RegioneEmilia-Romagna

9th HTAi Annual Meeting BILBAO | 2012

HTA in Integrated Care for a **Patient Centered System** HTAi

Methods in HTA – Health outcomes

Bringing patients' outcome at the forefront in HTA of diagnostic tests using the GRADE approach

Luciana Ballini
Luca Vignatelli, Susanna Maltoni, Antonella Negro, Fabio Trimaglio, Roberto Grilli

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Appropriateness of
FDG-PET in oncology: <u>3rd update</u>

**Since 2001 a permanent research activity
alongside the development and diffusion
of the technology**

➡ **An obsession ?**

… or an opportunity

- To reason on diagnostic-therapeutic strategies, rather than simply on diagnostic test

- To address research gaps (clinical effectiveness)

- To test a new methods for working groups developing diagnostic recommendations

Appropriateness of a diagnostic test

The value of any medical test is ultimately measured by whether the information it provides affects patient-relevant outcomes (Bossuyt 2010)

- Initial diagnostic assessment with subsequent therapeutic approach

- The potential of the new test to modify initial diagnostic assessment (e.g. stage of disease)

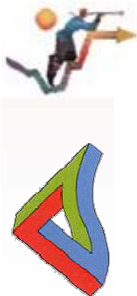- The change in management following change of diagnostic assessment

Rationale

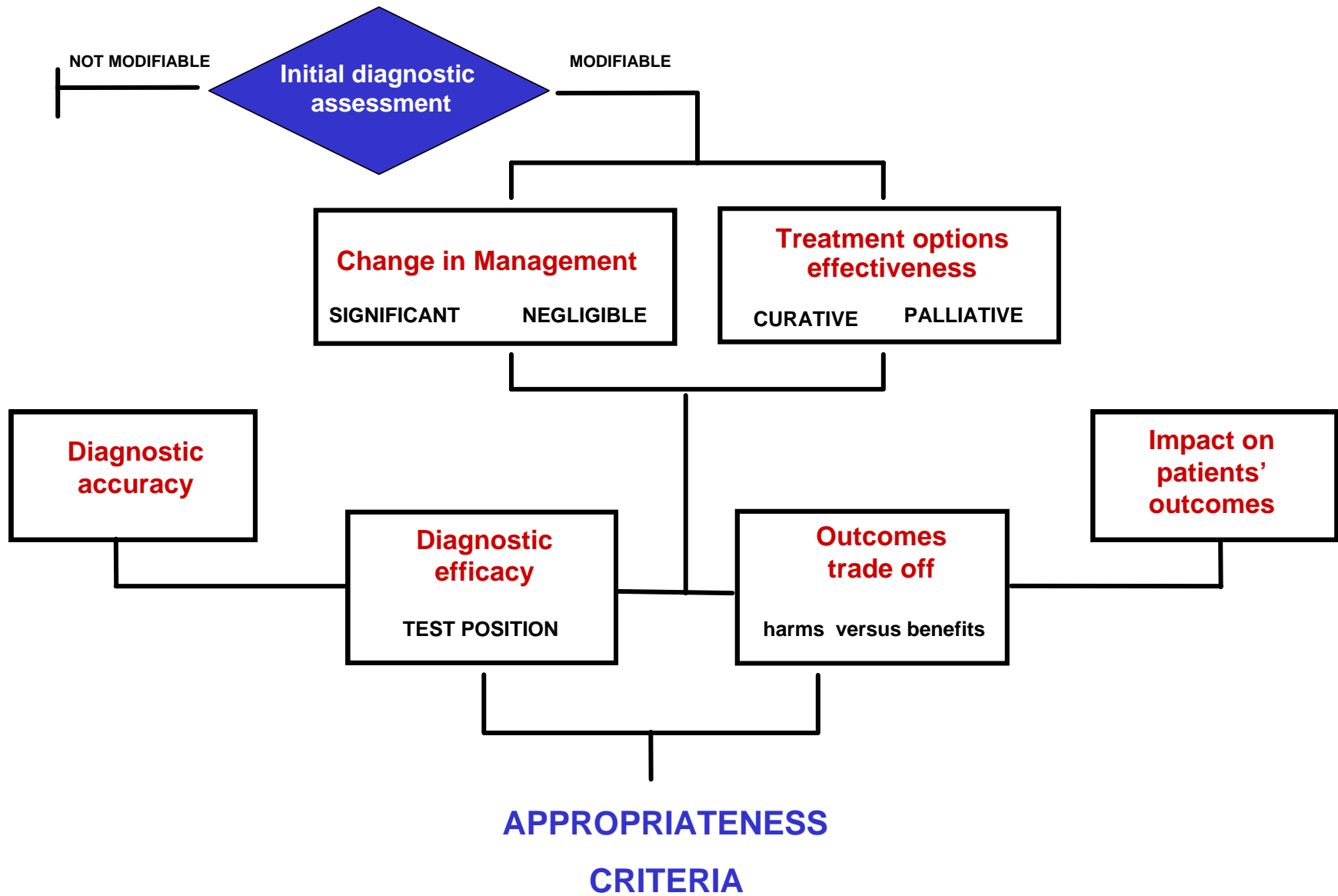- The diagnostic accuracy of the new test

Available evidence

- The resulting improvement in patients' outcome due to change in therapeutic approach induced by new test's results

?

GRADE

Schunemann et al BMJ 2008;336:1106-1110.

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Consequentialist Approach

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NOT MODIFIABLE

Initial diagnostic assessment

MODIFIABLE

Change in Management

SIGNIFICANT   NEGLIGIBLE

Treatment options effectiveness

CURATIVE   PALLIATIVE

Diagnostic accuracy

Diagnostic efficacy

TEST POSITION

Outcomes trade off

harms versus benefits

Impact on patients' outcomes

APPROPRIATENESS

CRITERIA

CLINICAL QUESTION 3: Role of FDG-PET in early response to preoperative chemoradiation of patients treated for locally advanced esophageal cancer

Rationale: As preoperative chemotherapy could increase the risk of postoperative mortality (ESMO 2010), a selection of respondents after the first cycles could spare non-respondents the risks of a futile full-length chemotherapy.

Effectiveness of treatment: in patients with locally advanced cancer, preoperative chemoradiation improves the 2-year survival by 13% (absolute difference) compared to surgical treatment only (Gebski 2007). On the other hand preoperative chemotherapy could increase the risk of postoperative mortality (ESMO 2010).

Research question: FDG-PET as replacement (new test)
Is FDG-PET accurate in evaluating the early response to preoperative chemoradiation of patients treated for locally advanced oesophageal cancer?

Pre-test probability: 43% of patients show an histopathological response to neoadjuvant chemotherapy (Ngamruengphong 2010, Lorenz 2007).

Diagnostic accuracy estimates: Level of evidence: low

FDG-PET	sensitivity (heterogeneous) range 44-100%	specificity: 74%
Comparator (current practice: all patients complete preoperative treatment)	sensitivity: 100%	specificity: 0%

Outcomes importance

Consequences of TEST for		Level of Importance* (1-9)
Patients Responders	True Responders: Responders complete clinically effective preoperative treatment, which could improve survival but might carries some risk of postoperative mortality	6 (2-9)
	False Non Responders: Responders interrupt clinically effective treatment, which could have improved survival, and proceed directly to surgery	8 (2-9)
Patients Non-responders	True Non Responders: Non-responders interrupt ineffective treatment, which would not have improved survival, and proceed directly to surgery, with lower risks of postoperative mortality	7 (2-9)
	False Responders: Non responders complete ineffective preoperative treatment, with no possible gain in survival but with some risk of postoperative mortality	6 (2-9)

* not important (score 1-3), important (4-6), and critical (7-9) to a decision
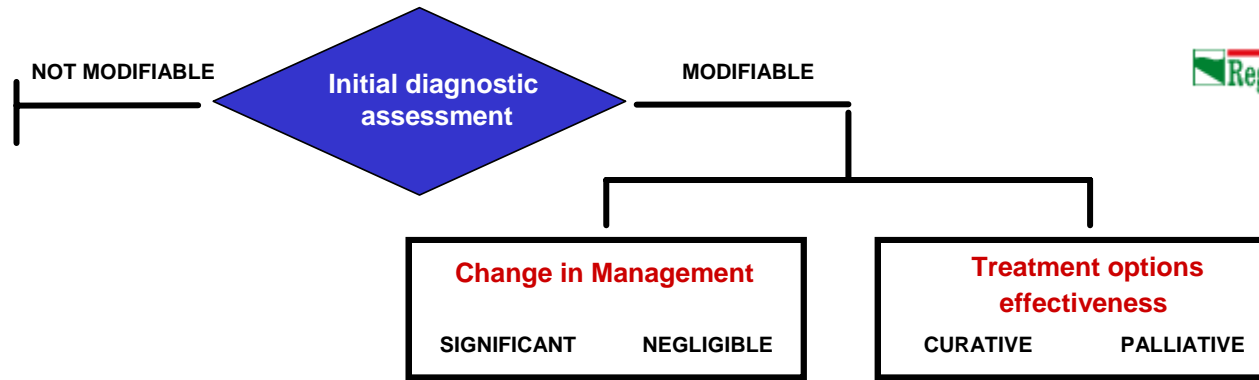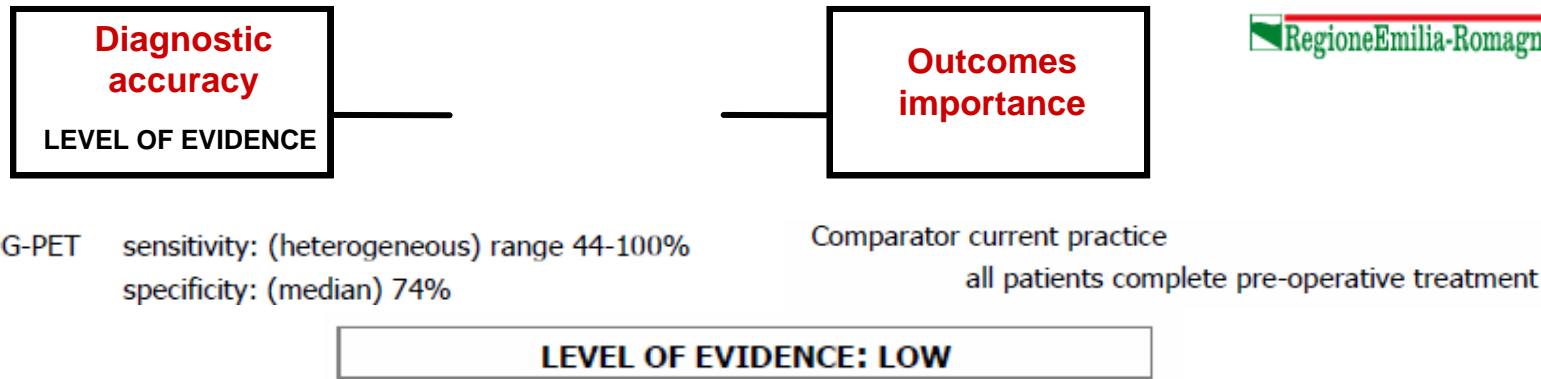
Matrix of natural frequencies

	Patients	According to PET	According to current practice
		N of patients out of 100 submitted to the exam	
Patients responders	True Responders	19 - 43	43
	False Non-responders	24 - 0	0
Patients non responders	True Non-responders	42	0
	False Responders	15	57
		100	100

CLINICAL QUESTION 3:

APPROPRIATENESS of FDG-PET 1-2-3 inappropriate 4-5-6 uncertain 7-8-9 appropriate	1	2	3	4	5	6	7	8	9
INDETERMINATE									

The consequentialist approach at work : information provided to the panel

NOT MODIFIABLE

Initial diagnostic assessment

MODIFIABLE

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Change in Management

SIGNIFICANT   NEGLIGIBLE

Treatment options effectiveness

CURATIVE   PALLIATIVE

CLINICAL QUESTION:

Role of FDG-PET in early response to pre-operative chemoradiation of patients treated for locally advanced esophageal cancer

Treatment effectiveness: **Preoperative chemo/radio therapy improves 2 year survival by 13% (absolute difference) compared to surgical treatment only (Gebski Lancet Oncology 2007)**

Rationale: **Preoperative chemo/radio therapy reduces tumour mass but increases risk of post-operative mortality (ESMO 2010). Early identification of non responders could avoid futile treatment and unnecessary risks**

RESEARCH QUESTION: FDG-PET as replacement

Is FDG-PET accurate in evaluating early response to pre-operative chemoradiation of patients treated for locally advanced esophageal cancer ?

Pre-test probability

43% of patients show an histopathological response to neoadjuvant chemotherapy (Lorenz 2007; Ngamruengphong 2010).
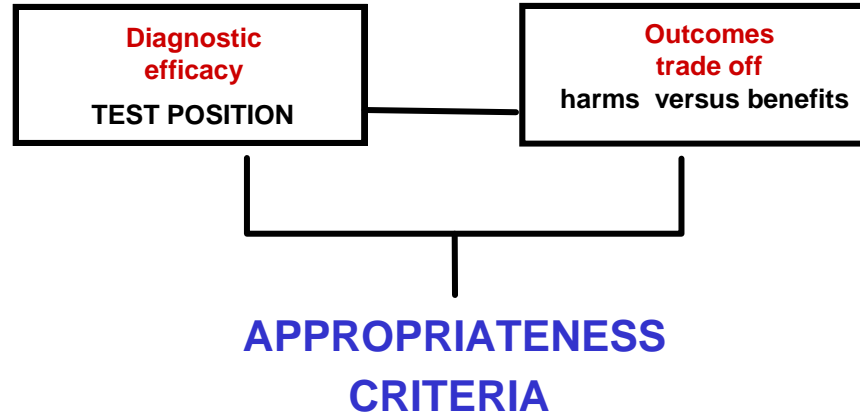
Diagnostic accuracy

LEVEL OF EVIDENCE

Outcomes importance

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FDG-PET   sensitivity: (heterogeneous) range 44-100%
           specificity: (median) 74%

Comparator current practice
           all patients complete pre-operative treatment

LEVEL OF EVIDENCE: LOW

Table 7.5.   Patient-important clinical outcomes and median scores of importance

PATIENT IMPORTANT OUTCOMES	Median score
Consequences of test for responders	
• True responders - responders complete clinically effective pre-operative treatment, which could improve survival but might carries some risk of post-operative mortality	7
• False non responders - responders interrupt clinically effective treatment, which could have improved survival, and proceed directly to surgery	8
Consequences of test for non responders	
• True non responders - non responders interrupt ineffective treatment, which would not have improved survival, and proceed directly to surgery, with lower risks of post-operative mortality	7
• False responders - non responders complete ineffective pre-operative treatment, with no possible gain in survival but with some risk of post-operative mortality	5

GRADE

Schunemann et al BMJ 2008;336:1106-1110.

Diagnostic
efficacy

TEST POSITION

Outcomes
trade off
harms versus benefits

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APPROPRIATENESS
CRITERIA

Table 7.6. "Natural frequencies" of patients assessed for response to therapy

		N of patients out of 100 submitted to the exam		Median scores of importance
		According to FDG-PET	According to current practice	
Patients responders	True responders	19 - 43	43	7
	False non responders	24 - 0	0	8
Patients non responders	True non responders	42	0	7
	False responders	15	57	5
		100	100	

INAPPROPRIATE

Not good enough

RAND/UCLA Appropriateness Method: Results
7 panels (60 experts) – 7 tumours

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Lung
Breast
Head & Neck
Esophageal
Colo-rectal
H Lymphoma
NH Lymphoma

55 questions

11 appropriate

4 indeterminate

13 inappropriate

27 Disagreement

5 appropriate

9 inappropriate

2 uncertain

11 disagreement

9 light Disagreement

2 Strong Disagreement
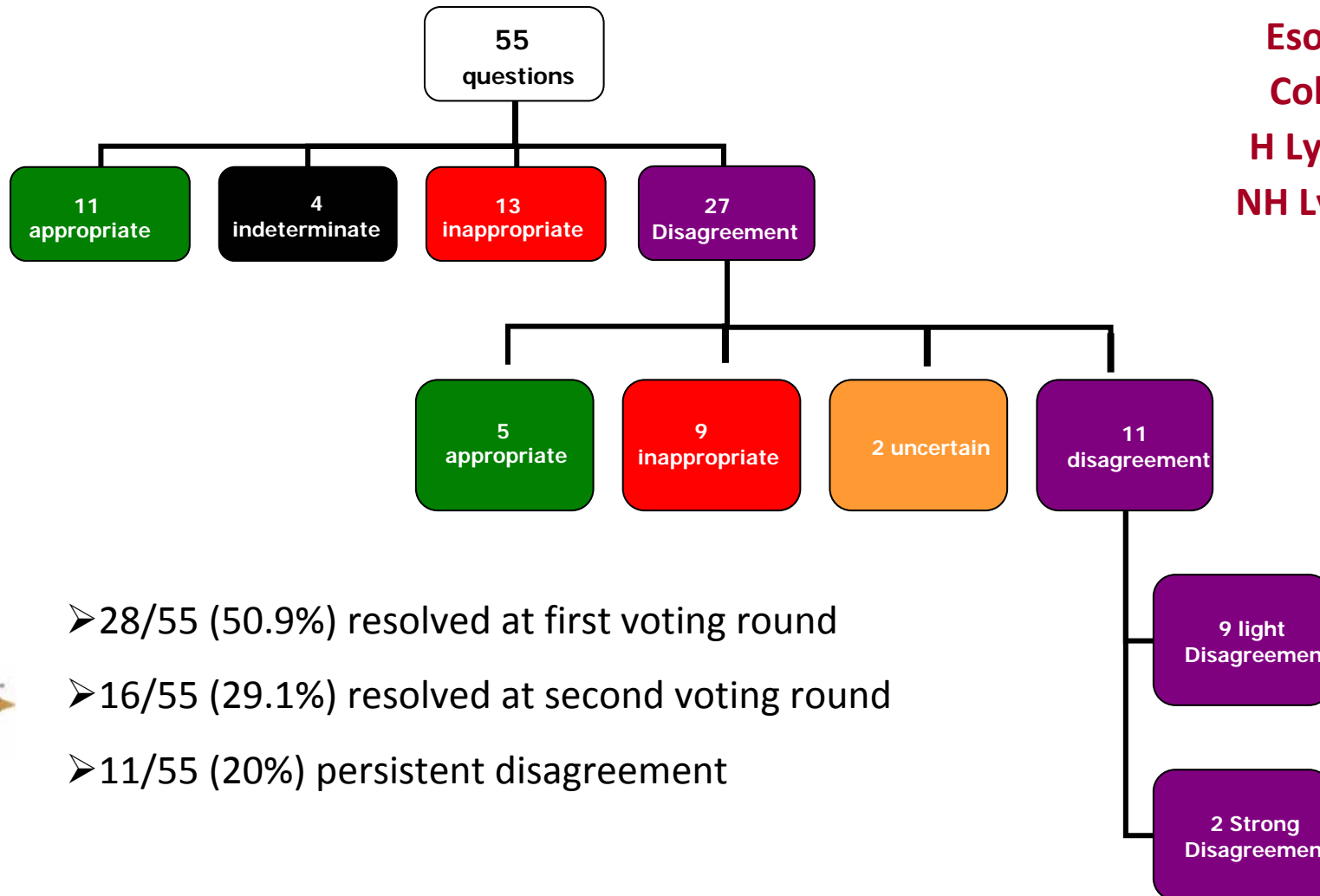
➢ 28/55 (50.9%) resolved at first voting round

➢ 16/55 (29.1%) resolved at second voting round

➢ 11/55 (20%) persistent disagreement

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The panelists

Valentina Ambrosini — Nuclear Physician, Azienda ospedaliero-universitaria di Bologna

Giorgio Baldari — Nuclear Physician, Azienda ospedaliero-universitaria di Parma

Mario Bertolani — Radiologist, A...

Filippo Bertoni — Radiotherapis...

Maurizio Boaron — Surgeon, Azie...

Alessandra Casolo — Nuclear Physic...

Claudio Corbelli — Nuclear Physic...

Maria Cristina Cucchi — Surgeon, Azie...

Valerio Di Scioscio — Radiologist, A...

Giorgio Fagioli — Nuclear Physic...

Stefano Fanti — Nuclear Physic...

Luca Fasano — Pneumologist,...

Luciano Feggi — Nuclear Physic...

Antonio Frassoldati — Oncologist, Az...

Patrizia Giacobazzi — Radiotherapis...

Nicola Lacava — Surgeon, Azie...

Giuseppe Longo — Oncologist, Az...

Andrea Martoni — Oncologist, Az...

Giorgio Mazzi — Health Directo...

Monica Agostini — Nuclear Physician, Azienda USL di Cesena

Salvatore Bacciu — Ear, Nose & Throat Specialist, Azienda ospedaliero-universitaria di Parma

Alessandra Bologna — Oncologist, Azienda ospedaliera di Reggio Emilia

Athos Borghi — Internist, Azienda ospedaliero-universitaria di Modena

Alba Brandes — Oncologist, Azienda USL di Bologna

Sebastiano Calpona — Oncologist,...

Paolo Campioni — Radiologist,...

Luigi Cavanna — Nuclear Phy...

Roberto De Maria — Surgeon, Az...

Ermanno Emiliani — Radiotherap...

Stefano Fanti — Nuclear Phy...

Giovanni Frezza — Radiotherap...

Riccardo Galassi — Nuclear phy...

Andrea Gardini — Surgeon, Az...

Cinzia Iotti — Radiotherap...

Moreno Marani — Ear, Nose &...

Federica Matteucci — Nuclear Phy...

Renzo Mazzarotto — Radiotherap...

Alberto Merighi — Gastroenter...

Barbara Melotti — Oncologist, Azienda Ospedaliero-Universitaria di Bologna

Francesco Merli — Haematologist, Azienda Ospedaliero-Universitaria di Reggio-Emilia

Stefano Nava — Pneumologist, Azienda ospedaliero-universitaria di Bologna

Alberto Ravaioli — Oncologist, Azie...

Francesca Re — Haematologist,...

Livia Ruffini — Nuclear Physicia...

Maura Scarlattei — Nuclear physicia...

Nicola Sciascia — Radiologist, Azie...

Davide Tassinari — Oncologist, Azie...

Enrico Tincani — Internist, Azien...

Lucia Zanoni — Nuclear Physica...

Giampaolo Zini — Radiotherapist,...

Stefania Zoboli — Nuclear Physicia...

Maurizio Zompatori — Radiologist, Azie...

Maurizio Miselli — Health Director, Azienda ospedaliero-universitaria di Modena

Manlio Monti — Oncologist, IRST Meldola

Andrea Moretti — Nuclear physician, Azienda USL di Forlì

Cristina Nanni — Nuclear Physician, Azienda ospedaliero-universitaria di Bologna

Silvia Palazzi — Radiotherapist, Azienda USL di Ravenna

Micaela Piccoli — Surgeon, Azienda ospedaliero-universitaria di Modena

Monica Silvotti — Radiologist, Azienda ospedaliera di Reggio Emilia

Annibale Versari — Nuclear Physician, Azienda ospedaliera di Reggio Emilia

Claudio Vicini — Ear, Nose & Throaty Specialist, Azienda USL di Forlì

Alessandro Volpe — Surgeon, Azienda ospedaliero-universitaria di Modena

Elena Zamagni — Hematologist, Azienda ospedaliero-universitaria di Bologna

Thank you

luballini@regione.emilia-romagna.it

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Criteria for appropriate use of FDG-PET in breast... ORIentamenti 4

Criteria for appropriate use of FDG-PET in esopha... ORIentamenti 6

Criteria for appropriate use of FDG-PET in lung cancer ORIentamenti 5

Criteria for appropriate use of FDG-PET in colorectal... ORIentamenti 7

Criteria for appropriate use of FDG-PET in head and neck cancer