VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013

Auditorium Antonianum, Viale Manzoni 1

LA PERSONALIZZAZIONE DELLO SCREENING

Marcello Anti

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

Published in final edited form as:
Per Med. 2013 July 1; 10(5): 453–462.

Personalized medicine: challenges and opportunities for translational bioinformatics

Casey Lynnette Overby[*,1] and **Peter Tarczy-Hornoch**[2,3,4]

[1]Program in Personalized & Genomic Medicine and Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA

[2]Department of Biomedical Informatics & Medical Education, University of Washington, Seattle, WA, USA

[3]Department of Pediatrics, University of Washington, Seattle, WA, USA

[4]Department of Computer Science & Engineering, University of Washington, Seattle, WA, USA

MEDICINA GENOMICA

… «The use of information from genomes (from humans and other organisms) and their derivatives (RNA, proteins and metabolites) to guide medical decision-making»…

DEFINIZIONE ATTUALE

… «Model of healthcare that is predictive, personalized, preventive and partecipatory («P 4 Medicine»)»…

… This model applies technologies to customize and deliver care and in practice provides a venue for adopting genomics applications»…

….e

… “can include many nongenomic personalized screening and diagnostic approaches»…

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

Personalized Medicine in Screening for Malignant Disease: A Review of Methods and Applications

F. Schmalfuss[1] and P.L. Kolominsky-Rabas[2]

[1]Institute of Pathology, Technische Universität München, Trogerstr, Munich, Germany. [2]Interdisciplinary Center for Health Technology Assessment (HTA) and Public Health, Friedrich-Alexander-Universität Erlangen-Nuremberg, Erlangen, Germany. Corresponding author email: f.schmalfuss@tum.de

Biomarker Insights 2013:8 9–14

APPROCCIO «PAZIENTE-SPECIFICO»

APPROCCIO «TARGETED» E «TAILORED»

BASSO/ALTO RISCHIO ⇨ RISCHIO INDIVIDUALIZZATO

INCREMENTO DELLA «EARLY DETECTION» E RIDUZIONE DEL «MISSED LESION RATE»

SUPPLEMENTAZIONE E OTTIMIZZAZIONE DELLE PROCEDURE STANDARDIZZATE

- **Adattamento del programma di screening al rischio individuale**
- **Aumento della sensibilità dei programmi convenzionali**
- **Incremento della qualità e dell' efficienza**

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

BIOMARCATORI: APPROCCIO POLIGENICO ALLA PREVENZIONE

A blood-based biomarker panel for stratifying current risk for colorectal cancer

Kenneth Wayne Marshall[1], Steve Mohr[1], Faysal El Khettabi[1], Nadejda Nossova[1], Samuel Chao[1], Weisheng Bao[1], Jun Ma[1], Xiao-jun Li[2] and Choong-Chin Liew[1,2]

Int. J. Cancer: 126, 1177–1186 (2010)

Table 2. Colorectal cancer (CRC) biomarker gene list and differential expression in the training set (112 CRC and 120 controls)

Gene symbol[5]	Gene name	Sequence accession ID	Fold change[1]	Fold change *p* value[2]	Expression ratio[3]	Expression ratio *p* value[2]	Expression ratio AUC[4]
ANXA3	Annexin A3	NM_005139	1.67	<0.001	1.71	<0.001	0.71
CLEC4D	C-type lectin domain family 4, member D	NM_080387	1.39	0.002	1.50	<0.001	0.66
IL2RB	Interleukin 2 receptor, beta	NM_000878	0.84	0.01	–	–	–
LMNB1	Lamin B1	NM_005573	1.31	<0.001	1.37	<0.001	0.68
PRRG4	Proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)	NM_024081	1.58	<0.001	1.72	<0.001	0.76
TNFAIP6	Tumor necrosis factor, alpha-induced protein 6	NM_007115	1.50	<0.001	1.58	<0.001	0.66
VNN1	Vanin 1	NM_004666	1.48	<0.001	1.53	<0.001	0.67

[1]Determined by qRT-PCR analysis using ACTB (reference) gene as denominator. [2]Calculated by Mann–Whitney test. [3]Determined by qRT-PCR analysis using IL2RB (underexpressed) gene as denominator. [4]Area under receiver-operating-characteristic curve. [5]Biomarker candidates were screened by microarray (5 μg of total blood RNA extracted from blood collected into EDTA tubes was hybridized to U133Plus2.0 GeneChip, Affymetrix).

A Plasma MicroRNA Panel for Detection of Colorectal Adenomas: A Step Toward More Precise Screening for Colorectal Cancer

Kanaan Z et al; *Ann Surg 2013; 258(3): 400-8*

…Un panel di 8 miRNAs discrimina i portatori di adenomi vs controlli con elevata accuratezza….

IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

PROGRAMMI DI PREVENZIONE "ORIENTATI":PERSONALIZZAZIONE DELL' OFFERTA

PREFERENZE DEL PAZIENTE

VALUTAZIONE DELL' ATTITUDINE

COINVOLGIMENTO NEL PROCESSO DECISIONALE

SCELTA DELLE OPZIONI

"SHARED DECISION-MAKING" VS "INFORMED"

CONSAPEVOLEZZA DEL LIVELLO DI RISCHIO

Vernon SW, Bartholomew LK, McQueen A, et al. A randomized controlled trial of a tailored interactive computer-delivered intervention to promote colorectal cancer screening: sometimes more is just the same. Ann Behav Med 2011;41(3):284–99.

Menon U, Belue R, Wabab S, et al. A randomized trial comparing the effect of two phone-based interventions on colorectal cancer screening adherence. Ann Behav Med 2011;42(3):294–303.

Sequist TD, Zaslavsky AM, Colditz GA, Ayanian JZ. Electronic patient messages to promote colorectal cancer screening: a randomized controlled trial. Arch Intern Med 2011;171(7):636–41.

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013

Auditorium Antonianum, Viale Manzoni 1

"TARGETED AND TAILORED INTERVENTIONS": TRIALS RANDOMIZZATI

Ronald E. Myers, PhD

A Randomized Controlled Trial of the Impact of Targeted and Tailored Interventions on Colorectal Cancer Screening

Cancer 2007;110:2083–91

Univariate Analysis of Screening Use by Study Group (N = 1546)

	No.	% Screening	OR*	95% CI	Raw $P^{\dagger}$	Hochberg $P^{\ddagger}$
Study group					<.001	
Control	387	32.56	1.00	—	—	—
SI	387	45.74	1.68	(1.25–2.53)	.001	.003
TI	396	43.78	1.58	(1.18–2.12)	.002	.010
TIP	386	48.45	1.91	(1.42–2.56)	<.001	.001
...						
TI vs SI	—	—	0.94	(0.71–1.25)	.683	.683
TIP vs SI	—	—	1.14	(0.86–1.51)	.372	.683
TIP vs TI	—	—	1.21	(0.91–1.61)	.193	.580

Control: nessun contatto
SI: offerta standard
TI: offerta standard + messaggio personalizzato
TIP: TI + telefonata di richiamo

"PHM: lower vs higher decision stage"

Paul C. Schroy III

Aid-Assisted Decision Making and Colorectal Cancer Screening

A Randomized Controlled Trial

Am J Prev Med 2012;43(6):573–583

Table 2. Patient outcomes by study group, *n* (%) or % (95% CI)

	Decision aid vs control			Decision aid vs decision aid +YDR		
Outcome	Decision aid alone	Control	Difference	Decision aid alone	Decision aid + YDR	Difference
Test ordered						
1 month	186 (69.1)	167 (60.5)	8.6 (0.7, 16.6)*	186 (69.1)	169 (60.4)	8.8 (0.8, 16.7)*
3 months	193 (71.8)	172 (62.3)	9.4 (1.6, 17.3)*	193 (71.8)	180 (64.3)	7.5 (−0.3, 15.2)
6 months	207 (77.0)	180 (65.2)	11.7 (4.2, 19.3)*	207 (77.0)	188 (67.1)	9.8 (2.4, 17.3)*
12 months	217 (80.7)	197 (71.4)	9.3 (2.2, 16.4)*	217 (80.7)	206 (73.6)	7.1 (0.1, 14.1)*
Test completed						
6 months	92 (34.2)	73 (26.4)	7.8 (0.1, 15.4)*	92 (34.2)	84 (30.0)	4.2 (−3.6, 12.0)
12 months	116 (43.1)	96 (34.8)	8.3 (0.2, 16.5)*	116 (43.1)	104 (37.1)	6.0 (−2.2, 14.2)

Note: Bold indicates significance.

* $p < 0.05$ by chi-square test of independence

YDR, *YourDiseaseRisk* personalized risk assessment tool with feedback

Decision Aid: DVD (modulo interattivo con touch-screen)

IRE ISTITUTO NAZIONALE TUMORI REGINA ELENA

ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

"TARGETED AND TAILORED INTERVENTIONS": TRIALS RANDOMIZZATI

NIH Public Access

A Randomized Controlled Trial of a Tailored Interactive Computer-Delivered Intervention to Promote Colorectal Cancer Screening: Sometimes More is Just the Same

Sally W. Vernon

Ann Behav Med. 2011 June ; 41(3): 284–299

Conclusions

Our results show that in a clinic setting, a patient-directed tailored intervention based on the trans-theoretical model was not more effective at increasing CRC screening than a public web site or only being surveyed. Positive changes in some of the intermediate psychosocial variables, although favoring the tailored group, did not translate into increased screening. We need to better understand what occurs between physicians' and patients and what system factors can be modified to increase adherence. To date, as a research community, we have yet to identify an intervention approach for CRC screening that is consistently more effective than usual care or minimal cues despite using the best available theoretical evidence and state-of-the-science methods [25].

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

ALTO RISCHIO: IBD

Guidelines for the management of inflammatory bowel disease in adults

Craig Mowat, Andrew Cole, Al Windsor, et al.

Gut 2011 60: 571-607

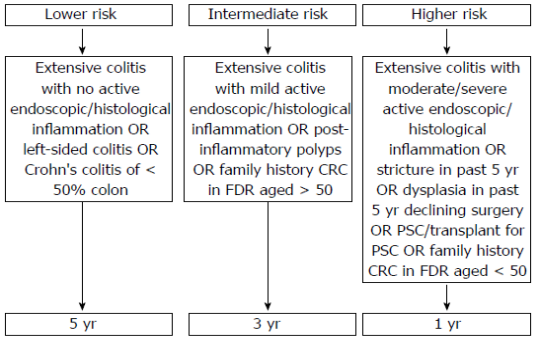
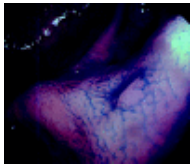


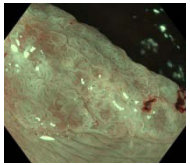
Figure 1 Surveillance recommendations for patients with colitis. OR: Odds ratio; CRC: Colorectal cancer; PSC: Primary sclerosing cholangitis; FDR: First degree relative.

Pancolonic dye spraying with targeted biopsy of abnormal areas is recommended (EL 2, RG A). If chromoendoscopy is not used, the strategy of random biopsy outlined in the 2002 surveillance guidelines should be followed.

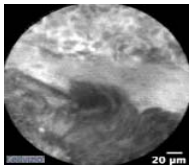
«TARGETED BIOPSIES»



Rutter MD, 2004
Hulstone DP, 2005
Kiesslich R, 2003



Dekker E, 2007 ?
Neumann H, 2011
Neumann H, 2013



Neumann H, 2011
Neumann H, 2011
Neumann H, 2013
De Palma G, 2011
De Palma G, 2013

ALTO RISCHIO: IBD

The risk of colorectal cancer in ulcerative colitis: a meta-analysis

J A Eaden, K R Abrams, J F Mayberry
Gut 2001;**48**:526–535

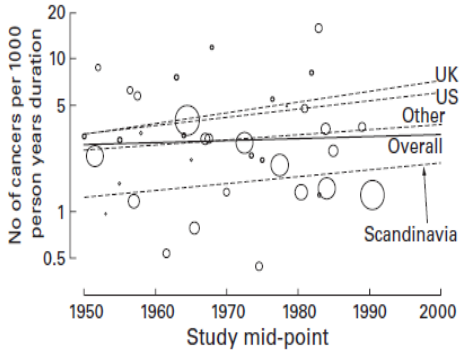


Figure 2 Temporal relationship of colorectal cancer, overall and by geographical location.

PREVALENZA: 3.7% (5.4% pancolite)

INCIDENZA NEL TEMPO

Rutter MD, 2006 ↓

Jess T, 2006 ↓

***Söderlund S*, 2009** ↓

CHEMIOPREVENZIONE: 5-ASA E SUOI DERIVATI

- **Inibizione crescita e sopravvivenza cellule CCR**
- **Inibizione generazione mutazioni «frameshift»**
- **Inibizione Pathway Wnt/β-Catenina**
- **Attivazione EGFR**
- **Attivazione PPAR-γ**

STUDI OSSERVAZIONALI

Eaden JA, 2001 ↑

Rubin DT, 2006 ↑

Velayos FS, 2005 ↑

***Bernstein CN*, 2011** ↓

***Terdiman JP*, 2007** ↓

VIII CONGRESSO NAZIONALE GISCoR

WORKSHOP SCREENING CCR REGIONE LAZIO

GISCoR Gruppo Italiano Screening Colorettale

ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

ALTO RISCHIO: S. DI LYNCH

Efficacy of Annual Colonoscopic Surveillance in Individuals With Hereditary Nonpolyposis Colorectal Cancer

CHRISTOPH ENGEL,* NILS RAHNER,‡ KARSTEN SCHULMANN,§ ELKE HOLINSKI-FEDER,‖ TIMM O. GOECKE,¶ HANS K. SCHACKERT,# MATTHIAS KLOOR,** VERENA STEINKE,†† HOLGER VOGELSANG,‡‡ GABRIELA MÖSLEIN,§§ HEIKE GÖRGENS,* STEFAN DECHANT,‖‖ MAGNUS VON KNEBEL DOEDERITZ,** JOSEF RÜSCHOFF,¶¶ NICOLAUS FRIEDRICHS,## REINHARD BÜTTNER,** MARKUS LOEFFLER,* PETER PROPPING,‡ and WOLFF SCHMIEGEL,§ on behalf of the GERMAN HNPCC CONSORTIUM

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2010;8:174–182

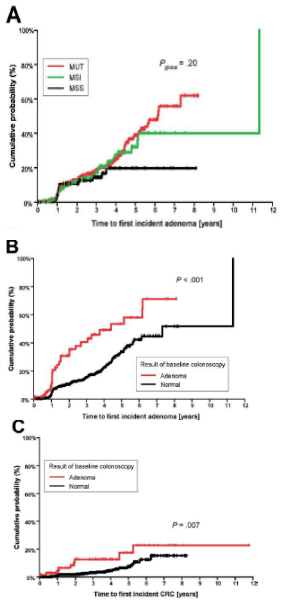


Figure 4. Time between baseline colonoscopy and first pathologic finding at follow-up colonoscopies. (*A* and *B*) End point adenoma; (*C*) end point CRC.

Revised guidelines for the clinical management of Lynch syndrome (HNPCC): recommendations by a group of European experts

Hans F A Vasen,[1] Ignacio Blanco,[2] Katja Aktan-Collan,[3] Jessica P Gopie,[4] Angel Alonso,[5] Stefan Aretz,[6] Inge Bernstein,[7] Lucio Bertario,[8] John Burn,[9] Gabriel Capella,[2] Chrystelle Colas,[10] Christoph Engel,[11] Ian M Frayling,[12] Maurizio Genuardi,[13] Karl Heinimann,[14] Frederik J Hes,[4] Shirley V Hodgson,[15] John A Karagiannis,[16] Fiona Lalloo,[17] Annika Lindblom,[18] Jukka-Pekka Mecklin,[19] Pal Møller,[20] Torben Myrhoj,[7] Fokko M Nagengast,[21] Yann Parc,[22] Maurizio Ponz de Leon,[23] Laura Renkonen-Sinisalo,[24] Julian R Sampson,[12] Astrid Stormorken,[20] Rolf H Sijmons,[25] Sabine Tejpar,[26] Huw J W Thomas,[27] Nils Rahner,[28] Juul T Wijnen,[4] Heikki Juhani Järvinen,[24] Gabriela Möslein,[29] (the Mallorca group)

Gut 2013;**62**:812–823.

Table 4 Outcome of colonoscopic surveillance in LS

Author/year	No of participants	Mean follow-up (years)	Interval recommend (years)	Risk interval cancer* By follow-up time	Risk interval cancer* By age 60 years	No of interval cancers	Location right colon (%)	Local stage (stage I & II) (%)	Death CRC
Mecklin *et al* (2007)[44]	420	6.7	2	–	M 35% F 22%	26	57	80	5
Engel *et al* (2010)[46]	1126	3.7	1	–	–	25	Not reported	95	Not reported
Vasen *et al* (2010)[45]	745	7.2	1–2	6%/10 years	–	33	62	83	0
Stuckless *et al* (2011)[47]	109	Ca 10	1–2	–	–	21	62	78	1

*Defined as CRC that develops after a negative screening colonoscopy.
CRC, colorectal cancer; LS, Lynch syndrome.

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

VIII CONGRESSO NAZIONALE GISCoR
WORKSHOP SCREENING CCR REGIONE LAZIO
GISCoR Gruppo Italiano Screening Colorettale
ROMA, 3 E 4 OTTOBRE 2013
Auditorium Antonianum, Viale Manzoni 1

Interval cancers in LS under surveillance

LS affected Under CRC surveillance	71 (30 families)
M/F	33/38
Mean age at baseline colonoscopy (range)	39,8 years (18-68 yrs)
MLH1/MSH2 deleterious mutation (n° carriers)	31/40

Table 1: baseline characteristics of patients enrolled in the study

N° of total colonoscopies performed	268
Mean follow-up (range)	61,6 months (12-371)
Interval CRC detected (n° of patients)	4/71 (5,6%)

Table 2: results of CRC surveillance

Mean age at diagnosis of interval CRC (range)	40 years (32-50).
Mean interval from previous colonoscopy (range)	24 months (16-30)
Suboptimal Bowel preparation	1/4
MLH1/MSH2 Deleterious mutations	2/2
Previous diagnosis of CRC	0/4

Table 3: characteristics of patients diagnosed with interval cancer

Sanchez-Mete L, IRE, 2013

Quality colonoscopy and risk of interval cancer in Lynch syndrome

Haanstra JF et al, ***Int J Corectal Dis, 2013 Jul 16***

….Interval cancers could be related to incompleteness of previous endoscopy and possibly residual adenomatous tissue. Further reduction of interval cancer risk may be achieved by optimizing endoscopy quality and individualization of surveillance guidelines….

IRE
ISTITUTO NAZIONALE TUMORI
REGINA ELENA
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO