Draft abstract for submission to SMDM (Due Monday May 23, 2022)

Clinical outcomes and cost-effectiveness of colorectal cancer screening among childhood cancer survivors previously treated with abdominal-pelvic radiation

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Abstract category: Applied Health Economics

Word count: 375 / 375

Introduction: Childhood cancer survivors treated with abdominal-pelvic radiation are at increased risk for colorectal cancer (CRC). The Children's Oncology Group (COG) recommends early initiation of CRC screening at age 30 with colonoscopy every 5 years, multitarget stool DNA [mtsDNA] testing every 3 years, or fecal immunochemical testing [FIT] every year. However, the benefits, costs, and cost-effectiveness of screening strategies among this patient population are unknown.

Methods: We used data from the Childhood Cancer Survivor Study to modify the SimCRC model from CISNET to reflect high CRC and competing mortality risks among survivors. Strategies evaluated varied by modality (no screening, colonoscopy, mtsDNA, FIT), screening start age (25, 30, 35, 40, 45), and screening interval (3, 5 or 10y for colonoscopy; 1, 2 or 3y for mtsDNA and FIT). Analyses assumed complete uptake and adherence to all screening and follow-up procedures. Utility weights and costs (2020 USD), including those from the health-care and patient perspectives, were derived from the Centers for Medicare & Medicaid Services publically-available resources and the published literature. We calculated incremental cost-effectiveness ratios (ICERs) and identified the cost-effective strategy at a willingness-to-pay threshold of 150K/quality-adjusted life-years gained (QALYG). Our primary analysis evaluated the cost-effective strategy when all strategies are compared against each other. Because the COG currently recommends 3 options for screening, each with a different screening modality, we also identified the cost-effective strategy within each modality. To more fully capture uncertainty in CRC risk in survivors of childhood cancer, we conducted the analyses with 100 calibrated natural history parameter sets and reported mean outcomes.

Results: QALYG from screening ranged from 226 to 326 per 1000 25-year-olds. Compared to no screening, nearly all strategies were cost-saving. Annual FIT starting at age 25 was the cost-effective strategy among all those evaluated and among just the FIT strategies. Among the colonoscopy strategies, 10-yearly screening starting at age 30 was cost-effective; among the mtsDNA strategies, triennial screening starting at age 30 was cost-effective. If the risk of CRC was 11% lower than the base-case, biennial FIT at age 25 is cost-effective.

Conclusion: Early initiation of screening, as recommended by the COG, may substantially reduce CRC mortality among high-risk childhood cancer survivors and is cost-effective. Decision-makers can use this information to guide screening recommendations for childhood cancer survivors.

Table. Model results (per 1000 survivors) for efficient screening strategies. We calculated incremental cost-effectiveness ratios (ICER) for all strategies compared against each other and by modality.

Strategy	QALYG*	CRC cases averted*	CRC deaths averted*	Total costs	ICER (all strategies)	ICER (by modality)
Colonoscopy†						
COL 45-75, 10	242	52	23	8,790,000	-	default
COL 40-75, 10	266	55	24	8,820,000	-	37K
COL 35-75, 10	286	58	25	9,470,000	-	78K
COL 30-75, 10	297	59	25	9,790,000	-	126K
COL 25-75, 10	307	60	26	10,810,000	-	247K
COL 25-75, 5	325	67	27	17,470,000	1025K	892K
FIT‡						
FIT 45-75, 1	235	46	23	8,000,000	default	default
FIT 40-75, 3	251	48	24	7,900,000	0K	0K
FIT 35-75, 3	265	49	24	7,810,000	3K	3K
FIT 30-75, 3	279	51	25	7,790,000	16K	16K
FIT 30-75, 2	286	52	25	7,800,000	31K	31K
FIT 25-75, 2	294	53	25	7,860,000	46K	46K
FIT 25-75, 1	303	56	26	8,270,000	143K	143K
mtsDNA						
mtsDNA 45-75, 3	226	43	22	10,610,000	-	default
mtsDNA 40-75, 3	249	47	23	10,980,000	-	53K
mtsDNA 35-75, 3	271	50	24	11,650,000	-	84K
Recommended by COG mtsDNA 30-75, 3	285	52	25	12,440,000	-	144K
mtsDNA 25-75, 3	293	53	25	13,340,000	-	275K
mtsDNA 25-75, 2	307	58	26	15,760,000	-	487K
mtsDNA 25-75, 1	316	63	27	21,870,000	-	1989K

*Compared to no screening

†The colonoscopy strategy recommended by COG (COL 30-75, 5) had 317 QALYG, averted 66 CRC cases, and averted 27 CRC deaths at a total cost of $15,840,000 and was dominated.

‡The FIT strategy recommended by COG (FIT 30-75, 1) had 294 QALYG, averted 55 CRC cases, and averted 25 CRC deaths at a total cost of $8,020,000 and was dominated.