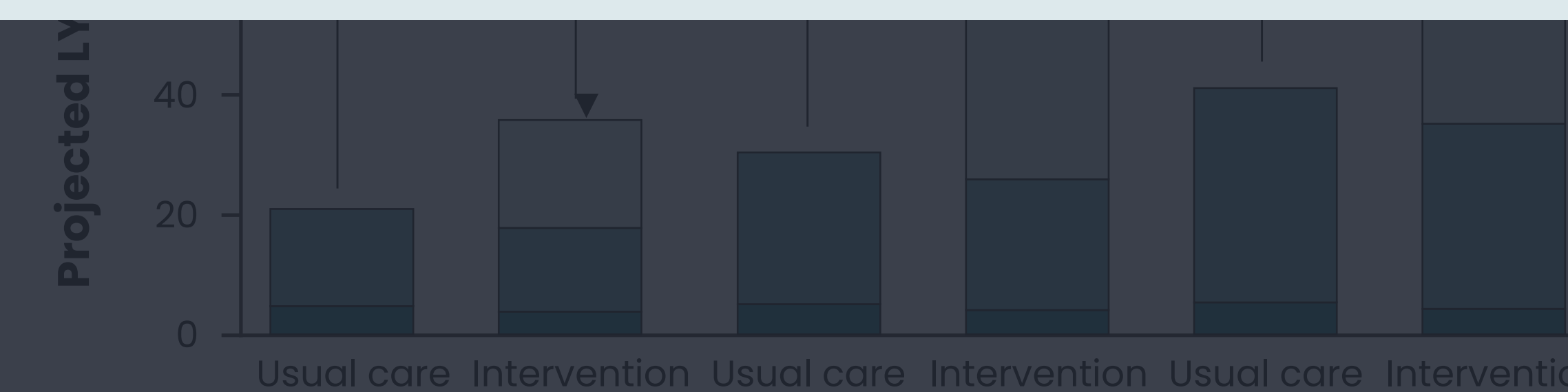
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OBJECTIVE

- To estimate the long-term clinical and economic impact of offering a choice of blood-based screening vs existing screening tests, based on adherence patterns observed for CRC screening with blood-based tests vs existing screening tests in real-world settings.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of different screening patterns across the studies' control and intervention arms.
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Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Stool DNA test
Specificity	-	0.97	0.97
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Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

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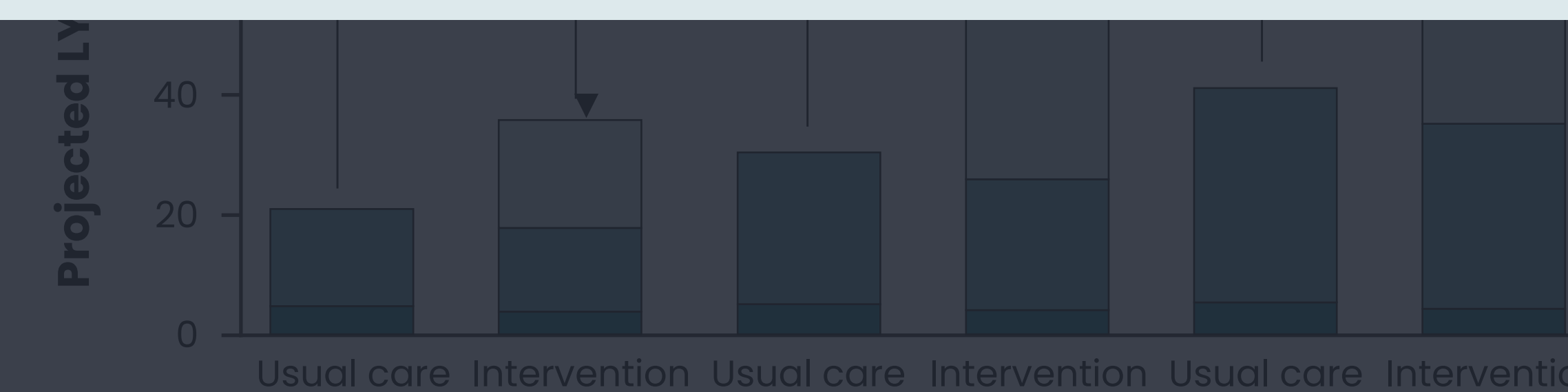
Model inputs for adherence patterns for follow-up colonoscopy

- In both Liang et al. and Coronado et al., 50% of the individuals who had a positive blood test result completed a follow-up colonoscopy, while the follow-up rate for fecal tests ranged from 0% to 70%^{9,10} (Table 3).
- As differences were not statistically significant, we assumed a rounded follow-up rate of 50% for both blood and fecal testing based on the overall average of 51.4%.
- To account for uncertainty, higher reported rates in literature, and potential future improvements, we also evaluated scenarios with 75% and 100% follow-up.

	Screened	Positive	Followed up ^a
Usual care	33	3	0 (0%)
Intervention	9	2	1 (50%)
Usual care	214	10	0.40
Intervention	204	22	7 (70%)
Usual care			11 (50%)
Intervention			0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



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- Emerging blood-based tests for CRC detection, free from some of the barriers associated with existing tests, such as bowel preparation, sedation, and colonoscopy, could potentially improve screening rates⁵⁻⁹.
- However, there is concern that replacing existing tests with blood-based tests could impact health outcomes and costs due to the lower sensitivity of blood-based tests for advanced precursor lesions¹⁰⁻¹².
- Two recent studies in patients who previously declined screening (one comparing a choice between blood-based screening vs existing screening or stool testing) increased overall adherence, with limited reported impact on screening^{3,8}.

OBJECTIVE

- To estimate the long-term clinical and economic impact of a choice of blood-based screening vs existing screening tests, based on adherence patterns observed for CRC screening with blood-based tests vs existing tests in two real-world settings.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of different screening patterns across the studies' control and intervention arms.
- The assumed performance for blood testing was 74% CRC sensitivity and 97% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based tests set by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma (AA) sensitivity was conservatively assumed.
- Assumed costs were based on CMS reimbursement rates, using existing test costs as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering a choice of blood-based screening vs existing tests.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Blood test (gFOBT)
Specificity	-	0.97	0.97
Sensitivity for non-AA ^a	0.75-0.85	0.07	0.07
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

^bThe model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

^cColonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

MODEL ASSUMPTIONS

Table 3. Adherence pattern for follow-up colonoscopy

Patients, n (%)	Liang et al., 2023 ⁸			Coronado et al., 2024 ⁹		
	Fecal testing	Blood testing	P value ^a	Fecal testing	Blood testing	P value ^a
Screened	33	9		214	204	
Positive	3	2		10	22	
Followed up ^b	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.^{2,3}

Screened	33	9		214	204	
Positive	3	2		10	22	
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.^{2,3}

RESULTS AND CONCLUSIONS

Modeling suggest that offering patients a choice of blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost.

Comparison of positive screening results with colonoscopy is higher when blood testing replaces some of the existing tests observed in Coronado et al.⁹

Isolated observed test utilization patterns from the screening round in patients who previously declined screening.

Need to understand the impact of first-line blood-based screening on adherence on projected benefits and costs.

1. 2023;73(3):233-254.

2. JAMA. 2021;325(19):1965-1977.

3. n. 2018;68(4):260-281.

4. National Colorectal Cancer Roundtable. Accessed February 16, 2024.

5. 0-in-every-community

6. 2021;13(5):1101.

7. 2010;38(5):499-507.

8. Colorectal Cancer Facts & Figures 2023-2025. Atlanta: American Cancer Society; 2023.

9. J Hepatol. 2023;21(11):2951-2957.e2.

10. 3(4):622-628.

11. Gastroenterology. 2024;167(2):368-377.

12. Gastroenterology. 2024;167(2):378-391.

13. Gastroenterology. Updated March 26, 2024. Accessed August 22, 2024.

14. Data-offer-reality-check-on-blood-based-colorectal-cancer-screening-2/

15. Cancer Intervention and Surveillance Modeling Network. Accessed August 27, 2024.

16. colorectal/#profiles-registry

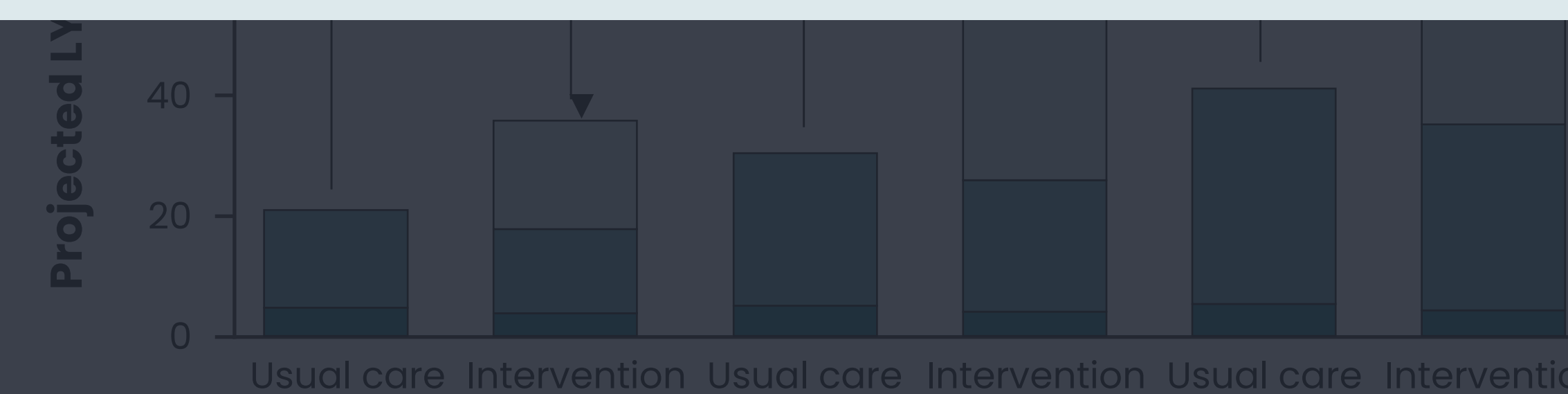
17. Centers for Medicare and Medicaid Services. Updated January 1, 2024. Accessed August 22, 2024.

18. ncd-coverage-database/view/ncd.aspx?NCDId=281

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Disclosures

RGSM: employee, Freenome Holdings Inc. AP: employee, Freenome Holdings Inc., with equity. LB: former employee, Freenome Holdings Inc., with equity. NMG: former employee, Freenome Holdings Inc. PSL: research support, Epigenomics, Freenome Holdings Inc., participation in advisory board, Guardant Health, Natera.



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LY, life-years gained; QALY, quality-adjusted life-years.

Projected Benefit and Cost-Effectiveness of Offering a Choice of Blood-Based Screening Versus Existing Screening Tests for Colorectal Cancer in Two Real-World Settings

Reinier G.S. Meester,^{1,2} Andy Piscitello,¹ Lance Baldo,^{1,a} Noelle M. Griffin,^{1,a} Peter S. Liang^{3,4}

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^aAffiliation at the time the study and/or analyses were conducted

INTRODUCTION

- Screening for colorectal cancer (CRC) reduces CRC-associated mortality¹ and is recommended for average-risk adults starting at age 45².
- Recent CRC screening statistics reveal that only 59% of eligible adults are screened, which is well below the US nationwide goal of 80%¹⁴.
- Emerging blood-based tests for CRC detection, free from some of the burdens associated with existing tests, such as bowel preparation, sedation, and discomfort, could potentially improve screening rates⁶⁻⁹.
- However, there is concern that replacing existing tests with blood-based tests could impact health outcomes and costs due to the lower sensitivity of blood-based tests to detect advanced precursor lesions¹⁰⁻¹².
- Two recent studies in patients who previously declined screening (one comparing a choice between blood-based screening vs existing screening or stool testing) increased overall adherence, with limited impact on screening¹³.

OBJECTIVE

- To estimate the long-term clinical and economic impact of offering a choice between blood-based screening vs existing screening tests, using observed adherence for CRC screening with blood-based tests vs existing screening tests.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of offering a choice between screening patterns across the studies' control and intervention arms.
- The assumed performance for blood testing was 74% CRC sensitivity and 95% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based screening tests from the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma sensitivity was conservatively assumed.
- Assumed costs were based on CMS reimbursement rates, using existing test costs as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering blood-based testing.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Colonoscopy
Specificity	-	0.97	0.97
Sensitivity for non-AA ^a	0.75-0.85	0.07	0.07
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

^bThe model defines non-AA as adenomas <10 mm in size and AA as adenomas ≥10 mm.

Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

RESULTS

Projected clinical and cost-effectiveness of blood-based testing using observed adherence patterns for screening and follow-up colonoscopy

- With 50% assumed adherence to colonoscopy follow-up and with observed screening patterns from Liang et al., offering blood testing in addition to existing tests was projected to result in 1.6 additional CRC deaths averted per 1000 persons, and to increase the LYG by 1.6 times, at a cost of \$39,100/QALY gained (Figure 1A).
- With observed screening patterns from Coronado et al., offering blood-based screening resulted in 2.9 projected CRC deaths averted per 1000 persons, and increased the LYG by 1.7 times, at a cost of \$112,700/QALY (Figure 1B).

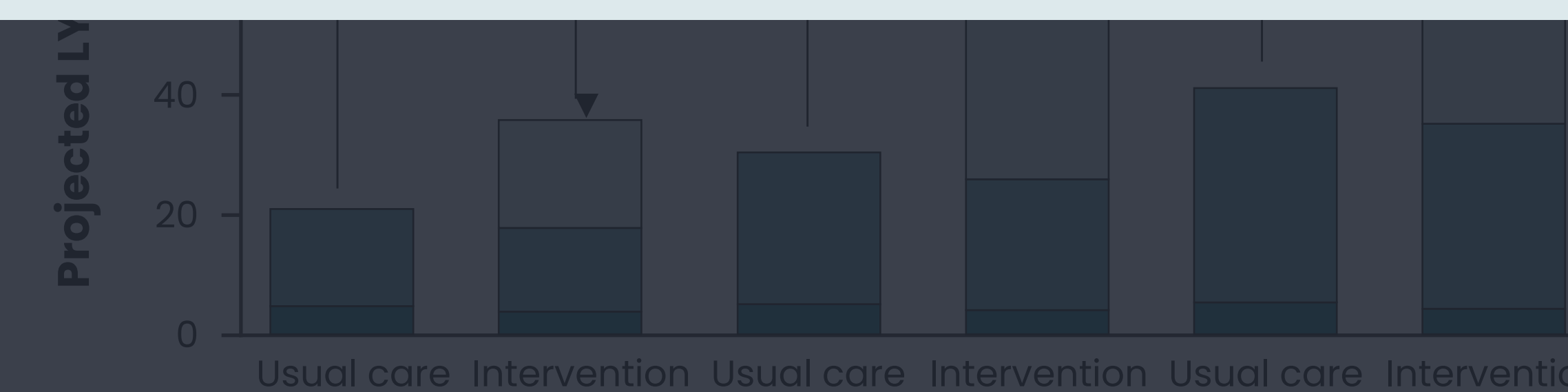
Projected clinical and cost-effectiveness of blood-based testing with higher assumed adherence to follow-up colonoscopy

- With assumed follow-up adherence of 75% and 100% and observed screening patterns from Liang et al., offering blood-based screening resulted in a steady increase in LYG per 1000 persons at a cost of \$25,900/QALY and \$18,500/QALY, respectively (Figure 1A).
- At 75% and 100% assumed follow-up adherence and observed screening patterns from Coronado et al., offering blood-based testing resulted in a steady increase in LYG per 1000 persons at a cost of \$68,900/QALY and \$49,000/QALY, respectively (Figure 1B).

Screened	33	9	214	204		
Positive	3	2	10	22		
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LYG, life-years gained; QALY, quality-adjusted life-years.

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Disclosures

RGS: employee, Freenome Holdings Inc. AP: employee, Freenome Holdings Inc., with equity. LB: former employee, Freenome Holdings Inc., with equity. NMG: former employee, Freenome Holdings Inc. PSL: research support, Epigenomics, Freenome Holdings Inc., participation in advisory board. Guardant Health, Natara.

DISCUSSION AND CONCLUSIONS

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Modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may improve outcomes at an acceptable cost.

Integration of positive screening results with colonoscopy is likely when blood testing replaces some of the existing tests observed in Coronado et al.⁹

Isolated observed test utilization patterns from the screening round in patients who previously declined screening.

We needed to understand the impact of first-line blood-based screening and adherence on projected benefits and costs.

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Cancer. JAMA. 2021;325(19):1965-1977.

N Engl J Med. 2018;68(4):260-281.

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ncd-coverage-database/view/ncd.aspx?NCDId=281

Disclosures were provided by Iyshwarya Balasubramanian, PhD (Healthcare Consultancy, Freenome Holdings, Inc). This study was sponsored by Freenome Holdings, Inc.

Projected Benefit and Cost-Effectiveness of Offering a Choice of Blood-Based Screening Versus Existing Screening Tests for Colorectal Cancer in Two Real-World Settings

Reinier G.S. Meester,^{1,2} Andy Piscitello,¹ Lance Baldo,^{1,a} Noelle M. Griffin,^{1,a} Peter S. Liang^{3,4}

¹Freenome Holdings Inc., South San Francisco, CA, US; ²Stanford University School of Medicine, Stanford, CA, US; ³VA New York Harbor Health Care System, New York, NY, US; ⁴NYU Langone Health, New York, NY, US

^aAffiliation at the time the study and/or analyses were conducted

INTRODUCTION

- Screening for colorectal cancer (CRC) reduces CRC-associated mortality¹ and is recommended for average-risk adults starting at age 45². Recent CRC screening statistics reveal that only 59% of eligible adults are up-to-date, which is well below the US nationwide goal of 80%¹⁴.
- Emerging blood-based tests for CRC detection, free from some of the burdens associated with existing tests, such as bowel preparation, sedation, and discomfort, could potentially improve screening rates⁵⁻⁹.
- However, there is concern that replacing existing tests with blood-based tests could impact health outcomes and costs due to the lower sensitivity of blood-based tests compared to colonoscopy¹⁰⁻¹².
- Two recent studies in patients who previously declined screening (Liang et al. and Coronado et al.) increased overall adherence, with limited reported impact on outcomes^{3,4}.

OBJECTIVE

- To estimate the long-term clinical and economic impact of offering a choice between blood-based screening vs existing screening tests (colonoscopy or stool testing) in patients who previously declined screening.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of offering a choice between blood-based screening vs existing screening patterns across the studies' control and intervention groups.
- The assumed performance for blood testing was 74% CRC sensitivity and 97% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based tests set by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% adherence rate was conservatively assumed.
- Assumed costs were based on CMS reimbursement rates, using the incremental cost of blood-based tests as a proxy for blood-based tests.
- Outcomes assessed were deaths averted, projected life-years gained, and incremental cost/quality-adjusted life-years (QALY) for offering a choice between blood-based screening vs existing screening tests.

Table 1. Inputs on test performance

Test characteristic	Colonoscopy	Fecal test (FIT)	Blood test (BT)
Specificity	-	0.97	0.97
Sensitivity for non-AA ^a	0.75-0.85	0.07	0.07
Sensitivity for AA	0.95	0.22	0.10
Sensitivity for CRC	0.95	0.74	0.74

^aThe input test performance for blood testing was defined as the minimum coverage criteria outlined by CMS.¹⁴

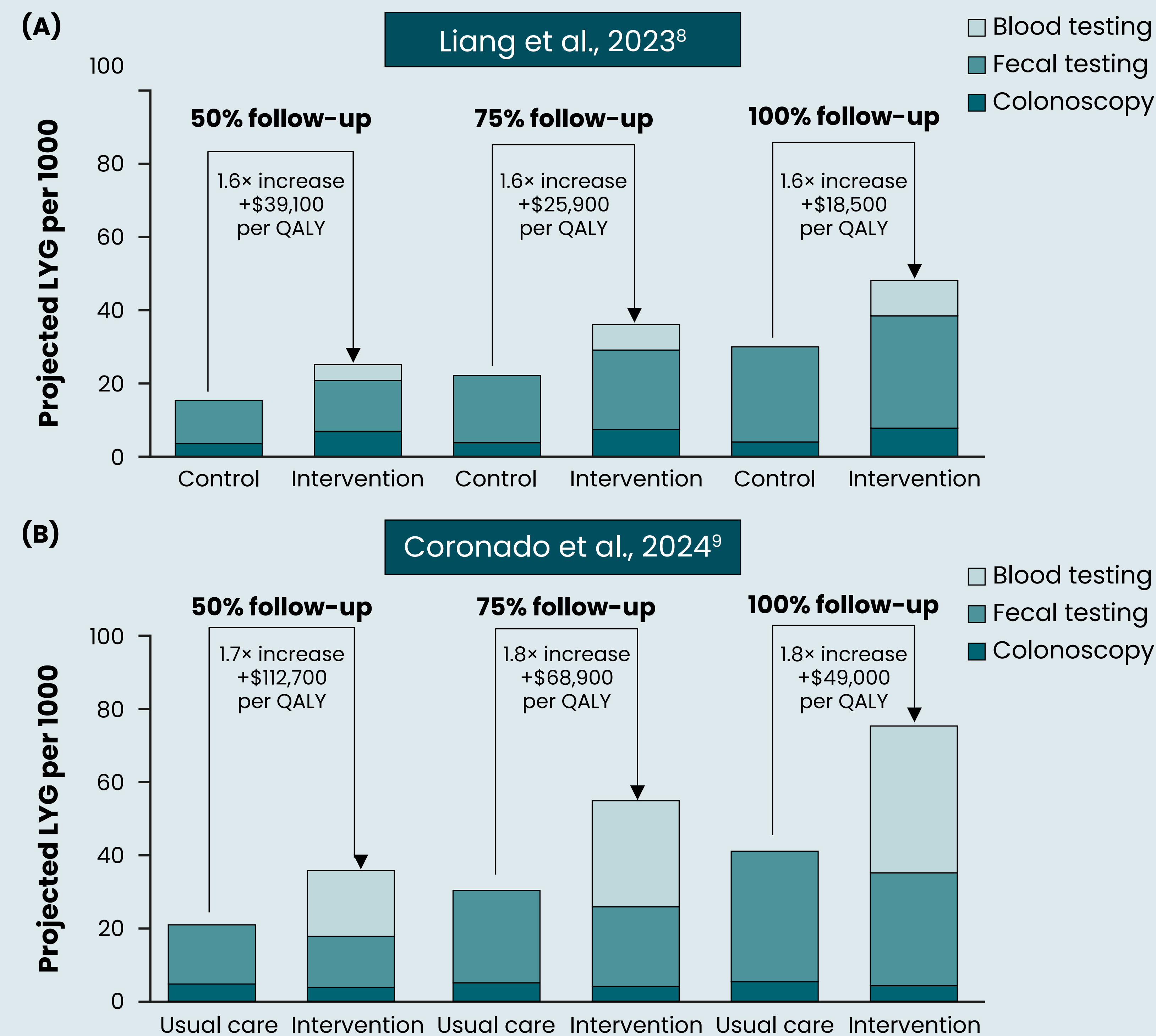
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Colonoscopy sensitivity differs for adenomas of 1-5 (75%) vs 6-9 mm (85%).

AA, advanced adenoma; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; FIT, fecal immunochemical test.

RESULTS

Figure 1. Projected benefit and cost-effectiveness of blood-based testing by adherence pattern for follow-up colonoscopy



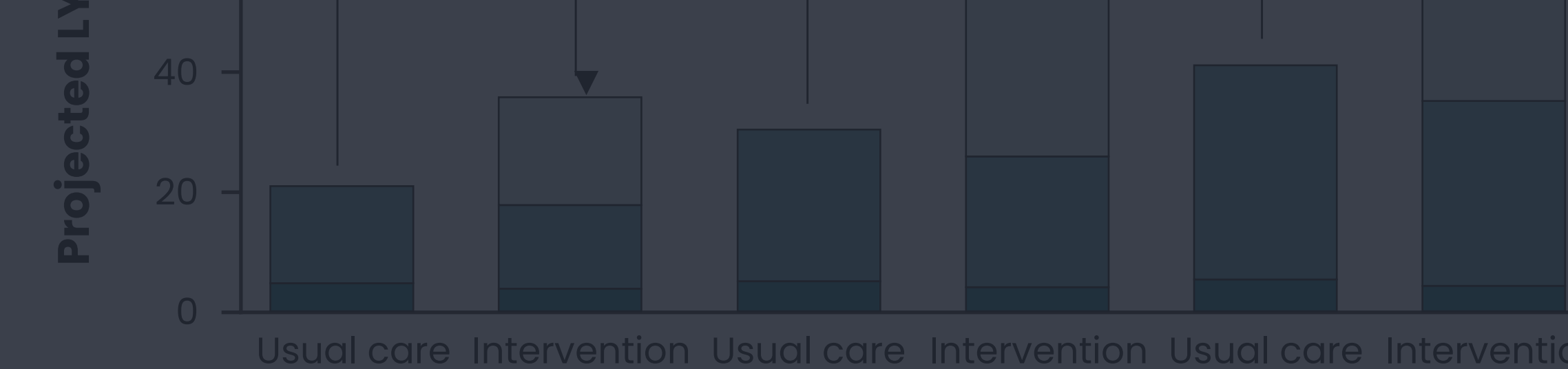
Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LYG, life-years gained; QALY, quality-adjusted life-years.

2 of 2

	Screened	Positive	Followed up ^a
Control	33	3	0 (0%)
Intervention	9	2	1 (50%)
Control	214	10	7 (70%)
Intervention	204	22	11 (50%)
Control	0.40	0.40	0.40
Intervention	0.45	0.45	0.45

^aUsing Fisher's exact test.

^bCurrent clinical guidelines state all positive results for non-colonoscopy tests should be followed up with a timely colonoscopy.¹⁵



Projected benefit and cost-effectiveness of offering a choice between blood-based screening vs existing tests for colorectal cancer in Liang et al. (A) and Coronado et al. (B). LYG, life-years gained; QALY, quality-adjusted life-years.

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Projected Benefit and Cost-Effectiveness of Offering a Choice of Blood-Based Screening Versus Existing Screening Tests for Colorectal Cancer in Two Real-World Settings

Reinier G.S. Meester,^{1,2} Andy Piscitello,¹ Lance Baldo,^{1,a} Noelle M. Griffin,^{1,a} Peter S. Liang^{3,4}

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- Screening for colorectal cancer (CRC) reduces CRC-associated mortality¹ and is recommended for average-risk adults starting at age 45².
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- Two recent studies in patients who previously declined screening (one comparing a choice between blood-based screening vs existing screening or stool testing) increased overall adherence, with limited impact on outcomes^{3,8}.

OBJECTIVE

- To estimate the long-term clinical and economic impact of offering a choice between blood-based tests vs existing screening tests, based on test utilization patterns observed for CRC screening with blood-based tests vs existing screening tests in two real-world settings.

MODEL ASSUMPTIONS

- An established Cancer Intervention and Surveillance Modeling Network (CISIM) model was replicated, validated, and then used to evaluate the impact of offering a choice between blood-based tests vs existing screening tests across the studies' control and intervention arms.
- The assumed performance for blood testing was 74% CRC sensitivity, 95% specificity (Table 1), satisfying the minimum US coverage criteria for blood-based tests set by the Centers for Medicare and Medicaid Services (CMS)¹⁴; a 10% advanced adenoma (AA) sensitivity was conservatively assumed.
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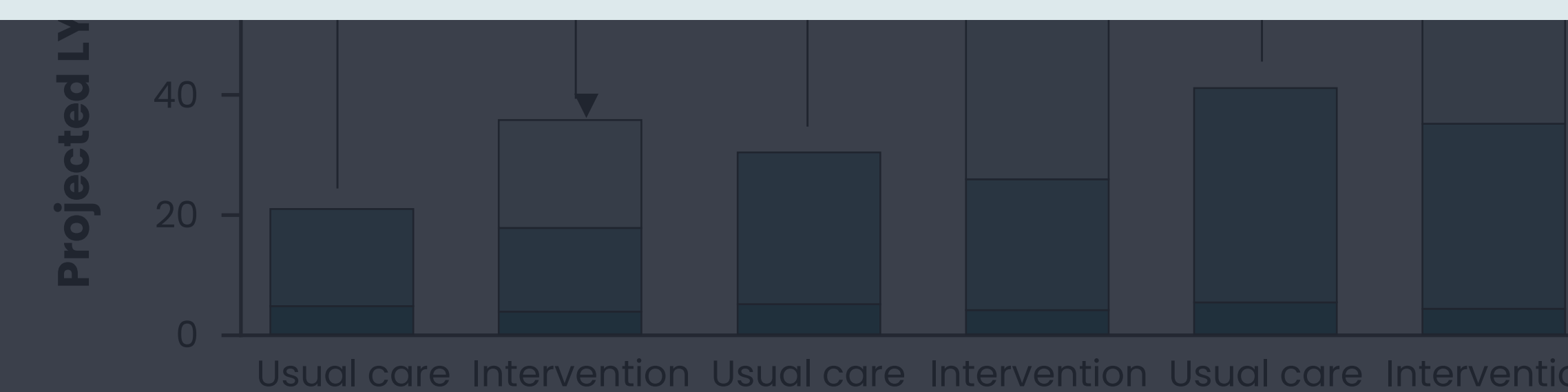
KEY FINDINGS AND CONCLUSIONS

- Trial data and modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may substantially improve outcomes at an acceptable cost.
- Adequate follow-up of positive screening results with colonoscopy is essential, especially when blood testing replaces some of the existing screening, such as observed in Coronado et al.⁹
- Our analysis extrapolated observed test utilization patterns from studies with a single screening round in patients who previously declined standard screening.
- More research is needed to understand the impact of first-line blood testing and longitudinal adherence on projected benefits and cost-effectiveness.

	Usual care	Intervention	Usual care	Intervention	Usual care	Intervention
Screened	33	9	214	204		
Positive	3	2	10	22		
Followed up ^a	0 (0%)	1 (50%)	0.40	7 (70%)	11 (50%)	0.45

^aUsing Fisher's exact test.

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DISCUSSION AND CONCLUSIONS

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Modeling suggest that offering patients a choice between blood-based CRC screening vs existing tests may substantially improve outcomes at an acceptable cost.

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