Economic Evaluation of Universal Lynch Syndrome Screening Protocols Among Newly Diagnosed Patients with Endometrial Cancer

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Geisinger IMPULSS
Implementing Universal Lynch Syndrome Screening

Background

- Between 2%-6% of endometrial cancer (EC) cases are attributable to Lynch Syndrome (LS) and the lifetime risk of endometrial cancer for women with LS is between 40%-60%.
- Universal tumor screening for LS in individuals with EC is recommended by several professional societies:

(2014)

SGO Society of Gynecologic Oncology

ACOG The American College of Obstetricians and Gynecologists

(2018)

NCCN National Comprehensive Cancer Network®

- Implementation of universal LS screening in healthcare systems remains inconsistent and suboptimal.

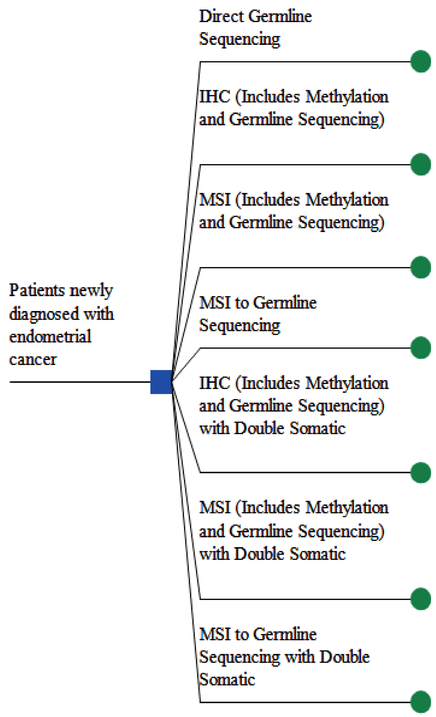
Methods

- We conducted economic evaluation from a healthcare system perspective by developing 7 decision analytic models reflecting current LS screening protocols on a hypothetical cohort of 1,000 newly diagnosed patients with EC.
- Used outcome measures that were deemed important for healthcare system decision-making - performance, costs, and efficiency (total costs/number of true LS cases identified).

Assumptions:

- 100% availability and success in blood and tumor tissue collection and 100% compliance with protocols (genetic counseling and consenting, all tests ordered and completed)
- Genetic testing used in all protocols for detecting LS cases is a next-generation sequencing (NGS) panel including MMR genes

Figure 1. Lynch Syndrome Screening Protocols



Note: IHC, immunohistochemistry; MSI, microsatellite instability. Germline sequencing refers to next generation sequencing (NGS) panel including MMR genes in all protocols.

Analysis Performed

Base-case analysis
using the best estimates (base-case values) for all model parameters and inputs

One-way sensitivity analysis
to assess the effects of changes in individual parameters on the estimated model outcomes

Probabilistic sensitivity analysis
with 1,000 model iterations based on assigned probability distributions for each parameter to evaluate the plausible ranges (reported as 95% CI) for model outcomes

Threshold analysis
to estimate the threshold cost of germline sequencing at which the direct germline sequencing protocol would reach equivalent efficiency as the most efficient protocol

Results

Base Case Results

- The Direct Germline Sequencing (DGS) protocol had the best performance, identifying all 40 out of the expected 40 true LS cases, and had similar efficiency to the MSI protocol.
- The IHC protocol was most efficient but missed more LS cases (than DGS), identifying 37/40 true LS cases.
- Adding double somatic testing to the IHC, MSI and MSI to germline sequencing protocols reduced the number of unexplained cases by 99%-100% and increased costs by 1%-18%.
- Threshold analysis showed that for the direct germline sequencing protocol to be as efficient as the IHC protocol, the cost of the germline sequencing panel would need to be $251.44.

Conclusions

- DGS would be as efficient as the IHC protocol if the cost of germline sequencing continues to decline and is already at similar efficiency to the MSI protocol.

Table 1. Base-Case and Probabilistic Sensitivity Analysis on Outcome Measures

	Protocols													
Outcomes	**DGS**		**IHC**		**MSI**		**MSIGS**		**IHCDS**		**MSIDS**		**MSIGSDS**	
	Base Case	(95% CI)	Base Case	(95% CI)	Base Case	(95% CI)	Base Case	(95% CI)	Base Case	(95% CI)	Base Case	(95% CI)	Base Case	(95% CI)
Performance														
Sensitivity of protocol	99.90%	(99.55-99.95%)	92.59%	(88.27-97.24%)	80.53%	(77.16-85.46%)	89.48%	(86.63-93.86%)	92.59%	(88.32-97.23%)	80.53%	(77.20-85.48%)	89.48%	(86.50-93.88%)
Specificity of protocol	99.50%	(95.47-99.53%)	99.98%	(99.78-99.98%)	100.00%	(99.96-100.00%)	99.91%	(99.00-99.90%)	99.98%	(99.78-99.99%)	100.00%	(99.96-100.00%)	99.91%	(98.95-99.90%)
Number of true LS cases expected to be identified*	40	(24-56)	37	(22-52)	32	(19-46)	36	(22-51)	37	(22-52)	32	(19-46)	36	(21-51)
Number of missed LS cases	0	(0-0)	3	(1-5)	8	(4-11)	4	(2-7)	3	(1-6)	8	(4-12)	4	(2-7)
Number of unexplained dMMR cases	NA	NA	32	(14-60)	4	(3-10)	163	(149-250)	0	(0-1)	0	(0-0)	2	(0-4)
Costs														
Cost per protocol for a 1,000 hypothetical cohort ($ millions)	$0.82	($0.48-$1.77)	$0.48	($0.37-$0.64)	$0.62	($0.46-$0.82)	$0.71	($0.56-$1.04)	$0.51	($0.39-$0.68)	$0.62	($0.46-$0.82)	$0.84	($0.70-$1.17)
Cost per EC case screened	$820	($484-$1,773)	$481	($371-$644)	$618	($460-$817)	$714	($555-$1,036)	$507	($393-$675)	$621	($465-$821)	$845	($695-$1,174)
Efficiency														
Cost per true LS case identified	$20,521	($10,315-$50,301)	$12,992	($8,378-$24,362)	$19,179	($12,749-$33,542)	$19,948	($13,089-$37,671)	$13,688	($8,831-$25,625)	$19,281	($12,281-$33,785)	$23,600	($16,011-$46,769)

Note: * The number of true LS cases expected to be identified is 40 (20–60) in the hypothetical cohort of 1,000 endometrial cancer patients based on LS prevalence of 4% (2–6%). DGS Protocol: Direct Germline Sequencing Protocol; IHC Protocol: Immunohistochemistry (Includes Methylation and Germline Sequencing) Protocol; MSI Protocol: Microsatellite Instability (Includes Methylation and Germline Sequencing) Protocol; MSIGS Protocol: Microsatellite Instability to Germline Sequencing Protocol; IHCDS Protocol: Immunohistochemistry (Includes Methylation and Germline Sequencing) with Double Somatic Protocol; MSIDS Protocol: Microsatellite Instability (Includes Methylation and Germline Sequencing) with Double Somatic Protocol; MSIGSDS Protocol: Microsatellite Instability to Germline Sequencing with Double Somatic Protocol.

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