



OncoSim

Formerly the Cancer Risk Management Model

Informing decisions in cancer control



Simulation of Sigmoidoscopy Trials for Colorectal Cancer Screening: A Microsimulation Validation Approach

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Acknowledgements

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Background

- Additional CRC screening methods include: fecal immunochemical test (FIT) and fecal occult blood test (FOBT) which are currently implemented in all Canadian provinces
- Alternative colorectal cancer (CRC) screening methods are being examined worldwide
- Sigmoidoscopy has received growing interest as a screening method for colorectal neoplasia detection
- In comparison to colonoscopy, sigmoidoscopy is less invasive but does not provide a complete examination of the colon
- OncoSim-CRC is part of suite of cancer models available in the OncoSim platform

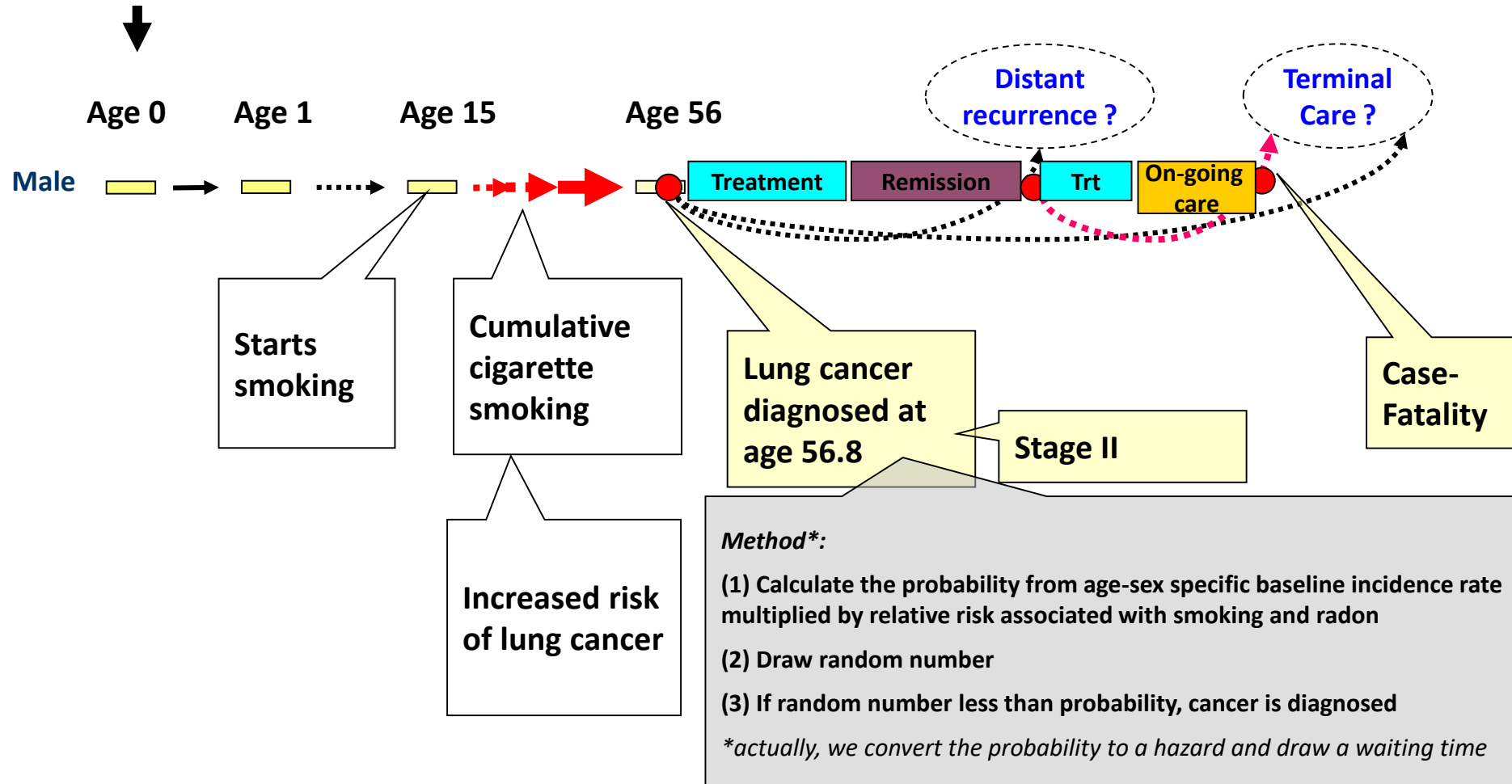
Objective

- To validate OncoSim-CRC against randomized controlled trials (RCTs) that examined the effect of sigmoidoscopy screening on reduction of incidence and mortality

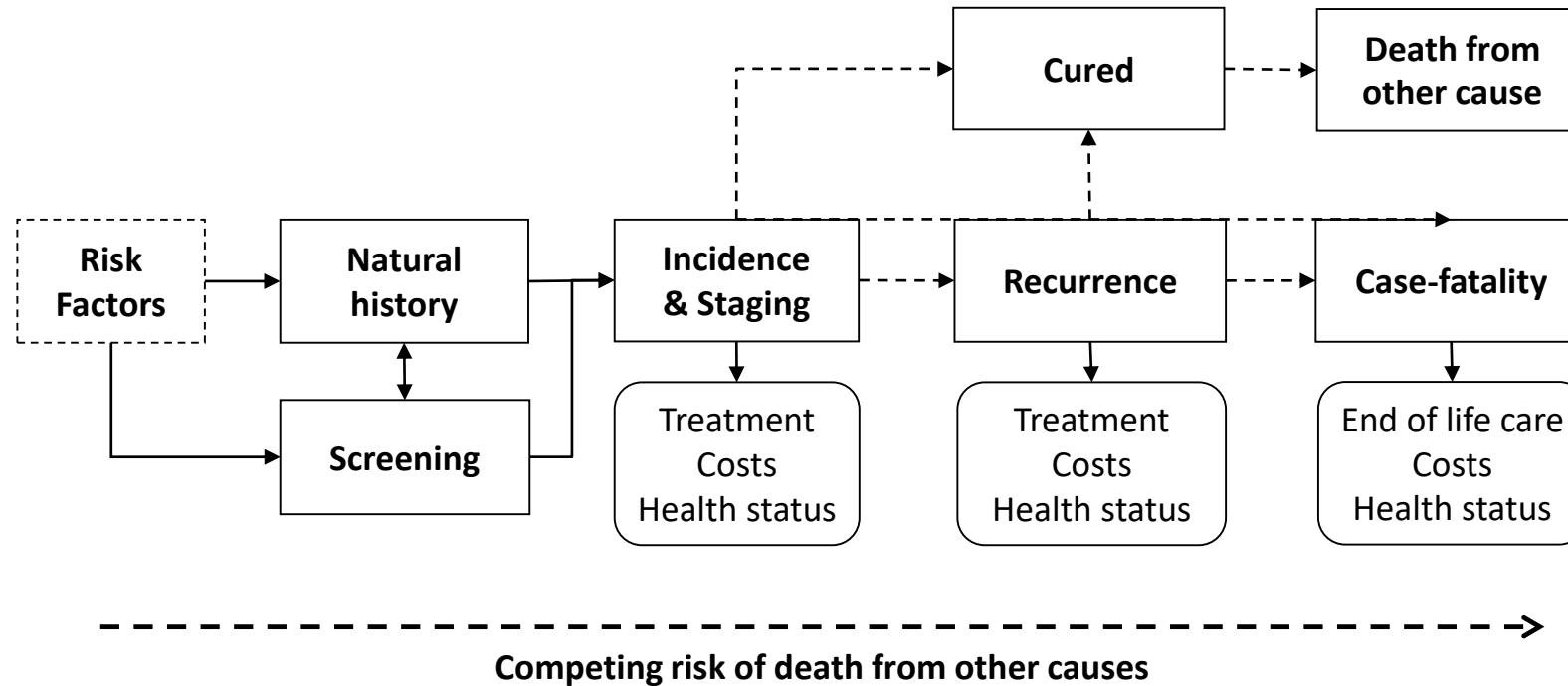
How does microsimulation work?

(non-interacting agent approach)

Let's start with one simulated person (who happens to get lung cancer)



Colorectal Cancer Model Diagram



Dashed arrows are times drawn from survival distribution

Sigmoidoscopy Trials

	UK Flex Sig	SCORE	PLCO	NORCCAP
Country	UK	Italy	USA	Norway
Age eligible	55-64	55-64	55-74	50-64**
Experimental Intervention	One time sigmoidoscopy	One time Colonoscopy reaching to sigmoid/ descending junction	Baseline sigmoidoscopy and at 3-5 years	One time sigmoidoscopy or one time sigmoidoscopy (colonoscope used)
Control Intervention	None	None	None	None
Randomized to Sigmoidoscopy	Males: 28,097	Males: 8,576	Males: 38,350	Males: 9,900
	Females: 29,157	Females: 8,572	Females: 39,115	Females: 10,103
Average follow-up time (years)	10.8	10.5	11.9	10.9
Randomization Ratio (Intervention:Control)	1:2	1:1	1:1	Intervention group randomized to sigmoidoscopy +/- Fecal Test

*Other exclusion criteria related to other trial randomizations

**Initial study included 55-64 only study was expanded in 2000 to recruit 50-54

Sigmoidoscopy Trials

	UK Flex Sig	SCORE	PLCO	NORCCAP*
Inclusion Criteria	Participating practices, persons willing to be randomized	Mixed across regions – willing to be randomized	Mass media and mailings	Random Invitation via population register, non-invited are controls
Exclusion Criteria	History CRC, adenoma or IBD >1 fam hist. CRC, sigmoidoscopy /colonoscopy < 3 years, Symptoms CRC	History CRC, adenoma or IBD, >1 1st deg fam hist. CRC, sigmoidoscopy/ colonoscopy ≤2 years, Symptoms CRC	History CRC, *sigmoidoscopy/ colonoscopy < 3 years	Apply to screen group only: Colorectal surgery, rad or chemo treatment, anti-coagulant therapy, medical kontras
Sigmoidoscopy Uptake Rate	Males: 20,519 (73%) Females: 20,155 (69%)	Males: 4,112 (48%) Females: 4,057 (47%)	Males: 33,048† (86.2%) (Age 55-64) - 86.2% Females: 31,610† (80.8%) (Age 55-64) – 82.1%	Males: 6,299 (64%) Females: 6,661 (66%)
Cancers Diagnosed in Control	Total: 1818	Total: 306	Total: 1287	Total: 1086
Cancers Diagnosed in Sigmoidoscopy Group	Total: 706 (screened=445)	Total: 251 (screened=126)	Total: 1012	Total: 253

*Results in this trial are for Sig and Sig+FIT combined. †For first round

Approach

- Trial cohorts and interventions of each RCT were examined
- OncoSim-CRC was configured to replicate the screening methods, cohorts, control and intervention groups
- OncoSim setup to mimic trial participation and trial protocols
- For each trial two scenarios representing the respective control and intervention arms were run

Approach

- Simulated outcomes were compared to the observed results of each RCT
- Outputs from the model were scaled to match the proportions of individuals in the control and intervention groups of each trial
- **Data from the four trials had not been used in the development of the model**

OncoSim Matched to Trial Characteristics

	Intervention	Age		Male : Female Ratio		Sigmoidoscopy Uptake		Follow-up Period
		Intervention	Control	Intervention	Control	Intervention	Control	Both arms
UK Flex	✓ One time sig	✓	✓	✓	✓	✓	N/A	✓ 11 years
SCORE	✓ One time colonoscopy to sigmoid	✓	✓	✓	✓	✓	N/A	✓ 11 years
PLCO	✓ Baseline sig + 3 year sig + 5yr sig	✓	✓	✓	✓	✓	✓ Simulated 25% contamination	✓ 11 years
NORCAAP	✓ One time sig plus One time sig and FIT	✓ 2 step process to match change in study age intake	✓	✓	✓	✓	N/A	✓ 11 years

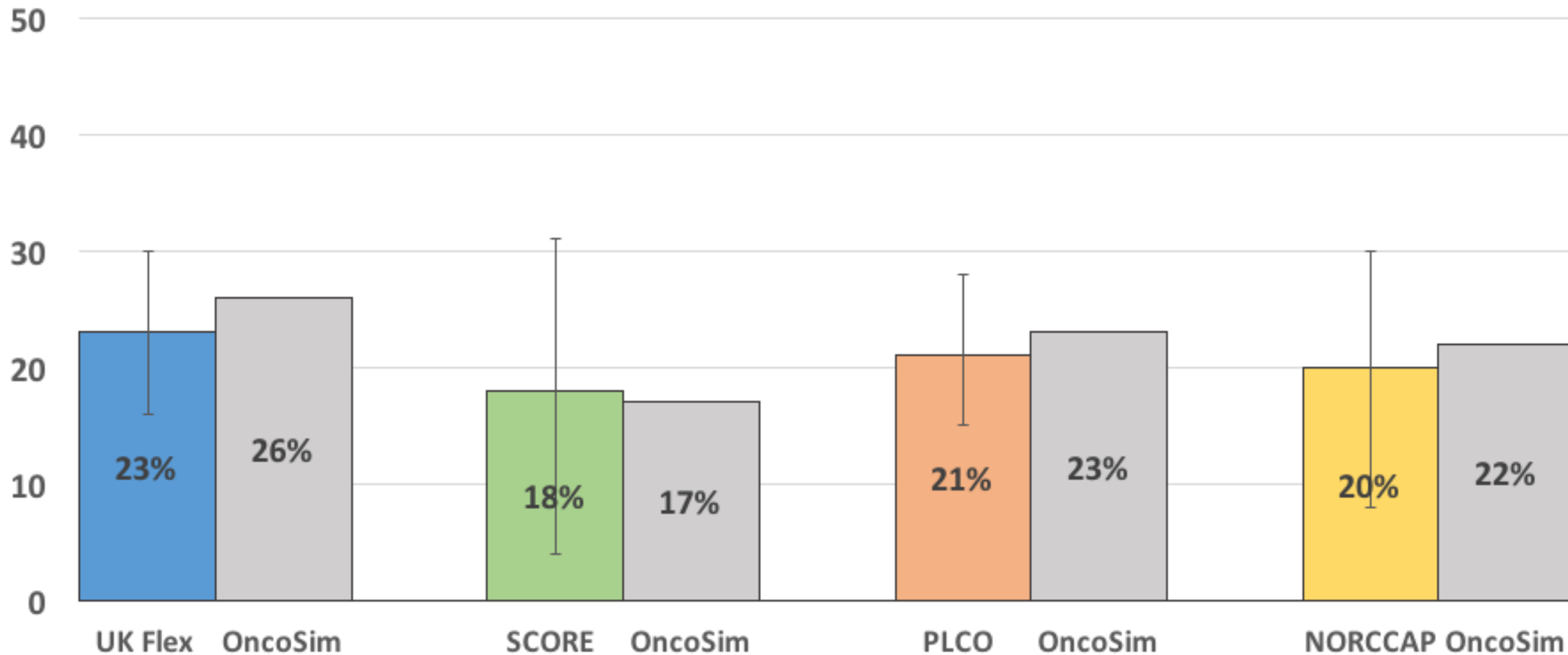
Model Assessment Results

OncoSim simulated results that closely approximate trial results

		% Reductions	
		Incidence	Mortality
UK Flex		23	31
OncoSim		26	27
SCORE		18	22
OncoSim		17	18
PLCO		21	26
OncoSim		23	22
NORCCAP		20	27
OncoSim		22	21

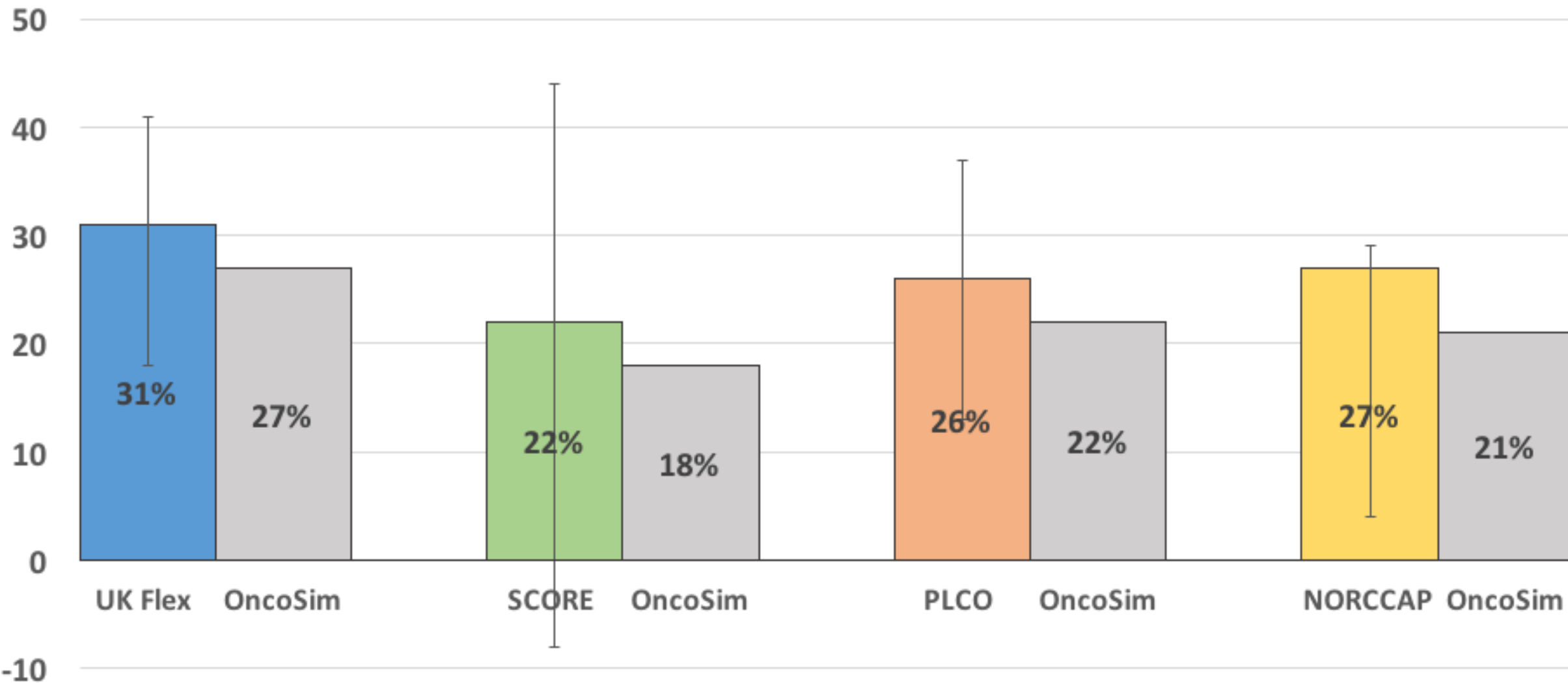
Trials VS OncoSim Incidence Reductions (%)

Percent



Trials VS OncoSim Mortality Reductions (%)

Percent



Conclusions

- ✓ **OncoSim-CRC** was **able** to match key cohort characteristics of each sigmoidoscopy RCT
- ✓ **OncoSim-CRC** was **able** to reproduce the incidence and mortality reductions from CRC in each RCT

Limitations

- In simulating the PLCO trial, there was uncertainty in knowing which individuals received screening outside the trial, in particular in the period after screening in the trial had concluded
- Agreement between RCTs and model prediction does not guarantee accuracy of longer term predictions but can provide further reassurance

Contact Us to Learn More!

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Appendix

Trial References

Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO)

- Prorok PC, Andriole GL, Bresalier RS, Buys SS, Chia D, Crawford ED, et al. Design of the prostate, lung, colorectal and ovarian (PLCO) cancer screening trial. *Control Clin Trials* 2000;21(6):273S-309S.
- Schoen RE, Pinsky PF, Weissfeld JL, Yokochi LA, Church T, Laiyemo AO, et al. Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. *N Engl J Med* 2012 Jun 21;366(25):2345-2357.

UK Flexible Sigmoidoscopy Trial (UKFS)

- Atkin WS, Edwards R, Wardle J, Northover JM, Sutton S, Hart AR, et al. Design of a multicentre randomised trial to evaluate flexible sigmoidoscopy in colorectal cancer screening. *J Med Screen* 2001;8(3):137-144.
- Atkin WS, Edwards R, Kralj-Hans I, Wooldrage K, Hart AR, Northover JM, et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. *Lancet* 2010 May 8;375(9726):1624-1633.

Screening for Colon Rectum (SCORE)

- Segnan N, Senore C, Andreoni B, Aste H, Bonelli L, Crosta C, et al. Baseline findings of the Italian multicenter randomized controlled trial of "once-only sigmoidoscopy"--SCORE. *J Natl Cancer Inst* 2002 Dec 4;94(23):1763-1772.
- Segnan N, Armaroli P, Bonelli L, Risio M, Sciallero S, Zappa M, et al. Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian Randomized Controlled Trial--SCORE. *J Natl Cancer Inst* 2011 Sep 7;103(17):1310-1322.

Norwegian Colorectal Cancer Prevention (NORCCAP)

- Bretthauer M, Gondal G, Larsen I, Carlsen E, Eide T, Grotmol T, et al. Design, organization and management of a controlled population screening study for detection of colorectal neoplasia: attendance rates in the NORCCAP study (Norwegian Colorectal Cancer Prevention). *Scand J Gastroenterol* 2002;37(5):568-573.
- Holme O, Loberg M, Kalager M, Bretthauer M, Hernan MA, Aas E, et al. Effect of Flexible Sigmoidoscopy Screening on Colorectal Cancer Incidence and Mortality A Randomized Clinical Trial. *JAMA* 2014;312(6):606-615.

OncoSim Data Sources

Data Type	Source
Mortality, Birth, Population projections	Vital Statistics (1950-2005), Census (2006, 2011)
Incidence, Staging, (Survival)	Canadian Cancer Registry (1992-2010)
Cancer Survival by stage	British Columbia Cancer Registry Data (1992-2012) Chart review (1991-92), Literature (1981, 1990-2000, 2005),
Smoking rates	Canadian Community Health Survey (2000-2007), National Population Health Survey (1994-2004) Canadian Health Survey (1979)
Time use data	General Social Survey (2005)
Earnings, Transfers, and Taxes	Census 2006, SPSPD/M v16.1 (2005)
Total health care expenditures	Canadian Institute for Health Information (2006)
Health care costs: diagnosis, treatment, follow-up, palliative and terminal care	Ontario Case Costing Initiative (2007-2008), Provincial formulary (2009), Provincial Ministries of Health (2009)
Current treatment practice	Expert Opinion, Ontario admin data
Screening, Lung cancer risk equation, Radon exposure, sexual network, HPV virus transmission	Canadian Breast Cancer Screening Database, British Columbia admin data, CCHS, Reports, Literature
Health status	Classification and Measurement System, CCHS

OncoSim Publications

General

Evans WK, Wolfson MC, Flanagan WM, et al. [Canadian Cancer Risk Management Model: Evaluation of cancer control](#). Int J Technol Assess Health Care. 2013 Apr; 29(2):131-9.

Lung cancer

Evans WK, Wolfson M, Flanagan WM, et al. [The evaluation of cancer control intervention in lung cancer using the Canadian Cancer Risk Management Model](#). Lung Cancer Manage. 2012; 1(1):25-33.

Louie AV, Rodrigues GB, Palma DA, et al. [Measuring the population impact of introducing stereotactic ablative radiotherapy for stage I non-small cell lung cancer in Canada](#). 2014 Aug; 19(8):880-5.

Fitzgerald NR, Flanagan WM, Evans WK, et al. [Eligibility for low-dose computerized tomography screening among asbestos-exposed individuals](#). Scand J Work Environ Health. 2015 Apr.

Flanagan WM, Evans WK, Fitzgerald NR, et al. [Performance of the Cancer Risk Management Model lung cancer screening module](#). Health Reports. 2015 May; 26(5).

Goffin JR, Flanagan WM, Miller AB et al. [The Cost-Effectiveness of Lung Cancer Screening in Canada](#). JAMA Oncology; 2015;1(6):807-813.

Evans WK, Flanagan WM, Miller AB, et al. [Implementing Low Dose CT Screening for Lung Cancer in Canada: Implications of Alternative At Risk Populations, Screening Frequency and Duration](#). Curr Oncol. 2016 Jun;23(3):e179-87. Epub 2016 Jun 9.

Goffin JR, Flanagan WM, Miller AB, et al. [Biennial lung cancer screening in Canada with smoking cessation—outcomes and cost-effectiveness](#). Lung Cancer. 2016 Nov; 101: 98-103.

Colorectal cancer

Coldman AJ, Phillips N, Brisson J, et al. [Using the Cancer Risk Management Model to evaluate colorectal cancer screening options for Canada](#). Curr Oncol. 2015 Apr; 22(2):e41-50.

Cervical cancer / HPV

Miller AB, Gribble S, Nadeau C et al. [Evaluation of the Natural History of cancer of the cervix, implications for prevention. The Cancer Risk Management Model \(CRMM\)- Human PapillomaVirus and Cervical components](#). Journal of Cancer Policy 4 (2015) 1–6.

Popadiuk C, Gauvreau CL, BhavsarM, et al. [Evaluating the health and economic impact of cytology versus primary HPV DNA cervical cancer screening in Canada using the Cancer Risk Management Model \(CRMM\)](#). Curr Oncol. 2016 Feb; 23(Suppl 1): S56–S63.

Lacombe J, Gauvreau CL, Memon S, Popadiuk C, Flanagan WM, Nadeau C et al. [Exploring the health outcomes of various pan-Canadian cervical cancer screening programs using microsimulation modeling](#). J. Epidemiol. 2016. 184(1): 78-80.