

**9TH AARHUS WORKSHOP IN BREAST SURGERY  
MAY 20TH 2021**

**ONCOPLASTIC BREAST CONSERVING SURGERY:  
RECOMMENDATIONS DEVELOPED WITH THE GRADE METHOD**

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**THE POTENTIAL ADVANTAGES OF ONCOPLASTIC BCS  
HAVE NOT BEEN VALIDATED IN ROBUST STUDIES  
THAT CONSTITUTE HIGH LEVELS OF EVIDENCE,  
DESPITE ONCOPLASTIC TECHNIQUES BEING WIDELY ADOPTED AROUND THE GLOBE**

**BY WE FELT THE NEED TO DEFINE THE PRECISE ROLE OF OPBCS IN THE TREATMENT OF EARLY BREAST  
WITH THE PRODUCTION OF RECOMMENDATIONS FOR CLINICAL PRACTICE**



**WE CONVENED A PANEL OF WORLD-RENOWNED BREAST SPECIALISTS TO  
EVALUATE EVIDENCE, EXPRESS PERSONAL VIEWPOINTS AND ESTABLISH RECOMMENDATIONS  
USE OF OPBCS VS. STANDARD BCS AS PRIMARY TREATMENT OF UNIFOCAL EARLY STAGE BREAST CA  
USING THE GRADE APPROACH**

Name	Specialty	Country
Werner Audretsch	Breast Oncoplastic Surgeon	Germany
John Benson	Breast Oncoplastic Surgeon	UK
Giuseppe Catanuto	Breast Oncoplastic Surgeon	Italy
Carmen Criscitiello	Medical Oncologist	Italy
Rosa Di Micco	Breast Oncoplastic Surgeon	Italy
Margarita Gjeloshi	Breast Nurse	Italy
Tibor Kovacs	Breast Oncoplastic Surgeon	Hungary/UK/China
Steven Kronowitz	Plastic Surgeon	USA
Henry Kuerer	Breast Oncoplastic Surgeon	USA
Laura Lozza	Radiation Oncologist	Italy
Giacomo Montagna	Breast Oncoplastic Surgeon	Switzerland/USA
Nahid Nafissi	Breast Oncoplastic Surgeon	Iran
Maurizio Bruno Nava	Breast Oncoplastic Surgeon	Italy
Rachel O'Connel	Breast Oncoplastic Surgeon	UK
Serena Oliveri	Psycho-oncologist	Italy
Loredana Pau	Patient Advocacy	Italy
Giancarlo Pruneri	Pathologist	Italy
Nicola Rocco	Breast Oncoplastic Surgeon	Italy
Gianfranco Scaperrotta	Breast Radiologist	Italy
Achilles Thoma	Plastic Surgeon	Canada
Zoe Winters	Breast Oncoplastic Surgeon	UK



## RATING QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

# GRADE: going from evidence to recommendations

The GRADE system classifies recommendations made in guidelines as either strong or weak. This article explores the meaning of these descriptions and their implications for patients, clinicians, and policy makers

BMJ | 10 MAY 2008 | VOLUME 336



**“CRITICAL OUTCOMES”  
FOR DECISION-MAKING IN ONCOPLASTIC BCS  
(PRIORITIZED AS FOLLOWS):**

**QUALITY OF LIFE  
PATIENT’S SATISFACTION WITH AESTHETIC OUTCOME  
LOCO-REGIONAL RECURRENCE  
RE-EXCISION RATE (FOR POSITIVE MARGINS)  
CONVERSION TO MASTECTOMY (FOR POSITIVE MARGINS)  
OVERALL SURVIVAL  
MARGIN POSITIVITY RATE  
DISEASE-FREE SURVIVAL  
SURGICAL COMPLICATIONS**

**GRADE**



## CERTAINTY OF EVIDENCE

FOR EACH SELECTED OUTCOME,  
AN EVALUATION OF THE CERTAINTY OF EVIDENCE  
WAS PERFORMED BASED ON THE GRADE APPROACH

LITERATURE WAS EXPLORED ACCORDING TO FIVE MAIN DOMAINS:  
STUDY LIMITATIONS, IMPRECISION, INDIRECTNESS, INCONSISTENCY AND PUBLICATION BIAS  
WITH A FINAL JUDGMENT ON THE CERTAINTY OF EVIDENCE  
(HIGH, MODERATE, LOW AND VERY LOW)

BASED ON THE STUDY DESIGN,  
THE CERTAINTY LEVEL STARTS AT A PRE-SPECIFIED LEVEL  
(HIGH CERTAINTY FOR RCTs)  
THE DETECTION OF LIMITATIONS IN ONE OR MORE OF THE FIVE DOMAINS  
CAN LEAD TO DOWNGRADING THE CERTAINTY OF THE EVIDENCE

**GRADE**



**ACCORDING TO THE GRADE METHOD, WE USED AN  
EVIDENCE TO DECISION (EtD) FRAMEWORK  
PROVIDING A TRANSPARENT AND STRUCTURED APPROACH TO SUPPORT DECISION-MAKING**

**IT ALLOWS EVIDENCE TO BE SUMMARISED IN RELATION TO  
PRIORITIZATION OF THE PROBLEM,  
EFFECTS OF THE INTERVENTION,  
BALANCE OF THE EFFECTS,  
CERTAINTY OF EVIDENCE,  
PATIENTS VALUES AND PREFERENCE,  
USE OF RESOURCES, EQUITY, ACCEPTABILITY AND FEASIBILITY**

**GRADE**



**DURING THE FACE-TO-FACE MEETING HELD IN MILAN IN DECEMBER 2019  
(MBN 2019 ONCOPLASTIC BREAST MEETING),  
THE PANELISTS WERE ASKED TO EXPRESS THEIR OPINION  
ON EACH OF THE EtD DOMAINS**

**GRADE**





## **INCLUDED STUDIES**

**THE ANALYSIS INCLUDED  
STUDIES COMPARING OPBCS (LEVEL I AND LEVEL II TECHNIQUES) VS SBCS  
FOR THE TREATMENT OF INVASIVE BREAST CANCER AND DCIS  
CONDUCTED IN THE US, UK, EUROPE, SOUTH AMERICA, CHINA, INDIA, CANADA, ISRAEL AND IRAN  
WITH INVOLVEMENT OF 193,833 PATIENTS  
AND A MEAN OF 6683 WOMEN PER TRIAL**

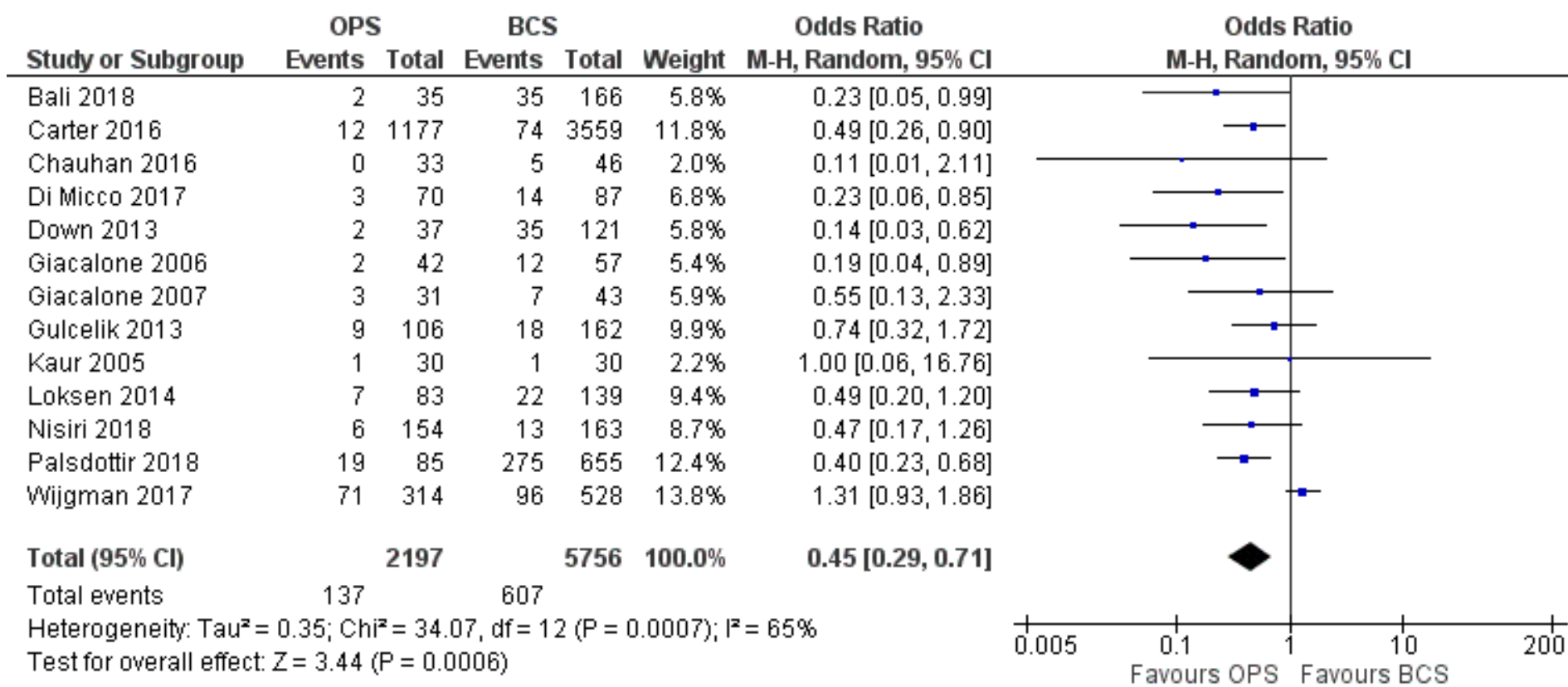
**STUDY DESIGN INCLUDED PROSPECTIVE COHORTS, CASE-CONTROL STUDIES,  
CROSS-SECTIONAL STUDIES AND DATABASE ANALYSES**



## EFFECTS OF INTERVENTIONS

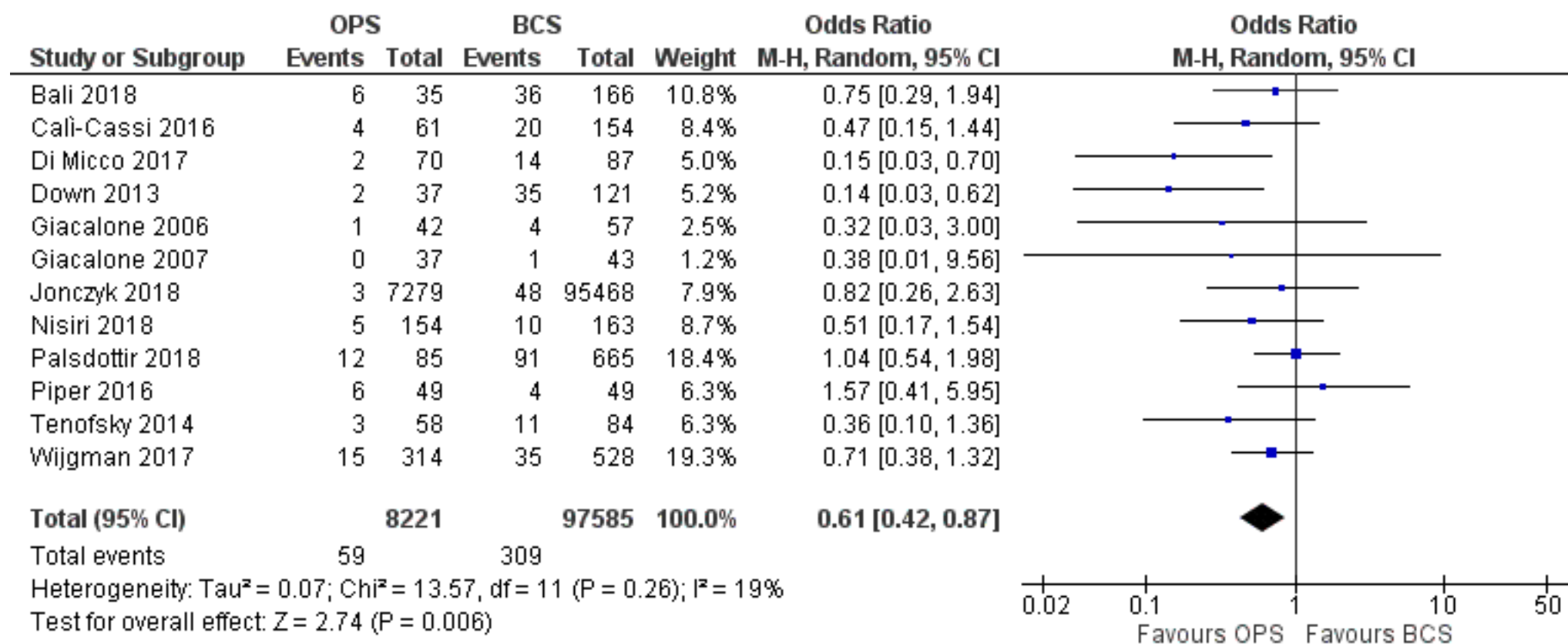


## MARGIN POSITIVITY



CERTAINTY OF EVIDENCE : LOW

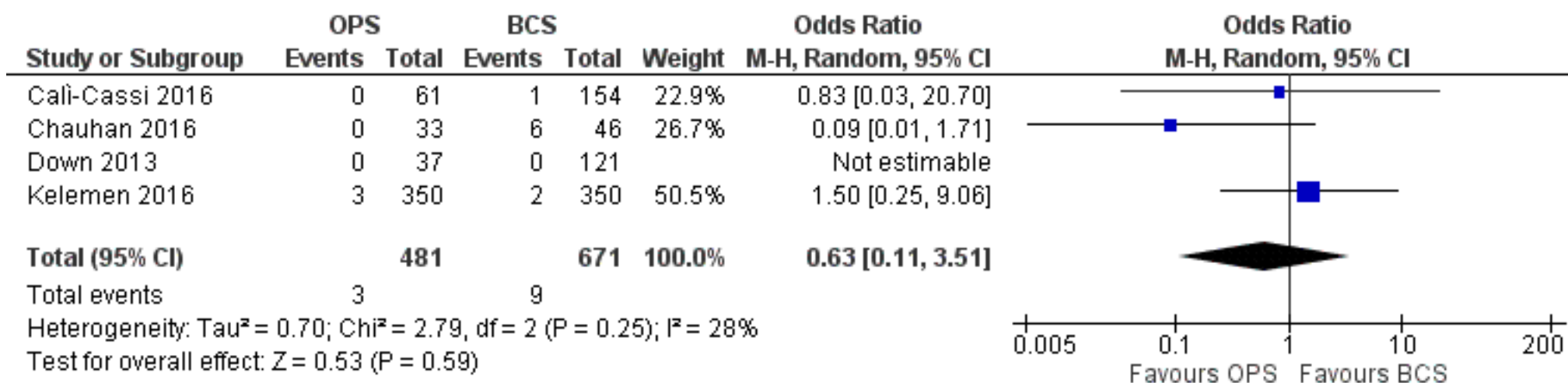
## RE-EXCISION OF POSITIVE MARGINS



CERTAINTY OF EVIDENCE : VERY LOW

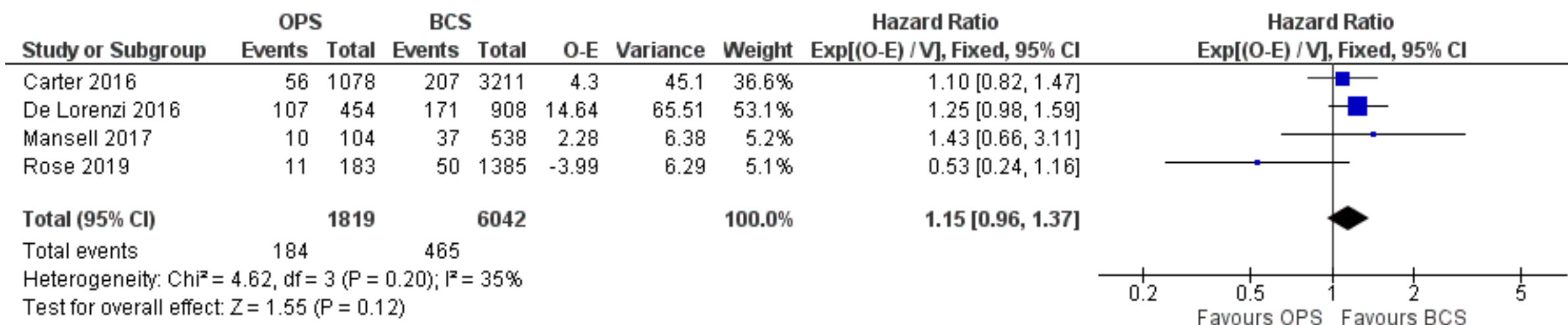


## LOCO-REGIONAL RECURRENCE



CERTAINTY OF EVIDENCE : VERY LOW

## DISEASE-FREE SURVIVAL

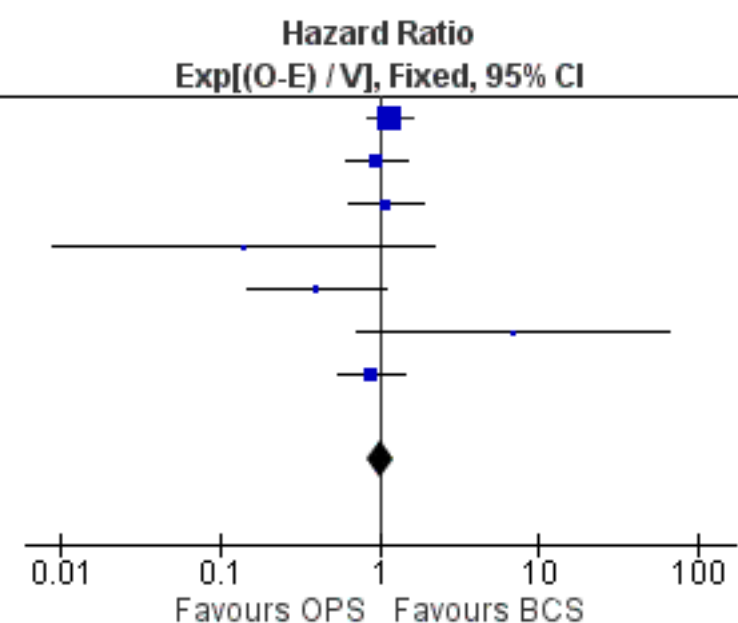


CERTAINTY OF EVIDENCE : VERY LOW



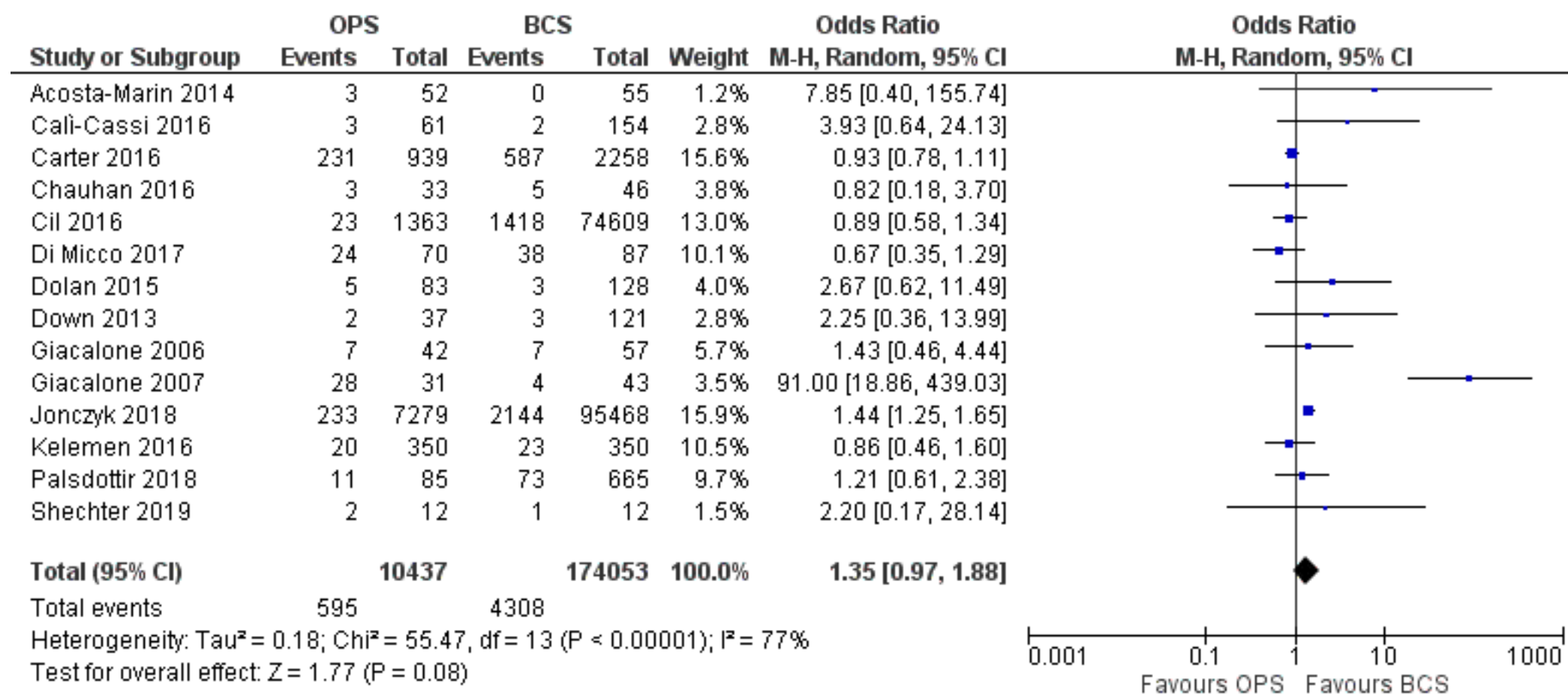
## OVERALL SURVIVAL

Study or Subgroup	OPS		BCS		O-E	Variance	Weight	Hazard Ratio	
	Events	Total	Events	Total				Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI
Carter 2016	48	1079	182	3213	5.6	37.74	41.1%	1.16 [0.84, 1.60]	
De Lorenzi 2016	30	454	60	908	-0.79	19.27	21.0%	0.96 [0.61, 1.50]	
Gulcelik 2013	24	106	34	162	1.32	13.87	15.1%	1.10 [0.65, 1.86]	
Kelemen 2016	0	350	2	350	-0.98	0.5	0.5%	0.14 [0.01, 2.25]	
Mansell 2017	2	104	26	538	-3.48	3.8	4.1%	0.40 [0.15, 1.09]	
Piper 2016	3	49	0	49	1.46	0.75	0.8%	7.01 [0.73, 67.35]	
Rose 2019	16	197	130	1399	-1.84	15.8	17.2%	0.89 [0.54, 1.46]	
<b>Total (95% CI)</b>		<b>2339</b>		<b>6619</b>			<b>100.0%</b>	<b>1.01 [0.83, 1.24]</b>	
Total events	123		434						
Heterogeneity: Chi <sup>2</sup> = 9.13, df = 6 (P = 0.17); I <sup>2</sup> = 34%									
Test for overall effect: Z = 0.13 (P = 0.89)									



CERTAINTY OF EVIDENCE : VERY LOW

## SURGICAL COMPLICATIONS



CERTAINTY OF EVIDENCE : VERY LOW





## QUALITY OF LIFE

**SURPRISINGLY ONLY FEW STUDIES COMPARING OPBCS AND STANDARD BCS ASSESSED QoL AND PATIENT'S SATISFACTION WITH THE AESTHETIC OUTCOME, EVEN THOUGH THE POSITIVE EFFECTS ON PROMs ARE AMONG THE STRONGEST SUPPOSED ADVANTAGES OF OPBCS COMPARED TO STANDARD BCS**

**ONLY 3 RCTs COMPARING OPBCS AND SBCS REPORTING DATA ON QoL ARE AVAILABLE IN LITERATURE, ALL DESIGNED AS C**

**HIGH HETEROGENEITY IN THE REPORTING OF QoL DID NOT ALLOW META-ANALYSES OF DATA**

**NO SIGNIFICANT DIFFERENCES IN TERMS OF QoL WERE REPORTED IN THE THREE INCLUDED STUDIES BETWEEN OPBCS AND SBCS**

**PATIENT'S SATISFACTION WITH AESTHETIC OUTCOME**

**7 STUDIES COMPARING OPBCS WITH SBCS REPORTING DATA ABOUT PATIENTS' SATISFACTION WITH THE AESTHETIC OUTCOME ARE AVAILABLE IN LITERATURE, ALL DESIGNED AS OBSERVATIONAL STUDIES**

**HIGH HETEROGENEITY IN THE REPORTING OF PATIENTS' SATISFACTION DID NOT ALLOW META-ANALYSES OF DATA**

**ONE STUDY REPORTED SIGNIFICANT WORSE OUTCOMES IN THE OPBCS GROUP**

**ALL THE OTHER STUDIES DID NOT FIND SIGNIFICANT DIFFERENCES IN TERMS OF PATIENTS' SATISFACTION WITH THE AESTHETIC OUTCOME BETWEEN OPBCS AND SBCS**

## BALANCE OF THE EFFECTS

**EVEN THOUGH THE EVIDENCE ABOUT  
THE EFFECTS OF OPBCS COMPARED TO SBCS IS VERY UNCERTAIN,  
THE SUPPOSED ADVANTAGES OF OPBCS IN TERMS OF  
IMPROVED QOL AND SATISFACTION WITH AESTHETIC OUTCOMES  
BALANCED WITH NO HIGHER RATES OF COMPLICATIONS  
BROUGHT THE PANELISTS  
TO CONSIDER THE INTERVENTION MORE FAVORABLE THAN SBCS**



## **CERTAINTY OF EVIDENCE**

**THE OVERALL CERTAINTY OF EVIDENCE WAS JUDGED AS VERY LOW  
DUE TO RISK OF BIAS, IMPRECISION OF ESTIMATES AND PUBLICATION BIAS**



## **PATIENTS' VALUES AND PREFERENCES**

**IT IS UNKNOWN WHAT VALUE PATIENTS CAN GIVE TO EACH CONSIDERED OUTCOME  
BECAUSE NO TOOLS ARE AVAILABLE TO INVESTIGATE PATIENTS' VALUES  
AND NONE OF THE INCLUDED STUDIES INVESTIGATED PATIENTS' VALUES AND PREFERENCES**

**WITHOUT ANY DATA, THE MAJORITY OF THE PANEL CONCLUDED THAT THERE IS LIKELY SIGNIFICANT UNCERTAINTY  
IN HOW PATIENTS COULD VALUE THE MAIN OUTCOMES**



## PATIENTS' VALUES AND PREFERENCES

**THE LACK OF ASSESSMENT IN THIS FIELD MAY REFLECT AN  
THAT SURGICAL INTERVENTIONS DESIGNED TO MAXIMIZE COSMETIC OUTCOMES MUST NECESSARILY IM**

**MORE STANDARDISED TOOLS FOR PATIENTS' PREFERENCE ASSESSMENT  
WITH CLINICAL UTILITY ARE URGENTLY REQUIRED  
AS THE IDENTIFICATION OF PATIENTS PREFERENCES IN TERMS OF OUTCOMES  
ARE A REAL-WORLD PRIORITY**



## **RESOURCES REQUIRED**

**PROCEDURES MAY REQUIRE LONGER OPERATIVE TIMES AND HIGHER RELATED COSTS IN TERMS OF OPERATING**

**NO PARTICULAR TOOLS ARE REQUIRED FOR OPBCS PROCEDURES**



## **COST EFFECTIVENESS**

**ONLY ONE STUDY ON THERAPEUTIC MAMMAPLASTIES  
WAS AVAILABLE IN LITERATURE FOR COMPLETE ECONOMIC EVALUATION**

**THE COST-UTILITY ANALYSIS PERFORMED IN THE USA  
UNDERLINED THE RELEVANCE ATTRIBUTED TO IMPROVED QOL  
WITH THE USE OF OPBCS**

**UTILITY VALUES WERE OBTAINED INDIRECTLY  
BASED ON THE OPINION OF SURGICAL EXPERTS  
(UNCERTAINTIES REMAIN THAT THEIR OPINION  
FULLY REFLECTS THAT OF THEIR PATIENTS)**





## **COST EFFECTIVENESS**

**ESTIMATES OF THE INCIDENCE OF COMPLICATIONS, POSITIVE MARGIN RATE, RE-EXCISION AND CONVERSION TO MASTECTOMY WERE OBTAINED FROM LITERATURE REVIEWS**

**THE ECONOMIC ANALYSIS WAS DONE ACCORDING TO THE PERSPECTIVE OF THIRD PARTY PAYMENT AND CONSIDERING THE DIRECT HEALTH COSTS (RELATED TO 2014 FOR THE USA)**



## COST EFFECTIVENESS

**THE COMPLETE ECONOMIC EVALUATION INDICATED  
AN OVERALL COST-EFFECTIVENESS  
OF THERAPEUTIC MAMMAPLASTIES VS. STANDARD LUMPECTOMIES**

**IT IS DOUBTFUL WHETHER THE COST ESTIMATES  
EVALUATED IN THESE ANALYSES  
CAN BE TRANSLATED INTO OTHER COUNTRIES CONTEXTS  
AND EXTRAPOLATED FOR OTHER TYPES OF OPBCS  
(DIFFERENT FROM THERAPEUTIC MAMMAPLASTIES)**

Chatterjee A, Offodile AC II, Asban A, Minasian RA, Losken A, Graham R, Chen L, Czerniecki BJ, Fisher C.  
**A Cost-Utility Analysis Comparing Oncoplastic Breast Surgery to Standard Lumpectomy in Large Breasted Women.**  
Advances in Breast Cancer Research 2018; 7 (2)



## **EQUITY**

**MORE EXTENSIVE SURGERY MAY INCREASE COSTS  
FOR NATIONAL HEALTHCARE SYSTEMS**

**HOWEVER INTRODUCTION OF ONCOPLASTIC TECHNIQUES (ESPECIALLY LEVEL 1)  
IS NOT EXPECTED TO GENERATE SIGNIFICANT DISPARITIES  
AND DOES NOT INVOLVE COMPLEX TECHNOLOGIES  
NOR DEMAND EXCEPTIONAL LEVELS OF SURGICAL SKILL AND TRAINING**

**IN SOME HEALTHCARE SYSTEMS,  
WELL TRAINED ONCOPLASTIC SURGEONS ARE CONFINED TO TERTIARY CARE HOSPITALS AND  
MORE PERIPHERAL BREAST UNITS MAY NOT HAVE ACCESS TO A FULL REPERTOIRE  
OF ONCOPLASTIC BREAST SURGERY**



# ACCEPTABILITY

**ONLY THREE STUDIES CONTAINED INFORMATION RELATING TO THE IMPACT OF  
ACCEPTABILITY OF OPBCS TO STAKEHOLDERS**

**THE AMERICAN SOCIETY OF BREAST SURGEONS  
FOUND A STRONG MOTIVATION AMONGST SURGEONS  
FOR PROVIDING ONCOPLASTIC SURGERY**

**SIMILAR ENTHUSIASM FROM SURGICAL GROUPS HAS BEEN NOTED  
IN OTHER NATIONAL REPORTS  
(UK ASSOCIATION OF BREAST SURGERY, DANISH BREAST CANCER GROUP)  
BUT SURGEONS ARE NOT THE ONLY STAKEHOLDERS INVOLVED IN THIS CONTEXT**

**NO INFORMATION IS AVAILABLE FROM NURSING REPRESENTATIVES,  
PATIENT ADVOCACY GROUPS OR MANAGERIAL HOSPITAL STAFF**



# FEASIBILITY

PROCEDURES ARE NOT ESPECIALLY CHALLENGING OPERATIONS AND THE NECESSARY SKILLS CAN BE A

NO CONCLUSIVE INFORMATION WAS AVAILABLE  
ON THE FEASIBILITY DOMAIN OF GRADE

SINGLE STUDIES REVEALED  
OBSTACLES TO THE IMPLEMENTATION OF ONCOPLASTIC SURGICAL SERVICES  
DUE TO THE POOR TRAINING OF JUNIOR DOCTORS IN THIS FIELD



## **FEASIBILITY**

**THE MAJORITY OF PANEL MEMBERS FELT THAT THIS INTERVENTION  
COULD BE RELATIVELY EASILY IMPLEMENTED**

**DEDICATED TRAINING PROGRAMMES  
INCORPORATING BASIC KNOWLEDGE AND PRINCIPLES OF ONCOPLASTIC SURGERY  
SHOULD BE ESTABLISHED BY POSTGRADUATE MEDICAL EDUCATION SYSTEMS  
UNDER THE AEGIS OF PROFESSIONAL ASSOCIATIONS ALLIED TO BREAST CANCER MANAGEMENT**



## LIMITATIONS OF THE STUDY

ALTHOUGH ALL MEMBERS OF THE PANEL CONSIDERED OPBCS TO BE A RESEARCH PRIORITY,  
SOME BREAST CANCER SPECIALISTS ARE SKEPTICAL AS TO WHETHER  
THIS NEEDS FORMAL EVIDENCE-BASED VALIDATION,  
AS IT COULD BE VIEWED AS SIMPLY A VARIANT FORM OF BCS  
THAT HAS ALREADY BEEN VALIDATED IN RCTs

OTHER LIMITATIONS RELATE TO A PAUCITY OF HIGH QUALITY PUBLICATIONS  
THAT EITHER FAIL TO ADDRESS KEY OUTCOMES OR INCLUDE POORLY DESIGNED STUDIES  
WITH MUCH HETEROGENEITY  
OR SUB-STANDARD METHODOLOGY FOR ASSESSMENT OF OUTCOMES



## LIMITATIONS OF THE STUDY

**THE PANEL PRIORITIZED OUTCOMES  
IN THE PRELIMINARY PHASE OF THE GRADE PROCESS  
AND IDENTIFIED QoL AND PATIENT-REPORTED AESTHETIC OUTCOME  
AS THE TWO MOST RELEVANT OUTCOMES FOR OPBCS,  
ALTHOUGH IRONICALLY THESE OUTCOMES WERE EXCLUDED  
FROM MOST STUDIES COMPARING ONCOPLASTIC VS. STANDARD BCS**

**ONLY THREE STUDIES ASSESSED QoL  
WITH ONE OF THESE USING STANDARD MEASUREMENT TOOLS  
INAPPROPRIATELY BY NOT APPLYING ALL THE DOMAINS**

**AMONGST THE STUDIES ASSESSING PATIENT-REPORTED AESTHETIC OUTCOME,  
ONLY HALF USED STANDARDIZED TOOLS**





## LIMITATIONS OF THE STUDY

**WITHOUT USE OF STANDARDISED TOOLS WITH MUCH VARIATION IN DEFINITION AND ASSESSMENT OF CURRENTLY AVAILABLE TOOLS FOR ASSESSMENT OF COMPLICATIONS SHOULD BE REFINED AND ADAPTED**

**DATA AVAILABLE IN LITERATURE DID NOT ALLOW ANY SUBGROUP ANALYSIS FOR LEVEL I VS. LEVEL II ONCOPLASTIC PROCEDURES**



# RESEARCH PRIORITIES

**THE GENERATION OF ROBUST EVIDENCE IS CHALLENGING FOR SURGERY AND LIMITED BY STANDARDIZATION OF TECHNIQUES AND TAILORED APPROACHES TO TREATMENT**

**PARAMOUNT AMONGST THE KNOWLEDGE GAPS IN BREAST CANCER RESEARCH AND TREATMENT IS THE NEED TO CAREFULLY EVALUATE THE EFFECTIVENESS OF OPBCS WHICH COULD REPRESENT AN ESCALATION OF SURGICAL COMPLEXITY**

**THERE ARE AREAS OF CONTROVERSY TO BE RESOLVED, ESPECIALLY RELATING TO COMPLICATIONS, COST-EFFECTIVENESS AND PATIENT REPORTED OUTCOMES**



# CONCLUSIONS

**OUR REVIEW HAS REVEALED A  
LOW LEVEL OF EVIDENCE FOR MOST OF THE IMPORTANT OUTCOMES IN ONCOPLASTIC BCS  
WITH LACK OF ANY RANDOMIZED DATA  
AND ABSENCE OF STANDARD TOOLS FOR EVALUATION OF CLINICAL OUTCOMES  
AND ESPECIALLY PATIENT'S VALUES**

**DESPITE AREAS OF CONTROVERSY,  
T ONE THIRD (36%) OF PANEL MEMBERS EXPRESSED A STRONG RECOMMENDATION IN SUPPORT OF O**

**PRESUMABLY, THIS REFLECTS A SYNTHESIS OF VIEWS ON  
THE RELATIVE COMPLEXITY OF THESE TECHNIQUES,  
ASSOCIATED COMPLICATIONS, IMPACT ON QUALITY OF LIFE AND COSTS**



SHOULD BE INFORMED OF THE FOLLOWING RECOMMENDATION BEFORE CONSENTING TO UNDERGO ANY BREAST SURGERY

**ONCOPLASTIC BCS SHOULD BE RECOMMENDED VERSUS STANDARD BCS  
FOR THE TREATMENT OF OPERABLE BREAST CANCER  
IN ADULT WOMEN WHO ARE SUITABLE CANDIDATES  
FOR BREAST CONSERVING SURGERY  
(WITH VERY LOW CERTAINTY OF EVIDENCE)**

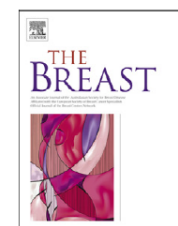
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journal homepage: [www.elsevier.com/brst](http://www.elsevier.com/brst)



Should oncoplastic breast conserving surgery be used for the treatment of early stage breast cancer? Using the GRADE approach for development of clinical recommendations



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G.RE.T.A.







## Group for Reconstructive and Therapeutic Advancements



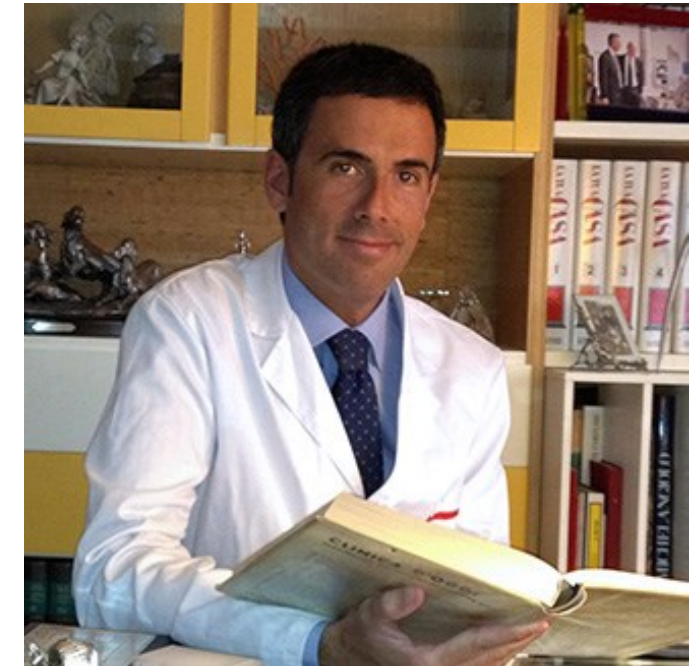
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