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A STUDY ON HRQOL OF PATIENTS WITH COLORECTAL NEOPLASM AND COST-EFFECTIVENESS ANALYSIS OF COLORECTAL CANCER SCREENING IN HONG KONG

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BACKGROUND

- Colorectal cancer (CRC) has become the commonest cancer in HK since 2011(except 2012 & 2019)
- CRC survival has extended with advances in diagnosis & treatment
- HRQOL can be affected by CRN & treatments
- CRC screening can prevent CRC & detect CRC early
- Population CRC screening was implemented in many countries, e.g. the UK, Canada & Australia before 2010
- Cost-effectiveness & optimal strategy of population screening in HK was uncertain

STUDY DESIGN – 2 PHASES

1. **HRQOL, preference & medical costs of CRN patients**
- Evaluate HRQOL & health preference of CRN survivors
- Explore factors associated with poor HRQOL
- Longitudinal change in HRQOL for adjustment in CEA modelling
- Costing study to estimate direct medical costs of CRN

2. CEA of five colorectal cancer screening strategies
- Determine the life years (LY) gained from reduction in incidence & progression of CRC by each screening strategy (literature review)
- Apply preference (SF-6D) & cost data derived from Phase 1 study
  - To determine the QALY gained by each CRC screening strategy by combining the preference value with LY
  - To identify the most cost-effective CRC screening strategy and determine the incremental cost per QALY gained by Markov modeling

PHASE I: SUBJECT CHARACTERISTICS

Sociodemographics (N=554)	
Age (Year, mean±SD)	63.3±11.3
Male	58.1%
Married	75.6%
Currently Working	24.4%
Ever Smoking	26.9%
Ever Drinking	27.4%
Household Monthly Income>HKD20,000	16.3%

Clinical Characteristics (N=554)	
Colorectal Polyp	30.2%
Colorectal Cancer	69.8%
Primary Site	
Colon	38.3%
Rectum	39.9%
Sigmoid	20.9%
Family History of CRC	18.5%
Duration of Diagnosis (Month, mean±SD)	46.7±55.8

HRQOL & PREFERENCE EVALUATION

Baseline (n=515) → 6 months (n=479) → 12 months (n=414)

- Interviewer-administration of questionnaires
  - Face-to-face or telephone
- HRQOL measures
  - SF-12V2, FACT-C, SF-6D (health preference)
- Clinical data extracted from medical records

CRN CARE COSTING STUDY (N=515)

- Estimate annual direct medical costs in the initial year of diagnosis based on the utilization of doctor consultations, diagnostic investigations, pre-treatment assessment, & treatments extracted from CMS

Diagnostic Ix/ pre-treatment assessment	Colonoscopy with/ without biopsy	Ultrasound for abdomen
	Histopathological examination	MRI contrast scan for pelvis
	Carcinoembryonic antigen test	PET scan
	CT contrast scan for abdomen & pelvis	
Treatments	Colorectal surgery	Target chemotherapy
	Hepatic resection	Radiotherapy
	Chemotherapy drugs	

- Estimate annual direct medical costs of subsequent years were estimated from the recommendations of established surveillance/clinical practice guidelines for CRN
- Unit costs of each doctor consultation, diagnostic investigations, pre-treatment assessment, & treatments were referenced from Government Gazette on HA fees and charges for non-eligible persons.

DATA ANALYSIS ON HRQOL & COSTS

- Comparison between CRN subject mean & HK normative SF-12V2 & SF-6D scores
  - Independent t-test
- Effects of stage at diagnosis, clinical & sociodemographic factors on HRQOL
  - Multivariate linear regressions
- Mean changes of HRQOL scores from baseline to 6 &12 m follow-up
  - Paired t-test
- Mean direct medical costs per person in incident year & subsequent years of CRN subjects by stage of disease

HRQOL OF CRN PATIENTS BY STAGE

N=515	Low Risk (n=85)	High Risk (n=66)	Stage I (n=80)	Stage II (n=99)	Stage III (n=109)	Stage IV (n=76)
FACT-C						
PWB	26.6±2.5	26.5±2.2	25.9±2.7	26.2±2.4	25.4±3.3	23.6±4.8
SWB	20.3±3.7	19.3±4.5	20.0±4.0	20.3±4.6	19.9±4.5	19.6±4.1
EWB	22.0±2.3	21.5±2.1	21.3±3.1	22.0±2.3	20.8±3.4	20.5±3.4
FWB	19.9±4.0	19.2±3.2	19.1±5.1	19.7±3.7	18.7±4.2	16.5±4.8
CCS	22.3±2.9	22.2±2.2	21.8±2.8	22.3±3.1	21.2±3.4	20.9±3.8
SF-12						
PCS	49.7±9.0	49.0±8.7	46.5±10.7	49.9±8.4	45.8±10.9	40.4±12.5
MCS	58.3±6.7	57.4±7.7	58.1±7.4	58.0±7.3	56.9±7.9	54.3±10.2
SF-6D	0.871±0.12	0.832±0.12	0.831±0.14	0.858±0.12	0.817±0.13	0.732±0.15

Notes: significant differences between advanced (III & IV) and early (polyps, I & II) stages of CRN

KEY FINDINGS ON HRQOL OF CRN PATIENTS

- Stage of illness is the strongest determinant of HRQOL & preference scores
- Advanced CRC was associated with significantly poorer HRQOL, lower preference, more bowel symptoms of diarrhoea, constipation, fatigue and appetite loss
- Rectal cancers were associated with worse HRQOL than colon or sigmoid cancers, because more symptoms & more likely to need a stoma

Direct Medical Costs	Unit Cost
Cost of Screening	
G-FOBT	$33[a]
FIT	$50[b]
Colonoscopy with / without biopsy plus Histopathology	$10,910[a]
Bleeding from colonoscopy Cx	$25,896[c]
Perforation from colonoscopy Cx	$84,162[c]
Cost of Initial CRN treatment [d]	
Low-risk Polyps	$15,142
High-risk Polyps	$39,435
CRC Stage I	$133,150
CRC Stage II	$154,086
CRC Stage III	$209,685
CRC Stage IV	$351,899
SOPC Follow-up	$700 [a]
CEA tests	$330 [a]

a. Government Gazette; b. Medix Biochemica, Finland
c. Tsoi & Ng et al .Alimentary Pharmacology & Therapeutics. 2008;28:353-63.
d. Wong & Lam et al. J Eval Clin Pract 2012;18:1203-10.

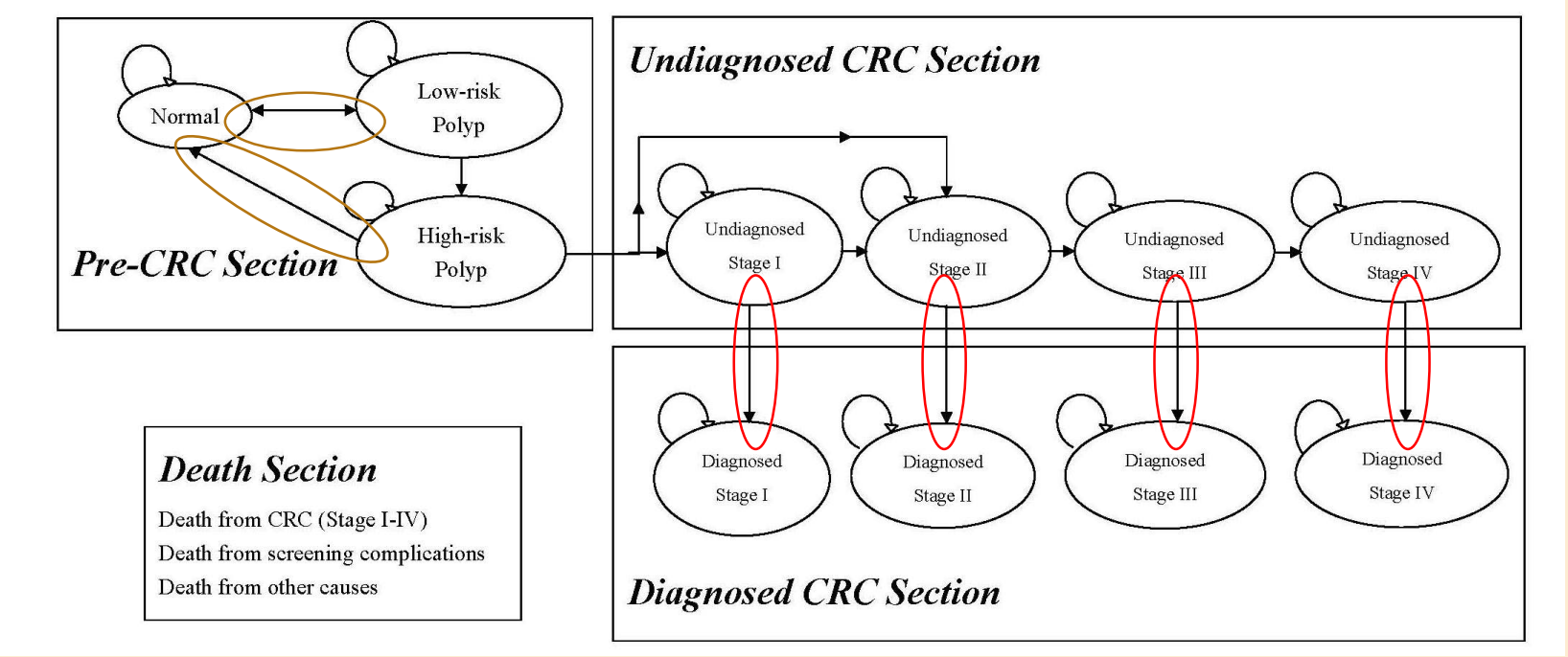
PHASE 2 – CEA OF CRC SCREENING STRATEGIES

- **5 screening strategies available in HK**
  - Annual Guaiac FOBT ---(+)--- > Colonoscopy
  - Biennial Guaiac FOBT ---(+)--- > Colonoscopy
  - Annual Faecal Immunochemical Test (FIT) ---(+)--- > Colonoscopy
  - Biennial FIT ---(+)--- > Colonoscopy
  - Colonoscopy every 10 years
- **Incremental cost-effectiveness ratio (ICER) of each of the five CRC screening strategies versus "no screening" & against each other**

COST-EFFECTIVENESS ANALYSIS

- Markov model on cohorts of 100,000 persons with normal state starting at age 50 y old per strategy
- Annual Markov cycle transitions, with a probability of progressing to CRN, until age 75 y old
- Cost of CRN treatment from healthcare provider perspective
- Outcome measures:
  - Cost per Life Year gained (LY)
  - Cost per Quality Adjusted Life Year (QALY)
  - ICER
- Costs and outcomes discounted at 3.5% annually

ANNUAL TRANSITION OF HEALTH STATES



Screening increases the probability of diagnosis of CRN

CRN States	Prevalence	Transit. Prob.	Symptomatic	Annual Mortality
Normal	69.90%	1.60%	0	
Low-risk polyp	17.62%	1.67%	0	
High-risk polyp	11.68%	3.26% (1) 1.74% (2)	0	
CRC	0.79%			
Stage I	0.08%	30%	20%	0%
Stage II	0.25%	45%	20%	1%
Stage III	0.28%	50%	65%	6%
Stage IV	0.18%		100%	38.70%

1. Transition to stage I CRC; 2. transition to stage II CRC

- Annual CRN prevalence & mortalities by stage of disease were extracted from the Hong Kong Cancer Registry in 2007 & local studies
- Transitional probabilities & Likelihood of symptomatic presentation were based on published studies in the literature

Screening Strat.	Compliance	Sens.	Specif.	Cx Rate
G-FOBT	60%	19.1%	79.6%	0
FIT	60%	62.0%	93.0%	0
Colonoscopy	60%	100%	100%	0
Perforation				0.13%
	(Death after perforation 5%)			
Bleeding				0.38%
	(Death after bleeding 1.47%)			
FU Colonoscopy	80%			

Sensitivities and specificities associated with G-FOBT and I-FOBT were based on the results of two local Hong Kong studies.
Complication rates based on published studies in the literature

COST & EFFECTIVENESS OF CRC SCREENING

Strategy (50-75 years old)	Cost (HKD) per person	Expected LYs per person	Expected QALY per person
No screening	19,816	15.64	14.75
Biennial G-FOBT	32,926	15.69	15.07
Annual G-FOBT	42,071	15.71	15.23
Colonoscopy every 10 years	37,066	15.74	15.36
Biennial FIT	35,425	15.74	15.42
Annual FIT	39,532	15.77	15.55

LY=Life-years; QALY=Quality-adjusted life-years

ICER OF CRC SCREENING STRATEGIES VS. NO SCREENING

Strategy (50-75 years old)	Incre'tal cost (HKD)	Incre'tal LYs	ICER (LYs)	Incre'tal QALYs	ICER (QALYs)
Biennial G-FOBT	13,110	0.0443	295,936	0.3207	40,879
Annual G-FOBT	22,255	0.0684	325,365	0.4860	45,792
Colonoscopy every 10 years	17,250	0.0965	178,756	0.6106	28,250
Biennial FIT	15,608	0.1009	154,688	0.6724	23,212
Annual FIT	19,716	0.1231	160,162	0.8012	24,608

•Thresholds of incremental cost per QALY gain recommended by UK guideline:GBP$20,000 (~HKD$240,000): HK 2013 annual GDP of ~HKD$260,000. .

CONCLUSIONS

- HRQOL of advanced CRN survivors are significantly impaired.
- Stage of CRN at diagnosis is the most significant determinant of HRQOL, supporting screening.
- Compared to "No screening", all screening strategies is cost-effective in terms of QALY gained.
- Biennial FIT is the most cost-effective screening strategy for HK adults aged 50-75 years.
- Annual FIT & colonoscopy every 10 y screening strategies are also cost-effective.
- G-FOBT is not recommended for CRC screening.

IMPACT ON POLICY, SERVICE & HEALTH

- **Policy**
  - Government subsidized population "CRC screening pilot programme" announced in the 2014 CE Policy Address.
- **Service**
  - Sept, 2016, Government subsidized "CRC screening pilot programme" for residents born 1946-1955 to receive biennial FIT
  - 2020 full implementation of Government subsidized CRC screening programme by biennial FIT for residents 50-75 yr old
- **Health benefit**
  - As of Nov 2021, 275,000 HK residents had FIT screening, in whom 33,900 were positive.
  - Colonoscopy of FIT positive subjects found 22,000 persons had colorectal adenomas & 2000 CRC (60% in stages II or earlier).

IMPACT ON RESEARCH

- Use of HA routine clinical medical record data for research
- Costing studies and cost-effectiveness evaluation of health services
- Seven HMRF from 2011 to 2020
  - 3 HMRF commissioned enhanced PC studies (EPC-HKU-2, EPC-HKU-1A & EPC-HKU-1B) to evaluate the QoC & CE of chronic disease management programmes of the HA, 2012-2016
  - HMRF (13142471) study on in-depth CEA of RAMP-HT, 2015-2017
  - HMRF (13142451) study on CEA of renal replacement therapy modalities for patients with ESRD, 2016-2017.
  - HMRF commissioned cohort study (CFS-HKU4) on outcomes and long-term CE of RAMP-DM, RAMP-HT & PSCC in DM & HT patients, 2019-2024.
  - HMRF (17181051) study on long-term impact of thyroidectomy on effectiveness and CE for relapsed Graves disease, 2020-2023.

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THANK YOU!

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