College of Family Physicians Singapore

National Cancer Centre Singapore
SingHealth

Role of Primary Care Physicians in Co-Management of Patients with Genetic Conditions

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Outline of presentation

- 1-Introduction
- 2-Materials and Methods
- 3-Main Findings
  - *3-1-Knowledge, Attitudes, and Practice Communication Behaviours*
  - *3-2-Facilitators & Barriers in Co-managing patients*
  - *3-3-Role of PCPs in co-management of patients with genetic conditions*
- 4-Case in point – Mrs Clara
- 5-Take home messages

1-Introduction

Primary care physicians (PCPs) are well placed to provide genomic education because they:

- care for patients from cradle to grave,
- across multiple disciplines,
- often look after more than one member of the family,
- develop a longitudinal relationship, trust
- patients look to their PCPs for medical advice

2-Materials & Methods

A narrative review of current literature (2019-2023) was conducted in Google Scholar, and PubMed using the keywords *Family Physicians, Genomics, Primary Care Physicians, Role*

Thirty-seven papers were selected and the information used in this review.

3-Main Results

- 3-1-Knowledge, Attitudes, Communication Behaviours
- 3-2-Facilitators and Barriers in Co-Managing Patients With Genetic Conditions
- 3-3-Role of FPs in Co-Management of Patients With Genetic Conditions

3-1: Knowledge, Attitudes, Communication Behaviours

❖ 4 Step-Model for Bridging Primary Care to Specialty Care

Qualitative Study on PCP in Ontario
10 in-depth interviews and 3 focus group (n=19)

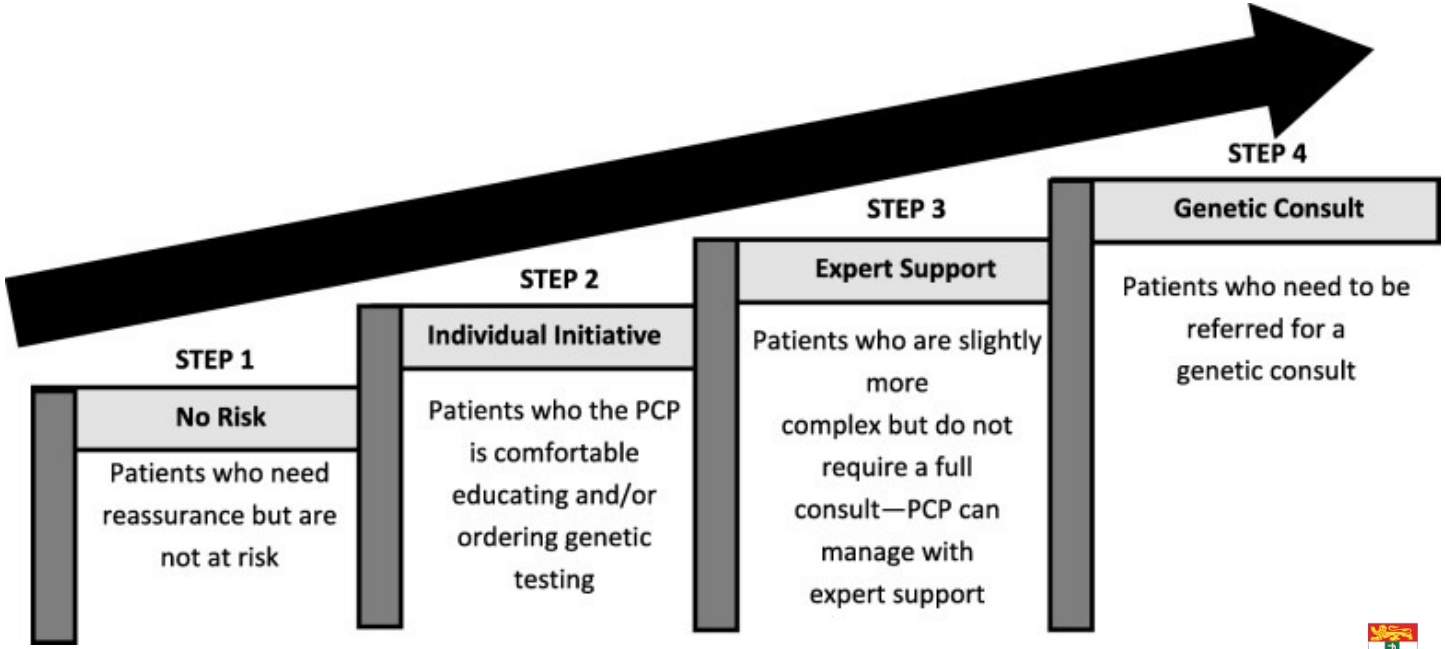
Findings:

✓ PCP have a **responsibility** to ensure their patients receive genetic care
✓ Need to **integrate** genetics into primary care practice

- Specific roles and responsibilities were poorly defined
- Recommended for **further education and resources** to enable them to provide care for individuals with genetic conditions

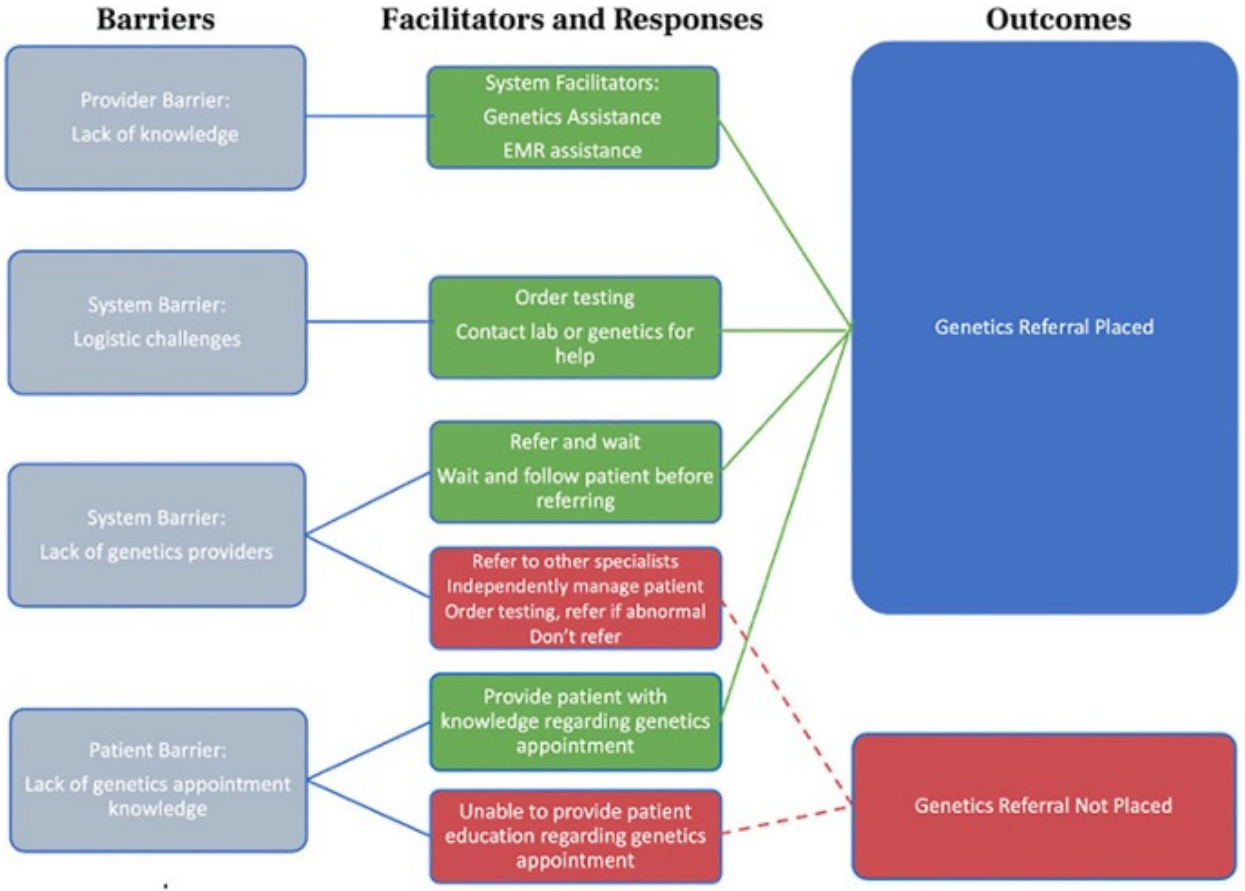
3-1: Knowledge, Attitudes, Communication Behaviours

- 4 Step-Model for Bridging Primary Care to Specialty Care



Harding, B., Webber, C., Rühland, L. *et al.* Bridging the gap in genetics: a progressive model for primary to specialist care. *BMC Med Educ* **19**, 195 (2019).

3-2: BARRIERS & FACILITATORS IN USE OF GENETIC SERVICES



Siebel E et al., JPC &CH 2021

3-3-Role of FPs in Co-Management of Patients with Genetic Conditions – 6 Tasks

- (1) Screening & Early Detection
- (2) Risk Assessment & Timely Referral
- (3) Safe Prescribing
- (4) Preventive Care
- (5) Care of Comorbidities & Continuity of Care
- (6) Managing Secondary Genomic Findings

4- Case in point

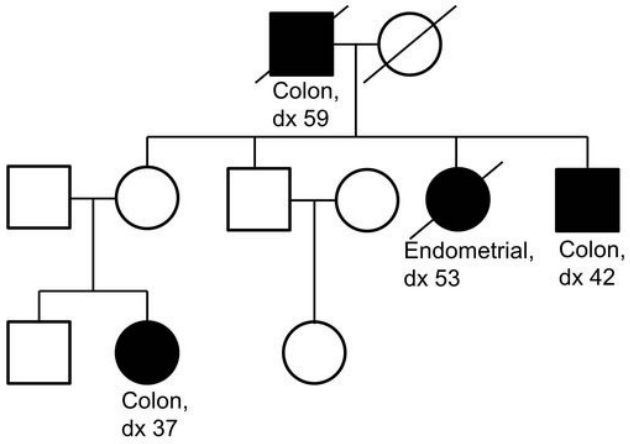
- Mrs Clara, 37 years' old, consults you her regular PCP for per rectal bleeding and loss of weight 2 kg

- Maternal aunt has endometrial cancer
- Maternal uncle has colorectal cancer
- Maternal grandpa passed away of colon cancer

Impression: ? Colorectal cancer

(i) Screening & Early detection: assess risk for hereditary cancer?

Lynch Syndrome Pedigree



1st degree relative: a person's parent, sibling or child.

Age of onset of cancer < 60 years old

*Screening: Colonoscopy not FIT

2019 Academy of Medicine, Singapore. Report of Screening Review Committee, Pg 14

History & Examination

Medical History:

- Hyperlipidaemia
- Diabetes Mellitus

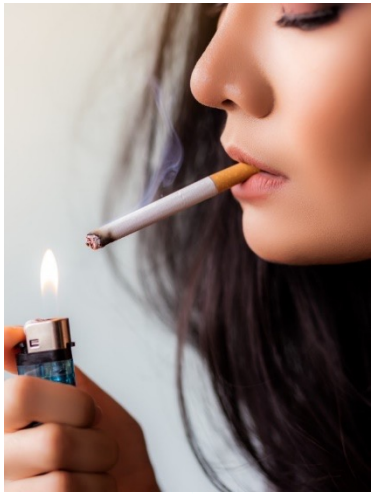
Medications:

- PO simvastatin 20 mg OD
- PO metformin 500 mg TDS

Social history:

- sedentary lifestyle
- Obese BMI = 31 kg/m^2)
- fast foods
- no regular exercise
- smokes 20 cigarettes/day, social drinker
- missed vaccinations

Diet



(ii) Risk assessment & timely referral (1)

- Demographic: young age
- Symptom: unintentional weight loss + bleeding PR
- Context: significant family history
- Predisposition: early referral warranted
- Safe netting: ED if active symptoms, unstable vitals
- Preferred modality of assessment: colonoscopy (biopsy for histology)

(ii) Risk assessment & timely referral (2)

- Colonoscopy: piles, no cancer
- Family history: suspicion for Lynch Syndrome
- Refer cancer genetic service at NCCS
- Positive for Lynch Syndrome → Risk Management & high risk surveillance clinic

LYNCH SYNDROME: LIFETIME CANCER RISK

	Cancer	Lynch syndrome	Population (Aus data)
Women	CRC	31%	6.6%
	Endometrial	33%	2-3%
	Ovarian	9%	1-2%
Men	CRC	38%	10%
Both	Gastric	6%	1%**
	Urothelial	<3%	1%
	Small bowel	<3%	0.01%

Male & Female: CRC, Gastric & urothelial cancers:
3 – 5 times higher risk

** Population risk of gastric cancer higher in Singapore for certain ethnicities (e.g. Chinese, Korean, Japanese, Chilean)

Sources: Dowty et al. Cancer risks for *MLH1* and *MSH2* mutation carriers. Hum Mutat 2013;34(3):490-497
Bonadona, et al. Cancer risks associated with germline mutations in *MLH1*, *MSH2*, and *MSH6* genes in Lynch syndrome. JAMA 2011;305(22):2304-2310.
Baglietto, et al. Risks of Lynch syndrome cancers for *MSH6* mutation carriers. J Natl Cancer Inst 2010;102(3):192-201.
Senter, et al. The clinical phenotype of Lynch syndrome due to germline *PMS2* mutations. Gastroenterology 2008;135(2):419-428.

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Female: Endometrial & Ovarian cancers: 5 - 10 times higher risk

Sources: Dowty et al. Cancer risks for *MLH1* and *MSH2* mutation carriers. Hum Mutat 2013;34(3):490-497
Bonadona, et al. Cancer risks associated with germline mutations in *MLH1*, *MSH2*, and *MSH6* genes in Lynch syndrome. JAMA 2011;305(22):2304-2310.
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LYNCH SYNDROME: RISK MANAGEMENT

Cancer	Recommendations	
Colorectal	Surveillance	Annual colonoscopy from age 25 Review frequency at age 60
	Risk-reducing medication	Consider aspirin (dose not yet defined)
Endometrial/ovarian	Surveillance	Annual TVU/endometrial sampling is an option (limited evidence)
	Surgical	Consider risk-reducing hysterectomy and bilateral salpingo-oophorectomy around age 40-45
Gastric/small bowel	Surveillance	2-3 yearly upper GI endoscopy from age 30-35 Test/treat H.pylori
Urothelial	Surveillance	Consider annual urinalysis from age 30-35 (limited evidence)

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Source: NCCN Guidelines v2.2016 (USA guidelines) and EviQ (Australian guidelines)

(iii) Safe prescribing

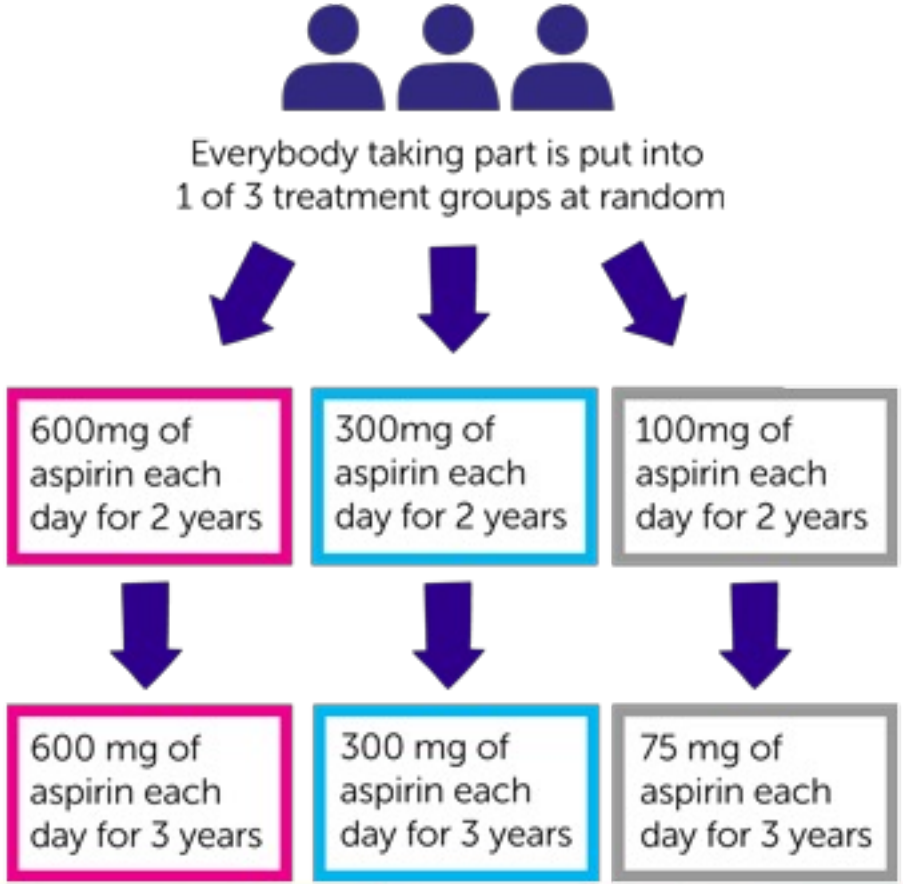
"Aspirin reduces risk of Lynch-associated colorectal cancer by greater than 50% and may reduce risk of other Lynch-associated cancers."

- Prescribed by specialists
- PCPs' role to ensure medication adherence and watch for adverse effects

Source: Yurgelun MB, Hampel H. Recent Advances in Lynch Syndrome: Diagnosis, Treatment, and Cancer Prevention. American Society of Clinical Oncology Educational Book-208341. 2018

Burn, J., Sheth, H., CAPP2 Investigators (2020). Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial. *Lancet (London, England)*, *395*(10240), 1855–1863.

Trials looking at different doses of aspirin to prevent cancer in people who have Lynch syndrome (CaPP3)



Optimal dosage & duration currently being evaluated

(iv,va) Preventive care & Care of comorbidities

- Risk factors of Colorectal cancer

Modifiable	Non modifiable
Diet	Family history
Obesity	Race
Exercise	Genetic pathogenic variants eg Lynch Syndrome
Comorbidities: Diabetes Mellitus	

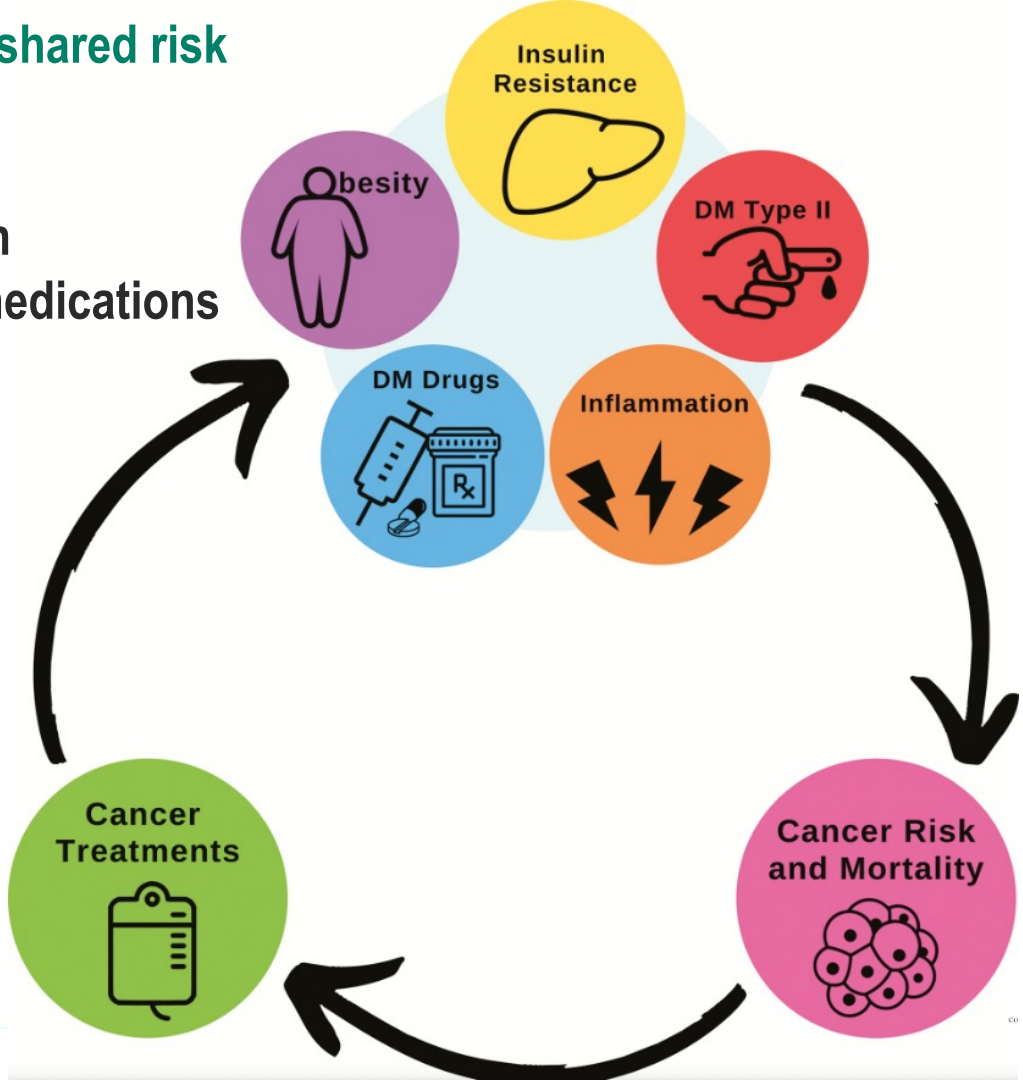
Diabetes, Obesity and Cancer

- Obesity and diabetes have both been associated with an increased risk of cancer

- The strongest and most robust associations are for:
  - ✓ postmenopausal breast cancer
  - ✓ endometrial cancer
  - ✓ colorectal cancer

Potential mechanisms/ shared risk factors

- Hyperinsulinemia
- chronic inflammation
- antihyperglycemic medications



Diabetes

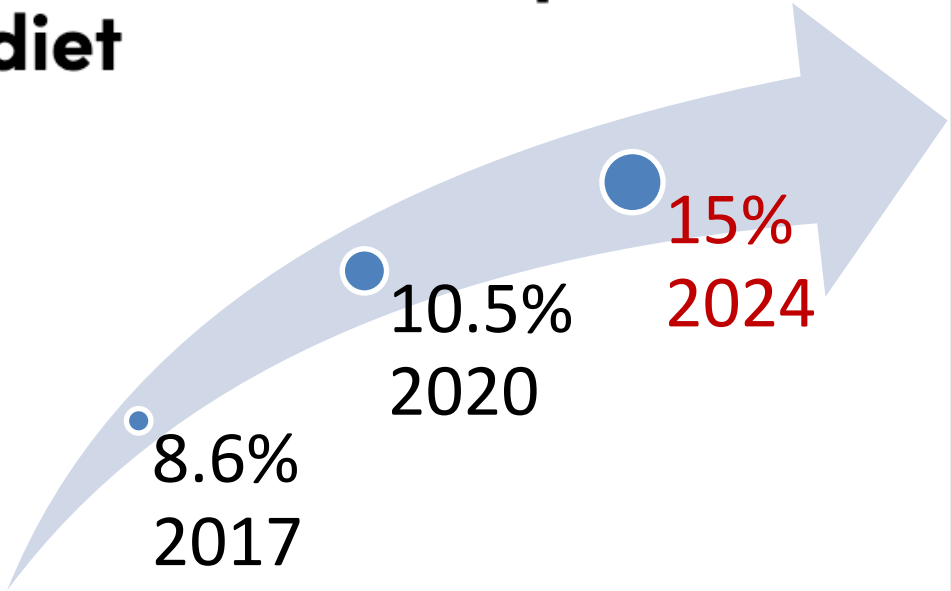
Cancers

Endocr Rev, Volume 41, Issue 1, Feb 2020, Pages 33–52, https://doi.org/10.1210/endrev/bnz014

Obesity rate rises to highest level since 2010; MOH urges public to exercise and adopt healthier diet

Rising obesity

BMI >= 30 kg/m2



https://www.channelnewsasia.com/singapore/obesity-rate-rises-highest-level-2010-moh-urges-public-exercise-and-adopt-healthier-diet-2322321

Ministry of Health, Singapore. *National Population Health Survey 2019/20*

(v-b) Continuity of care

- Ensure regular follow up and surveillance
- Early detection
- Genetic testing for family members
- Access to resources and referrals

Psychooncology. 2018 Mar;27(3):998-1004. doi: 10.1002/pon.4627. Epub 2018 Jan 24.

Factors influencing the decision to share cancer genetic results among family members: An in-depth interview study of women in an Asian setting

Shao-Tzu Li [1], Shirley Sun [2], Désirée Lie [3], Marie Met-Domestici [1], Eliza Courtney [1], Sapna Menon [1], Geok Hoon Lim [4], Joanne Ngeow [1 5 6]

3 facilitator themes

1.Close relationship of **family bond**

2.Perception of **Acceptance** from family members:

- Ability to understand, emotional maturity, correct timing
- Emotional impact – fear, anxiety, worries

3.Medical **implications**:

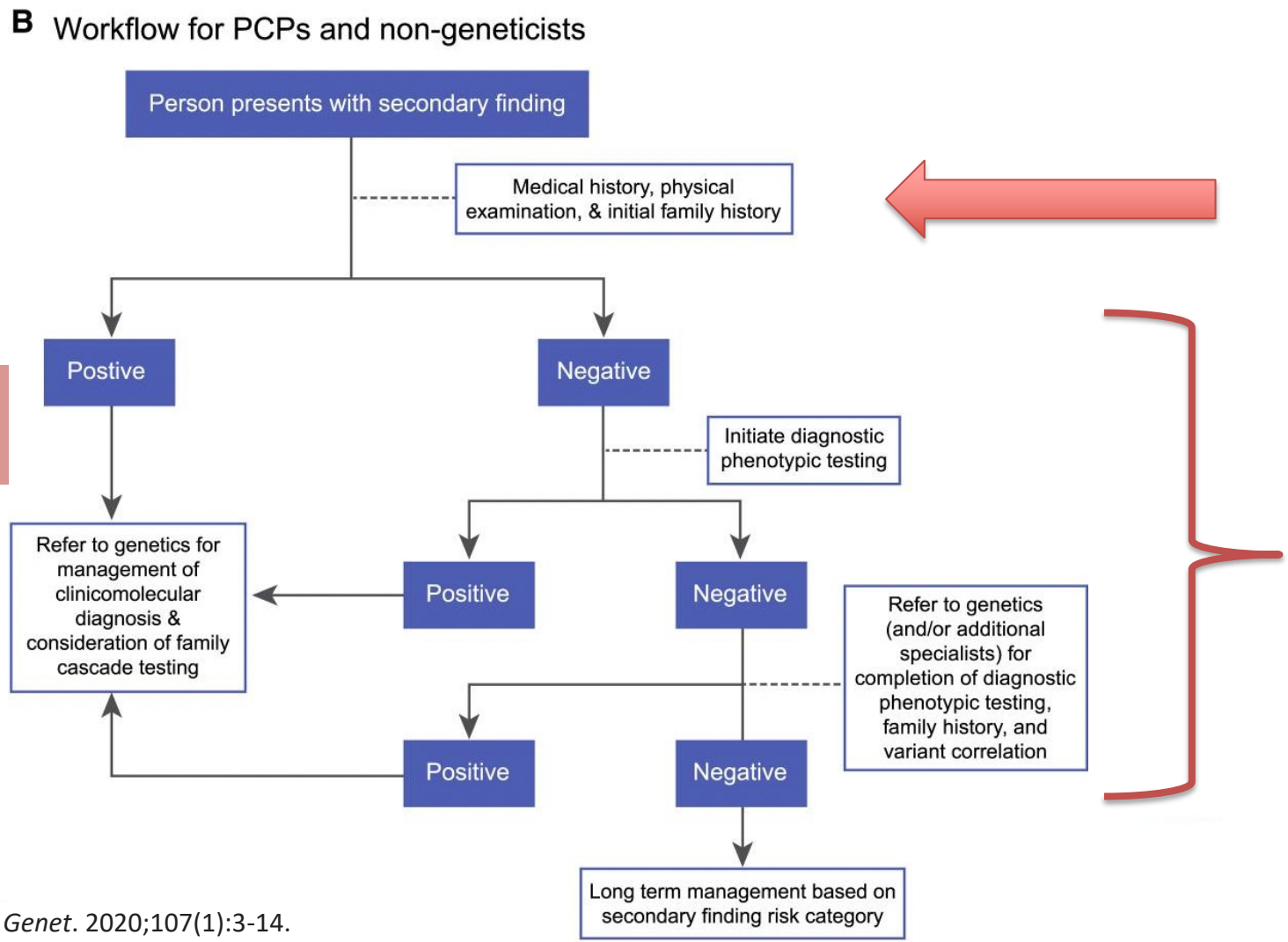
- Actionable intervention – surveillance, lifestyle modification

(vi) Managing secondary genomic findings

- Definition:
- *A secondary finding is defined as a genomic variant of potential medical value that is unrelated to the primary reason for testing*
- likely pathogenic variants
- 1%–4% of individuals

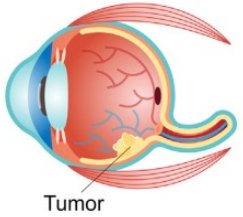
- e.g. A haematocrit or haemoglobin result below the reference range is not equivalent to a clinical diagnosis of anaemia, but rather a data point that can be used and contextualized to help make a clinical diagnosis

If in doubt, refer Genetics



Katz AE, et al. *Am J Hum Genet*. 2020;107(1):3-14.

Case: likely pathogenic secondary finding in RB1, a gene associated with retinoblastoma



40 yo with RB1 likely PV → History: No eye disease or cancer → Exam: unremarkable, VA normal → Genetic Testing: variant in his father → Refer Eye: NAD → Plan: co-manage with Eye

Back to the Case: Mrs. Clara

Medical History:

- Hyperlipidaemia
- Diabetes Mellitus

Optimize comorbidities & Cardiovascular Risk Factors

Medications:

- PO simvastatin 20 mg OD
- PO metformin 500 mg TDS

Social history:

- sedentary lifestyle
- Obese BMI = 31 kg/m^2)
- fast foods
- no regular exercise
- smokes 20 cigarettes/day, social drinker
- missed vaccinations

Increase physical activity

Healthy diet, weight

Stop smoking

Vaccinations

5-Take Home points:

PCPs play an essential role in clinical genomics:

- improving access
- co-managing patients with GHPs
- support patient & family in complex decisions

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