MASCC 2018, *Workshop 3*: What Does the Future Hold?
Prognostication in Advanced Cancer and Clinical Decision Making

Future Research in Prognostication: Maximizing Patient Outcomes

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Masanori Mori, MD, Tatsuya Morita, MD,

Palliative Care Team, Division of Palliative and Supportive Care,

Seirei Mikatahara General Hospital, JAPAN

Faculty Disclosure

X	No, nothing to disclose
	Yes, please specify:

Company Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*

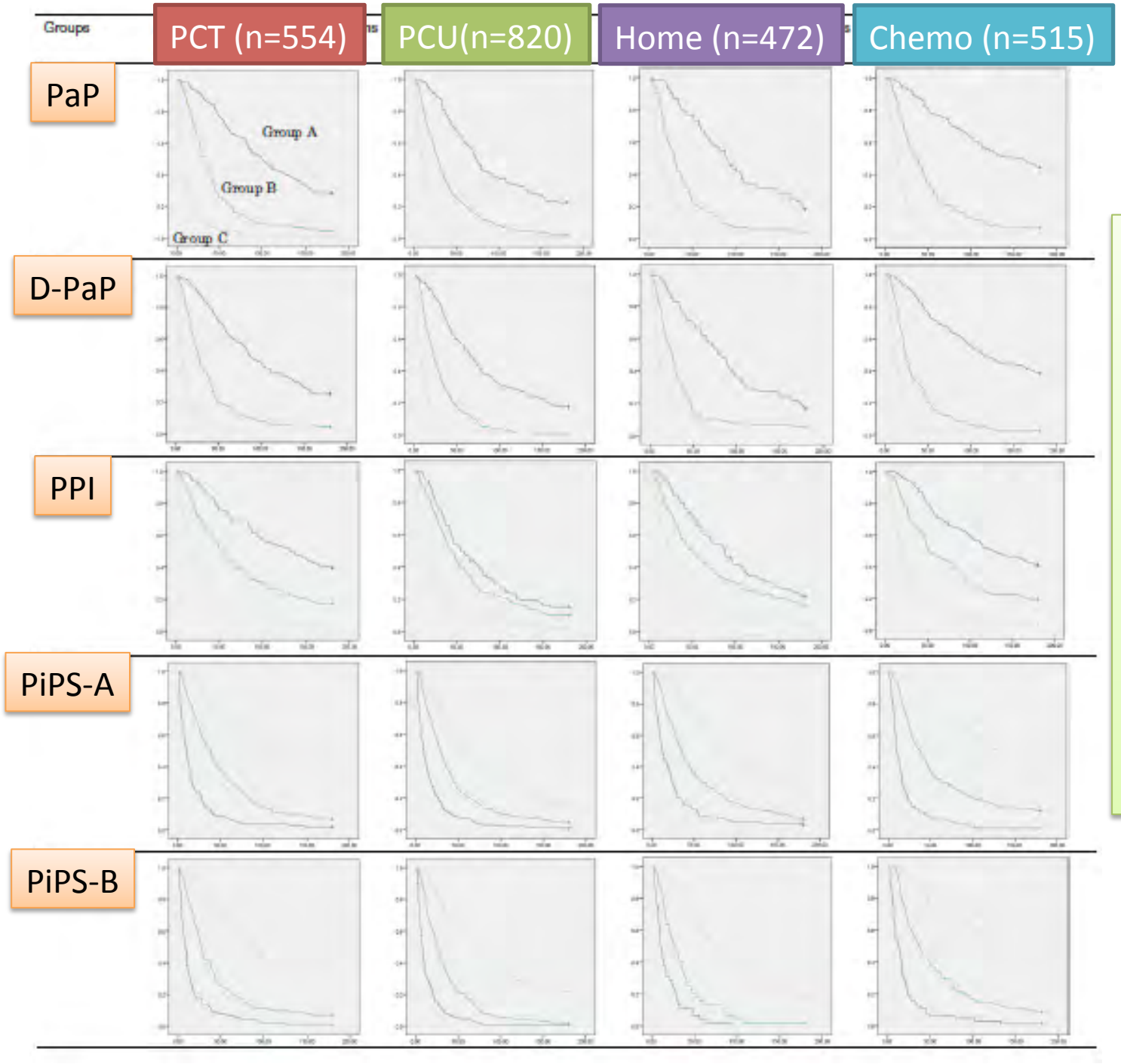
Future Research in Prognostication Topics

- How to improve the accuracy?
- How to identify tools that best fit specific goals?
- How to improve the reliability?
- How to identify best outputs?
- Potential clinical trials of prognostic disclosure to maximize outcomes?

Overview of Major Prognostic Factors

	1990s	2000s	2010s
Subjective	CPS (-1990s)	SQ (1 year)	SQ (30 days, 7days)
Signs & Symptoms	Dyspnea, delirium, anorexia, edema Impending death signs	Anorexia-cachexia complex Depression	Impending death signs
PS, QOL	KPS, QOL	PPS	
Comorbidities		Comorbidities	
Objective	WBC, %Lymph	B_{12} CRP Index, GPS	VS, Phase angle
Models	SUPPORT model PaP PPI		Feliu prognostic nomogram OPS, OPPS, SAP PiPS, Modified PiPS Simplified PPI

Moss AH. JPM 2010;13:837-40. Hamano J. Oncologist 2015;20:839-44. Morita T. AJHPC 1998;15:217-22. Benedetti FD. SCC 2013;21:1509-17. Hui D. Oncologist. 2014; 19: 681-7. Hui D. Cancer 2015;121:960-7. Hui D. JPSM 2015;50:488-94. Bruera S. JPSM 2014; 48: 510-7. Hwang IC. SCC 2013;21:835-40. Chen YT. JPSM 2015;49:690-6. Hui D. Cancer 2015;121:3914-21. Hui D. Cancer 2014;120:2207-14. Hui D. JPSM 2017;53:571-7. Downing GM. JPC 2007;23:245-252. Seow H. JCO 2011;29:1151-8. Vigano A. Arch Intern Med 2000;160:861-8. Maltoni M. JCO 2005;23:6240-8. Satin JR. Cancer 2009;115:5349-61. Tamburini M. JPSM 1996;11:32-41. Read WL. JCO 2004;22:3099-3103. Geissbuhler P. JPSM2000;20:93-103. Forrest LM. BJC 2005;92:1834-6. Knaus WA. Arch Intern Med 1995;122:191-203. Pirovano M. JPSM 1999;17:231-9. Morita T. SCC 1999;7:128-33. Feliu J. JNCI 2011;103:1613-20. Suh ST. SCC 2010;18:151-7. Uneno Y. PLoS One 12(8):e0183291. Gwilliam B. BMJ 2011;343:d4920. Baba M. JPSM 2015;49:853-60. Hamano J. JPSM 2015;50:542-7.



ProVal study

- Multicenter prospective cohort study
- 2426 advanced ca patients at 58 PC services (19 PCTs, 16 PCUs, and 23 home PC)
- The feasibility and accuracy of PaP, D-PaP, PPI and PiPS investigated

Baba M, et al.
Eur J Cancer 2015;
51:1618–29.

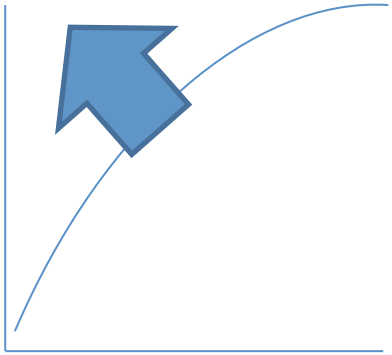
To Improve the Accuracy

Better use of variables by:

- Increasing the number of variables (e.g., PiPs)
- Identifying novel prognostic factors (e.g., phase angle)
- Utilizing technology to measure changes over time (e.g., sheet-shaped body vibrometer, wearable device)

Better use of statistical models by:

- TRIPOD statement (e.g., Fractional polynomial model)
- Deep learning



Other

- Identification of factors a/w inaccuracy

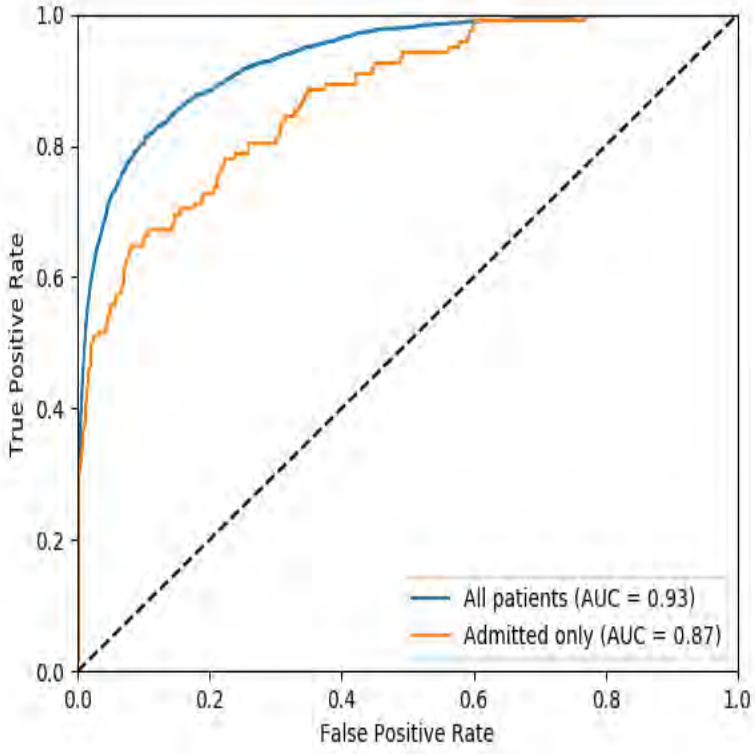
Moons KGM, et al. Ann Intern Med 2015;162:W1-W73.

To Improve the Accuracy Deep Learning

- To predict all-cause 3-12 month mortality
- Algorithm: Deep Neural Network trained on the EHR data from the previous years.
- Clinical data at Stanford (1995-2014), included 221,284 patients

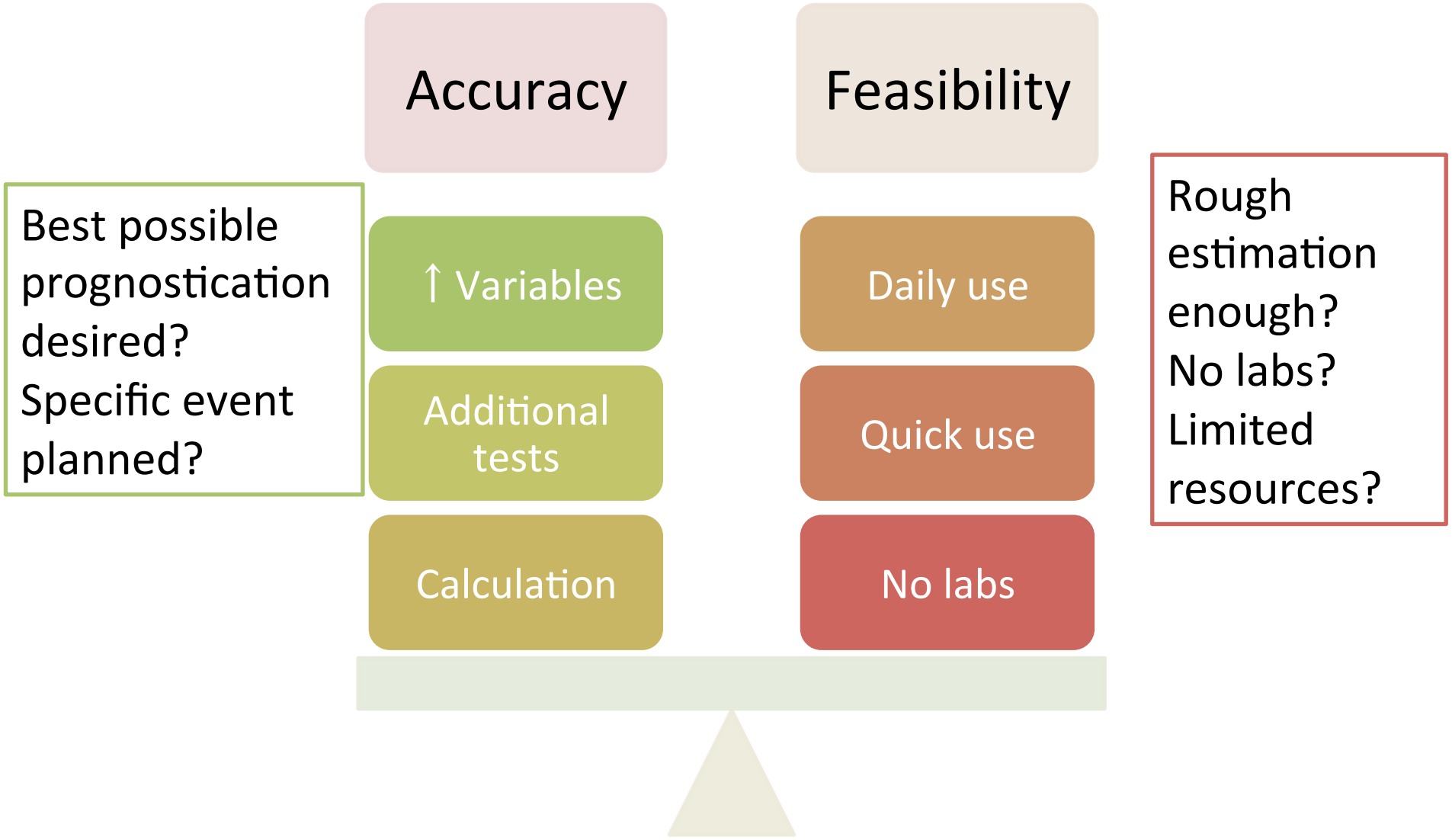
Patient MRN	XXXXXXX
Probability score	0.946

Factors	Code	Value	Influence	Description
Top Diagnostic factors	V10.51	4	0.0051	Personal history of malignant neoplasm of bladder
	V10.46	5	0.0019	Personal history of malignant neoplasm of prostate
	518.5	1	0.0012	Pulmonary insufficiency following trauma and surgery
	518.82	1	0.0008	Other pulmonary insufficiency
	88.75	1	0.0006	Diagnostic ultrasound of urinary system
Top Procedural factors	88331	1	0.0017	Pathology consultation during surgery with FS
	75984	1	0.0014	Transcatheter Diagnostic Radiology Procedure
	72158	1	0.0013	MRI and CT Scans of the Spine
	Code_Type_Count	76	0.0011	Summary statistic (count of all ICD/CPT codes)
	76005	1	0.0007	Fluroscopic guidance and localization of needle or catheter tip for spine
Top Medication factors				
Top Encounter factors	Hx Scan	21	0.0012	Number of scan encounters of all types
	Inpatient	60	0.0004	Number of days patient was admitted
	Var_Codes_per_Day	8	0.0002	Summary statistic (variance in number of codes assigned per day)
	Code_Day_Count	88	0.0001	Number of days any encounter code was assigned
Top Demographic factors	Age	81	0.0010	Age of patient in years at *prediction time*

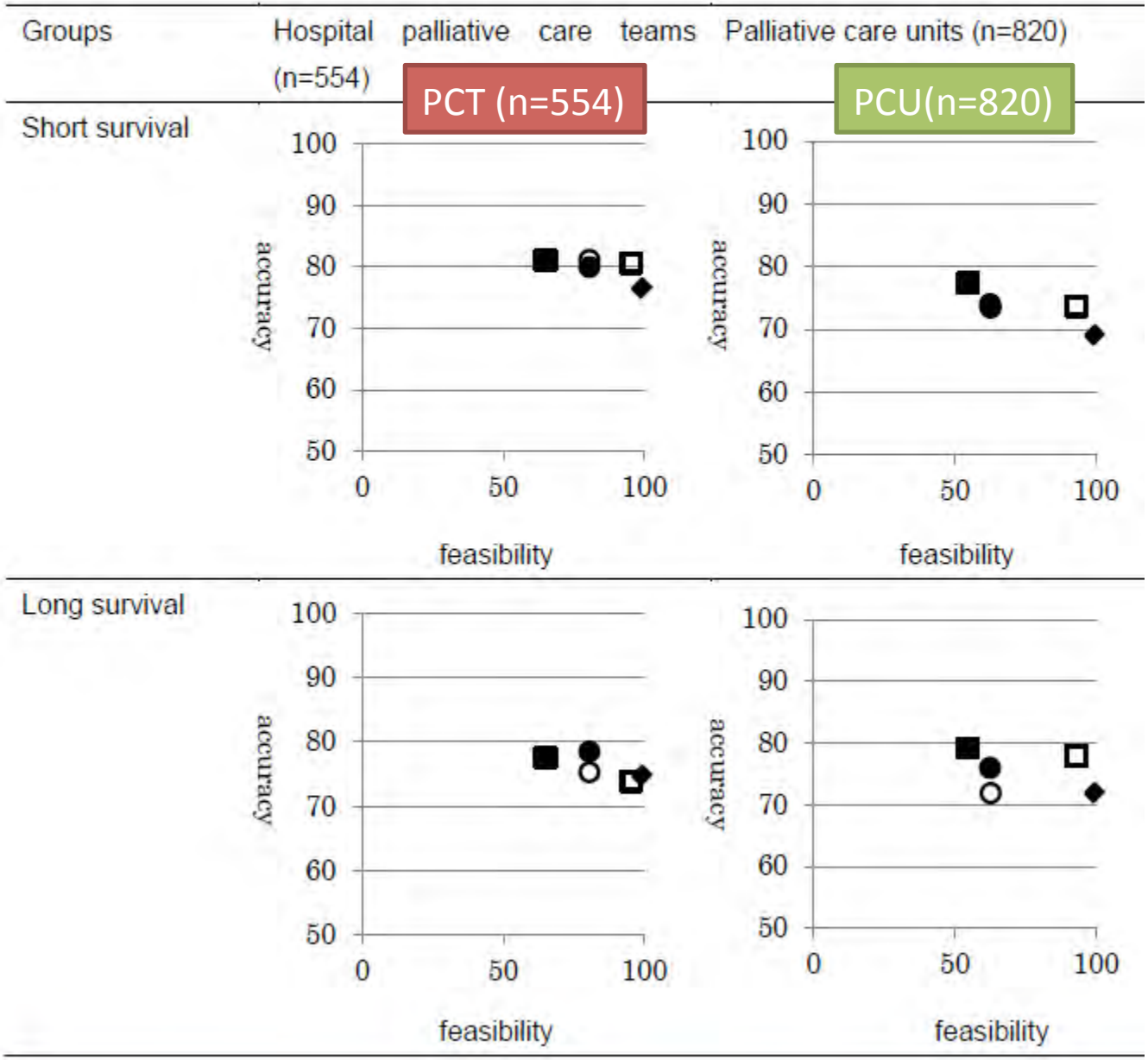


Avati A, et al. arXiv:1711.06402v1 [cs.CY] 17 Nov 2017

Accuracy and Feasibility



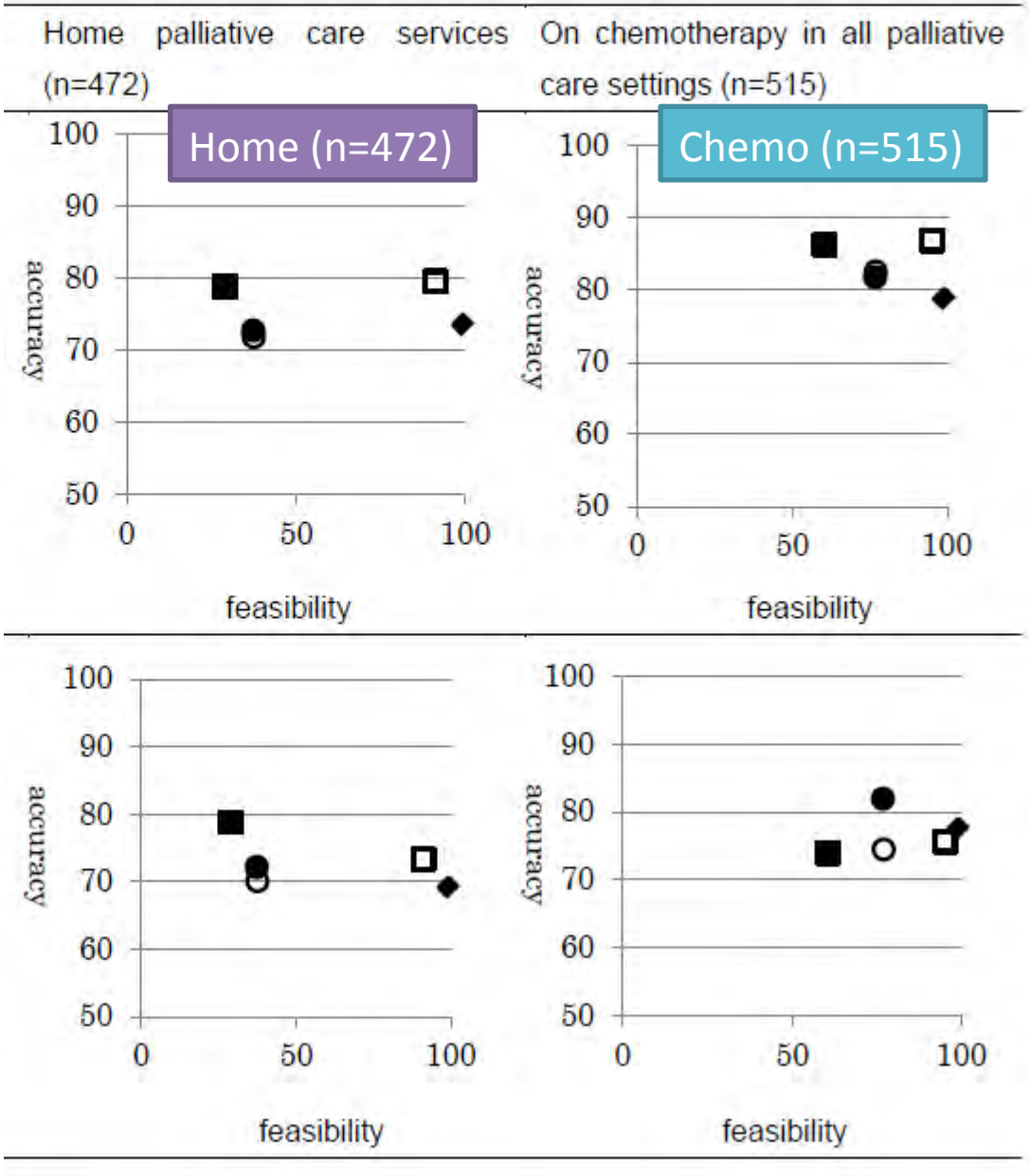
Accuracy x Feasibility



PaP
D-PaP
PPI
PiPS-A
PiPS-B

ProVal study
Baba M, et al.
Eur J Cancer 2015;
51:1618–29.

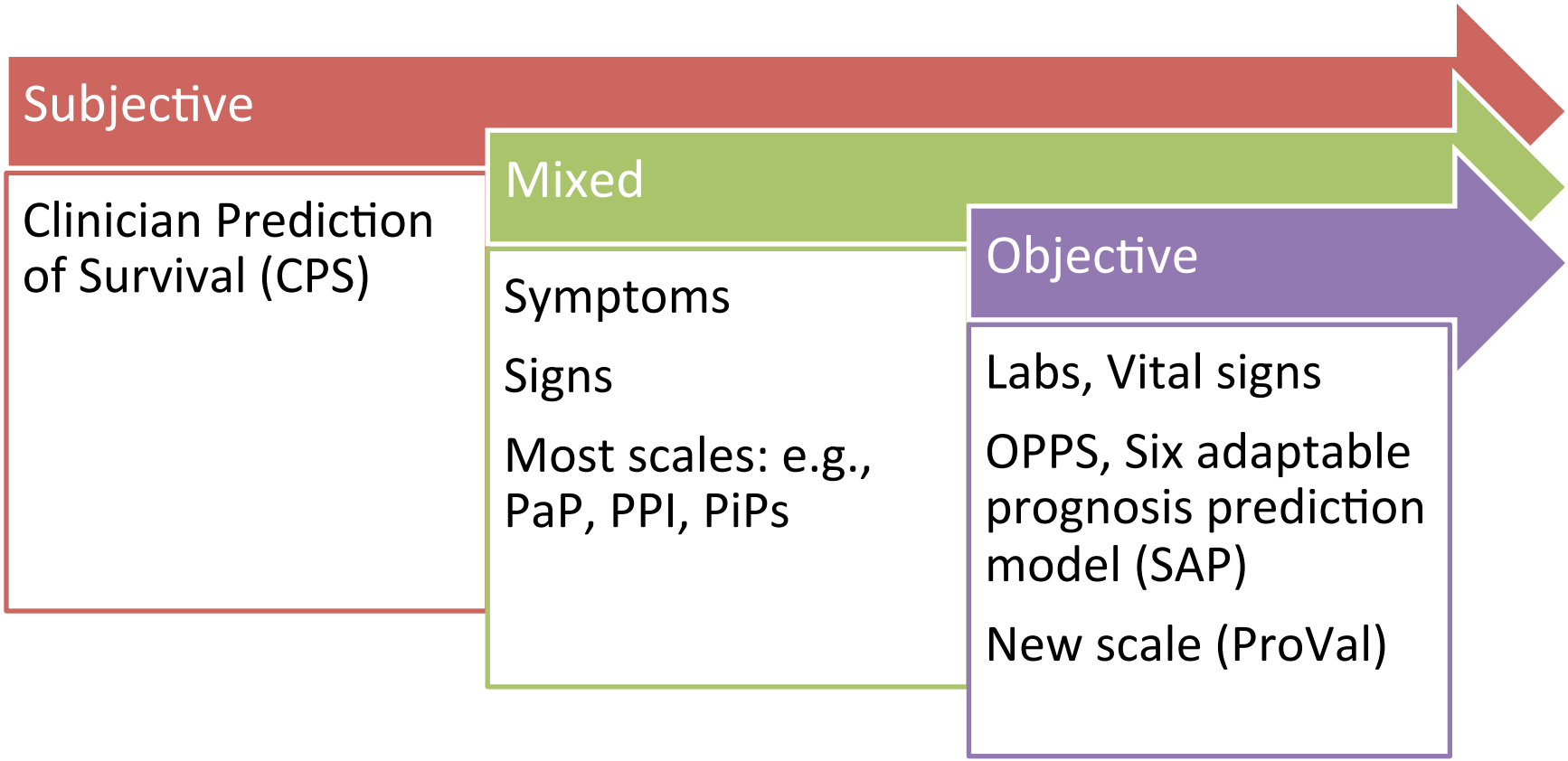
Accuracy x Feasibility



PaP
D-PaP
PPI
PiPS-A
PiPS-B

ProVal study
Baba M, et al.
Eur J Cancer 2015;
51:1618–29.

To Improve the Reliability



Chen YT, et al. JPSM 2015;49:690-696. Uneno Y, et al. PLoS One 12(8):e0183291.

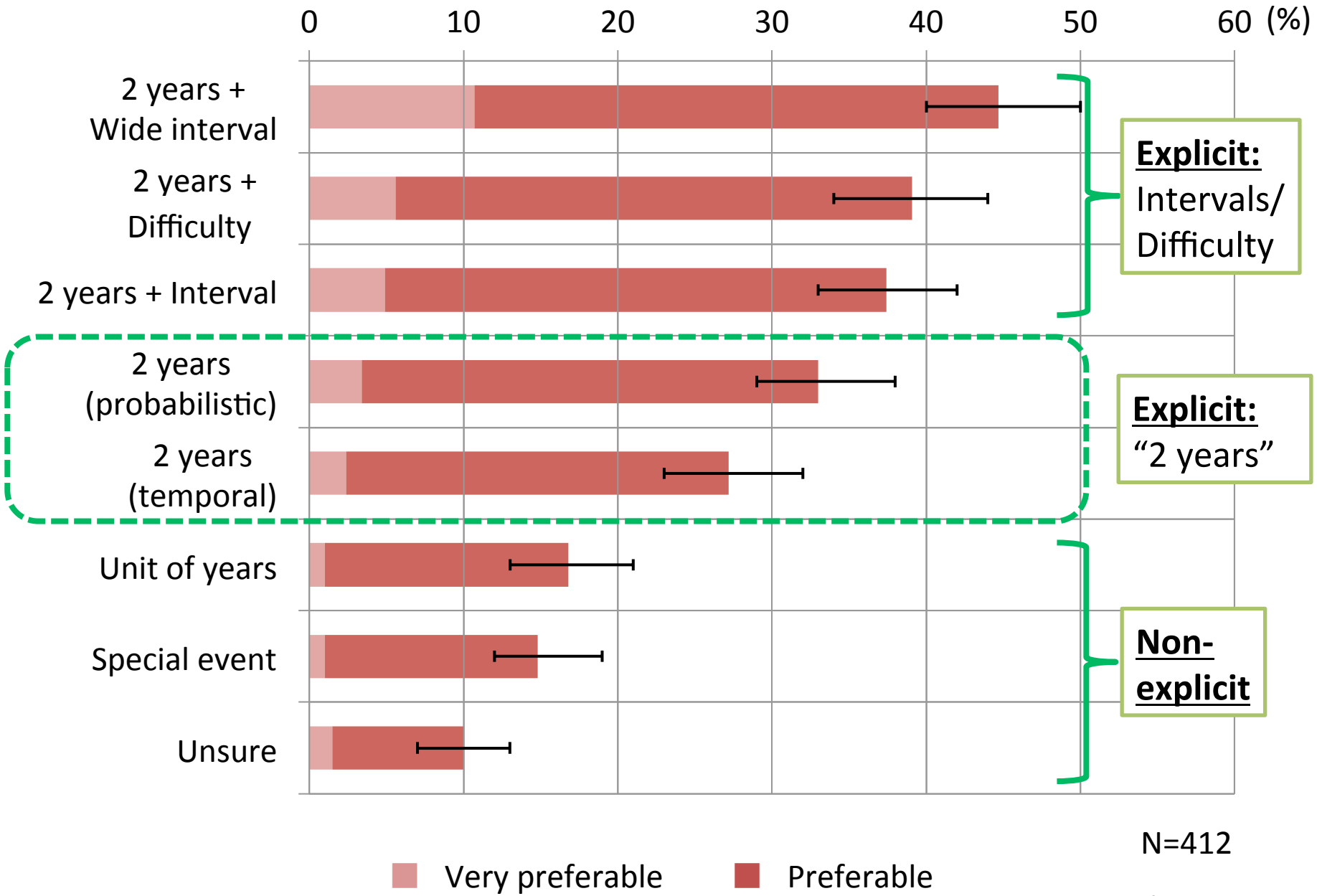
Ideal Output

- To match the info with patients' and families' need to better help them engage in ACP.
- What specific prognostic info do patients want within or beyond health care?
  - Temporal, probabilistic?
  - Definitive, probable, possible information?
  - Function until specific event?
  - Other output potentially important for the rest of their life?
- Methods
  - Qualitative study → website for patients and families

Concept	Examples of Output
Median	"A half of typical patients in your situation would live more than a year, and the other half would live less than a year."
Typical (x 1/2 – x 2)	About half of similar patients would live for somewhere between 6 months and 2 years (half to double the predicted median)
Best/Worst cases (x 1/4 – x 3-4)	• Best case – about 10% of patients could expect an excellent response to treatment with prolonged control and survival beyond 3 years • Worst case - about 10% of patients will experience rapid progression and death
Function (Opinion)	"You may be able • to walk without assistance for XX months, • to eat without severe appetite loss or difficulty swallowing for XX months, and • to talk with your loved ones for XX months. So if you would like to complete your XX (tasks), you may wish to do so by XX (specific month) just in case"

Kiely EB, et al. J Clin Oncol 2010;28:2802-4.

Pt Preferences of Explicit vs. Non-explicit Px Disclosure (n=412)



Mori M, et al. JSMO 2017

Potentially Useful Website for Pts (Japanese Example in Financing)

長期投資予想／アセットアロケーション分析

投資信託の「長期保有」や「積立て投資」の運用結果を予想し、グラフで表示します

1. アセットアロケーション（資産配分）の入力

いま保有する資産の配分、あるいはこれからの配分予定を入力してください。おおまかでもかまいません

資産クラス	投資金額	配分比率	期待リターン	リスク
日本債券	100 万円	19.61 %	1.00 %	5.40 %
日本株式	110 万円	21.57 %	4.80 %	22.15 %
先進国債券	200 万円	39.22 %	3.50 %	13.25 %
先進国株式	50 万円	9.80 %	5.00 %	19.59 %
新興国株式	50 万円	9.80 %	9.25 %	26.25 %
（信託報酬など			△ 0.00 %	）
計算結果	510 万円	100.00 %	4.00 %	9.70 %

期待リターン、リスクの値も変更可能です。またこのページ下部にある相関係数の値も変更可能です。
変更した結果はすぐ計算に反映されます。

2. あなたの運用資産の期待リターンとリスク

アセットアロケーションが決まると、資産全体の「期待リターン」と「リスク」が自動的に計算できます

期待リターン（年率）
4.00 %

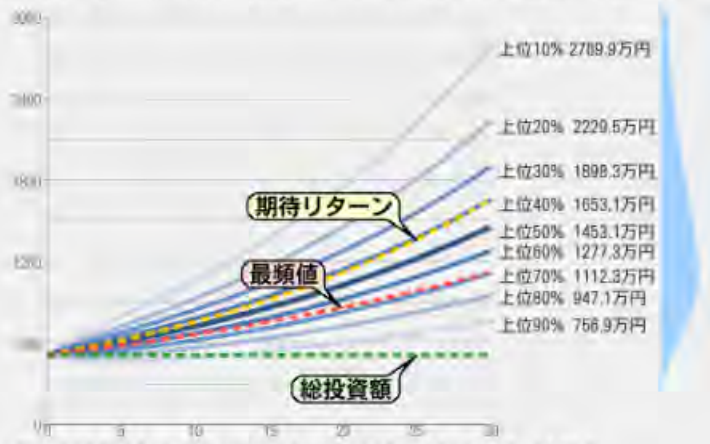
リスク（年率）
9.70 %

元本
510 万円

3. 長期投資による運用結果の予想

期待リターンとリスクをこのまま維持し続けた場合の、将来の運用結果が予想できます

積み立て投資の場合は、毎月の積立額を入力してください： 0 万円
（期待リターン 4.00 % ／ リスク 9.70 % ／ 元本 510 万円 ／ 年数 30 年）



期待値：1654.6　標準偏差：901.0　中央値：1453.1　最頻値：1120.8

- 30年間の総投資額は **510.0万円** です。
- いちばん起こりそうな運用結果は **1120.8万円** です（最頻値）。年率にして**約 2.7 %**です。
- 運用結果が **1112.3万円** 以上になる可能性は高く（確率70%）、
  もしかしたら **1453.1万円** 以上になるかもしれません（確率50%）。
  しかし、 **1898.3万円** 以上になる可能性はそれほど高くありません（確率30%）。
- 期待リターンの複利では **1654.6万円** になります（期待値）。ただしその確率は **39.9%** です。
- 元本割れする確率は **2.0%** です。
- 表示される確率や金額は「連続複利年率の収益率が正規分布する」ことを前提に計算されています。

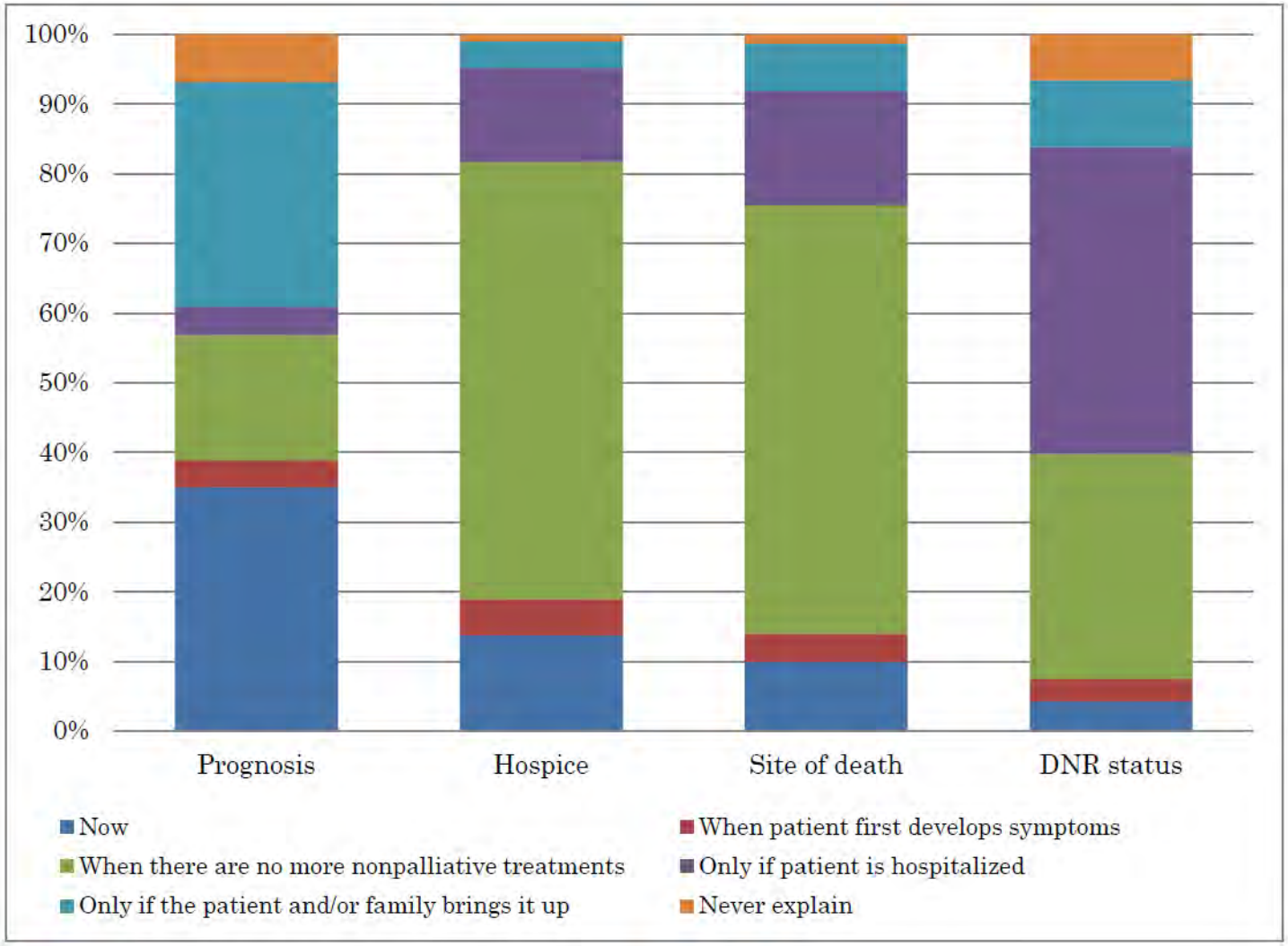
http://guide.fund-no-umi.com/tools/aa.html

Ideal Characteristics?

Prognosis	Aims of prognostication	Characteristics
Years	Initiation of ACP (global goals of care: GOC)	Rough idea
Months	ACP (Specific GOC: e.g., Cessation of chemotherapy, place of EOL)	High sensitivity
Weeks	Family's sick leave	High specificity
Days	Family's rest at home	High sensitivity
	Calling family living far away	High specificity
	Moving to a private room	High specificity
	Appropriateness of sedation	High specificity

Timing of EOLd Varies

479 JSMO Oncologists on a hypothetical patient with newly diagnosed metastatic cancer

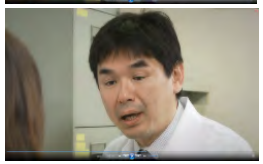


Mori M, et al. Oncologist 2015;20:1304-11.

A Video-Vignette Study to Explore the Best Practice in Prognostic Disclosure in Asia

- Design: Randomized, 2x2 cross-over video-vignette study
- P: 105 Women with invasive breast ca s/p surgery, w/o recurrence/metastasis
- I/C: 4 Videos (Explicitness +/- x Eye contact +/-)
- Explicitness +
  - ↓ Uncertainty, ↑ satisfaction without increasing anxiety
- Eye contact +

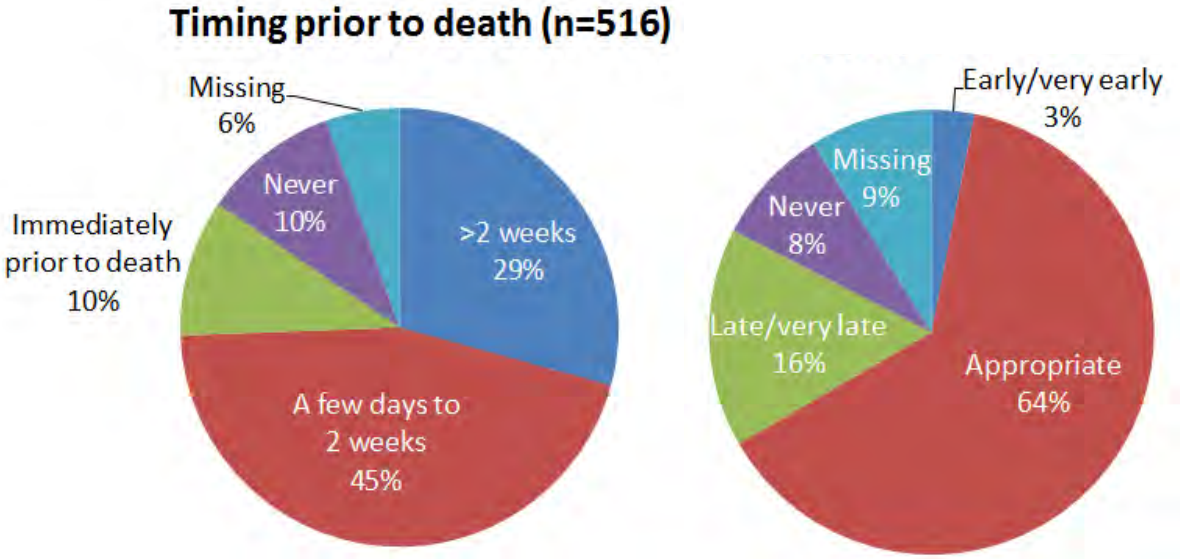
↑ Trust & c n, ↓ anger/sadness/fear/disgust/surprise



Mori M, Fujimori M, et al. MASCC 2018 (Oral)
Fujimori M, Mori M, et al. MASCC 2018 (ePoster)

Explanation about Impending Death to Families: When and How?

- Nationwide survey of 818 bereaved families of ca pts who died at PCUs
- Family-perceived need for improvements in the explanation about impending death
- Families' experiences



Variables	OR	95% CI	p
Patient's age	0.97	0.95 – 0.99	0.009
Explicit explanation about physical signs of impending death	0.67	0.51 – 0.88	0.004
Explanation of how long the patient and family could talk	0.67	0.51 – 0.88	<0.001
Excessive warning of impending death	1.45	1.03 – 2.03	0.033
Uncertainty caused by vague explanations about future changes	1.77	1.38 – 2.27	<0.001

Mori M. et al. BMJ Support Palliat Care 2018;8:221-8.

ACP + Prognostic Information

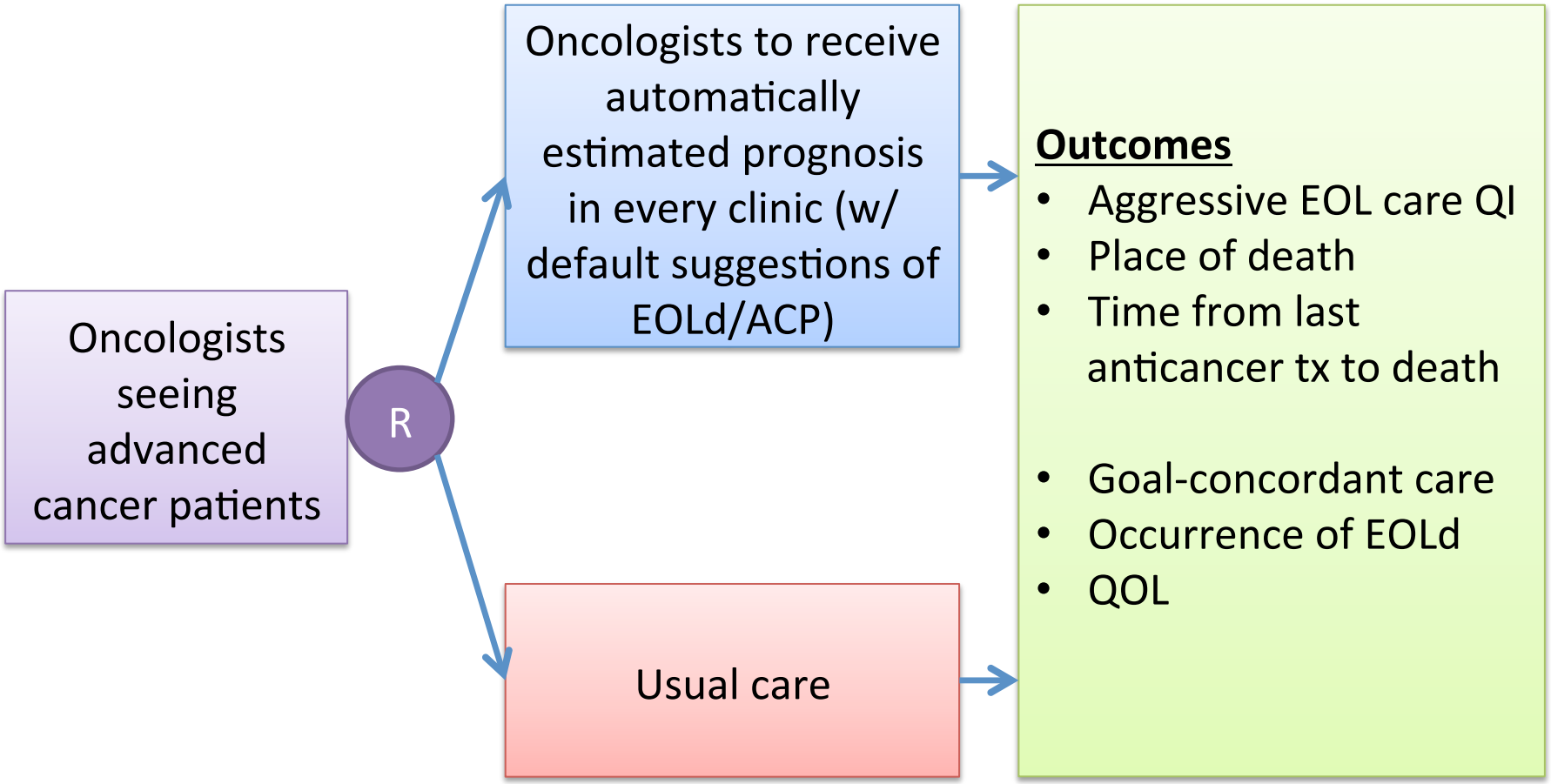
- Australian ACP Study
  - Adapted Respecting Patient Choices model + prognostic information

Table 3 Details and comparison between three randomised controlled trials (RCTs) of Advance Care Planning (ACP) in cancer care

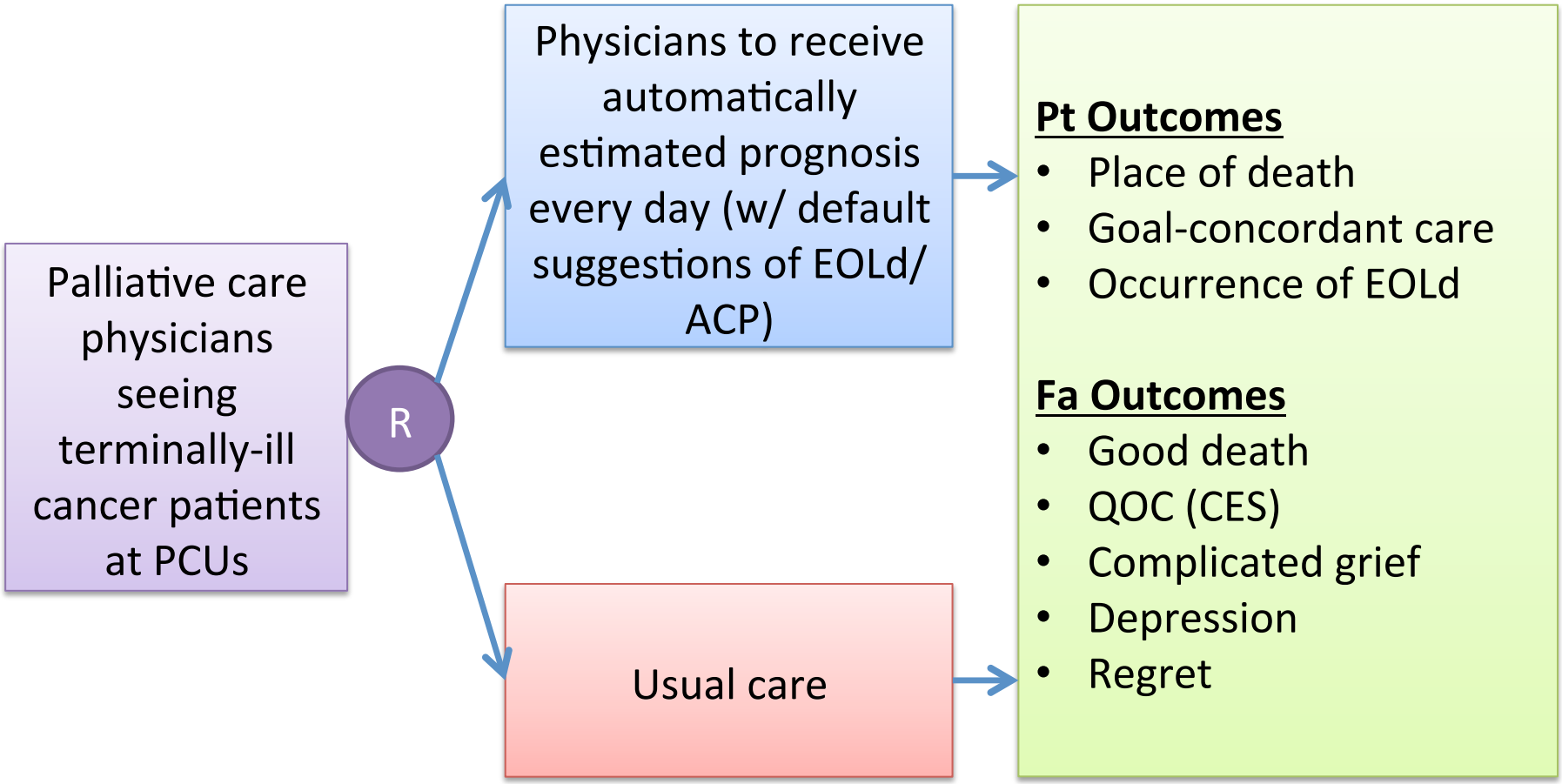
Study name	Study design	Sample size	Population	Intervention	Primary outcome	Shared patient outcomes	Additional features of each study
ACTION Study[27]	Cluster RCT in 6 European countries (BE, DK, IT, NL, SI, UK)	1360	Patients with advanced lung or colorectal cancer with an average life expectancy of 12 months	Respecting Choices model	Quality of life and symptoms	Goal concordant care Quality of life Quality of death/quality of end-of-life (EOL) care Satisfaction with the intervention	Qualitative study of patients, relative's and professional caregivers' experiences of involvement in ACP
Bernacki *et al*[26]	Cluster RCT, USA	426	Patients with advanced incurable cancer and a life expectancy of <12 months	A multicomponent, structured communication intervention	Receipt of goal-concordant care, and peacefulness at the EOL	Timing, place and prevalence of documentation about EOL care Place of death	Clinician outcome data—attitudes, confidence, acceptability, prognostic evaluation
Australian ACP study	One-to-one randomisation RCT, Australia	210	Patients with advanced cancer, and a life expectancy of 3–12 months	Adapted Respecting Patient Choices model + prognostic information	Family/friend-reported: (1) discussion with the patient about their EOL wishes and (2) perception that the patient's EOL wishes were met	Resource use/cost analysis Bereavement outcomes in relatives	Estimating and discussing survival scenarios

Johnson S, et al. BMJ Open 2016;6:e012387

Idea #1: Clinical Trial on Prognostication To Maximize Patient Outcomes (Tx)



Idea #2: Clinical Trial on Prognostication To Maximize Patient Outcomes (PCU)



Future Research in Prognostication Conclusions

- May improve the accuracy
  - ↑ Variables, statistics
- May identify tools that best fit specific goals
  - Balance between feasibility and accuracy
- May improve the reliability
  - Objective variables
- May identify best outputs
  - Within and beyond health care
- May conduct clinical trials utilizing prognostic disclosure to improve short- and long-term patient and family outcomes