CONTRALATERAL PROPHYLACTIC MASTECTOMY

WHO IS IT FOR???

PAUL WILLEMSE

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INTRODUCTION

BREAST CANCER → MOST FREQUENTLY DIAGNOSED CANCER IN WOMEN

- ✓ AVERAGE LIFETIME RISK = 12.2%

WHAT IS CPM? → REMOVAL OF THE UNAFFECTED BREAST AT THE TIME OF THERAPEUTIC MASTECTOMY FOR UNILATERAL CANCER

THE PRIMARY OBJECTIVE OF CPM IS RISK REDUCTION OF CBC

IN THE LAST DECADE THERE HAS BEEN A SUBSTANTIAL INCREASE IN THE NUMBER OF AVERAGE RISK WOMEN WITH EARLY-STAGE BC UNDERGOING THERAPEUTIC MASTECTOMY +CPM

- ✓ RATE OF CPM INCREASES BY 1%/YEAR IN NORTH AMERICA
  - 1.8%(1998) → 12.7% (2012)
- ✓ ESPECIALLY IN YOUNGER WOMEN WITH LOW-RISK DISEASE
- ✓ PREDOMINANTLY PATIENT DRIVEN
  - PATIENT MISPERCEPTIONS ABOUT RECURRENCE AND SURVIVAL
  - DESIRE TO REDUCE CBC
  - PEACE OF MIND

FACTS!!!!!

- NO SURVIVAL BENEFIT WITH CPM EXCEPT BRCA1/2 (SEE LATER)
- CBC RISK AT 10 YEARS FOR AVERAGE RISK WOMEN = 3-5%
- AFTER UNILATERAL SPORADIC BC, THE RISK FOR DEVELOPING CBC VARIES
  - ✓ TUMOR BIOLOGY
  - ✓ AGE AT DIAGNOSIS OF FIRST CANCER
  - ✓ FAMILY HISTORY
- RATES OF CBC ARE DECREASING DUE TO ADJUVANT ENDOCRINE THERAPY
- BENEFIT OF CPM:
  1. 95% RISK REDUCTION IN CBC
  2. BREAST SYMMETRY
- CONCERNS OF CPM
  1. DOUBLES THE RISK OF POSTOPERATIVE INFECTION/BLEEDING
  2. COULD POSSIBLY RESULT IN CHRONIC PAIN/BODY IMAGE ISSUES
- CYTOTOXIC CHEMOTHERAPY REDUCES THE RISK OF CBC BY 30%
- CPM DOES NOT PREVENT LOCAL/DISTANT RECURRENCE OF INDEX CANCERS

RATIONALES THE PATIENT MAY HAVE

1. WILL CPM REDUCE MORTALITY RISK?
2. WILL CPM REDUCE THE RISK OF CBC?
3. CAN I AVOID FURTHER SCREENING AFTER CPM?
4. WILL I HAVE BETTER BREAST SYMMETRY AFTER CPM?

WILL CPM REDUCE MORTALITY RISK? WHAT IS THE SURVIVAL BENEFIT?

CBC TENDS TO PRESENT AT A MORE FAVORABLE STAGE VS PRIMARY BREAST CANCER

- ✓ EARLIER STAGE
- ✓ SMALLER TUMOR
- ✓ MORE NODE NEGATIVE DISEASE

IN ORDER TO HAVE A SURVIVAL BENEFIT FROM CPM, PATIENTS WOULD NEED TO SURVIVE THEIR INDEX CANCER AND THEN DEVELOP AND SUCCUMB TO CBC

- ✓ MULTIPLE RETROSPECTIVE STUDIES
- ✓ CONTRADICTORY RESULTS
- ✓ SOME STUDIES DID SUGGEST A SURVIVAL BENEFIT, BUT THE MAGNITUDE OF SURVIVAL BENEFIT WAS GREATER THAN THE INCIDENCE OF CBC IN THE CONTROL GROUP → REVEALING THAT THEY CHOSE HEALTHIER, LOWER RISK WOMEN FOR THE PROCEDURES

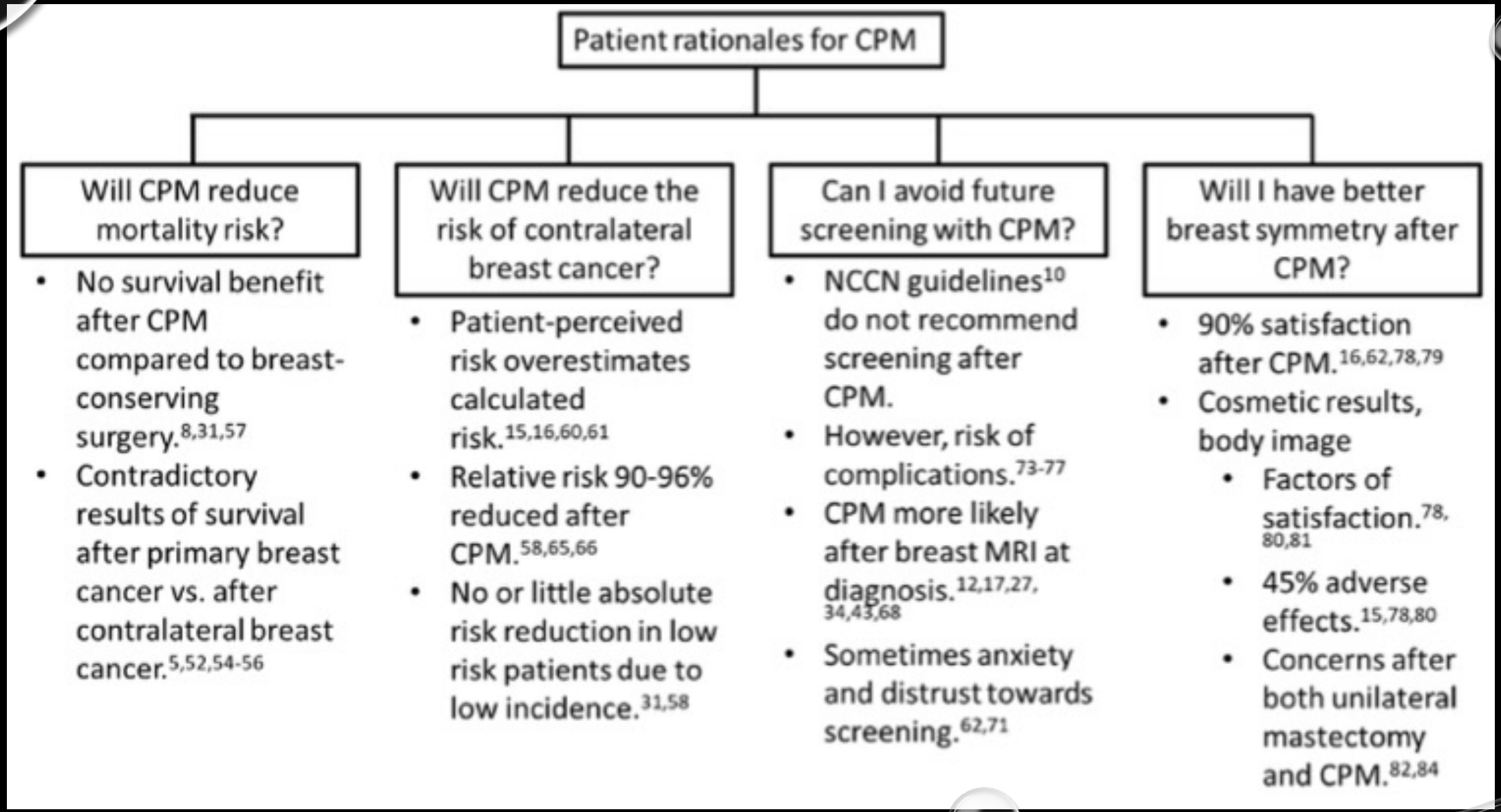
EXAMPLE

BEDROSIAN ET AL

- 4.8% ABSOLUTE REDUCTION IN BC MORTALITY WITH CPM IN WOMEN AGED 19-49 WITH STAGE1/2 ER NEGATIVE CANCER
- THE INCIDENCE OF CBC IN THE CONTROL GROUP WAS 0.9%!!!!!!

PROMPTED PORTSCHY ET AL TO DEVELOP A MARKOV MODEL TO ELIMINATE POTENTIAL SELECTION BIAS

- WOMEN WITH STAGE I/II SPORADIC BREAST CANCER
- ***ABSOLUTE 20-YEAR SURVIVAL BENEFIT FORM CPM = <1%***
- ALL AGES
- ER STATUS
- CANCER STAGES


Patient rationales for CPM
Will CPM reduce mortality risk?
• No survival benefit after CPM compared to breast-conserving surgery.[8,31,57]
• Contradictory results of survival after primary breast cancer vs. after contralateral breast cancer.[5,52,54-56]
Will CPM reduce the risk of contralateral breast cancer?
• Patient-perceived risk overestimates calculated risk.[15,16,60,61]
• Relative risk 90-96% reduced after CPM.[58,65,66]
• No or little absolute risk reduction in low risk patients due to low incidence.[31,58]
Can I avoid future screening with CPM?
• NCCN guidelines[10] do not recommend screening after CPM.
• However, risk of complications.[73-77]
• CPM more likely after breast MRI at diagnosis.[12,17,27,34,43,68]
• Sometimes anxiety and distrust towards screening.[62,71]
Will I have better breast symmetry after CPM?
• 90% satisfaction after CPM.[16,62,78,79]
• Cosmetic results, body image
• Factors of satisfaction.[78,80,81]
• 45% adverse effects.[15,78,80]
• Concerns after both unilateral mastectomy and CPM.[82,84]

FACTORS INFLUENCING CBC RISK

1. GERMLINE MUTATIONS/GENETICS
2. HISTORY OF CHEST WALL IRRADIATION
3. AGE
4. FAMILY HISTORY
5. TUMOR
6. PATIENT FACTORS
7. THOUGHTS ON MALE BREAST CANCER

SOME FACTS ON CBC RISK IN GENERAL

CUMULATIVE INCIDENCE OF CBC	
Annual Risk	0.4%/year
5 years	1.9%
10 years	4.6%
20 years	10.5%

- CBC IS 1.3-1.9 TIMES HIGHER THAN PRIMARY CANCER IN THE GENERAL POPULATION
- RISK OF DISTANT METASTASIS AT 5 YEARS = 10-12%
  - ✓ EXCEEDS THE RISK OF DEVELOPING CBC

BRCA1/2

	NON-Carriers	BRCA1	BRCA2
Annual	0.4%	2-3%	2-3%
5-year	1.9%	13%	8%
10-year	5.1%	21.1%	10.8%

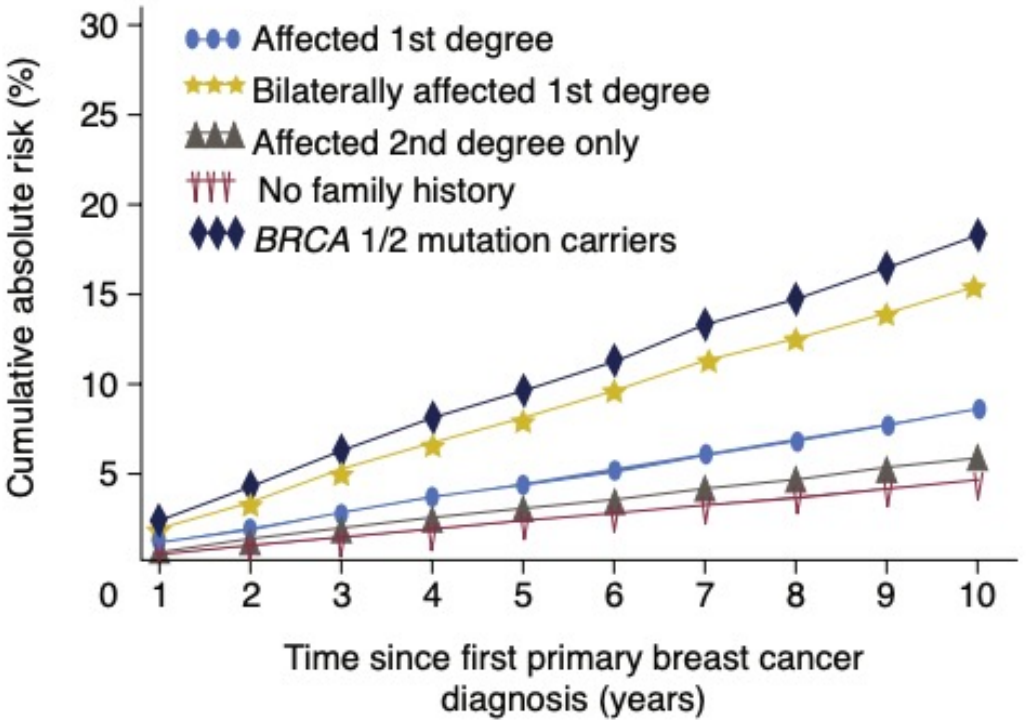
STRONGEST PREDICTOR OF CBC

- NON-CARRIER LIFETIME RISK OF CBC = 6.8%
- RISK INCREASES WITH YOUNGER AGE

RETROSPECTIVE STUDY → GRAESER ET AL

- 25 YEAR CUMULATIVE RISK FOR CBC FOR BRCA1 CARRIERS WITH 1ST BREAST CANCER DIAGNOSIS:

- <40 → 62.9%
- 40-50 → 43.7%
- >50 → 19.6%



OTHER GENETICS

TYPE	RISK
TP53	Li Fraumeni syndrome No studies estimating CBC risk
CHECK 2	Meta analysis by *Akdeniz et al*… • Increased CBC risk • Associated with bilateral BC • 2-6-fold increased risk for Bilateral breast cancer
PTEN	Cowden syndrome No studies estimating CBC risk
CDH1	No studies
PALB2	No studies

HISTORY OF CHEST WALL IRRADIATION

- HODGKIN'S LYMPHOMA AS ADOLESCENTS
- MANTLE FIELD RADIATION
- 25-30% RISK OF DEVELOPING BREAST CANCER BEFORE AGE 50
- BILATERAL BREAST CANCER IS COMMON IN THESE WOMEN
  - ✓ 50% PRESENT WITH SYNCHRONOUS BREAST CANCER
  - ✓ 20% PRESENT WITH METACHRONOUS BREAST CANCER AT 5 YEARS

FAMILY HISTORY/AGE

FAMILY HISTORY

VERY STRONG FAMILY HISTORY = 2/MORE 1ST DEGREE RELATIVES WITH BREAST/OVARIAN CANCER → VERY HIGH RISK FOR CBC

WECARE STUDY → WOMEN'S ENVIRONMENTAL CANCER RADIATION EPIDEMIOLOGY

- STRONG RELATIONSHIP BETWEEN FAMILY HISTORY OF BREAST CANCER AND THE RISK OF CBC
- 1ST DEGREE RELATIVE → DOUBLES THE RISK FOR CBC

AGE

WECARE → INCREASED RISK OF CBC WITH EARLIER DIAGNOSIS

- GENERALLY <45

TUMOR/PATIENT FACTORS

TUMOR

- HIGHER GRADE OF PRIMARY TUMOR
- SIZE OF PRIMARY TUMOR
- ER/PR NEGATIVE BC
- LOBULAR HISTOLOGY

PATIENT

- HIGHER BREAST DENSITY
- HIGH BMI

THOUGHTS ON MALE BREAST CANCER

- RARE IN GENERAL POPULATION
- BRCA2 – LIFETIME RISK = 5-10%
- BRCA 1 – 1-5%
- OF THOSE MEN ONLY 2-4% DEVELOP CONTRALATERAL BREAST CANCER
- CPM NOT RECOMMENDED

Table 2 Summary of risk factors for CBC and levels of evidence [8]

Family history—<45 years with a first-degree relative (RR 2.5)—<55 years with first degree relative (RR 1.5)—first degree relative with bilateral disease (RR 3.5)Level II evidence (Reiner AS JCO—2013) [18]
Gene mutation status—*BRCA1/2* mutation (RR4) Level II evidence (Metcalfe 2004 JCO; Evans 2013) [4, 25]
Chest radiotherapy for Hodgkin's lymphoma—rate of CBC unknown
Young age at diagnosis—<30 years 0.5–1.3 % annual CBC rateLevel II evidence (Nichols, Lacey JCO 2011) [2]
ER status—ER positive (reference point RR 1)—ER negative (RR 1.3) Level II evidence [26]
Anti-endocrine treatment (risk reduction), tamoxifen 50 % Aromatase inhibitor 70 % Level I evidence [27, 28]
DCIS—0.6 % annual CBC risk of DCIS and/or invasive carcinoma(RR 1.0)Level I evidence [21]
Lobular histology combined with family history (RR2.0)
Oophorectomy under 40 years (risk reduction) (RR0.5)
Early menopause <45 year (risk-reduction)—published as abstract [29]

HOW TO PREDICT RISK?

- **CBC RISK PREDICTION MODELS**

1. MANCHESTER FORMULA
2. CBCRISK
3. PREDICT CBC

MANCHESTER FORMULA:

1. 80 – PATIENT AGE = NR OF YEARS OF CBC RISK
2. NR OF YEARS OF CBC RISK X 0.5 = LIFETIME CBC RISK
3. MODIFY THE RISK BASED ON PATIENT'S PERSONAL RISK PROFILE
   - ER+ AND ON ENDOCRINE THERAPY – MULTIPLY BY 0.5% (50% RISK REDUCTION)
   - GENE CARRIERS – MULTIPLY BY 4 (2% ANNUAL INCIDENCE)
   - OOPHORECTOMY UNDER 40 YEARS – MULTIPLY BY 0.5 (50% RISK REDUCTION)
   - FAMILY HISTORY – MULTIPLY BY 2 (UNPUBLISHED DATA

Low risk
<10 % remaining life-time risk of CBC
Above average risk
10–20 % remaining life-time risk of CBC
Moderate risk
20–30 % remaining life-time risk of CBC
High risk
>30 % remaining life-time risk of CBC

SURGICAL OPTIONS/AXILLA

SURGICAL OPTIONS:

1. SIMPLE MASTECTOMY
2. SKIN SPARING
3. NIPPLE SPARING
4. RECONSTRUCTION

AXILLA:

- **NAGARAJA ET AL**

- OCCULT INVASIVE DISEASE IN THE CONTRALATERAL BREAST – 1.8%
- SLN + = 1.2%
- SLNB NOT RECOMMENDED

GUIDELINES

TABLE I Consensus Guidelines

	ASBrS	NCCN
CPM Discouraged	1. Average-risk women with unilateral breast cancer 2. Women with advanced index cancer (e.g., inflammatory breast cancer, T4 or N3 disease, stage IV disease) 3. Women at high risk for surgical complications (e.g., patients with comorbidities: obesity, smoker, diabetes) 4. Woman tested *BRCA* negative with a family of *BRCA+* carriers 5. Male breast cancer, including *BRCA* carriers	
CPM Considered	1. Deleterious mutations of *BRCA1/2* 2. Greater than 25 % lifetime risk (Gail Model) of breast cancer primarily due to family history in the absence of deleterious mutations 3. History of mantle radiation (typically for Hodgkin lymphoma) before age 30 4. Gene carrier of non-*BRCA* gene (e.g., *CHEK-2, PALB2, p53, CDH1*).	Women with a known *BRCA1/2* pathogenic or likely pathogenic variant, typically between 35 and 40 years of age

ASBrS, American Society of Breast Surgeons; *NCCN*, National Comprehensive Cancer Network.

EUROPEAN MANCHESTER GUIDELINES

STATES → IT IS NOT POSSIBLE TO BE PRESCRIPTIVE IN TERMS OF WHO SHOULD BE ALLOWED OR REFUSED CONTRALATERAL RISK REDUCING MASTECTOMY

THEY DESCRIBE A 5-STEP PROCESS:

1. TAKING A HISTORY AND DETERMINE THE PATIENT'S REASON FOR CBC 1ST
2. CALCULATE THE RISK
3. COOL OFF – PATIENT SHOULD NOT MAKE A DECISION UNTIL THE PRIMARY CANCER TREATMENT HAS BEEN COMPLETED
4. MDT MEETING WITH BREAST CARE NURSE/SURGEON/ONCOLOGIST/PATHOLOGIST AND RADIOLOGIST TO DISCUSS THE PATIENTS CPM REQUEST
5. PATIENT SIGNS CONSENT TO CONFIRM HER DECISION