ASGO Webinar #45

When to Stop Chemotherapy for Gynecologic Cancer Patients?

2024/02/22

St. Luke International Hospital MediLocus
Mikiko Asai-Sato MD. Ph. D.

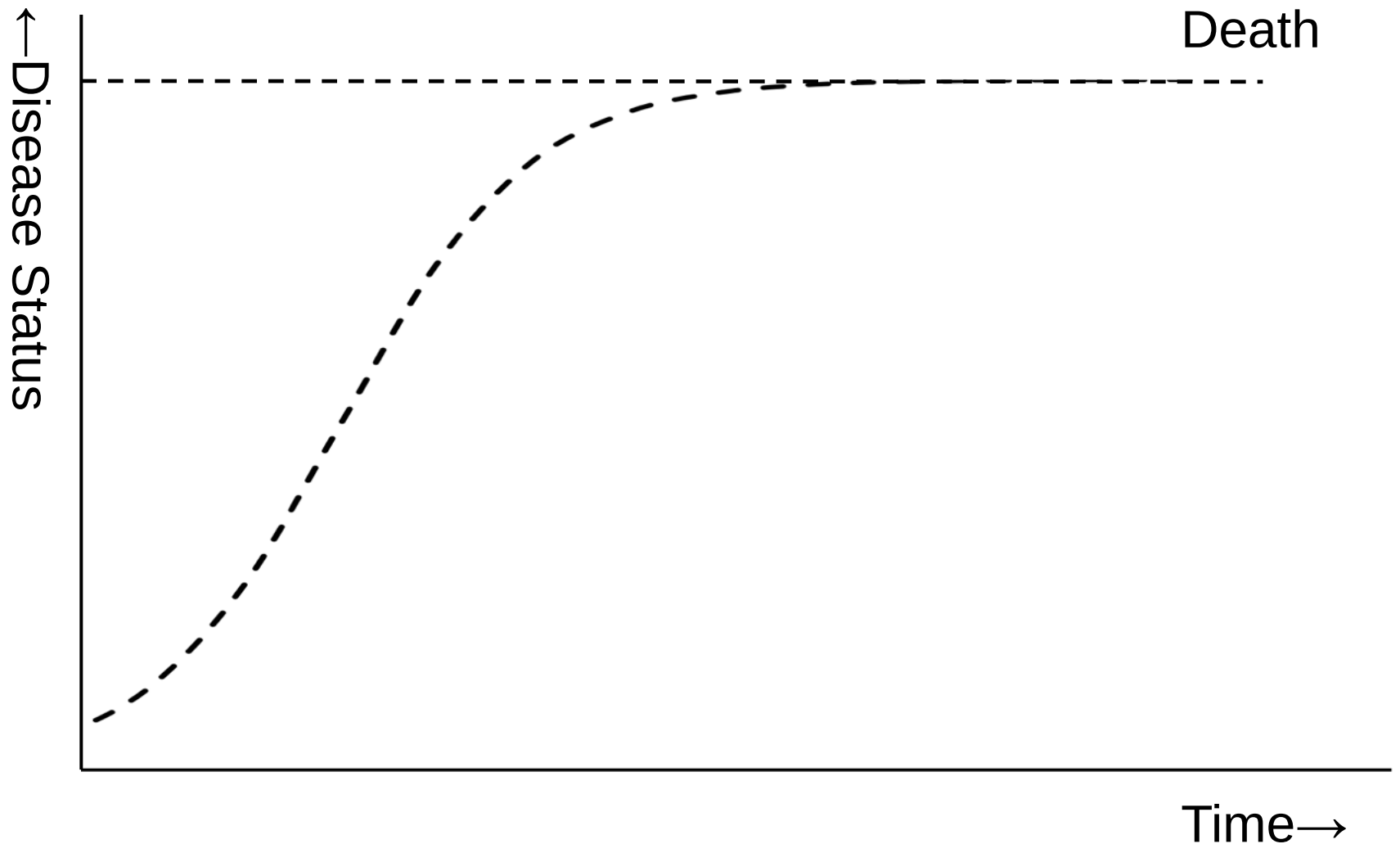
ASGO Webinar #45
Disclosure of Conflict of Interest

Mikiko Asai-Sato

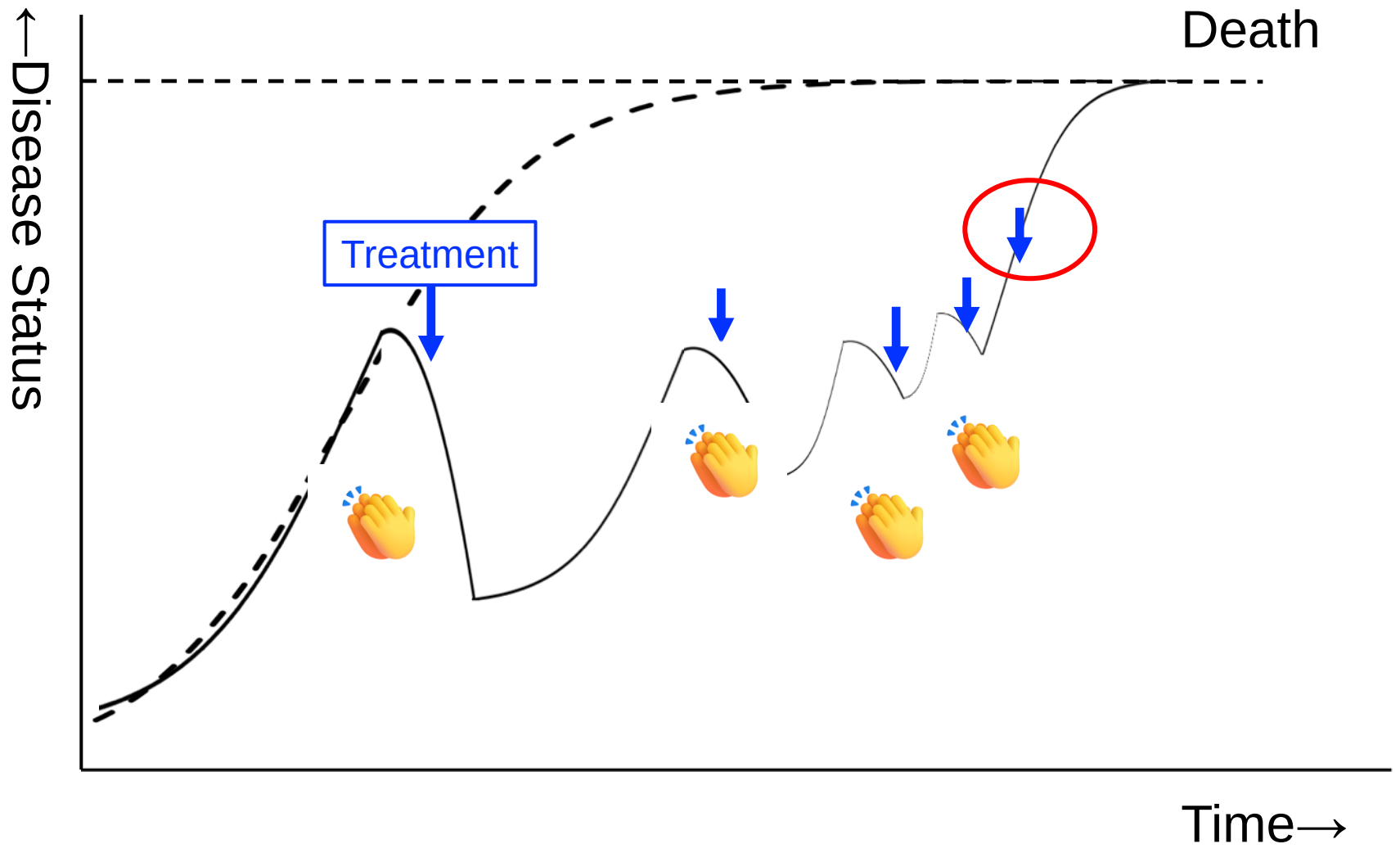
I have no COI

With regard to our presentation

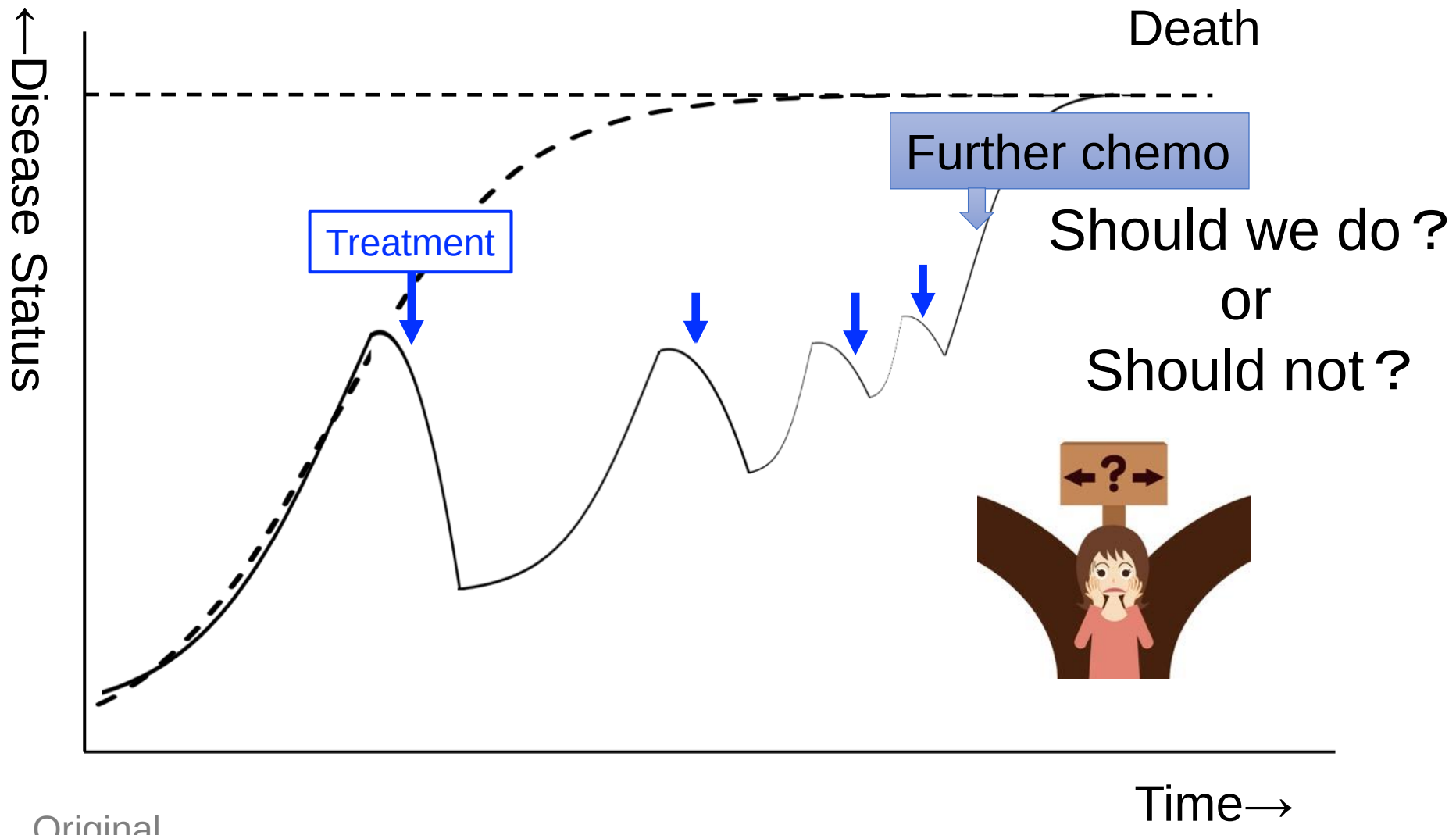
Process of advanced ovarian cancer (an example)



Process of advanced ovarian cancer (an example)



Process of advanced ovarian cancer (an example)



Original

J Gynecol Oncol. 2021 Mar;32(2):e49
https://doi.org/10.3802/jgo.2021.32.e49
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Practice Guideline

Check for updates

The 2020 Japan Society of Gynecologic Oncology guidelines for the treatment of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer

7. CQ 30: For patients being considered for chemotherapy beyond third-line chemotherapy, is further chemotherapy recommended?

Recommendation:

After adequate discussion with the patients and careful assessment of their condition, the administration of chemotherapy with different regimens is suggested if they are judged to be less disadvantageous owing to their adverse effects.

Grade 2 (↑); level of evidence: C; consensus: 100%

I will be presenting the data behind this CQ recommendation.

How many patients undergo late-line treatment?

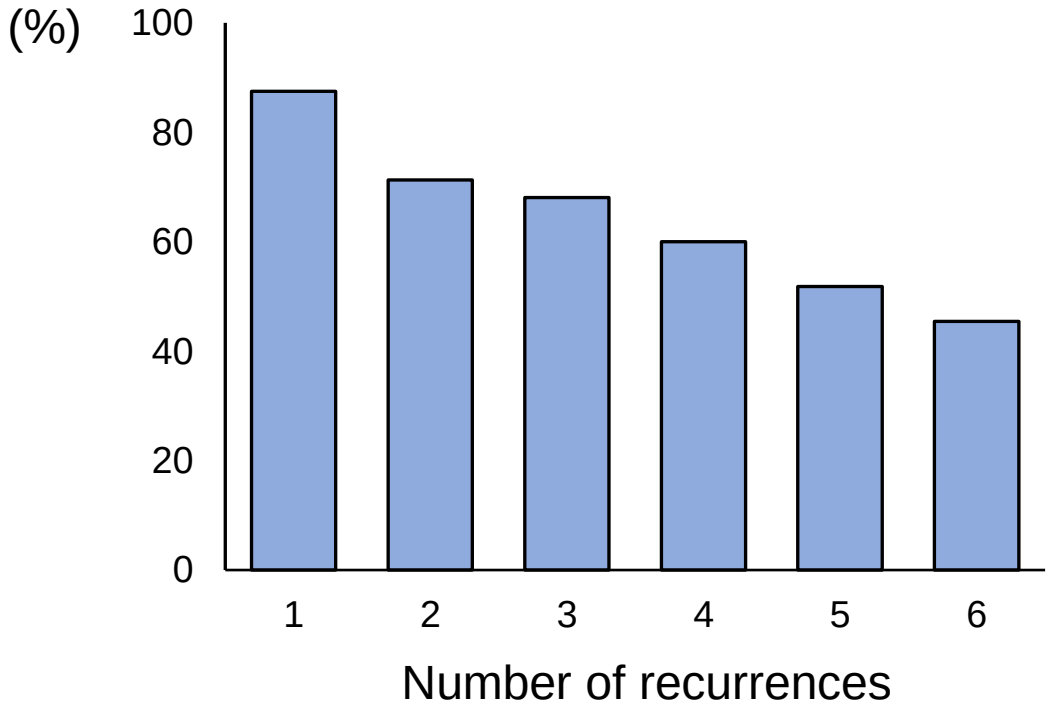
Table 2
Overall survival from diagnosis and each subsequent relapse/progression

	Median OS (months)	Overall survival %				
		1 year	2 years	3 years	4 years	5 years
From diagnosis						
n = 136	32	87	63	41	27	19
From 1st relapse						
A (n = 120)	11	49	26	12	0	
T (n = 105)	14	53	28	14	0	
NT (n = 15)	4	22	60	0		
From 2nd relapse						
A (n = 101)[a]	10	36	9	6	0	
T (n = 72)	14	42	13	8	0	
NT (n = 29)	8	0				
From 3rd relapse						
A (n = 69)	6	28	8	0		
T (n = 47)	6	37	12	0		
NT (n = 22)	2	6	0	0		
From 4th relapse						
A (n = 45)[a]	4	21	4	0		
T (n = 27)	7	30	5	0		
NT (n = 18)	1	6	6	0		
From 5th relapse						
A (n = 27)	3	7	0			
T (n = 14)	8	13	0			
NT (n = 13)	1	0	0			
From 6th relapse						
A (n = 11)	4	0				
T (n = 5)	5	0				
NT (n = 6)	2	0				

Hoskins JK et.al. Gynecol Oncol. 2005

Single-center retrospective analysis for 120 cases of recurrent epithelial ovarian cancer

Percentage undergoing chemotherapy after relapse
(Data from the paper was graphed by the speaker.)



How effective is late-line treatment?

Hoskins JK et.al. Gynecol Oncol. 2005

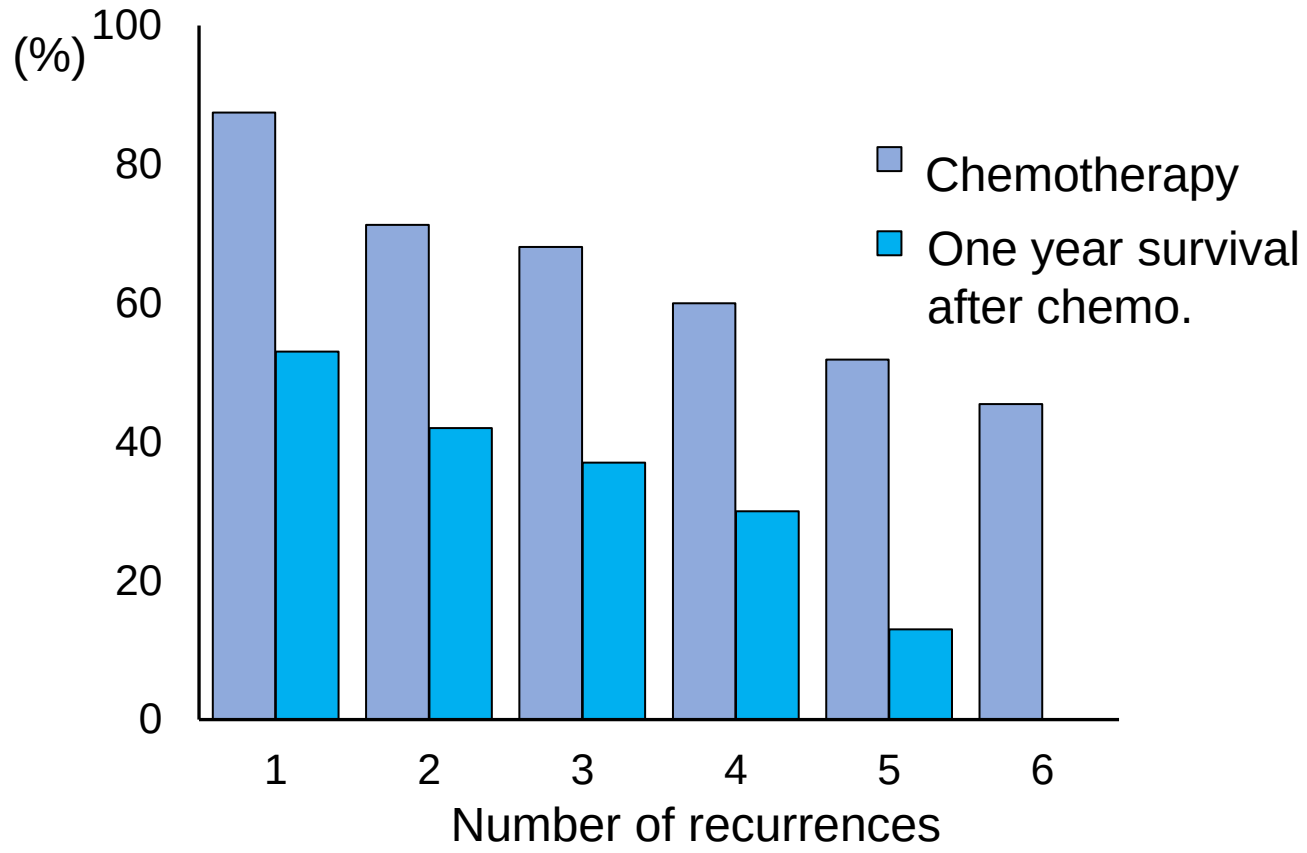
Single-center retrospective analysis for 120 cases of recurrent epithelial ovarian cancer

Table 2
Overall survival from diagnosis and each subsequent relapse/progression

	Median OS (months)	Overall survival %				
		1 year	2 years	3 years	4 years	5 years
From diagnosis						
n = 136	32	87	63	41	27	19
From 1st relapse						
A (n = 120)	11	49	26	12	0	
T (n = 105)	14	53	28	14	0	
NT (n = 15)	4	22	60	0		
From 2nd relapse						
A (n = 101)[a]	10	36	9	6	0	
T (n = 72)	14	42	13	8	0	
NT (n = 29)	8	0				
From 3rd relapse						
A (n = 69)	6	28	8	0		
T (n = 47)	6	37	12	0		
NT (n = 22)	2	6	0	0		
From 4th relapse						
A (n = 45)[a]	4	21	4	0		
T (n = 27)	7	30	5	0		
NT (n = 18)	1	6	6	0		
From 5th relapse						
A (n = 27)	3	7	0			
T (n = 14)	8	13	0			
NT (n = 13)	1	0	0			
From 6th relapse						
A (n = 11)	4	0				
T (n = 5)	5	0				
NT (n = 6)	2	0				

Percentage undergoing chemotherapy after relapse

(Data from the paper was graphed by the speaker.）



Efficacy of late-line chemotherapy for recurrent ovarian cancer (ROC)

Griffiths RW et al. Int J Gynecol Cancer. 2011

A retrospective study of 274 cases of platinum-resistant ROC

	Line of Therapy After Platinum Resistance				
	First	**Second**	**Third**	**Fourth**	**Fifth+**
n	274	196	127	62	30
Radiological response rate (CR + PR), %	15.7	8.1	3.1	1.6	0
Clinical benefit rate (CR, PR + SD), %	36.9	30.6	18.1	17.7	3.3
Serological response rate, %	49.3	37.1	32.2	23.7	13.3
PFI, median (95% CI), wk	18 (15–21)	16 (14–18)	13 (10–16)	13 (8–17)	8 (7–9)
OS, median (95% CI), wk	61 (53–69)	48 (40–56)	40 (33–47)	38 (22–53)	26 (21–31)

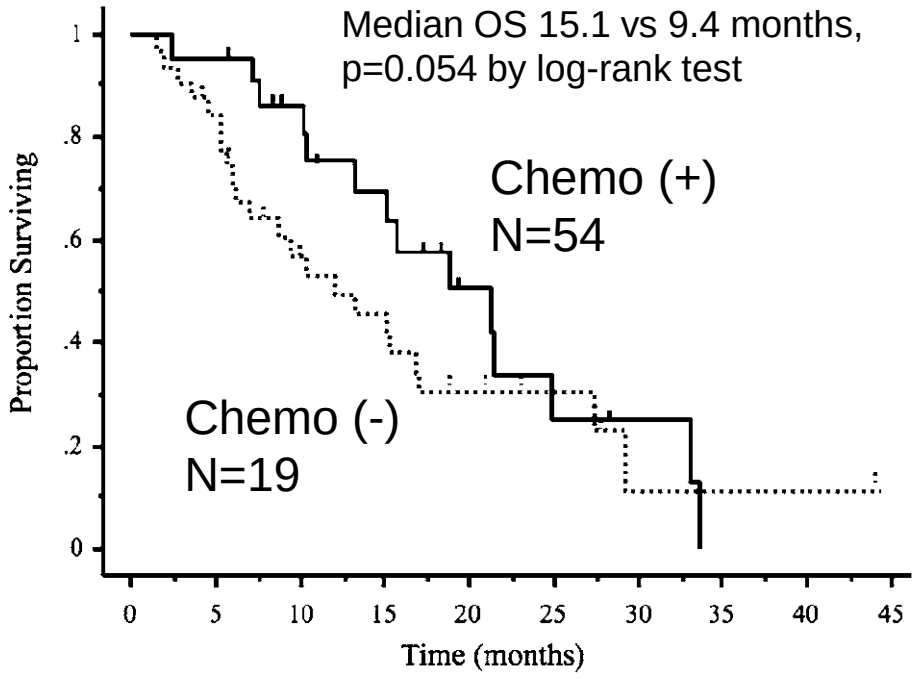
DISEASE STATUS[e,cc,dd] **THERAPY FOR PERSISTENT DISEASE OR RECURRENCE[m,ff,gg,hh]**

[ii] Patients who progress on two consecutive therapy regimens without evidence of clinical benefits have diminished likelihood of benefitting from additional therapy. Decisions to offer clinical trials, supportive care only, or additional therapy should be made on a highly individual basis.

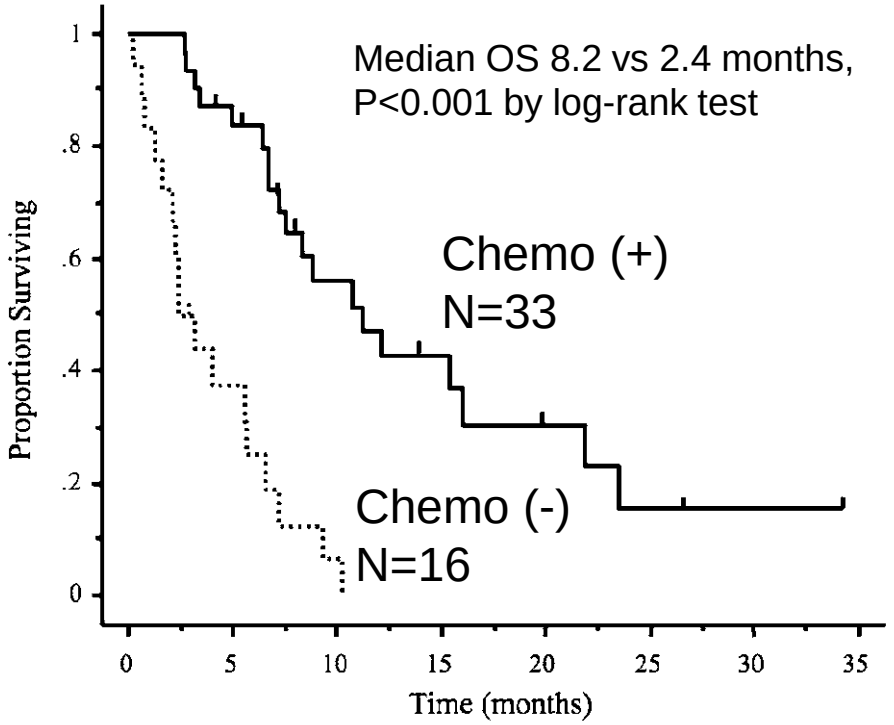
Does late-line chemotherapy for ROC contribute to a better prognosis?

Nishio S et. al., J Cancer Res Clin Oncol. 2009

Single-center retrospective analysis for 111 patients of ROC



Overall survival at 3rd line chemo.



Overall survival at 4th line chemo.

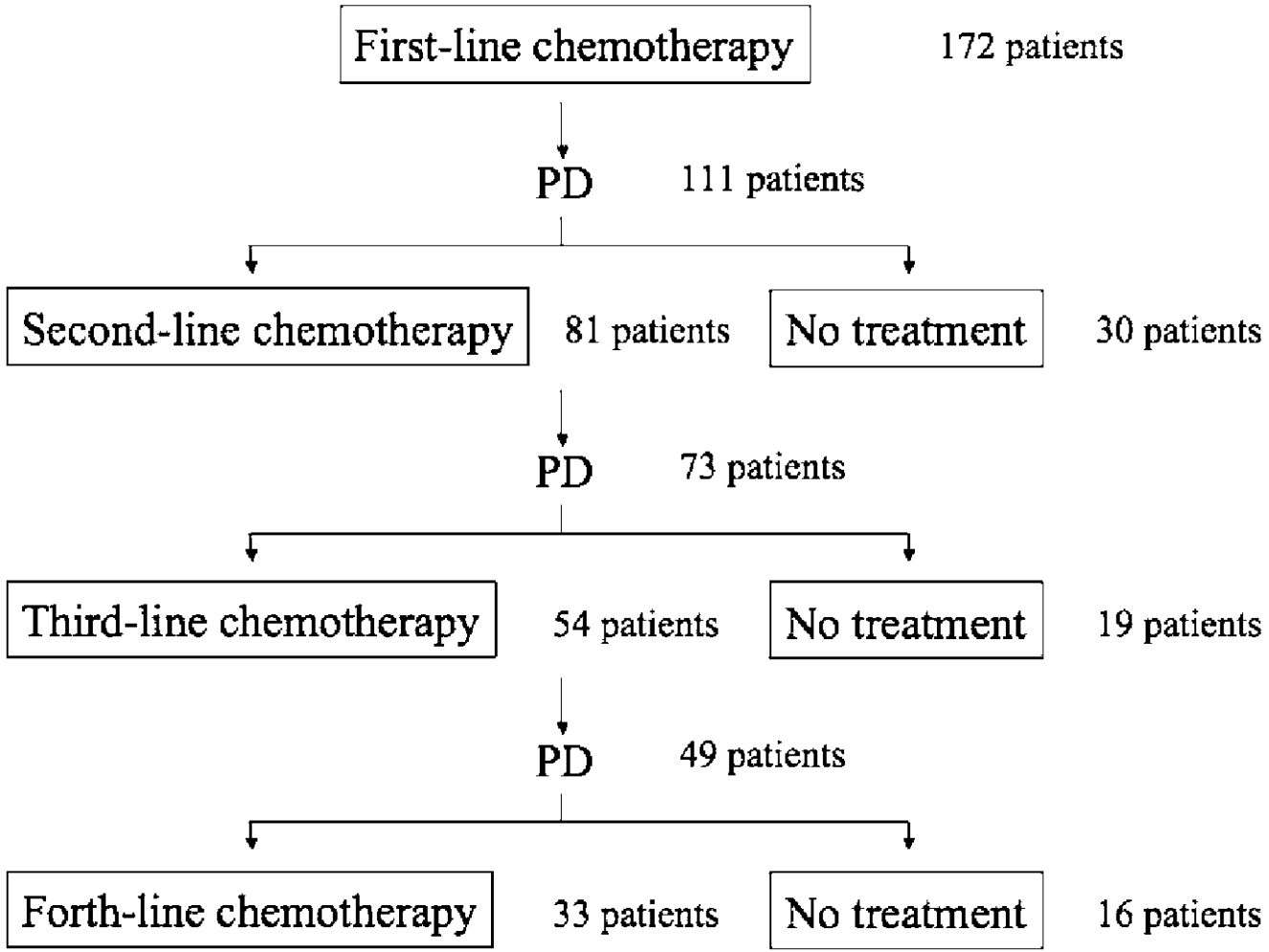


Fig. 1 Schema of treatment

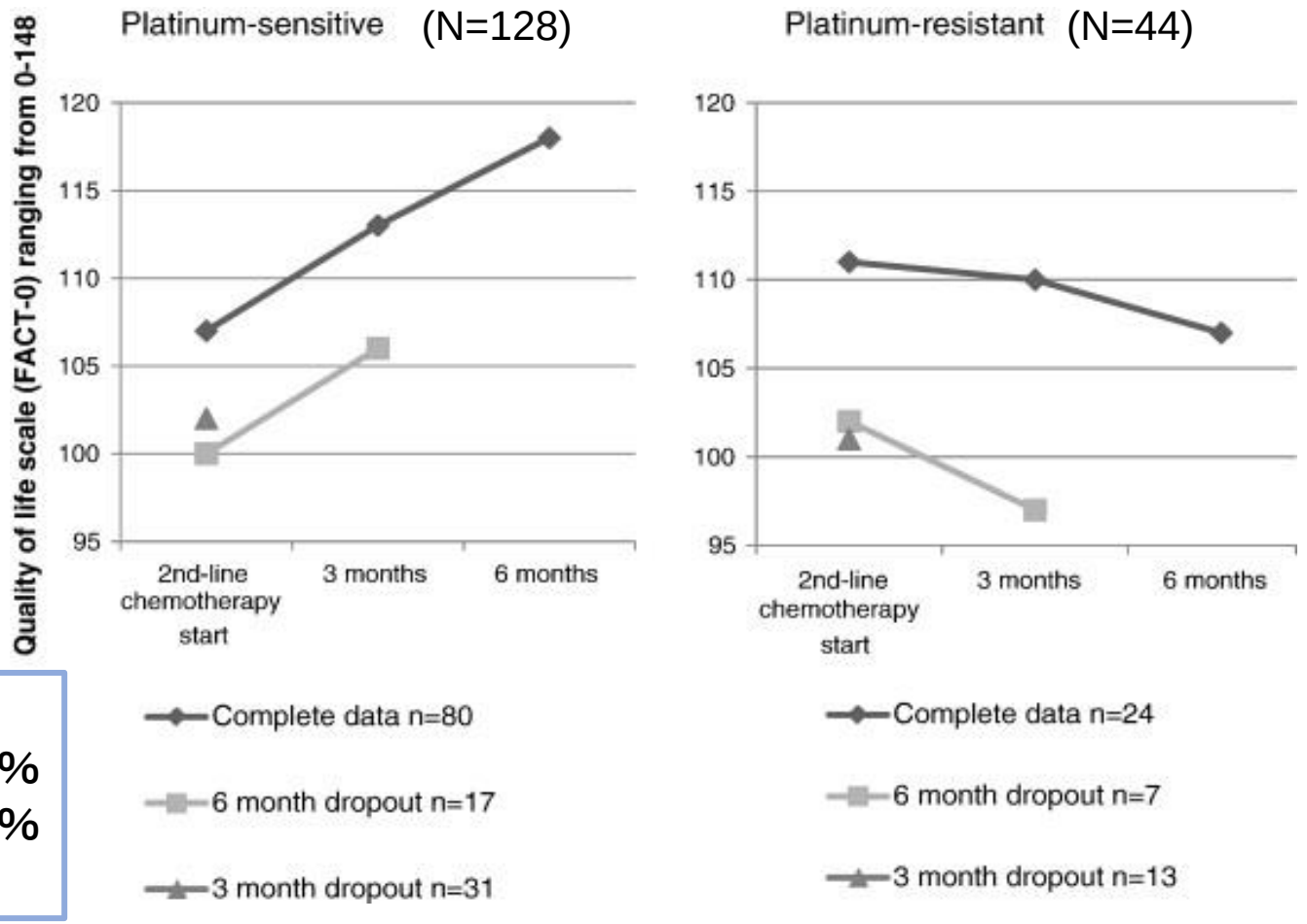
This study has a selection bias to treat only those likely to benefit from chemo.

Nishio S et. al., J Cancer Res Clin Oncol. 2009

Does late-line chemotherapy for ROC contribute to better QOL?

Beesley VL et. al, Gynecol Oncol 2014

Assessment of QOL change over time after 2nd-line chemotherapy (N=172)



Beneficial to some patients, harmful to about the same number of patients

QOL
Improved 51%
No change 40%
Worsen 9%

QOL
Improved 26%
No change 42%
Worsen 31%

Factors of ROC Patients Benefiting from Late-line Chemo.

Possibly beneficial

- Good response to the previous chemotherapy (Villa 1999)
- Optimal primary tumor debulking and platinum sensitivity (Hanker 2012)
- Primary drug-free interval more than 6 months (Nishio 2009)

Possibly unbeneficial

- Poor PS and/or QOL (Griffinths2011, Utsumi 2017, Roncolato 2017 etc)
- Disease progression on 2 consecutive lines (Hanker 2012, Griffiths2011)
- TFI less than three months after second-line chemotherapy (Yoshihama 2015)
- TFI less than 6 months since two previous treatment (Hoskins 2005)
- Abdominal/gastrointestinal symptom (Roncolato 2017, Walczak 2017)
- High CA125, WBC, Cr level Griffiths 2011, Utsuni 2017)

There is no decisive factor to judge.

Original

J Gynecol Oncol. 2021 Mar;32(2):e49
https://doi.org/10.3802/jgo.2021.32.e49
pISSN 2005-0380·eISSN 2005-0399

JOURNAL OF GYNECOLOGIC ONCOLOGY

Practice Guideline

The 2020 Japan Society of Gynecologic Oncology guidelines for the treatment of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer

7. CQ 30: For patients being considered for chemotherapy chemotherapy, is further chemotherapy recommended?

Recommendation:

After adequate discussion with the patients and careful assessment of their condition, the administration of chemotherapy with different regimens is suggested if they are judged to be less disadvantageous owing to their adverse effects.

Grade 2 (↑); level of evidence: C; consensus: 100%

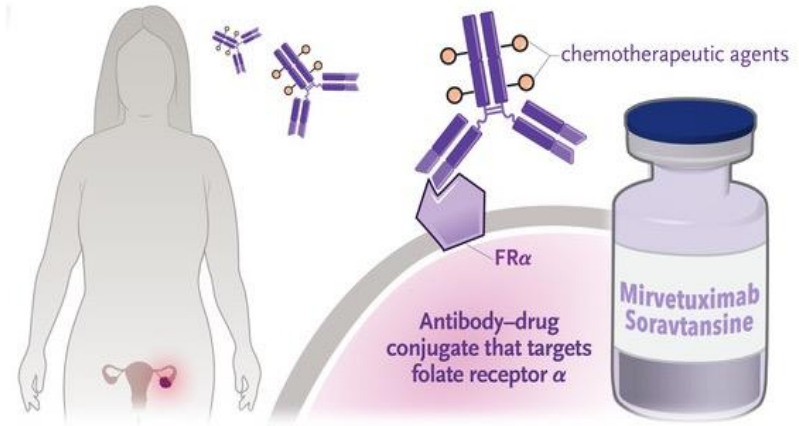
You may find this recommendation vague.

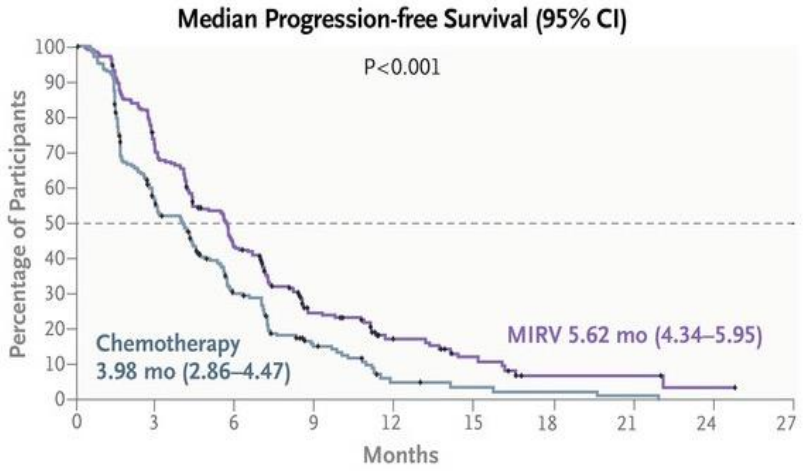
The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Mirvetuximab Soravtansine in FRα-Positive, Platinum-Resistant Ovarian Cancer

Moore KN et al. DOI: 10.1056/NEJMoa2309169





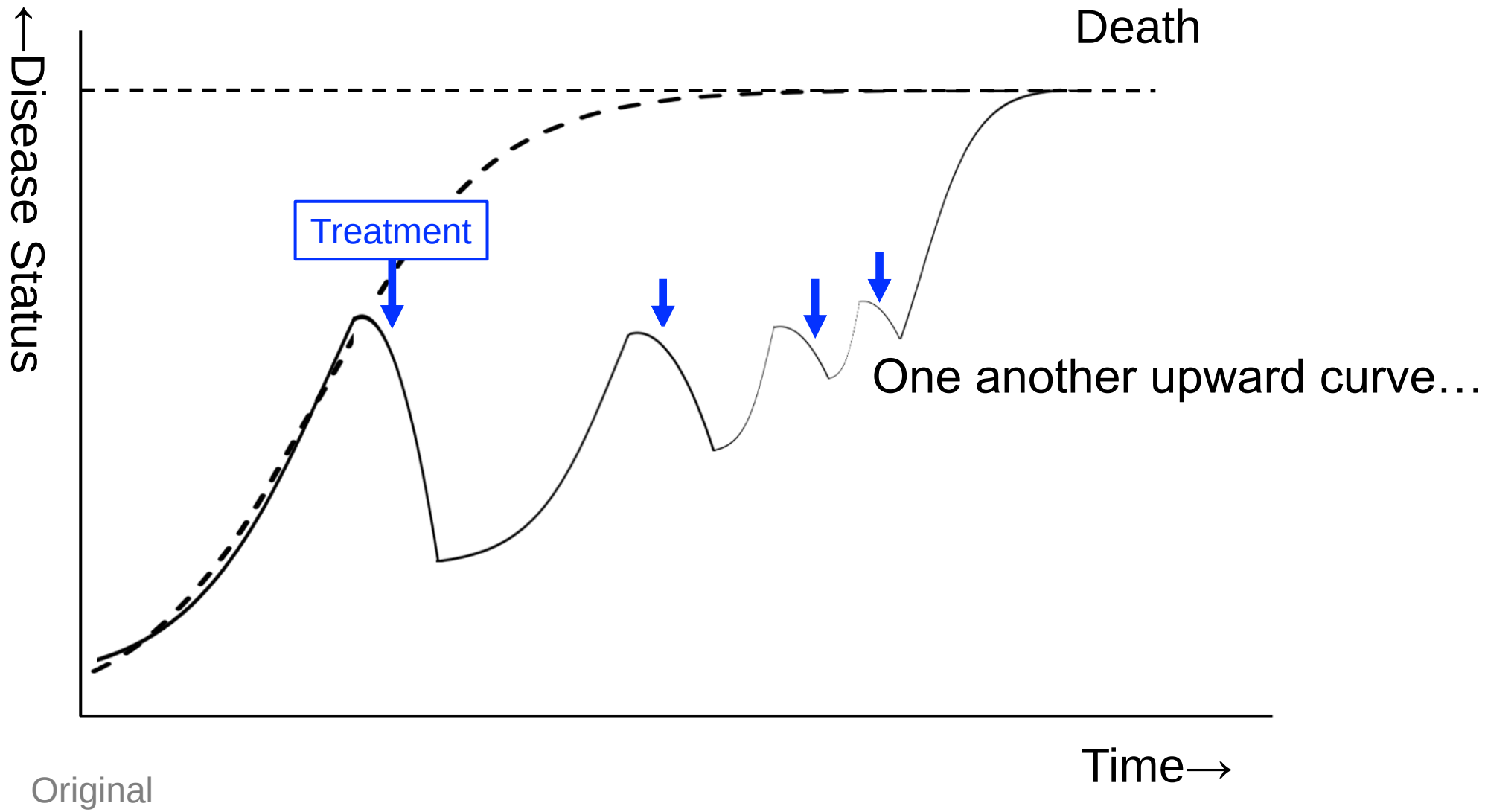
A great game-changer has descended!

Various other immunotherapy and molecular-targeted therapy drugs may become available in the future!

But still…

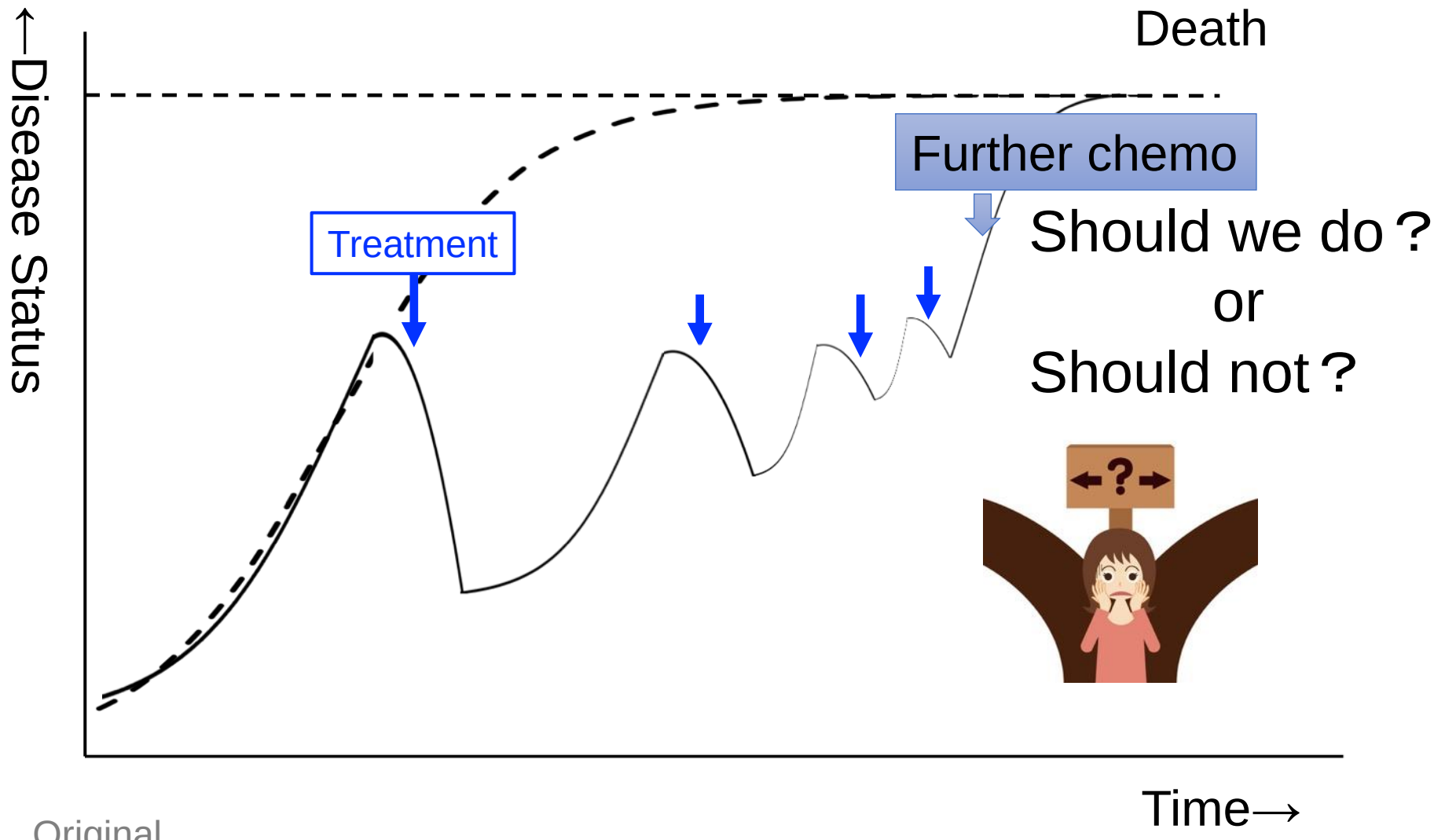
KN Moore et al. N Engl J Med 2023;389:2162-2174.

Process of advanced ovarian cancer (an example)



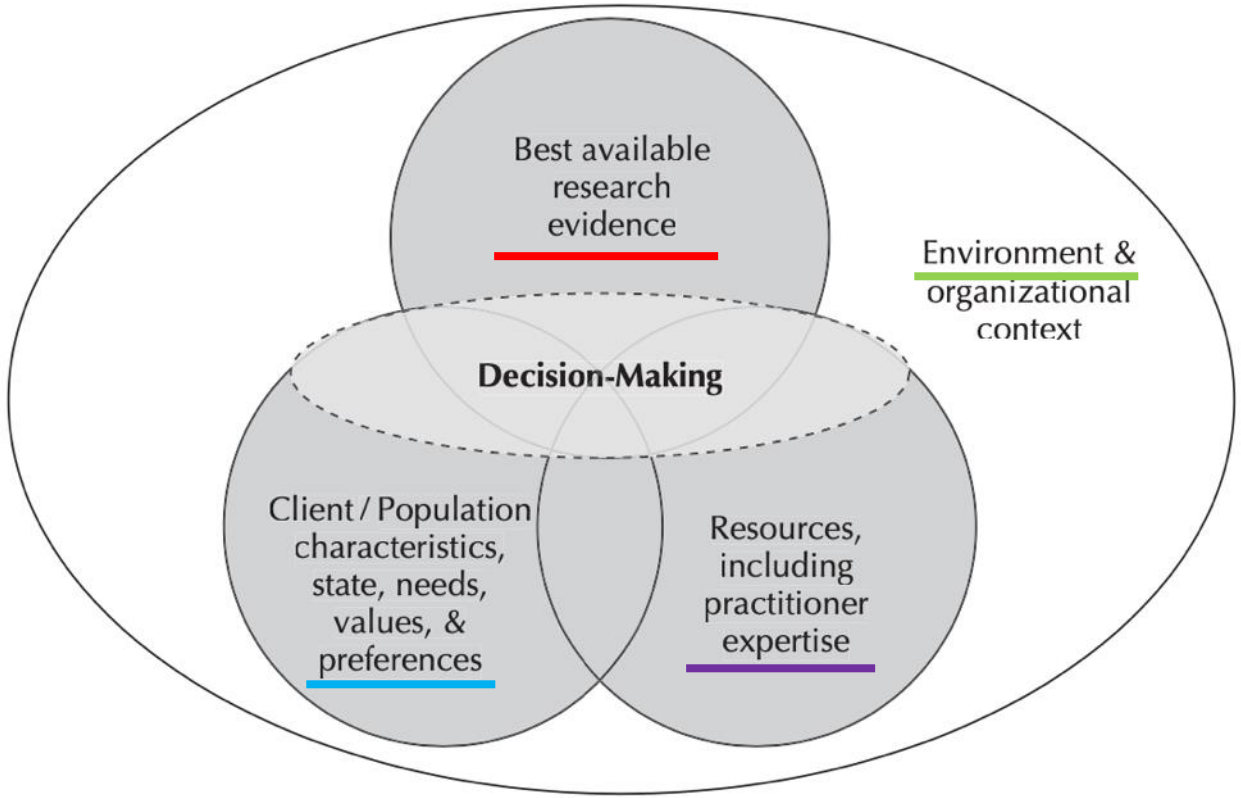
Original

Process of advanced ovarian cancer (an example)



Original

Evidence-based clinical decisions



Decision is made upon combination of
Research evidence
Environment & Organizational Context
Patients' preferences
Experts' experience and knowledge

In situations where there is little scientific evidence, medical decisions are made based on the **patient's preferences** and the practitioner's experience.

Shared Decision Making is essential in this situation.

Spring, B. and Hitchcock, K. (2010). Evidence-Based Practice. In The Corsini Encyclopedia of Psychology (eds I.B. Weiner and W.E. Craighead)

Shared Decision Making:

A collaborative process that involves a person and their healthcare professional working together to reach a joint decision about care.

NICE Guideline, No. 197

London: National Institute for Health and Care Excellence (NICE); 2021 Jun 17.
ISBN-13: 978-1-4731-4145-2

Shared Decision Making: **A collaborative process** that involves a person and their healthcare professional working together to reach a joint decision about care.

Concierge:
Perhaps he would like typical Japanese cuisine.

Tourist:
I am searching for a restaurant to have dinner.
Today is my first day in Japan.

Shared Decision Making: **A collaborative process** that involves a person and their healthcare professional working together to reach a joint decision about care.

Concierge:
We have a great sushi place in our hotel.

The fancy Sushi restaurant is a bit too expensive for me….

I am fond of raw seafood dishes, but I would like to visit a casual restaurant today.

Shared Decision Making: **A collaborative process** that involves a person and their healthcare professional working together to reach a joint decision about care.

How about trying out the local Japanese restaurant (Izakaya) near our hotel? They serve delicious seafood and rice bowls.

Shared Decision Making: **A collaborative process** that involves a person and their healthcare professional working together to reach a joint decision about care.

How about trying out the local Japanese restaurant near our hotel? They serve delicious seafood and rice bowls.

They may not even speak English at a local place. I am exhausted after a long flight…

Today, we prefer a restaurant where tourists can easily enter.

Shared Decision Making: **A collaborative process** that involves a person and their healthcare professional working together to reach a joint decision about care.

There is a Japanese restaurant in the next block. They have the menu book in English.

We go there. Thank you!

Shared Decision Making: **A collaborative process** that involves a person and their healthcare professional working together to reach a joint decision about care.

The outcome: Japanese restaurant for tourists.

It may be less tasty than a Sushi restaurant or local restaurant.
It may be more expensive than a local restaurant.

I am going to that local restaurant tomorrow.
Maybe the Sushi restaurant on the last day.

The discussion served for…
Satisfaction
and
Future decision making

What is necessary for the success of shared decision-making？

Medical provider (Concierge)

- ✓ Information
- ✓ Ability to perceive other’s feeling
- ✓ Communication skill

Patient (Tourist)

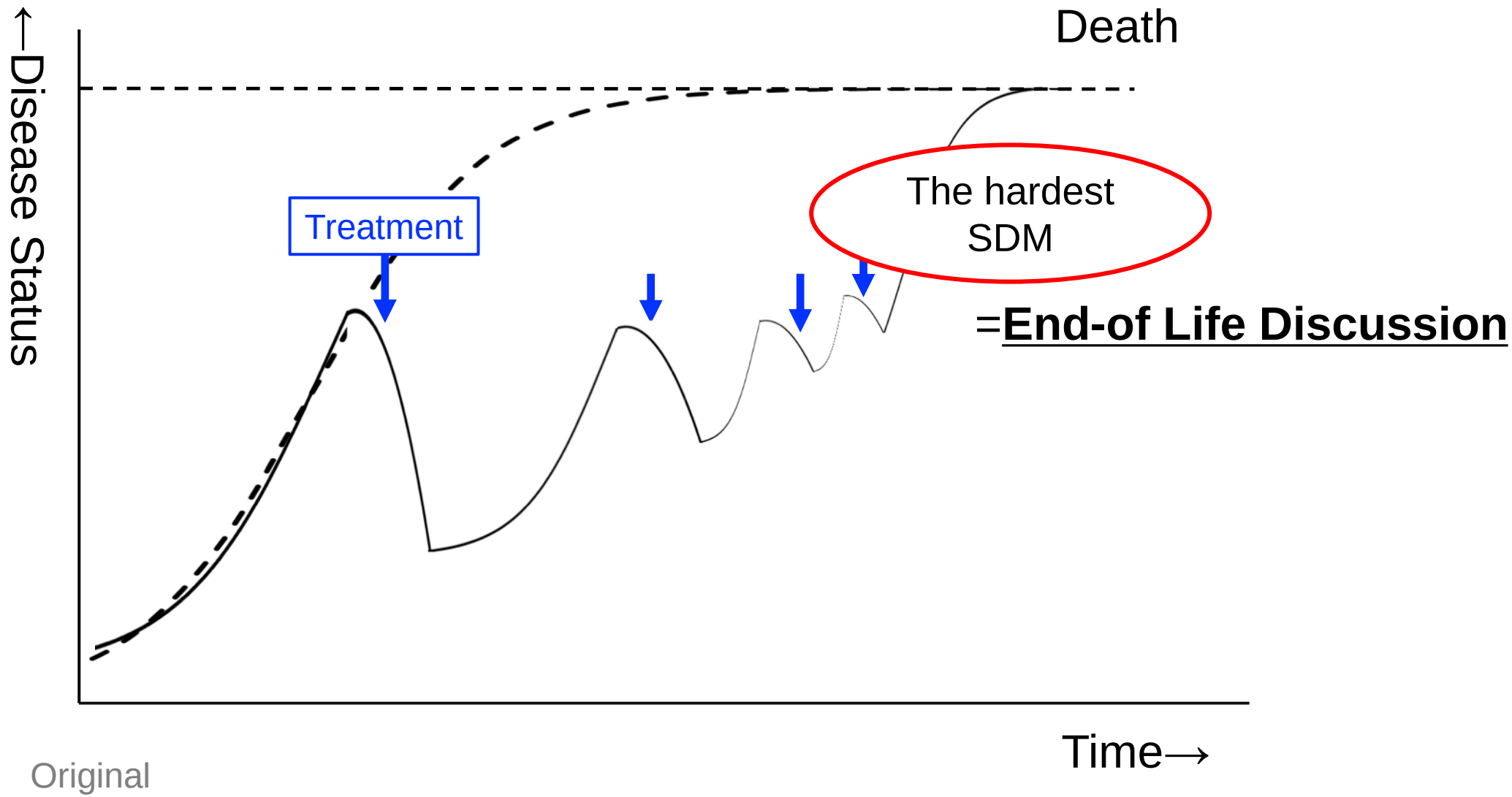
- ✓ Knowledge
- ✓ Understanding of one's own needs
- ✓ Verbally express one’s needs

Interaction

- ✓ Relationship of trust

We need practice for SDM!

Process of advanced ovarian cancer (an example)



Original

What is necessary for the success of shared decision-making？

Medical provider (Concierge)

- ✓ Information
- ✓ Ability to perceive other’s feeling
- ✓ Communication skill

Patient (Tourist)

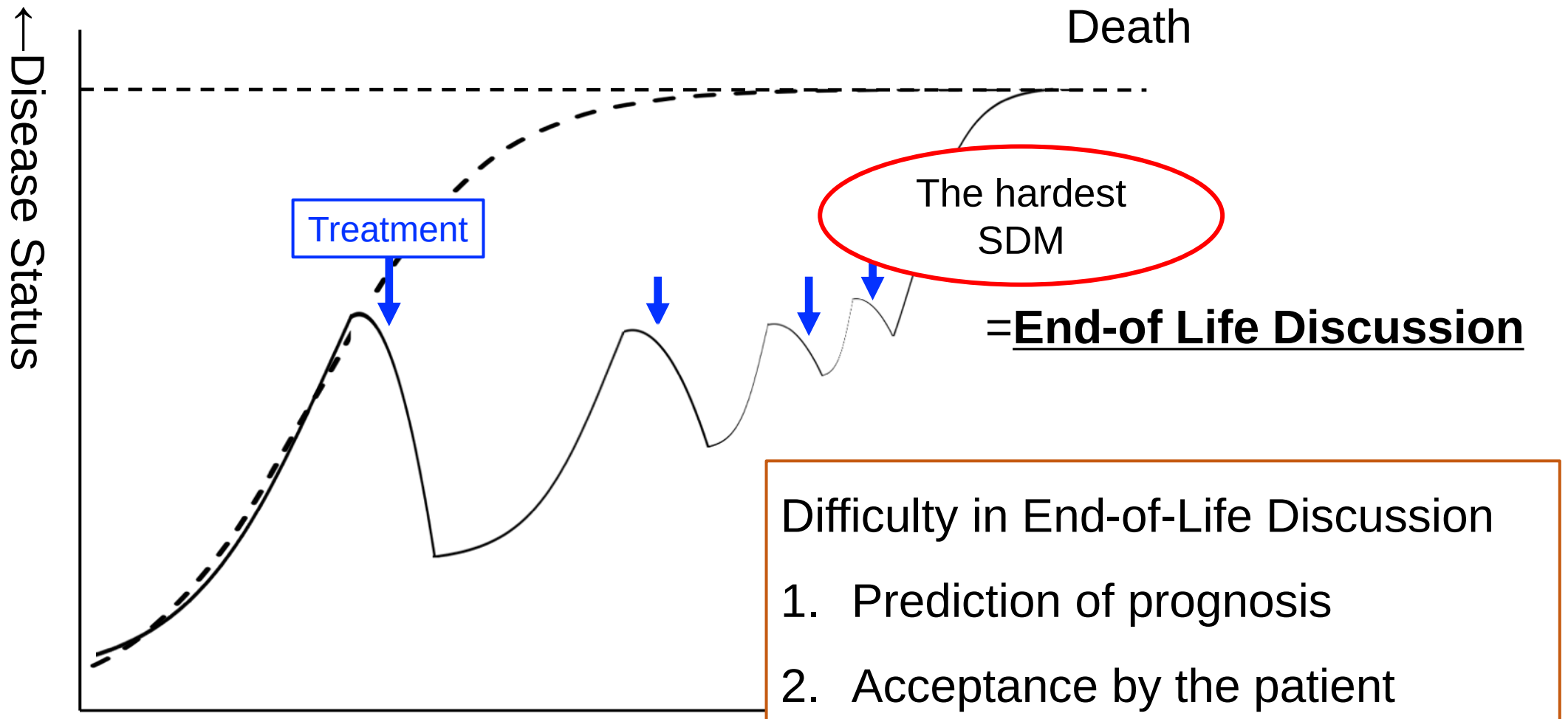
- ✓ Knowledge
- ✓ Understanding of one's own needs
- ✓ Verbally express one’s needs

Interaction

- ✓ Relationship of trust

We need practice for SDM!

Process of advanced ovarian cancer (an example)

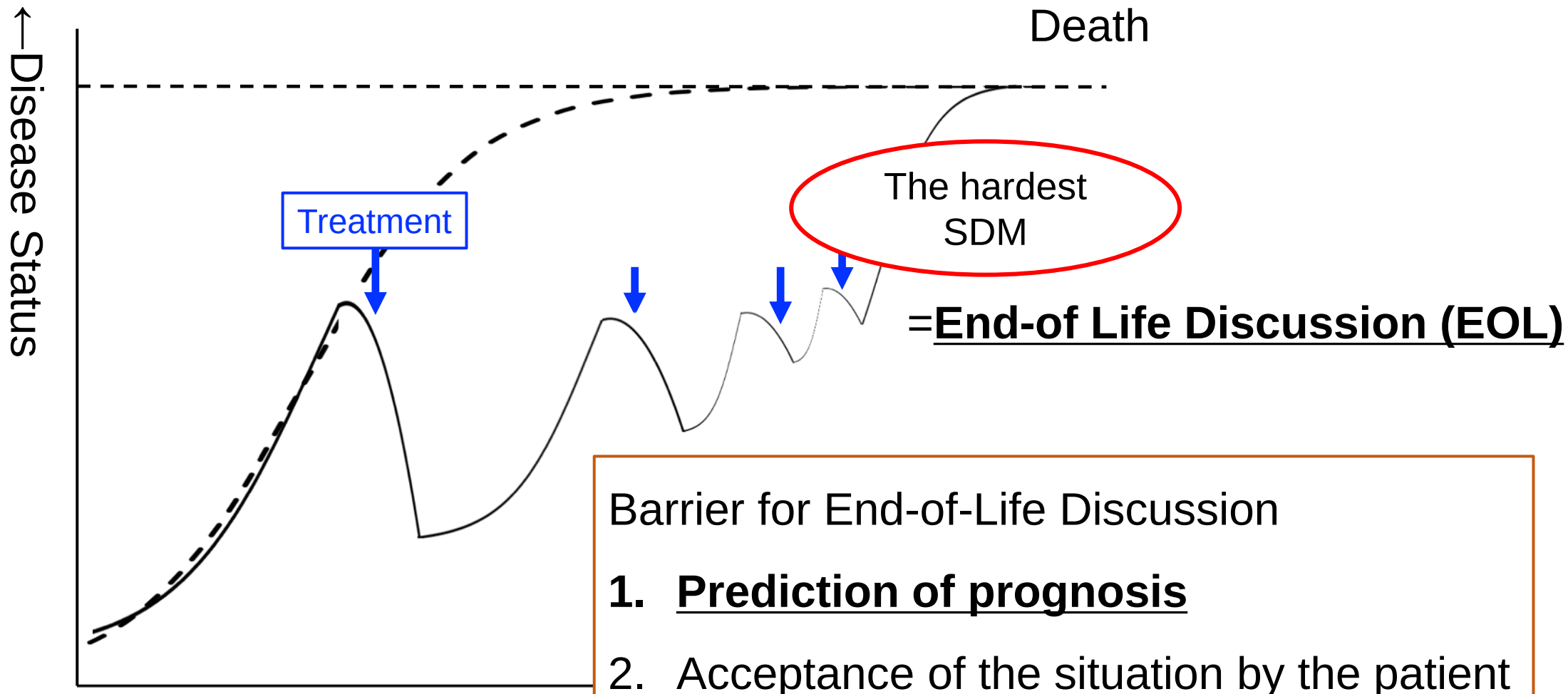


Original

Difficulty in End-of-Life Discussion

1. Prediction of prognosis
2. Acceptance by the patient
3. The pain of discussing bad news

Process of advanced ovarian cancer (an example)



Original

Barrier for End-of-Life Discussion

1. **Prediction of prognosis**
2. Acceptance of the situation by the patient
3. The pain of discussing bad news

Predicting survival in cancer patients is difficult

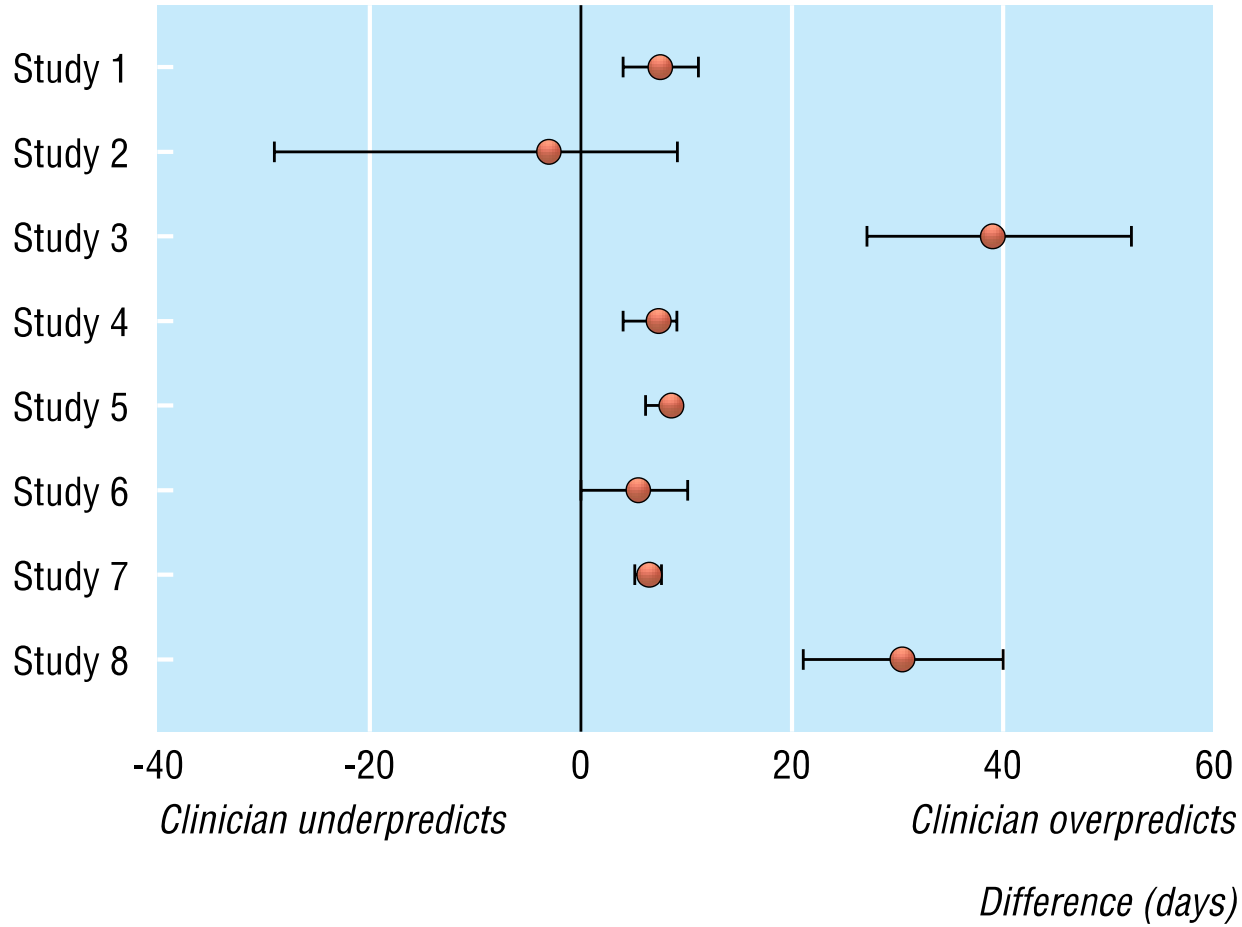


Fig 3 Difference between actual survival and clinical prediction of survival for terminally ill cancer patients (median and 95% confidence interval)

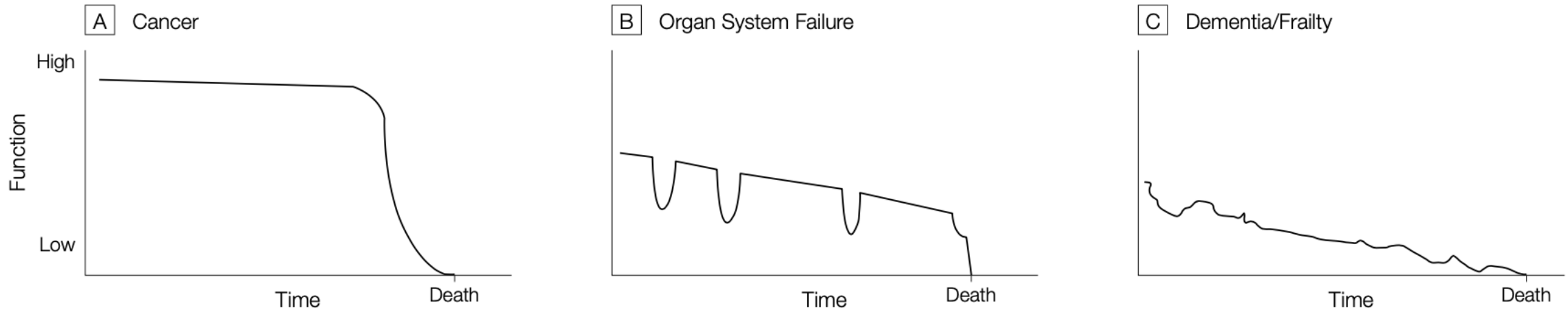
Clinicians often overestimate survival.

- Clinicians like to be optimistic about their patients' condition
- Cancer prognosis prediction is challenging due to the disease's nature.

Systematic review by Glare P, et al BMJ. 2003

Predicting survival in cancer patients is difficult

Figure. General Trajectories of Function and Well-being Over Time in Eventually Fatal Chronic Illnesses



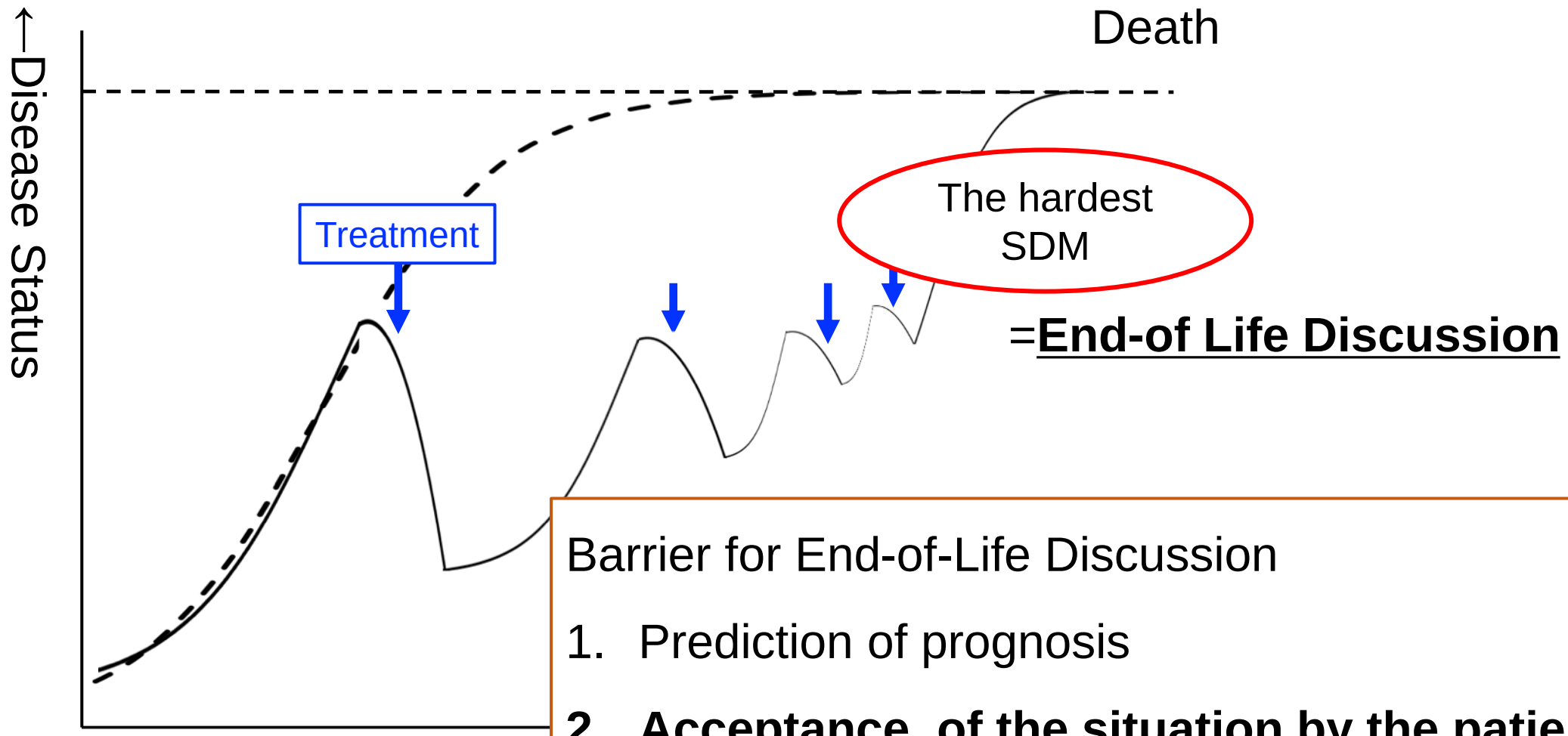
Rapid decline a few months prior to their death.

The gradual decline over time slowly.

Lynn J. et al. JAMA 2001

- It is hard to predict when the change is coming.
- As a result, we need to start EOL in advance.

Process of advanced ovarian cancer (an example)



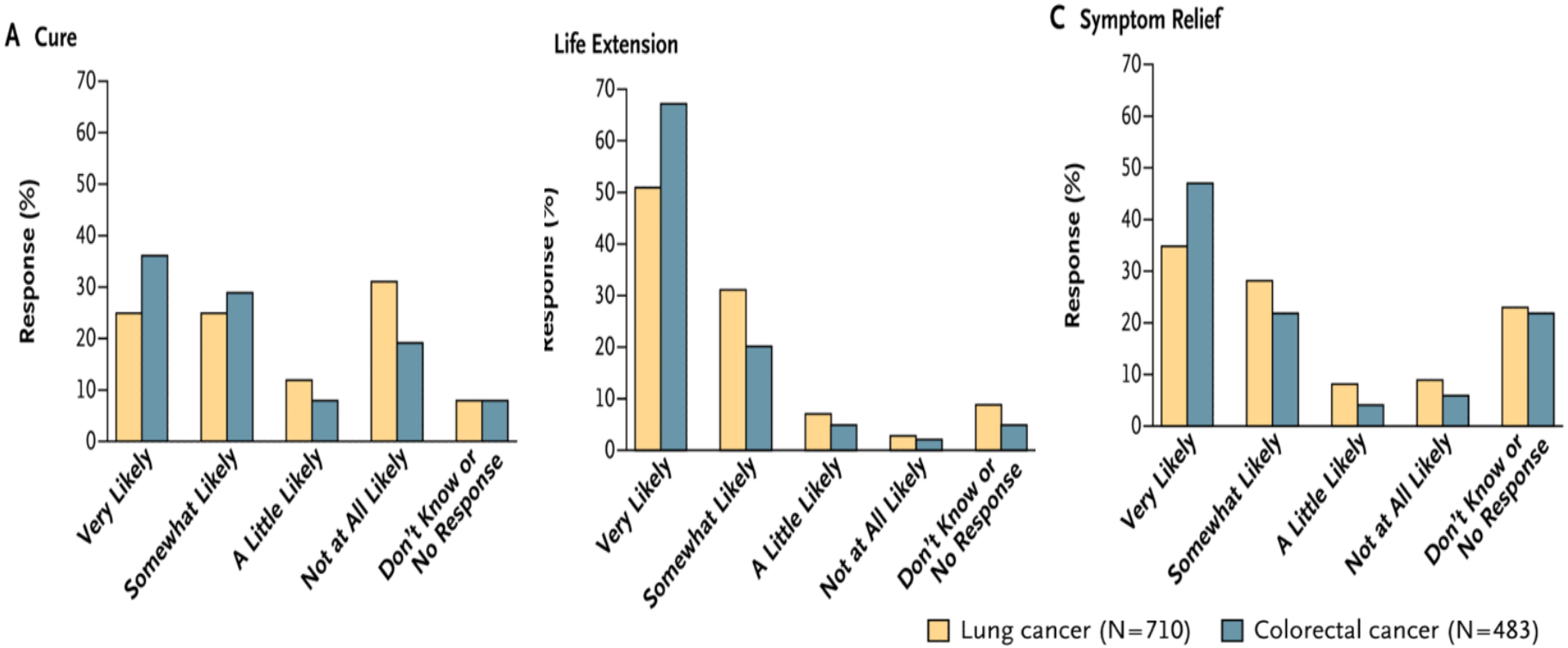
Original

Barrier for End-of-Life Discussion

1. Prediction of prognosis
2. **Acceptance of the situation by the patient**
3. The pain of discussing bad news

How much do patients expect about the effect of chemotherapy?

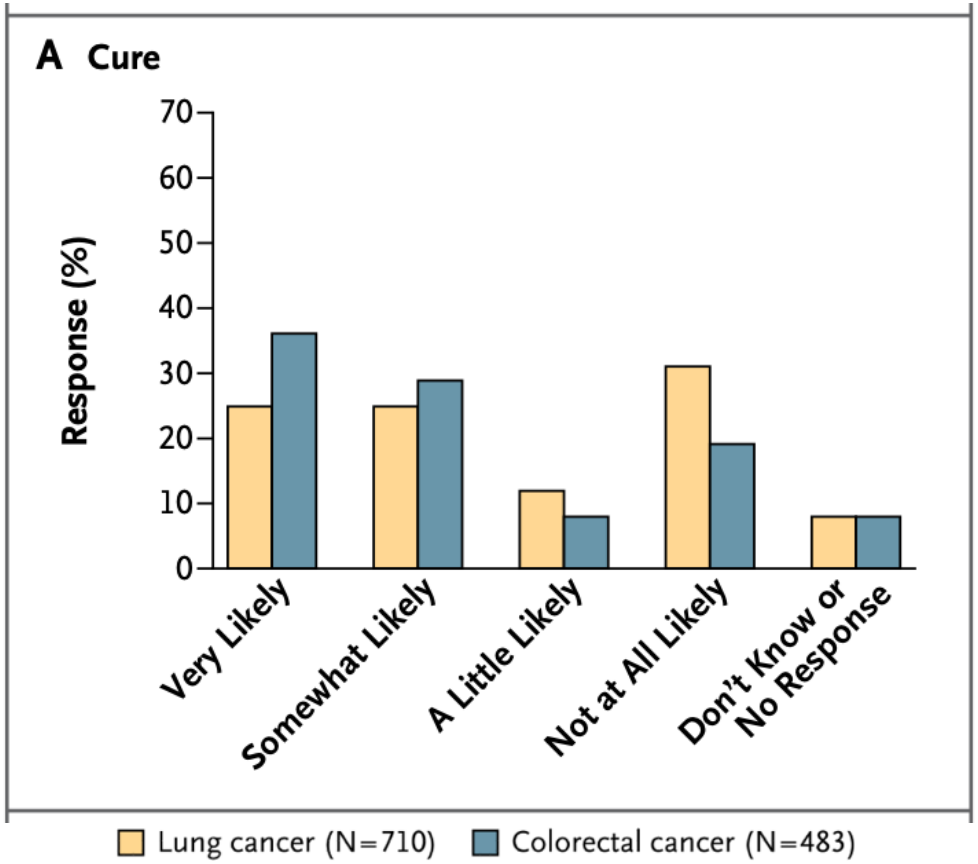
Survey target: Patients with stage IV lung or colorectal cancer
Question: How much do you expect about the effect of chemotherapy?



Weeks JC et al. N Engl J Med. 2012

How much do patients expect about the effect of chemotherapy?

Survey target: Patients with stage IV lung or colorectal cancer
Question: How much do you expect about the effect of chemotherapy?



There is a gap between patient expectations and reality.

Weeks JC et al. N Engl J Med. 2012

How much risk would patients put on chemotherapy?

Survey target: Patients with lung cancer and benign disease
Question: Would you receive chemo if you had a 1% chance of benefit?

Table 3. Subjects to Accept Treatments Giving Minimum Benefit

	L group (%)	N group (%)	P
Intensive treatment			
Chance of cure (1%)	41	24	0.01
Response (1%)	34	15	0.004
Relief of symptoms (1%)	26	15	0.09
Prolonging life (1 month)	12	8	0.18
Less-intensive treatment			
Chance of cure (1%)	43	28	0.05
Response (1%)	36	23	0.05
Relief of symptoms (1%)	30	21	0.24
Prolonging life (1 month)	15	12	0.19

Many cancer patients are willing to undergo treatments with more harm and less benefit in return.

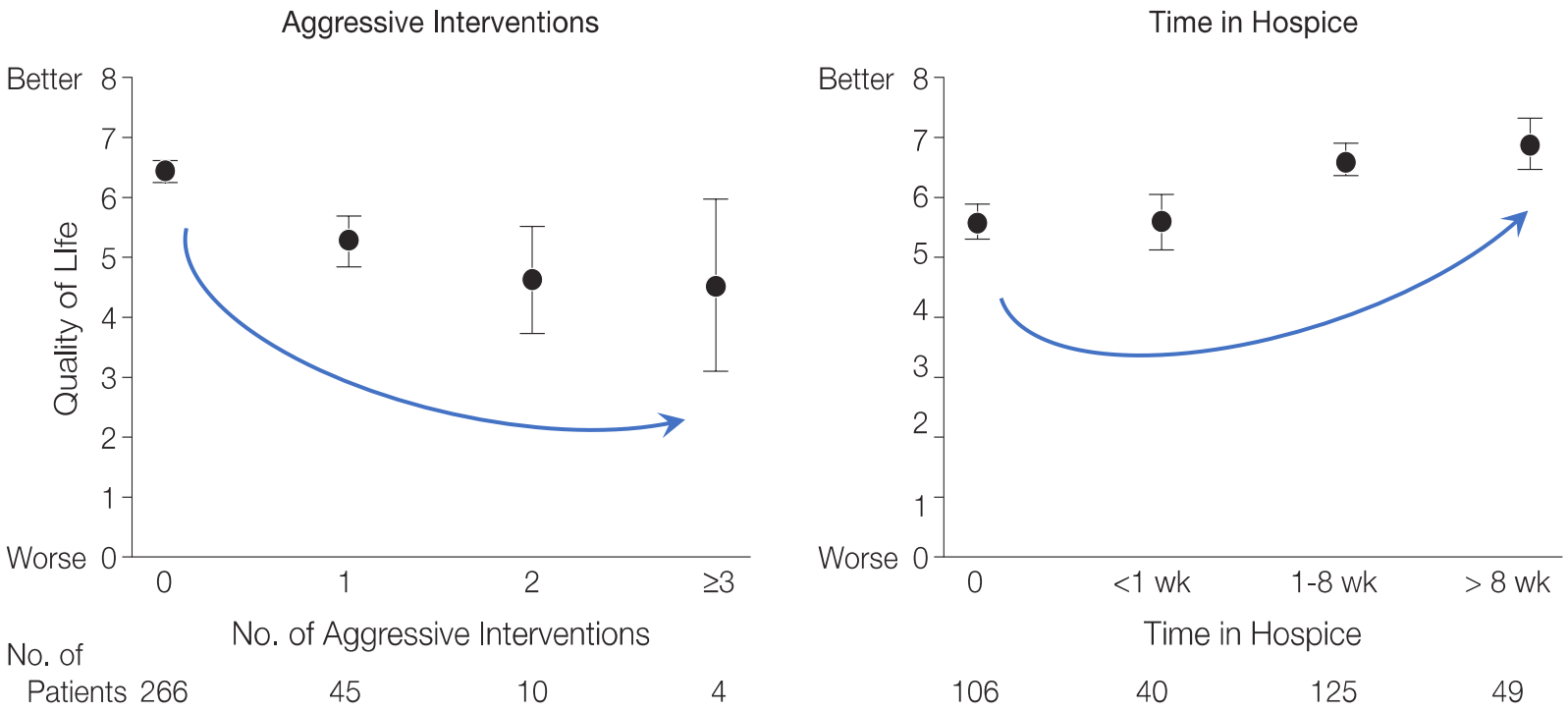
→ Chemo to support patients' feelings…?

Hirose T et al. Intern Med. 2005 Feb;44(2):107-13.

Aggressive interventions and QOL at EOL

Survey target: Caregivers at the EOL of cancer patients.

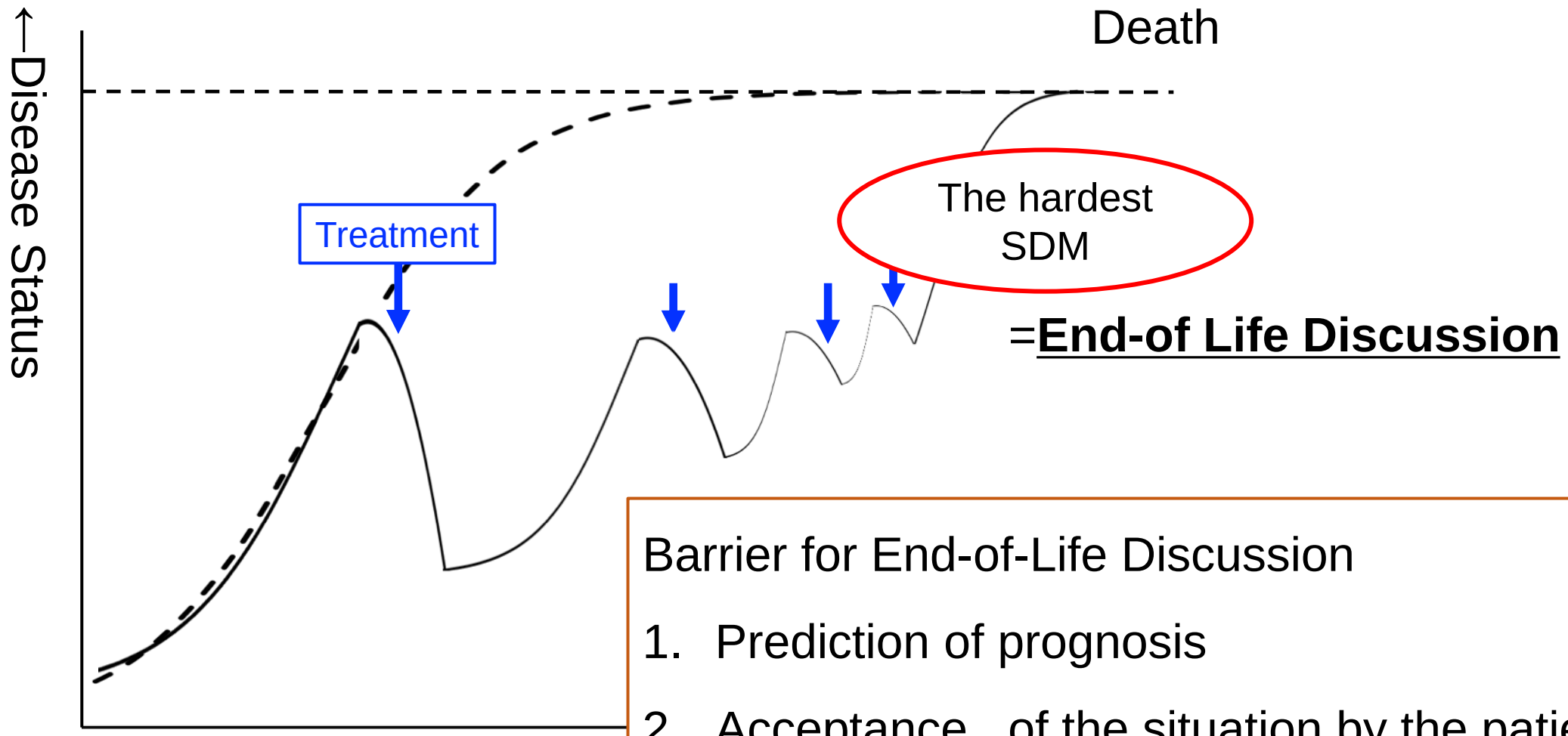
Figure. Relationship Between Quality of Life and End-of-Life Care



Less aggressive medical intervention and longer hospice stays are associated with higher QOL at EOL.

Wright AA. et al. JAMA. 2008 Oct 8;300(14):1665-73.

Process of advanced ovarian cancer (an example)



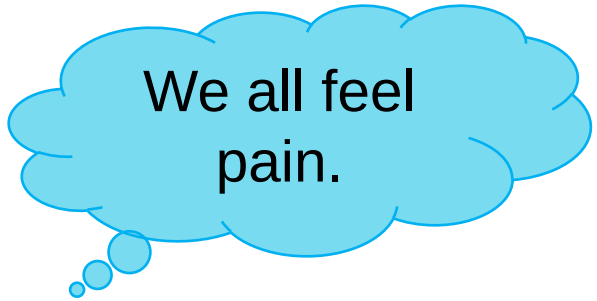
Original

Barrier for End-of-Life Discussion

1. Prediction of prognosis
2. Acceptance of the situation by the patient
3. **The pain of discussing bad news**

The burden on Gy oncologists for End-of-life discussion.

- ✓“Such discussion is simply too difficult and painful.” *(Harrington et al. JAMA 2008)*
- ✓We feel uncomfortable abandoning aggressive treatment after encouraging the patient.
- ✓We develop close relationships with the patients; thus, it’s tempting to be optimistic.
- ✓We feel guilty for not being able to cure the patient. This could result in avoiding facing the patient/burnout



（Bluhm M. J Oncol Pract. 2016, Herrington SE. JAMA2008, Temel JS JCO 2016)

How do we overcome these problems?

- **Team approach** (multidisciplinary collaboration）
- Seamless coordination between aggressive treatment and palliative care (e.g., early introduction of palliative care)
- Advance Care Planning (discussion of EOL at the early phase)
- Training on Shared Decision Making and End-of-Life discussion

Yet achieving these goals requires a variety of system modifications.

（Bluhm M. J Oncol Pract. 2016, Herrington SE. JAMA2008, Temel JS JCO 2016)

Take home message

- Scientific evidence for late-line ROC chemo
- Shared Decision Making: Try to do it at every visit
- End-of-Care Discussion: Understand the feelings of the patients and ours and work as a team.

Thank you for listening…
and Special thanks to ASGO Educational Committee

If you have any question,
e-mail sato.mikiko.45@luke.ac.jp