癌因性疲憊症於癌症早期緩和醫療之臨床角色

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癌症診療品質認證 (107年)

【加分項目】基準3.3	
癌症防治醫療機構應針對晚期癌症病人建立緩和醫療之照護標準與流程。	
評分說明	符合項目： 1. 已建立晚期癌症病人接受緩和醫療之照護標準與流程。 2. 在兩種癌別或兩個腫瘤相關病房（安寧病房除外）開始實行。
準備文件	1. 晚期癌症病人接受緩和醫療之照護標準與流程。 2. 緩和照護團隊之成員名單。 3. 緩和照護之執行紀錄□例如：照護服務單紀錄或病歷紀錄□□ 4. 緩和照護團隊教育訓練課程大綱。
重點	1. 晚期癌症定義：癌症出現遠處轉移或復發，但透過治療仍可延長病人生命（生命預期存活期＞6個月）。 2. 照護標準與流程應包含啟動轉介緩和醫療之條件、轉介流程與照護服務內容等。 3. 緩和照護團隊除需包含醫師（安寧專科醫師或腫瘤治療專科醫師）、護理師、社工師、心理師外□亦可自行增加其他相關人員（如靈性關懷人員等□。可由現有安寧緩和照護團隊或多專科團隊中成立功能小組負責辦理。 4. 緩和照護團隊成員應接受相關教育訓練，課程內容至少應涵蓋身心症狀處理、共同醫療決策及照護者支持等面向。

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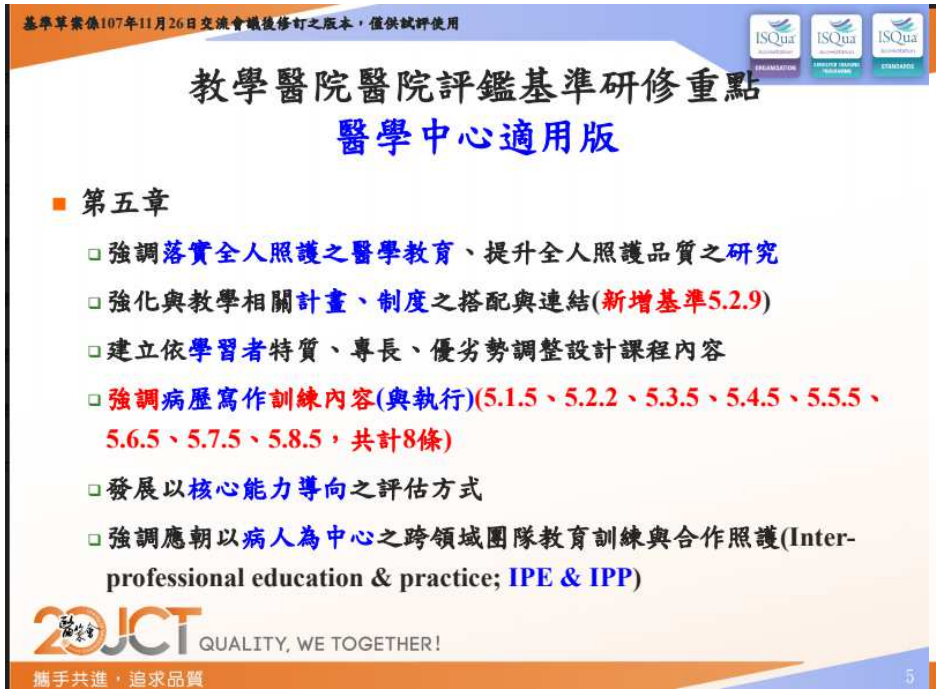
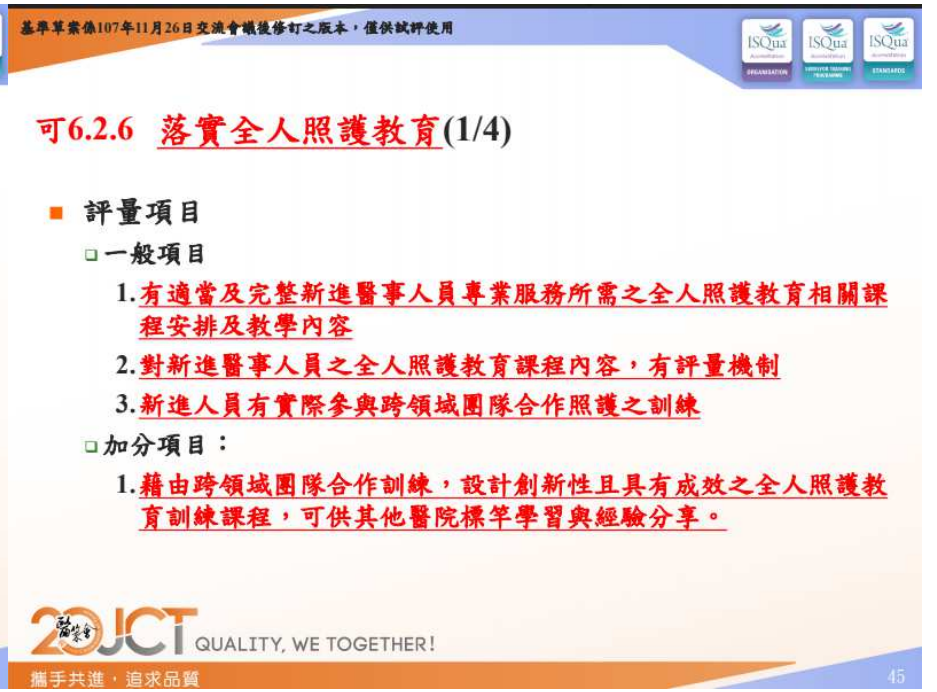
108年醫學中心版教學醫院基準研修





- 西醫、牙醫、中醫之醫學生(clerk)、PGY、住院醫師教學訓練計畫需加入全人照護
- 醫事類人員也需要落實全人照護教育

Curtesy of Dr . 黃姚儒

全人醫療　Holistic medicine

- A form of healing that considers the whole person -- body, mind, spirit, and emotions -- in the quest for optimal health and wellness.

Curtesy of Dr. 謝瑞坤

癌症患者的醫療還包含多種層面

Many aspects of supportive care

Nutrition

Anaemia

Diarrhoe/Obstipation

Pulmonary Tox.

Infections

Cardiotoxicity

Neutropenia

Antiemesis

Paravasation

Fertility

Tumorlysis

Fatigue

Pain

Neurotoxicity

Thrombocytopenia

Psychological support

Supportive measures in radiation therapy

Renal toxicity

Bone complications

Lymphedema

New Toxicities (Targeted drugs)

Venous Thromboembolism

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Palliative care

- an interdisciplinary approach to specialized medical and nursing care for people with life-limiting illnesses
- It focuses on providing relief from the symptoms, pain, physical stress, and mental stress at any stage of illness. The goal is to improve quality of life for both the person and their family

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因化療讓患者感到痛苦的事

1983

- **Being sick (vomiting)**
- **Feeling sick (nausea)**
- Loss of hair
- Thought of coming for treatment
- Length of time treatment takes at the clinic
- Having to have an injection
- Shortness of breath
- Constantly tired
- Difficulty sleeping
- Affects family or partner

1995 5-HT3 / dex

- **Feeling sick (nausea)**
- Loss of hair
- **Being sick (vomiting)**
- Constantly tired
- Having to have an injection
- Constipation
- Thought of coming for treatment
- Affects family or partner
- Feeling low, miserable (depression)
- Feeling anxious

Curtesy of Dr. 謝瑞坤

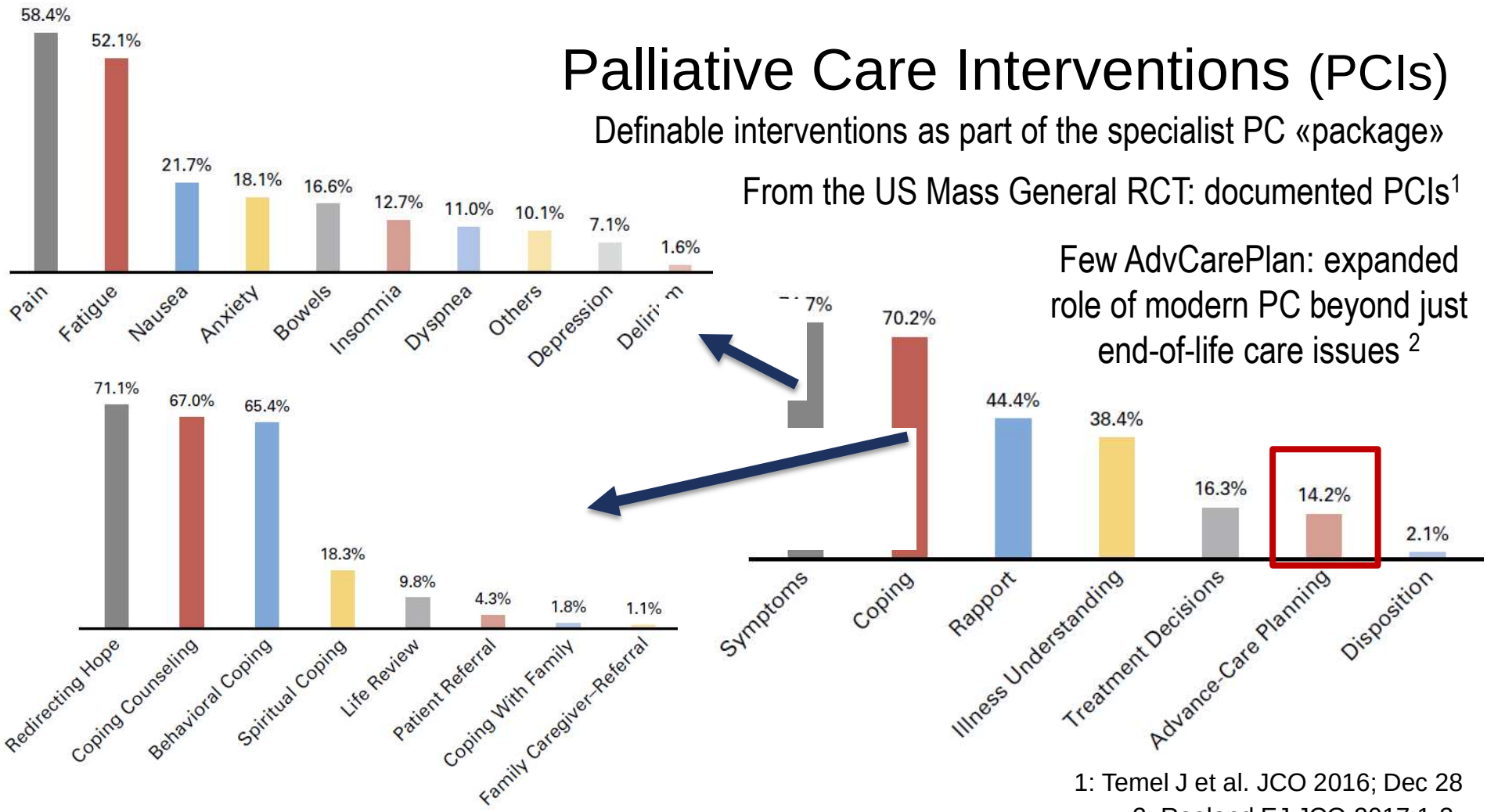
面對癌症患者的生理 病理以及心理層面

Palliative Care Interventions (PCIs)

Definable interventions as part of the specialist PC «package»

From the US Mass General RCT: documented PCIs[1]

Few AdvCarePlan: expanded role of modern PC beyond just end-of-life care issues [2]

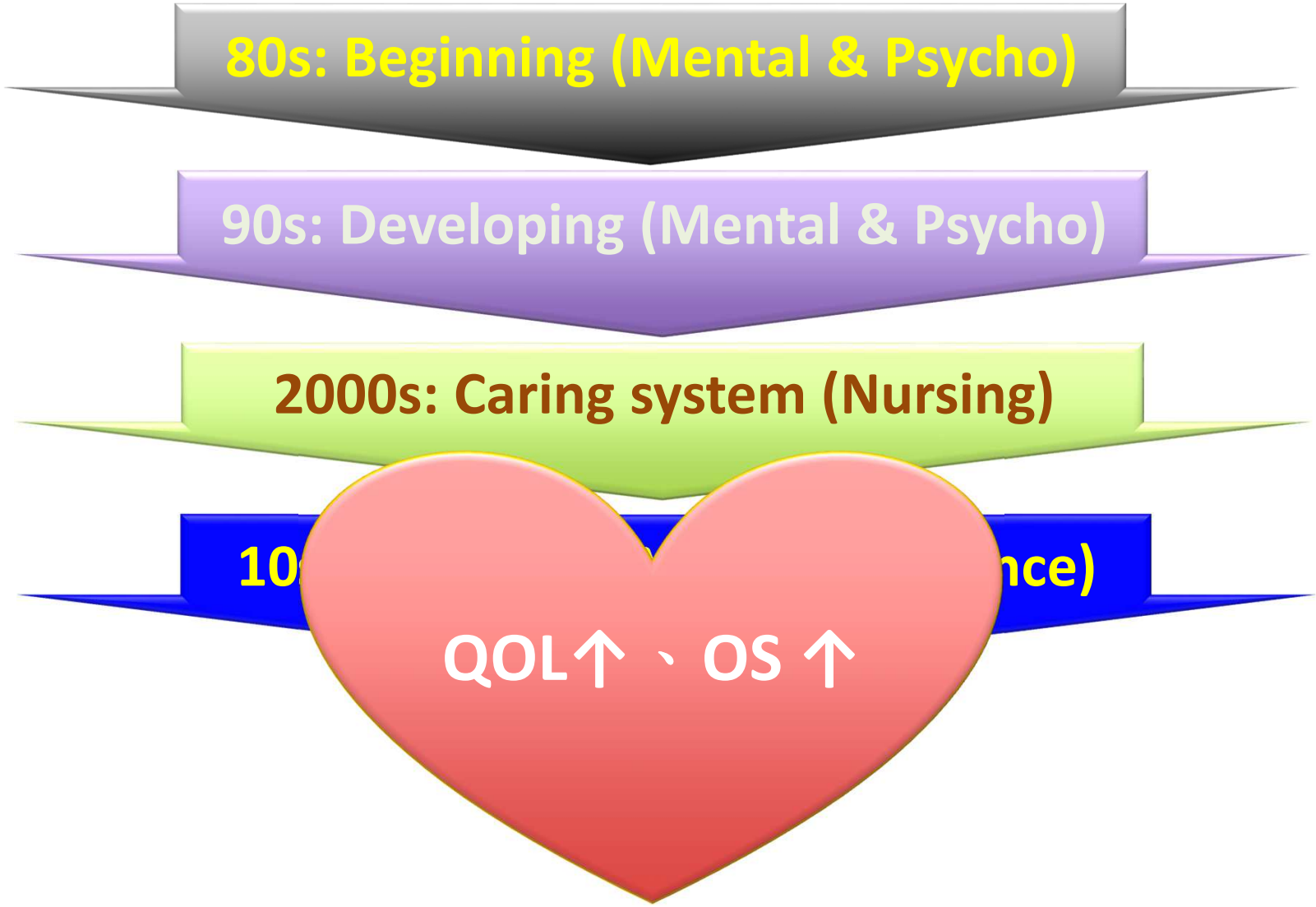


1: Temel J et al. JCO 2016; Dec 28

2: Roeland EJ JCO 2017;1-3

Curtesy of Dr. 謝瑞坤

Palliative medicine in cancer care



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全人醫療:
早期緩和醫療
Early Palliative care
Improve QOL and Save Life

Curtesy of Dr. 謝瑞坤

2013年彙整

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Early Specialty Palliative Care — Translating Data in Oncology into Practice

Ravi B. Parikh, A.B., Rebecca A. Kirch, J.D., Thomas J. Smith, M.D., and Jennifer S. Temel, M.D.

N Engl J Med 369;24 December 12, 2013

早期緩和醫療的介入可以維持生活品質及延長存活

N Engl J Med 369;24 December 12, 2013

Table 1. Randomized Trials of Early Specialty Palliative Care Interventions in Patients with Cancer.

Trial	Population	Intervention	Results

5 (or, really, 7) RCTS now show...

- ✓ **No harm in any trial**
- ✓ Better satisfaction
- ✓ Usually better Quality of life
- ✓ Sometimes better symptom control
- ✓ LESS depression and anxiety
- ✓ 2 show better survival, one significant 2.7 months in NSCLC

- ✓ No increased cost in any trial
- ✓ Usually markedly lower costs per day – at least $300/day
- ✓ 10-fold increase in hospice referrals

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Patient Satisfaction and QOL

Trial	Population	Intervention	Results- Pt sat	Results- QOL
Gade et al	517 people “surprise ?” 31% cancer	Inpatient PC MDT consult	Increased satisfaction	No difference
Bakitas et al	322 people ~1 yr prognosis 100% cancer	Phone based PC by APN		Improved QOL Improved mood
Temel et al	151 people 100% newly dx metastatic NSCLC	Outpatient PC >=monthly MD or APN and Inpatient PC consult		Improved QOL Improved mood
Zimmerman et al	442 people 100% cancer 6mo-2yr prognosis	Outpatient PC >=monthly	Increased satisfaction	Improved QOL

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倡議早期緩和介入

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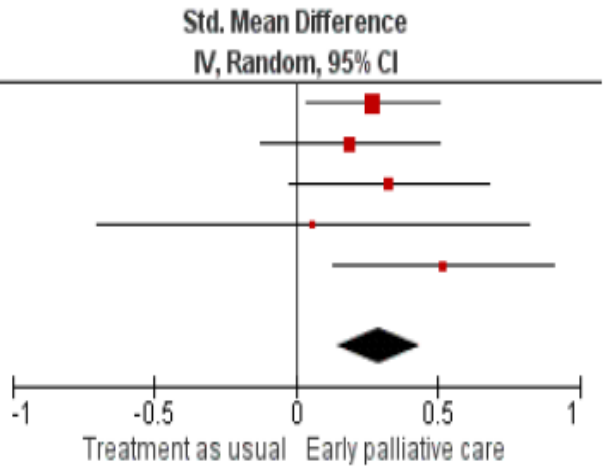
Quality of life is improved by early palliative care compared with standard care

Figure 8. Forest plot of comparison: 1 Early palliative care vs standard oncological care, outcome: 1.5 Health-related quality of life (sensitivity analysis for study design including RCTs only).

Study or Subgroup	Std. Mean Difference	SE	EPC Total	TAU Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bakitas 2009	0.27	0.12	145	134	40.6%	0.27 [0.03, 0.51]
Bakitas 2015	0.19	0.16	72	83	22.9%	0.19 [-0.12, 0.50]
Maltoni 2016	0.33	0.18	64	65	18.1%	0.33 [-0.02, 0.68]
Tattersall 2014	0.06	0.39	13	13	3.8%	0.06 [-0.70, 0.82]
Temel 2010	0.52	0.2	60	47	14.6%	0.52 [0.13, 0.91]
Total (95% CI)			**354**	**342**	**100.0%**	**0.29 [0.14, 0.44]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.14$, $df = 4$ ($P = 0.71$); $I^2 = 0\%$

Test for overall effect: $Z = 3.81$ ($P = 0.0001$)



Cochrane Database Syst Rev. **2017** Jun 12;6:CD011129.

Curtesy of Dr. 謝瑞坤

Project ENABLE

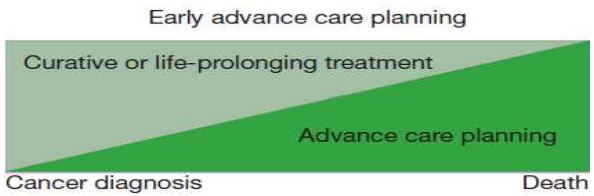
322 patients within 8-12 weeks of a new diagnosis of GI, lung, GU or breast cancer with a prognosis of approximately one year

- ENABLE intervention
- Usual Care

Outcome Measures

Patient-reported Outcomes
1. FACIT Palliative Care
2. ESAS (symptom intensity)
3. CES-D (depression)

Health Service Utilization
1. Number of days in hospital, intensive care unit and emergency department
2. Use of advanced directives
3. Referral to palliative care or hospice



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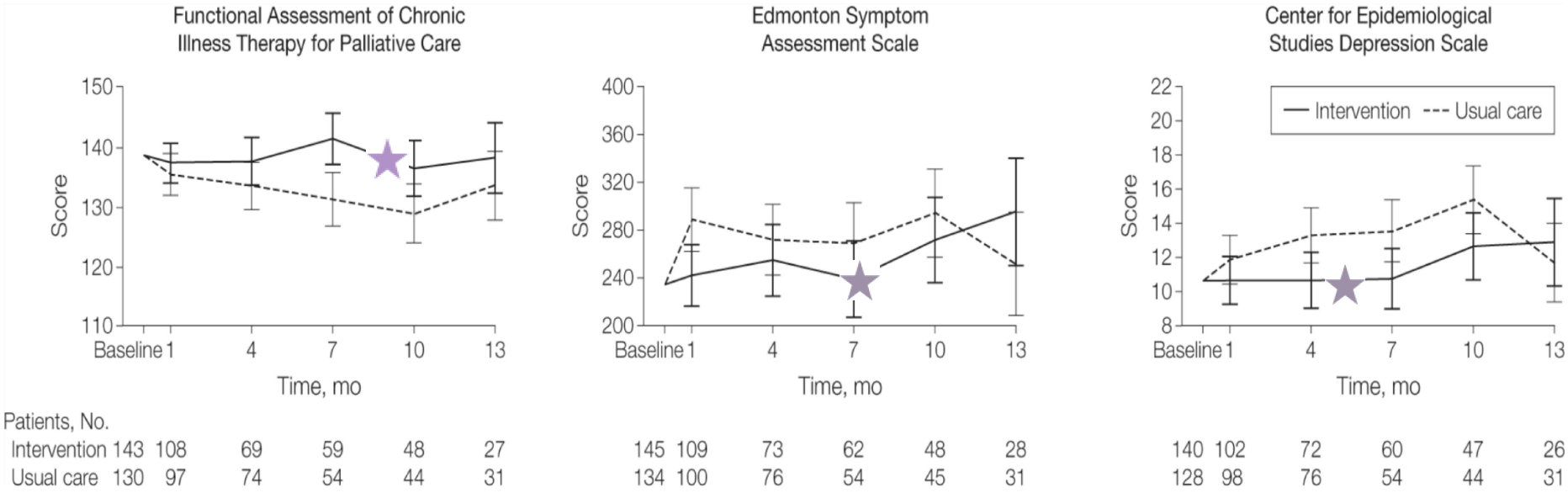
Nature of the Intervention

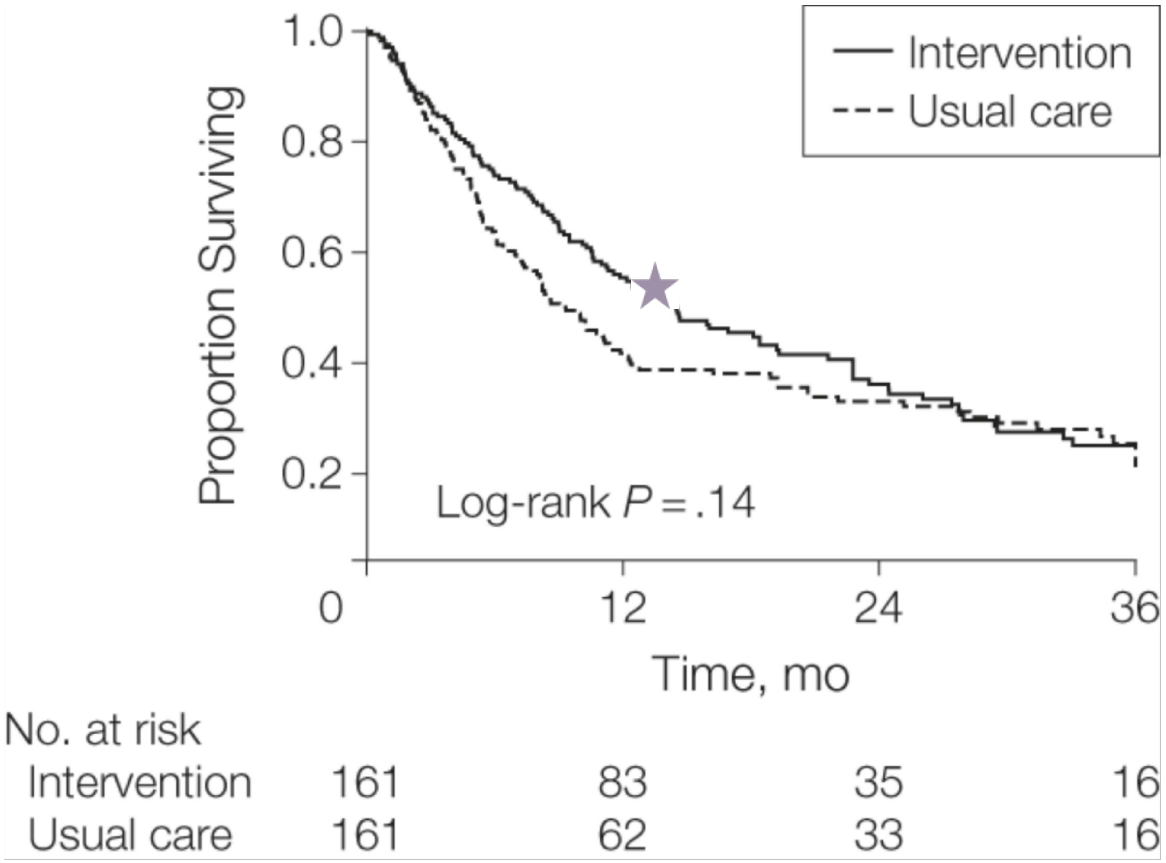
- Case management, educational approach to encourage patient activation, self-management and empowerment.
- Delivered in a manualized, telephone-based format (to administer to a rural population).
- Administered by advanced practice nurses with palliative care training.
- Included 4 initial structured educational and problem-solving sessions and at least monthly telephone follow up.

Curtesy of Dr. 謝瑞坤

Palliative care nursing education in addition to usual oncology care – in RCT – allowed improved quality of life, fewer symptoms, and less depression. Bakitas M, et al. Project ENABLE. JAMA. 2009 Aug 19;302(7):741-9.



Palliative care in addition to usual oncology care led to a trend for improved lifespan. Bakitas M, et al. Project ENABLE. JAMA. 2009 Aug 19;302(7):741-9.



Randomized Trial in Patients with Lung Cancer

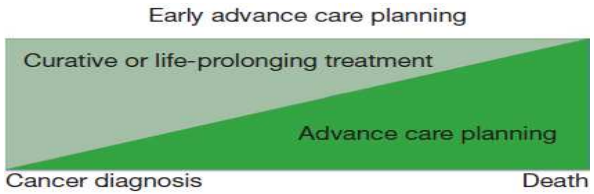
150 patients within 8 weeks of diagnosis of metastatic NSCLC with an ECOG PS 0-2

- Integrated care
- Standard care

Outcome Measures

<u>Patient-reported Outcomes</u>
1. FACT Lung
2. HADS (mood)
3. PHQ-9 (depression)
4. Prognostic awareness

<u>Health Service Utilization</u>
1. Hospice referrals
2. Chemotherapy administration
3. Documentation of resuscitation preferences



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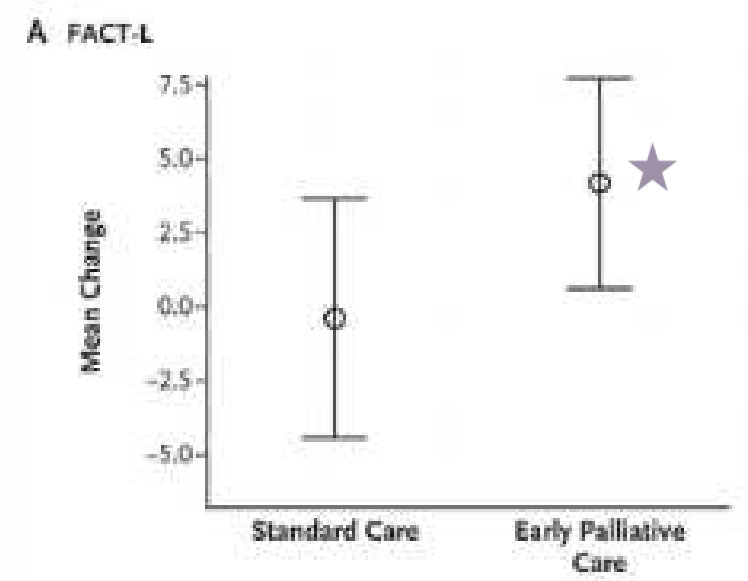
Nature of the Intervention

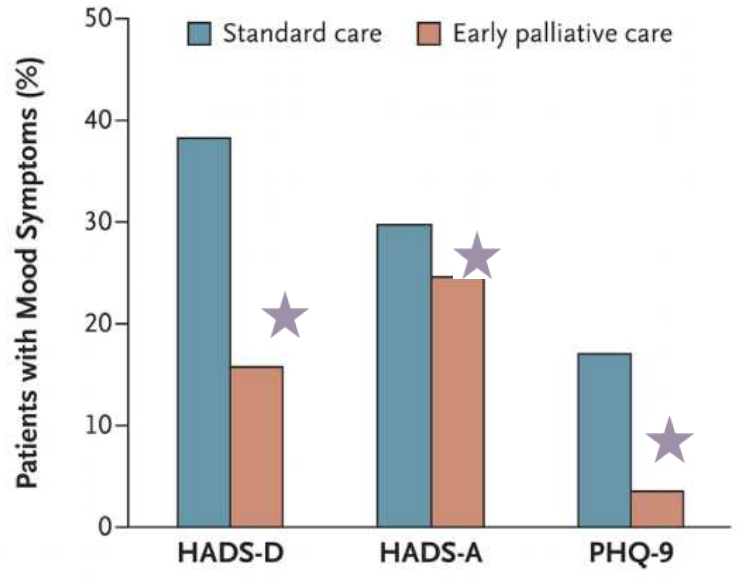
- Palliative care visits within 3 weeks of enrollment and at least monthly.
- Visits performed by physicians or advanced practice nurses within the Cancer Center (medical oncology or chemotherapy visits).
- Palliative care visits were not scripted or manualized but followed general guidelines for as per the national consensus project.
- If patients were admitted to the hospital, they were also followed by the palliative care team.

Curtesy of Dr. 謝瑞坤

Palliative care in addition to usual oncology care allowed lung cancer patients to have *much better quality of life* (FACT) and *less anxiety and depression.*

Temel J, et al. NEJM 2010; Temel J, et al, JCO 2011





Quality of life Better

生活品質改善顯著

Mood Better, LESS depression

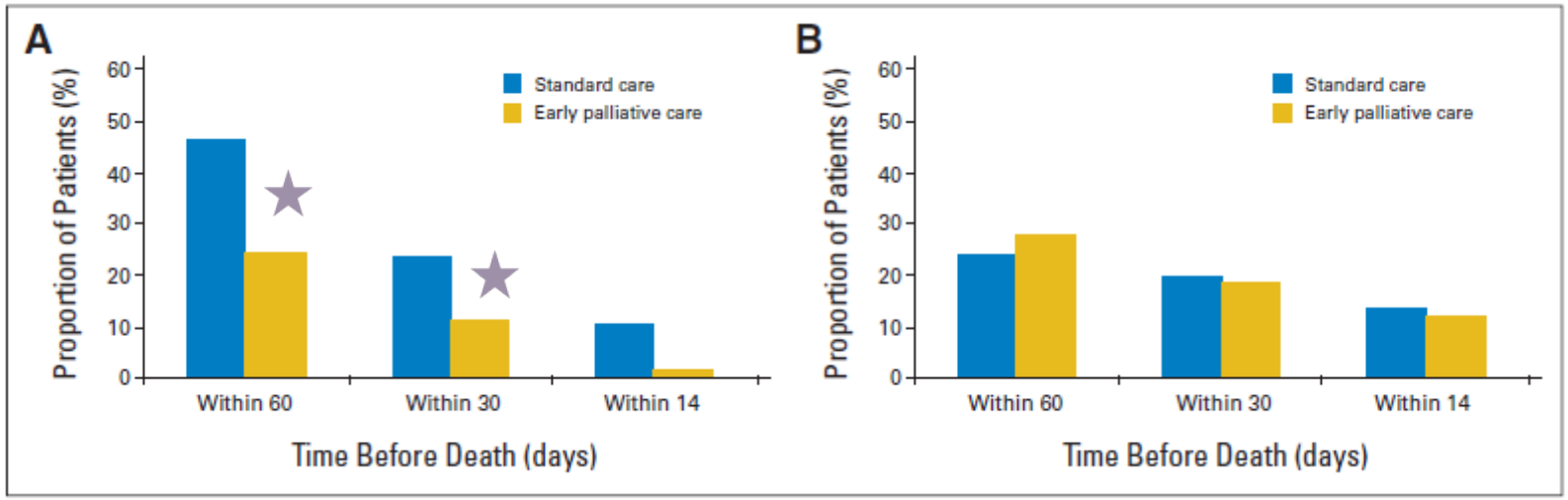
心情較佳 憂鬱較少

Final Chemotherapy at the EOL

臨終前期靜脈化學治療的使用顯著減少

IV Chemotherapy

Oral Chemotherapy

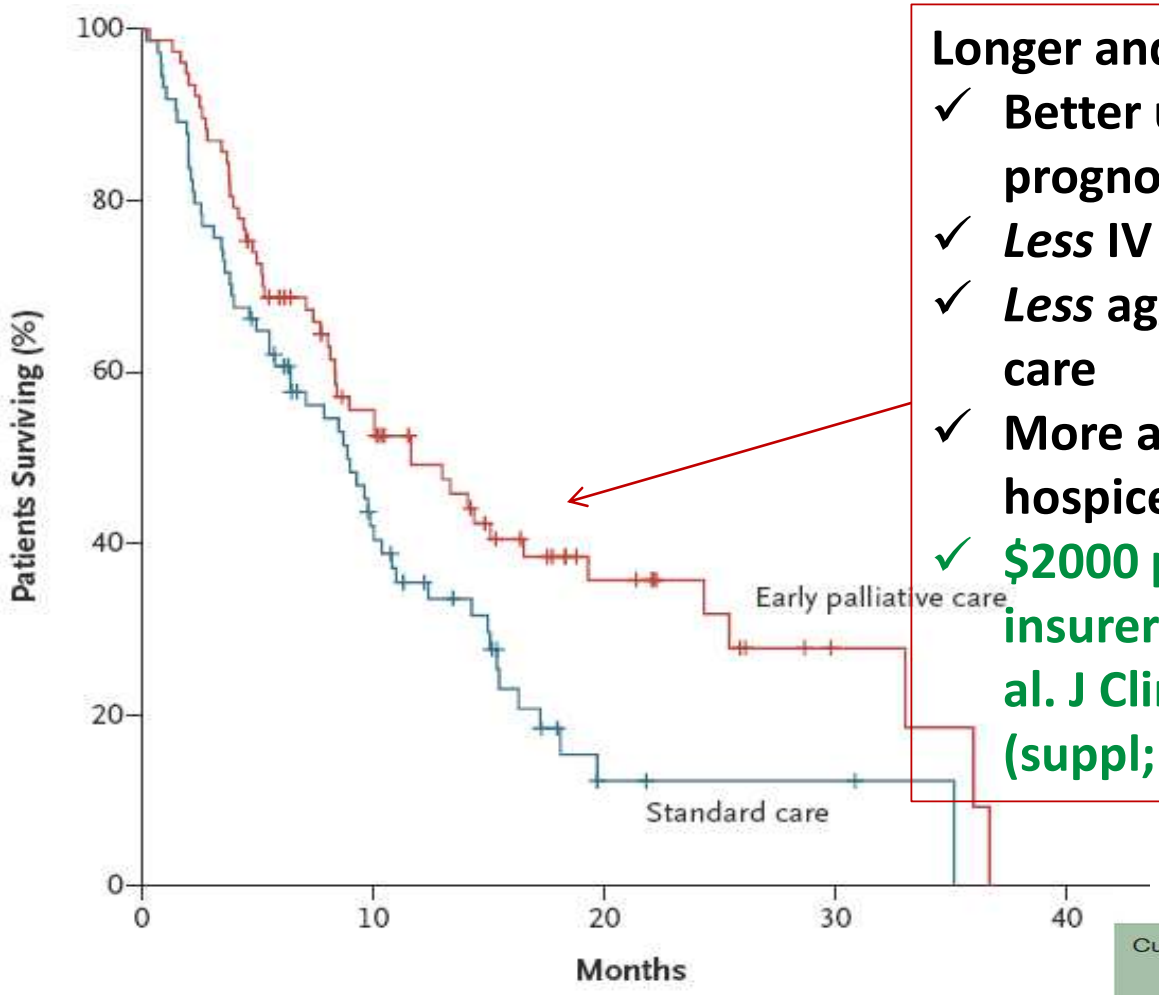


IV chemo within 60 DOD
46% v 24% p=0.01

Greer, JCO 30 (4) 2012

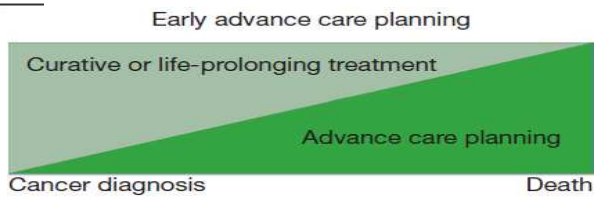
Palliative care in addition to usual oncology care allowed lung cancer patients to live almost 3 months longer than those who got usual oncology care.

Temel J, et al. NEJM 2010; Greer J, et al. JCO 2011



Longer and better survival

- ✓ **Better understanding of prognosis →**
- ✓ ***Less* IV chemo in last 60 days**
- ✓ ***Less* aggressive end of life care**
- ✓ **More and longer use of hospice**
- ✓ **$2000 per person savings to insurers and society (Greer, et al. J Clin Oncol 30, 2012 (suppl; abstr 6004))**



What do these studies tell us?

- Palliative care improves patients' QOL, mood and other aspects of care including prognostic awareness, satisfaction and quality of EOL care.
- Many palliative care delivery models work.
- A more "intensive" palliative care model may be needed to impact EOL care measures.

In summary

- Clinicians should routinely and periodically screen adult caregivers for practical and emotional needs while caring for a patient near the end of life.
- Periodic screening by caregivers for the patient's supportive needs should be a routine part of care for patients with serious chronic illness.

Integrating Palliative Care Into Oncology: A Way Forward

Simutaneous

Palliative care and Acute Oncology Care

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急性癌症醫療以及緩和醫療的整合

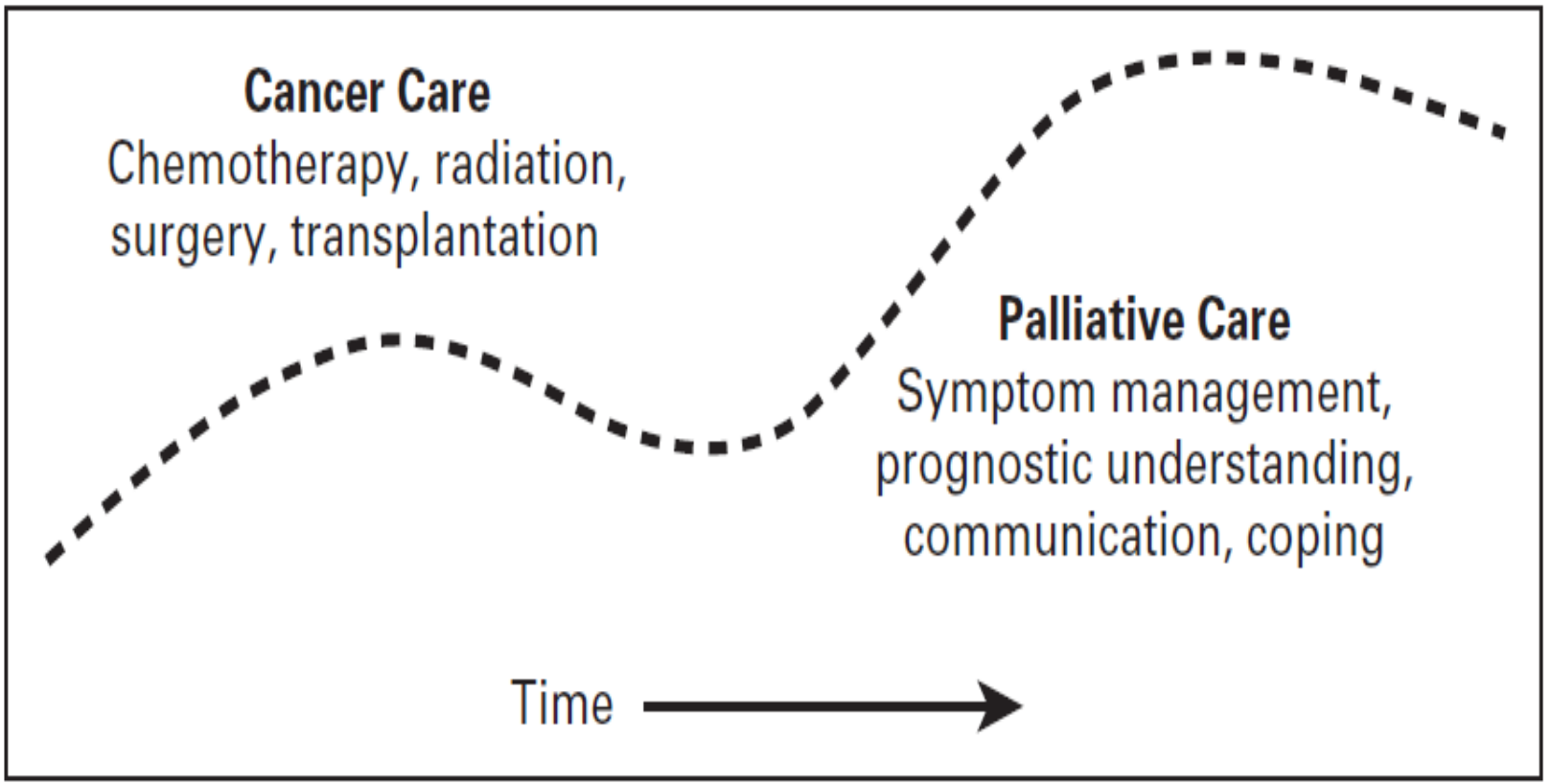

Fig 1. Palliative care integration in modern cancer care.

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To cancer treatment

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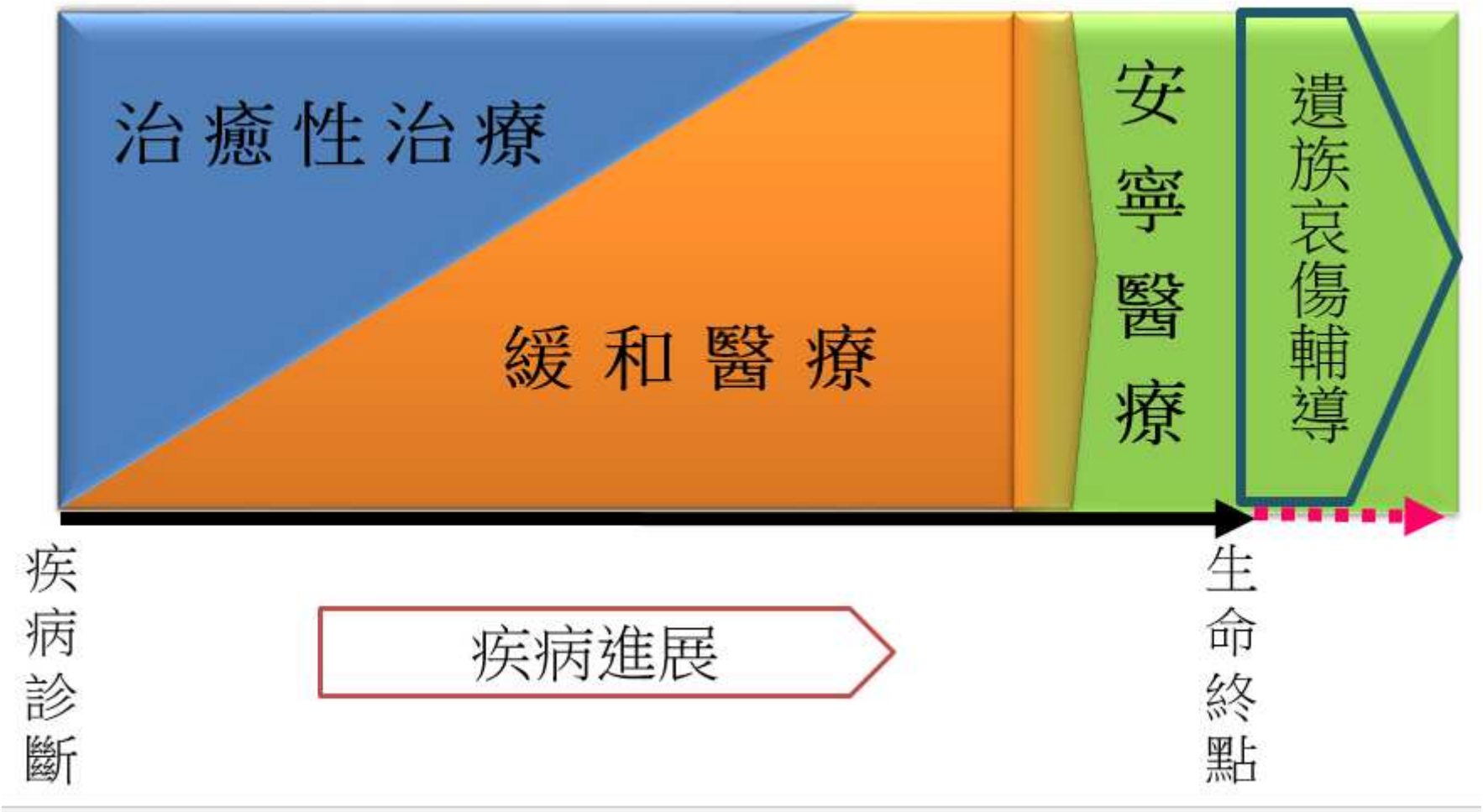
And to hospice care



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Palliative Care Is

- ✓ Excellent, evidence-based medical treatment
- ✓ Vigorous care of pain and symptoms throughout illness
- ✓ Care that patients want *at the same time* as efforts to cure or prolong life

Palliative Care Is NOT

- ✗ Not "giving up" on a patient
- ✗ Not in place of curative or life-prolonging care
- ✗ Not the same as hospice or end-of-life care

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Who should deliver Supportive & Palliative Care Interventions ?

- Role of Medical Oncologist
- Evidence for specialized PC teams
- Medical Oncology Curriculum includes many palliative topics

Primary Palliative Care by Oncologists:

Bickel KE et al. JOP 2016;12:e828-38

The World Health Organization (WHO)

- palliative care as services designed to prevent and relieve suffering for patients and families facing life-threatening illness, through early management of pain and other physical, psychosocial, and spiritual problems.

Palliative Care – WHO

- Uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated;
- Will enhance quality of life, and may also positively influence the course of illness;

- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

ASCO Guidelines 2016

- "Palliative care means patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering.
- Palliative care throughout the continuum of illness involves addressing physical, intellectual, emotional, social, and spiritual needs and to facilitate patient autonomy, access to information, and choice."

The American Society for Clinical Oncology (ASCO) recommends

- Considering the combination of palliative care with standard oncology care early in the course of treatment for patients with metastatic cancer and/or a high symptom burden

The National Comprehensive Cancer Network (NCCN)

- All cancer patients should be repeatedly screened for palliative care needs, beginning with their initial diagnosis and thereafter at intervals as clinically indicated
- Palliative care should be initiated by the primary oncology team and then augmented by collaboration with palliative care experts

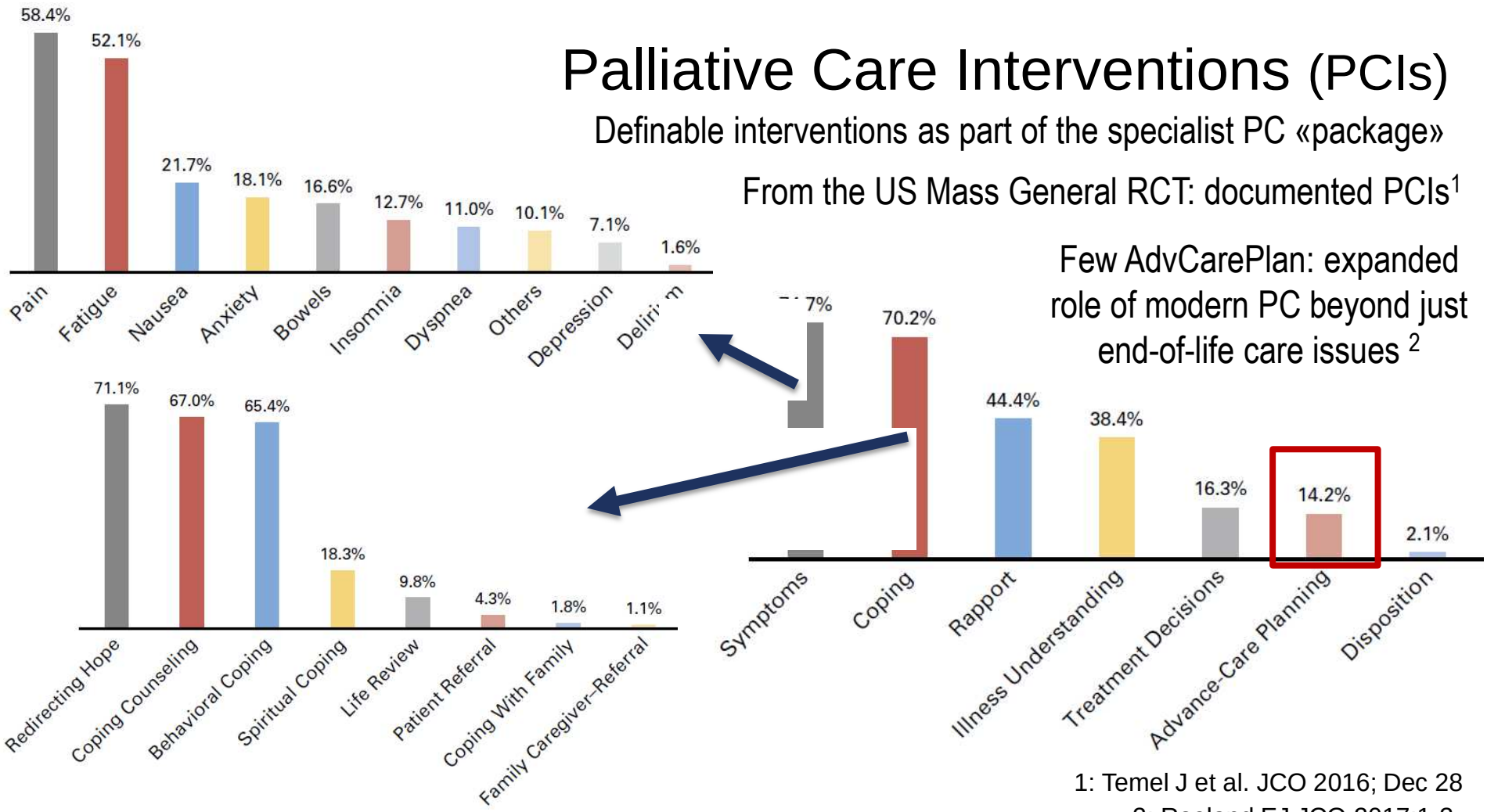
The National Comprehensive Cancer Network (NCCN)

- All health care professionals should receive education and training to develop palliative care knowledge, skills, and attitudes

NCI – Palliative care

- Palliative care is care given to improve the quality of life of patients who have a serious or life-threatening disease, such as cancer.
- Patients may receive palliative care in the hospital, an outpatient clinic, a long-term care facility, or at home under the direction of a physician.

面對癌症患者的生理 病理以及心理層面



Palliative Care Interventions (PCIs)

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From the US Mass General RCT: documented PCIs[1]

Few AdvCarePlan: expanded role of modern PC beyond just end-of-life care issues [2]

1: Temel J et al. JCO 2016; Dec 28

2: Roeland EJ JCO 2017;1-3

癌因性疲憊症: NCCN

與癌症或癌症治療相關而且和

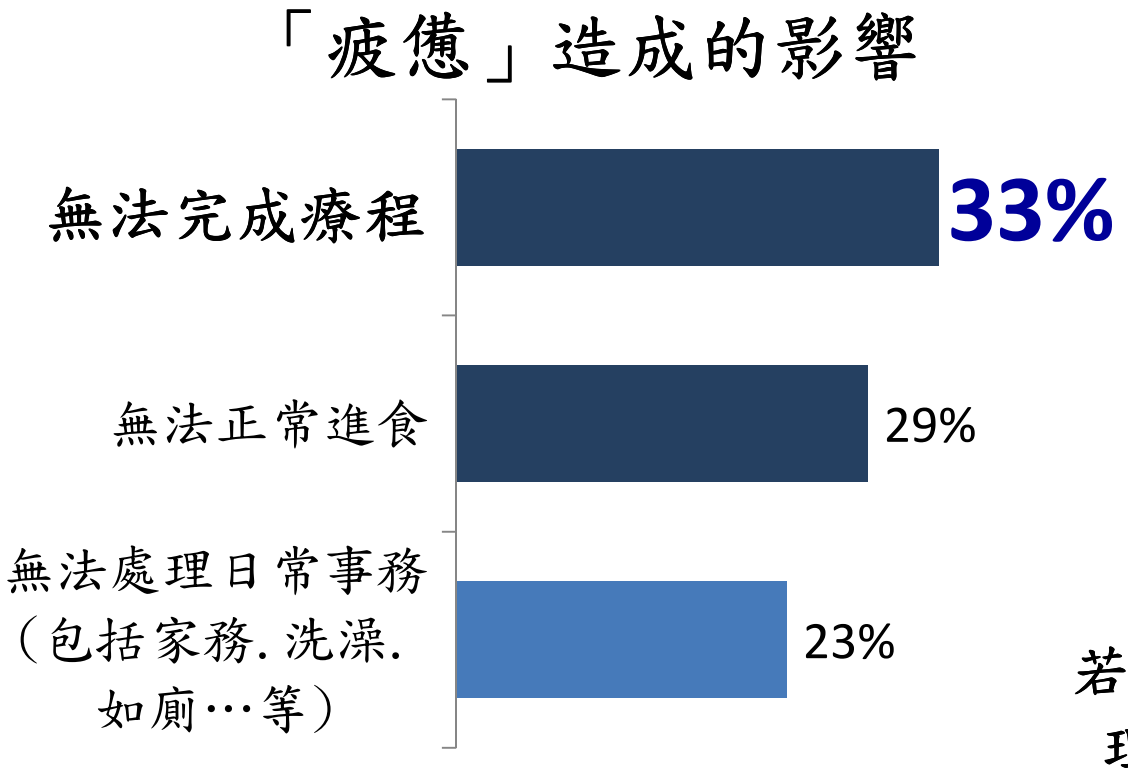
近期活動量不成比例的疲累感，

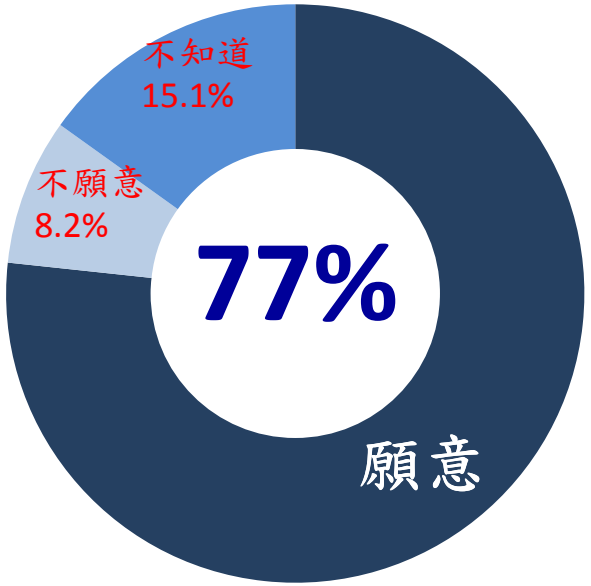
具有持續、令人感到不適、

而**主觀**的特性，且足以**影響正常生活**

1. NCCN. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue, Version 2.2017; 2017. https://www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf
2. Yeh ET et al. BMC Cancer 2011; 11:387.

1/3病人因疲憊中斷癌症治療

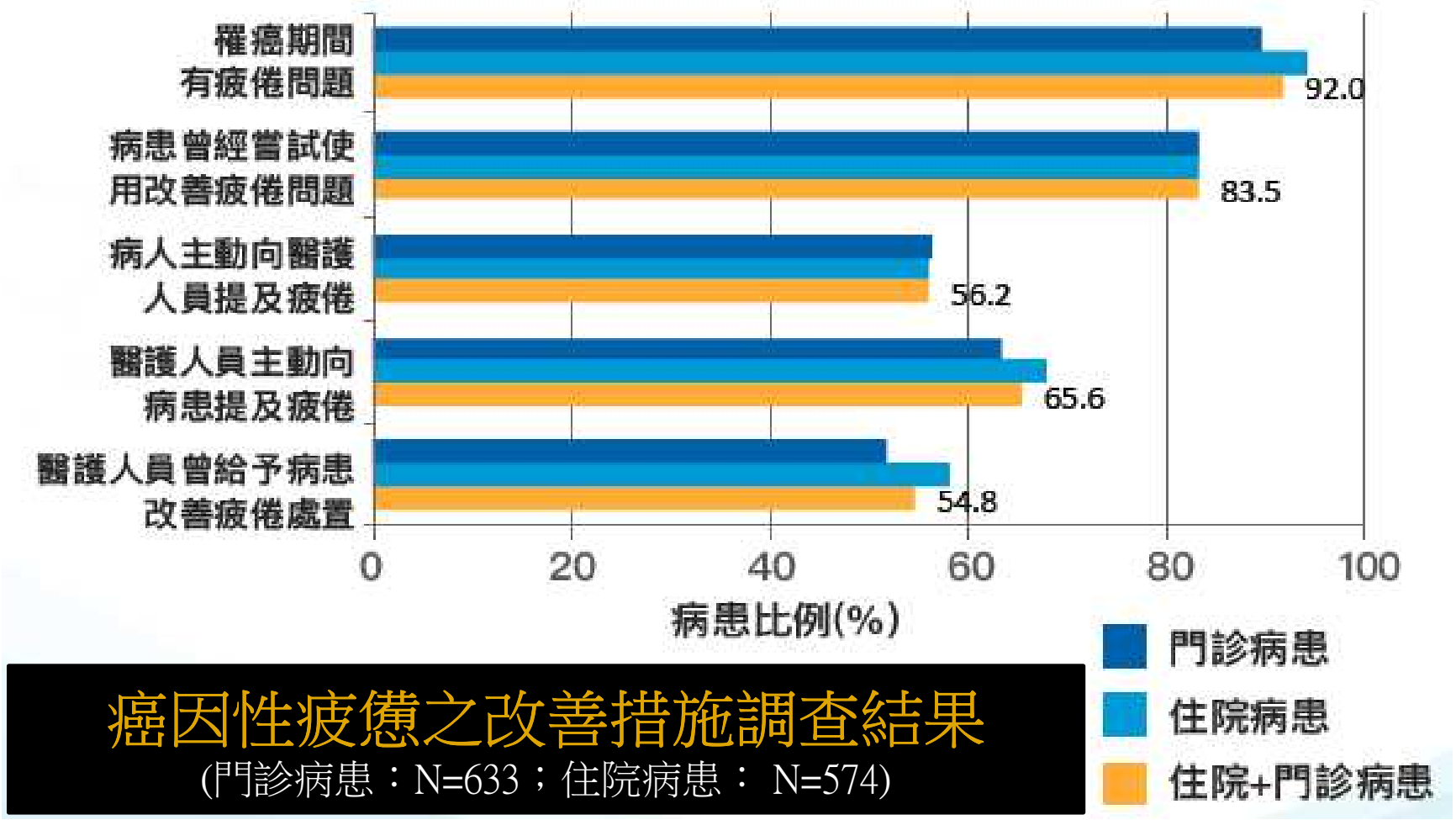




若有方法能有效且安全的處理我的疲憊，我願意嘗試

Ref. 台灣癌症基金會 https://www.canceraway.org.tw/uploads/FCF_201179932211.pdf. 樣本數:電訪74位癌症病人。

92% 台灣癌症患者罹癌期間有疲憊問題，約一半癌症病患主動向醫護人員提及疲憊



癌因性疲憊之改善措施調查結果

(門診病患：N=633；住院病患： N=574)

癌因性疲憊症之臨床治療指引

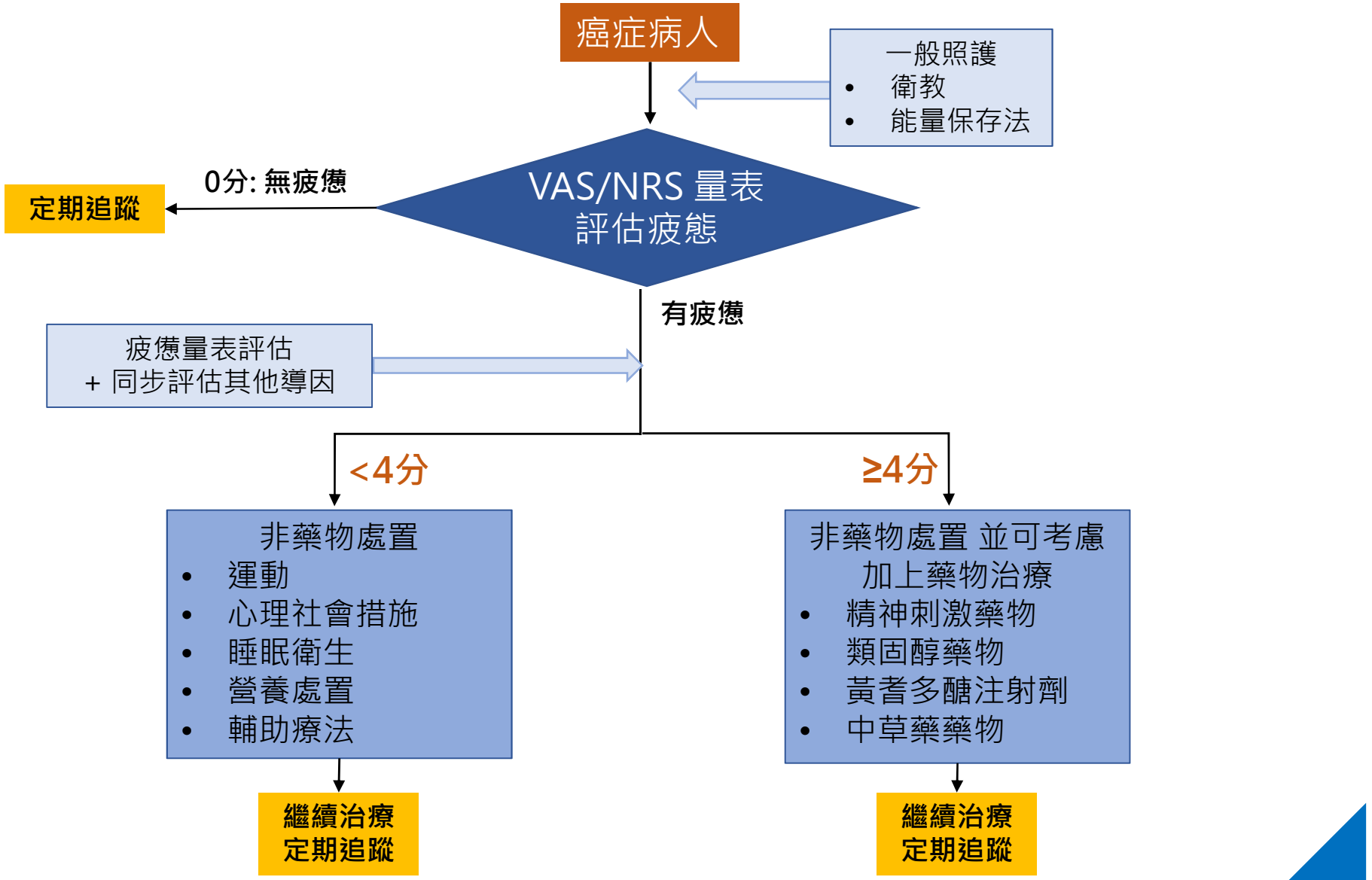
MANAGEMENT OF CANCER-RELATED FATIGUE – A GUIDELINE FOR TAIWAN –

2017年 11月 第一版

台灣癌症安寧緩和醫學會

台灣腫瘤護理學會

癌因性疲憊症的評估與處置流程



癌因性疲憊症的定義: ICD-10

符合 A–D 四大要件

A 最近一個月至少有**連續兩週期間**，每天或幾乎每天出現**至少六項** A1–A11 的症狀（ A1 為必需 ）

A1 感到明顯的疲累、缺少活力、或需要增加休息，且與近期活動程度不成比例

A2 感到全身虛弱、沉重

A3 感到很難集中精神或注意力

A4 感到平常習慣做的事都變得乏味而不想去做

A5 感到難以入睡、睡得不安穩、早起有困難、或是睡得太多

A6 感到睡覺起來還是覺得疲累，精神沒有恢復

A7 感到做什麼事情都必須經過一番掙扎，勉強自己去做

A8 因為疲累而感到悲傷、失意、或煩躁

A9 因為疲累不堪而事情做一半就做不下去了

A10 感到記性變差

A11 只要做了費力的事就會持續感到病懨懨、不舒服

Yeh ET et al. BMC Cancer 2011; 11:387.

癌因性疲憊症的定義: ICD-10

符合 A–D 四大要件

- **B** 疲累不堪的感覺會干擾到職場工作、家務處理、或人際互動。
- **C** 病歷、身體檢查、或生化檢查有記錄顯示疲憊症狀為癌症或癌症治療所引起。
- **D** 疲憊症狀不是由精神共病 (如重度憂鬱症、身體化疾患、心身症、或譫妄) 所引起。

Yeh ET et al. BMC Cancer 2011; 11:387.

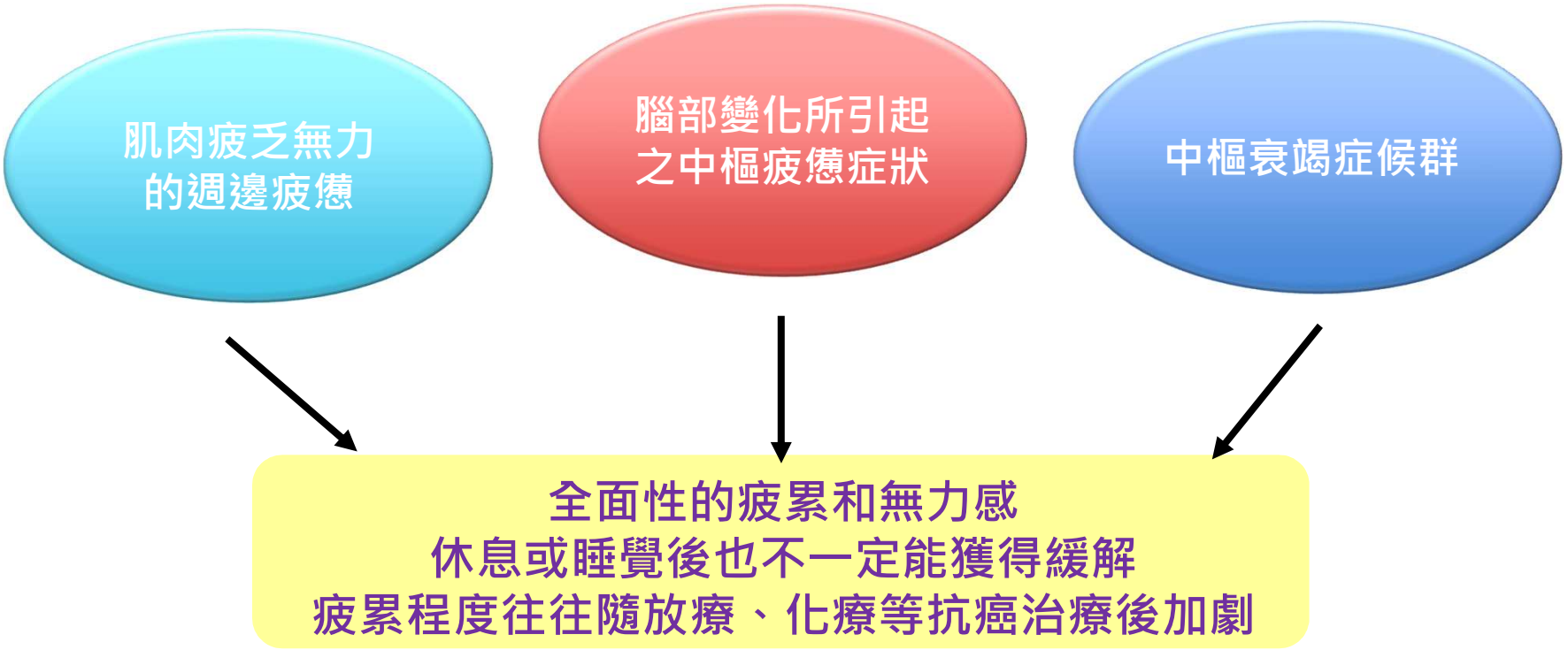
癌因性疲憊症的評估：NRS及VAS量表

數字等級量表 (Numerical Rating Scale, NRS) 及 視覺類比量表 (Visual Analogue Scale, VAS)

臨床驗證顯示 4 分以上的疲憊感即會影響正常生活，NCCN指引建議應特別關注這類病人[1]

1. NCCN. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue, Version 2.2017; 2017. https://www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf

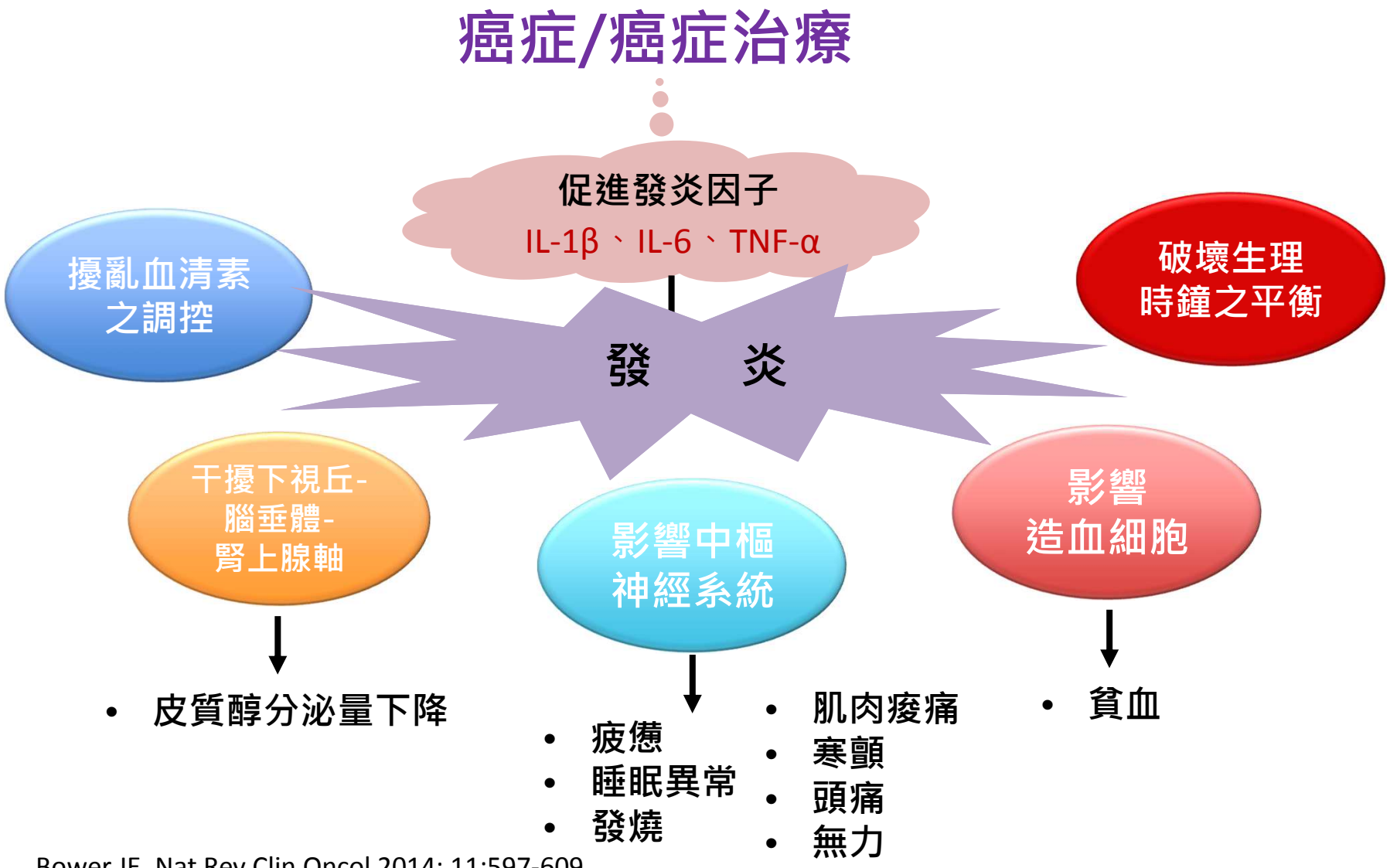
癌因性疲憊症有三種疲憊層面



- 疲憊是癌症病人最常見也最令人感到困擾的症狀之一，擾人的程度甚至超越疼痛、睡眠困難、食慾不振、和憂鬱等症狀[1]。
- 癌因性疲憊症包含三種疲憊層面，會造成全面性的疲累[2]。

1. Hsieh RK et al. J Clin Oncol 2015; 33(29_suppl):77.
2. Christensen Holz SA & Smith SR. Arch Phys Med Rehabil 2017; 98:1717-8.

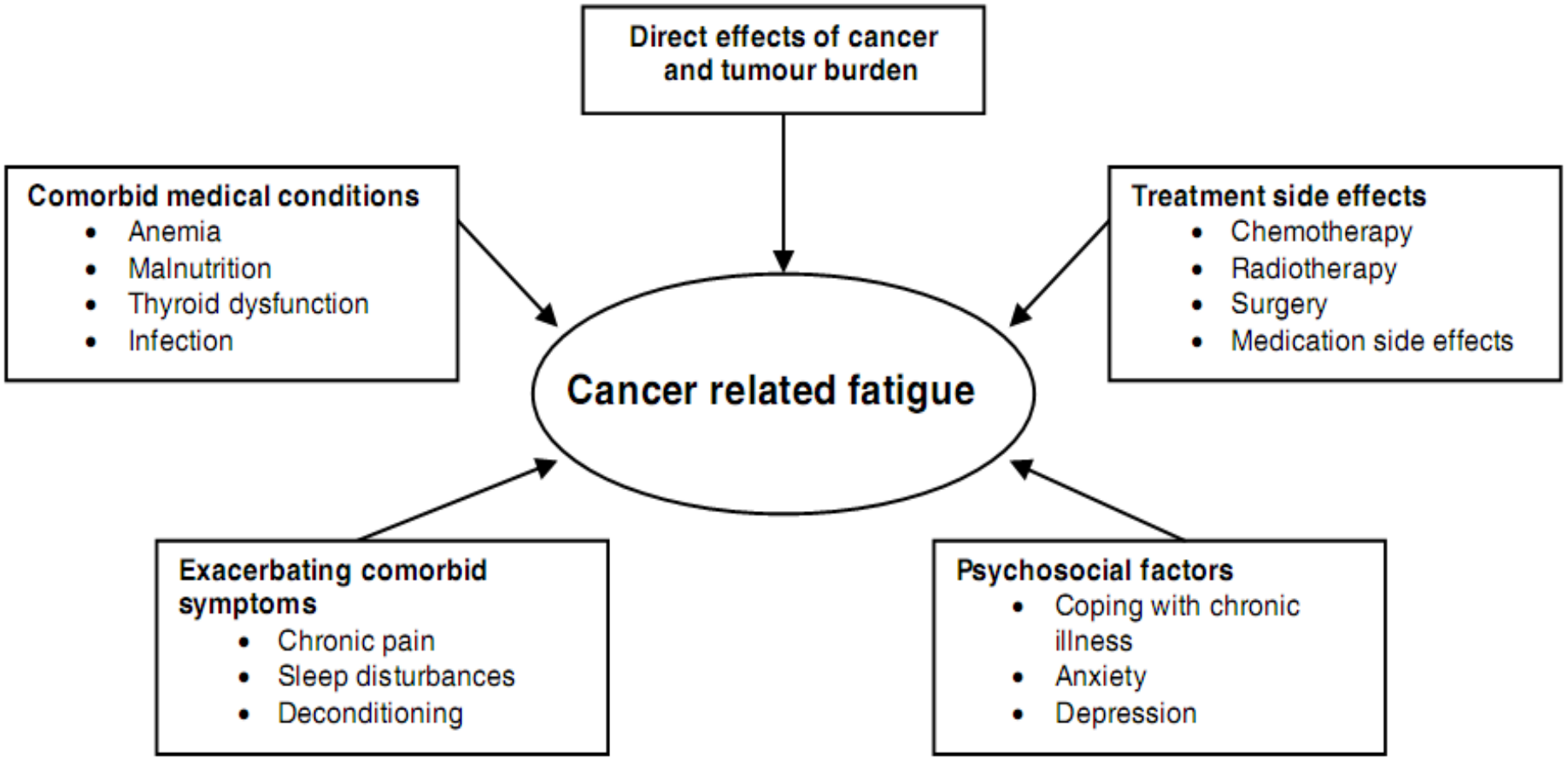
癌因性疲憊症之可能機轉~發炎假說



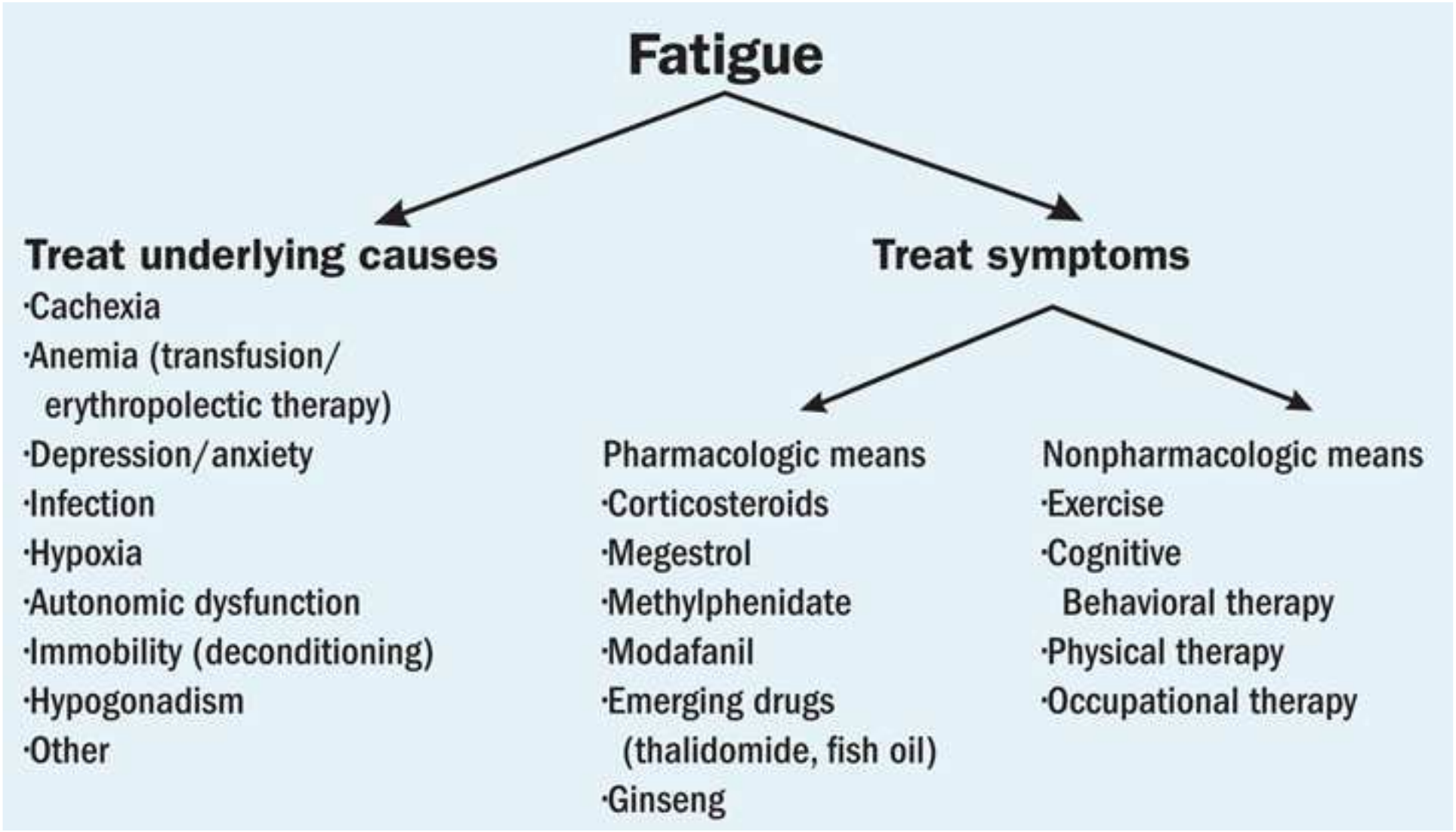
1. Bower JE. Nat Rev Clin Oncol 2014; 11:597-609.
2. Saligan LN et al. Support Care Cancer 2015; 23:2461-78.
3. Wang XS & Woodruff JF. Gynecol Oncol 2015; 136:446-52.


Cachexia
Autonomic failure
Muscular/neuromuscular abnormalities
Pain/drug side effects
Anemia
Psychological distress
FATIGUE
Hypogonadism
Cytokines
Infection
Dehydration
Metabolic problems
Chemotherapy/ radiotherapy

癌因性疲憊



British Journal of Cancer (2004) 91, 822–828


Fatigue
Treat underlying causes
·Cachexia
·Anemia (transfusion/ erythropolectic therapy)
·Depression/anxiety
·Infection
·Hypoxia
·Autonomic dysfunction
·Immobility (deconditioning)
·Hypogonadism
·Other
Treat symptoms
Pharmacologic means
·Corticosteroids
·Megestrol
·Methylphenidate
·Modafanil
·Emerging drugs (thalidomide, fish oil)
·Ginseng
Nonpharmacologic means
·Exercise
·Cognitive Behavioral therapy
·Physical therapy
·Occupational therapy

癌因性疲憊症的治療原則

- 癌症病人**在診斷後均應接受疲憊相關評估**，以期能及早發現疲憊問題並了解可能的導因，再進行處置和改善。
- 一般處置建議**從非藥物治療開始**，但如果無法改善疲憊或緩和疲憊的惡化，且已處理或排除其他可能的導因，就**應考慮進行藥物治療**。

NCCN. NCCN Clinical Practice Guidelines in Oncology: Cancer-Related Fatigue, Version 2.2017; 2017. https://www.nccn.org/professionals/physician_gls/PDF/fatigue.pdf

癌因性疲憊評估與治療

以NRS或BFI-T
評估疲憊

<4分
輕度疲憊

非藥物治療
運動、營養飲食、
認知行為治療、
睡眠衛生等

≥4分
中重度疲憊

加上藥物治療
- 癌因性疲憊適應症處方用藥
  PG2 Injection
- 其他用藥
  類固醇、中樞神經興奮劑

癌因性疲憊症之藥物治療

黃耆多醣注射劑有初步臨床試驗顯示可改善中重度癌因性疲憊症。 (Level IA, Grade A)	**蔘類**在臨床試驗顯示可以改善癌因性疲憊，但因中藥在使用上會因原料製備等影響，建議使用前應諮詢醫療團隊。 (Level IB, Grade B)
Methylphenidate 臨床研究顯示使用於疲憊程度或病情較嚴重的病人較具效果；但在用藥前應審慎考量劑量、用藥時間、濫用風險、及病人個人疾病等臨床情形，充分評估相關風險與效益。 (Level IA, Grade A)	**Methylprednisolone、dexamethasone**等類固醇藥物有臨床證據顯示可以改善癌症病人的疲憊和生活品質，但長期使用有安全風險，故建議只用於癌症末期、合併疲憊與厭食症、或有腦部或骨骼轉移而疼痛的癌症病人。 (Level IB, Grade B)

黃耆
(Astragalus membranaceus)

黃耆為豆科植物的根，在中藥中被列為上藥。古代醫家認為其功能為補氣升陽(增加元氣，提升能量)，益衛固表(提升免疫力)，利水消腫，托瘡生肌(肌肉增生)，為諸藥之長(中藥中的長老)，故名耆。

黃芪(耆)

- 補氣類中藥
- 【來源】

  – 始載於《神農本草經》，為豆科多年生草本植物蒙古黃芪或膜莢黃芪的乾燥根。

  –《本草綱目》中釋其名曰：“耆，長也。黃耆色黃，為補藥之長，故名。”

- 【性味歸經】

  甘，微溫。歸脾、肺經。

- 【功效】

  補氣升陽，益衛固表，利水消腫，托毒生肌。

- 【主治】

  內傷勞倦，脾虛泄瀉，脫肛、子宮脫垂、胃下垂等內臟下垂，婦女崩漏，自汗，盜汗，水腫，及一切氣虛血虧之証。

補氣藥之王：黃耆

《關於黃耆，你所不懂的》

鑑別	晉耆(紅皮耆)	北耆(白皮耆)
品種	多序岩黃耆	膜夾黃耆、蒙古黃耆
表皮	紅棕色	黃白色或黃褐色
甜味	甜味重	微甜
豆腥味	較淡或無	較重

資料提供：長庚紀念醫院中醫內兒科主治醫師王品涵

黃耆在中藥中被列為上藥，其功能為補氣升陽(增加元氣，提升能量)，益衛固表(提升免疫力)，利水消腫，托瘡生肌(肌肉增生)，為諸藥之長(中藥中的長老) ，故名耆。

在各種類黃耆中，產地在蒙古北部的蒙古黃耆，又稱為北耆，所含的黃耆多醣效果最佳。

北耆 膜莢黃耆

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Zhou L et al. Sci Rep. (2017)

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Cao Y et al. Oncotarget. (2017)

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Liu D et al. Int J Biol Macromol. (2018)

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1. Anti-tumor potential of **astragalus polysaccharides** on breast cancer cell line mediated by macrophage activation.
Li W, Song K, Wang S, Zhang C, Zhuang M, Wang Y, Liu T.
Mater Sci Eng C Mater Biol Appl. 2019 May;98:685-695. doi: 10.1016/j.msec.2019.01.025. Epub 2019 Jan 8.
PMID: 30813073

Wu et al. Cancer Cell Int (2017) 17:115
https://doi.org/10.1186/s12935-017-0487-6

Cancer Cell International

PRIMARY RESEARCH Open Access

Anticancer activity of *Astragalus* polysaccharide in human non-small cell lung cancer cells

Chao-Yan Wu[1], Yuan Ke[2], Yi-Fei Zeng[2], Ying-Wen Zhang[1] and Hai-Jun Yu[2*]

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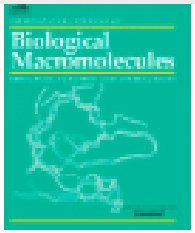
International Journal of Biological Macromolecules

Volume 106, January 2018, Pages 596-601

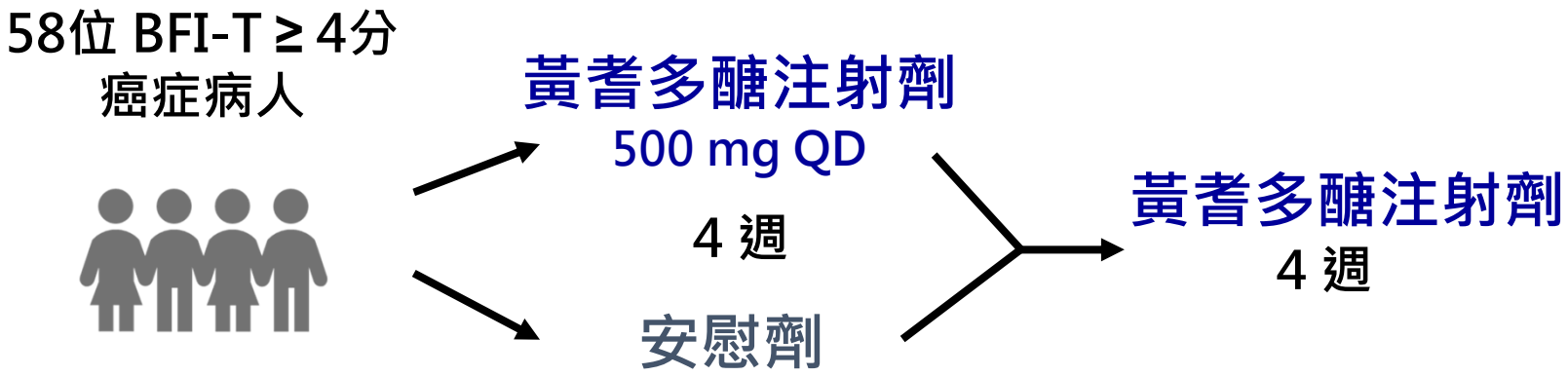


Immunomodulatory effects of herbal formula of astragalus polysaccharide (APS) and polysaccharopeptide (PSP) in mice with lung cancer

Xing Zhou [a], Zijing Liu [b], Tingting Long [a], Lijng Zhou [a], Yixi Bao [a]

黃耆多醣注射劑樞紐試驗設計

Phase II/III樞紐試驗

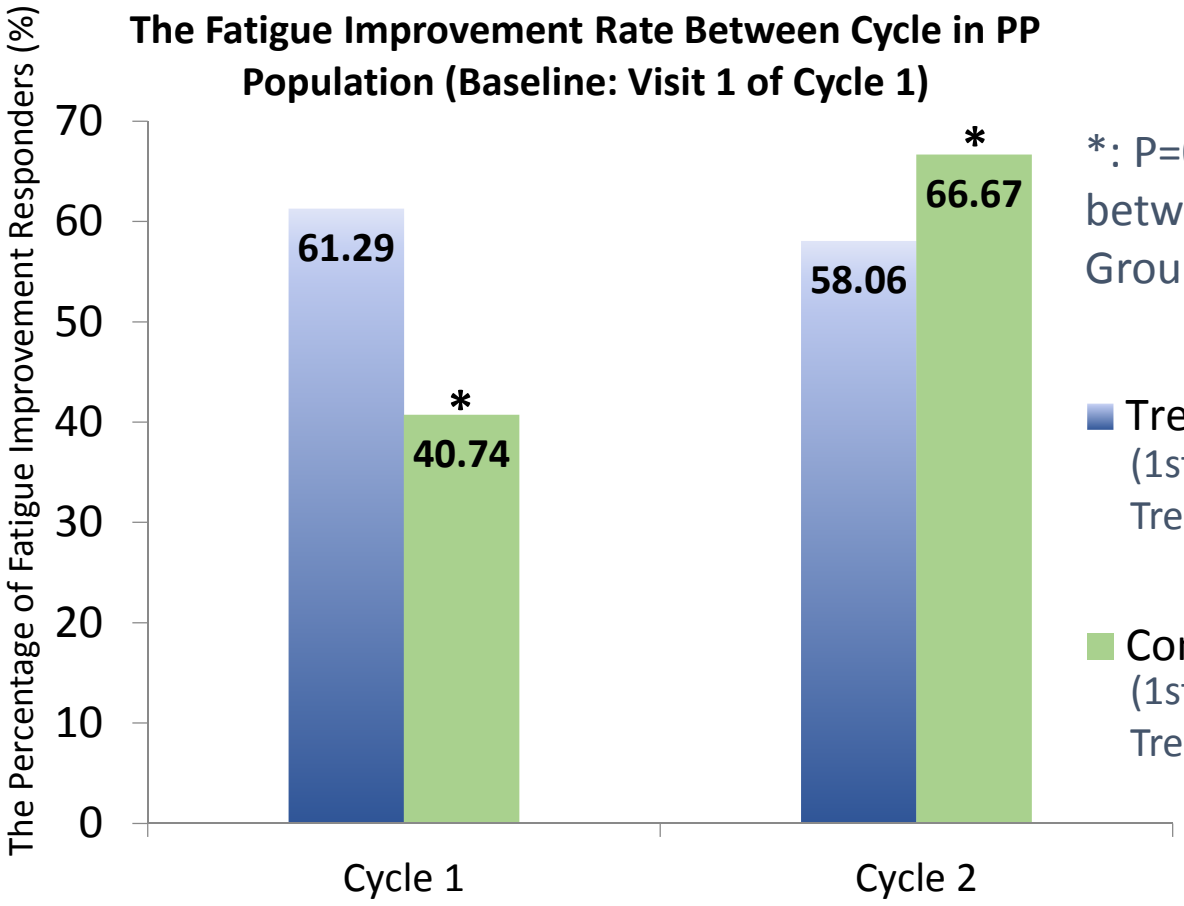


- 試驗首週後，疲憊改善的病人比率在黃耆多醣注射劑組較高 **(57% vs. 32%, P = 0.043)**
- 雙盲階段結束時，有**42.9%**的黃耆多醣注射劑組達到BFI-T分數降低20%以上的改善幅度。
- 試驗結束後，**82%**的黃耆多醣注射劑組受試者之癌因性疲憊症明顯改善，顯示長達8週的療程對病人有正面效果。

Chen HW et al. Clin Invest Med 2012; 35:E1-11.

黃耆多醣注射劑可有效改善疲憊

Phase II/III樞紐試驗



*: P=0.020 (The comparison between two cycles in the Control Group by McNemar's test)

Treatment Group
(1st and 2nd Cycle PG2 and PG2 Treatment; n=31)

Control Group
(1st and 2nd Cycle Placebo and PG2 Treatment; n=27)

- 改善幅度最大的BFI-T項目為行走能力和情緒
- 黃耆多醣注射劑組的不良反應發生率或嚴重程度未明顯高於安慰劑組
- 主要不良反應為輕微的皮疹、濕疹、或搔癢症，多不須額外處置即恢復

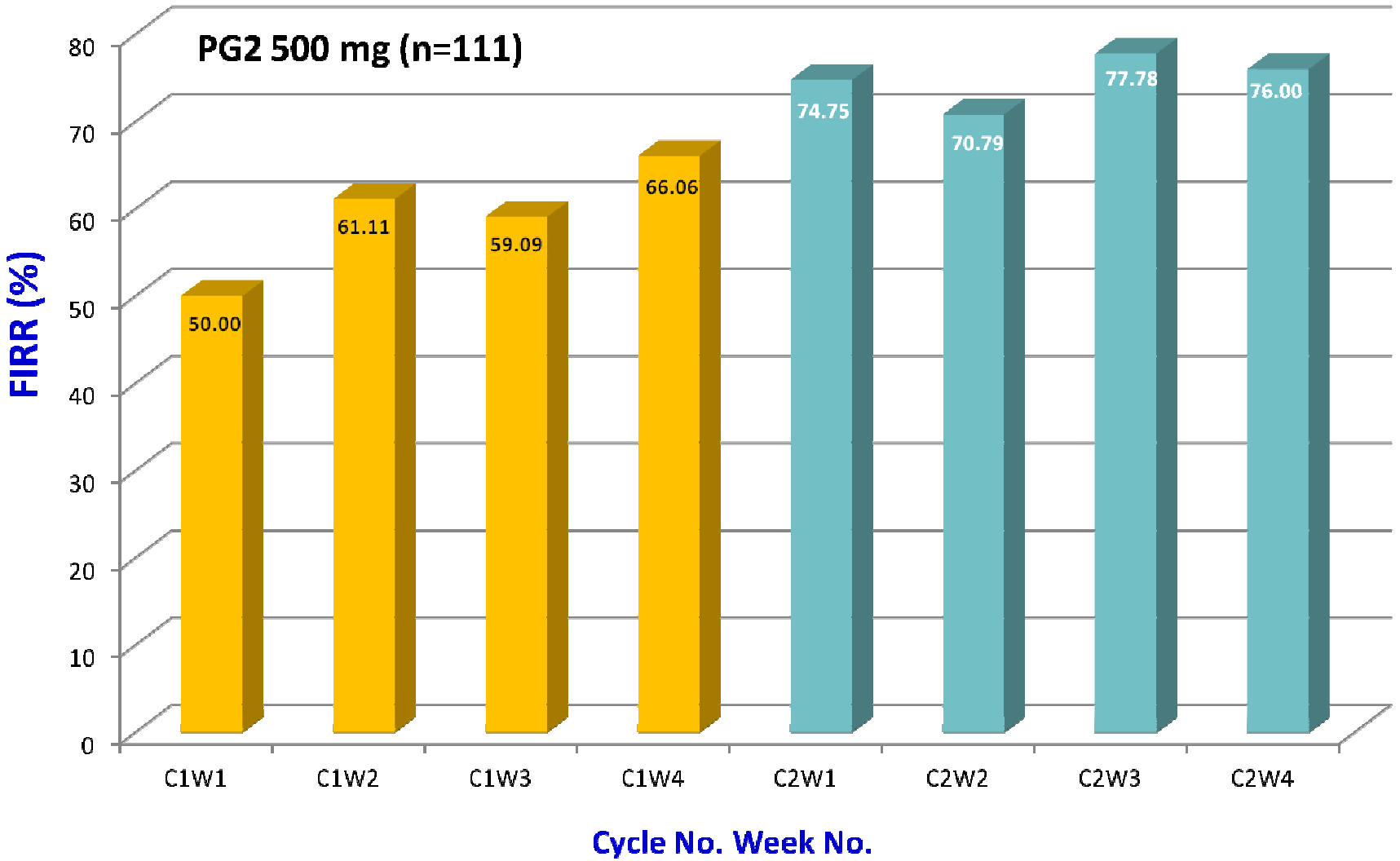
Chen HW et al. Clin Invest Med 2012; 35:E1-11.

PG2 Phase IV Trial

Center	馬偕，雙和，基隆長庚情人湖院區，三總，彰基，奇美柳營，中醫大，林口長庚，高雄長庚
Trial Objective	To evaluate the efficacy and safety of different doses of PG2 for relieving fatigue among advanced cancer patients who are under standard palliative care (SPC).
Blinding/ Randomization	Double-blinded/Randomized
Treatment Regimens	Two parallel arms: 1. PG2 500 mg by IV infusion for 3 days per week 2. PG2 250 mg by IV infusion for 3 days per week
Study Period	8 weeks
Primary Endpoint	Fatigue Improvement Response Rate (FIRR)
Sample Size	Enrolled Patient No.: 323 Evaluable Patient No.: 214 (1:1 ratio)

FIRR by Week during the Whole Study Period

Cut-off Point of FIR: 10 %



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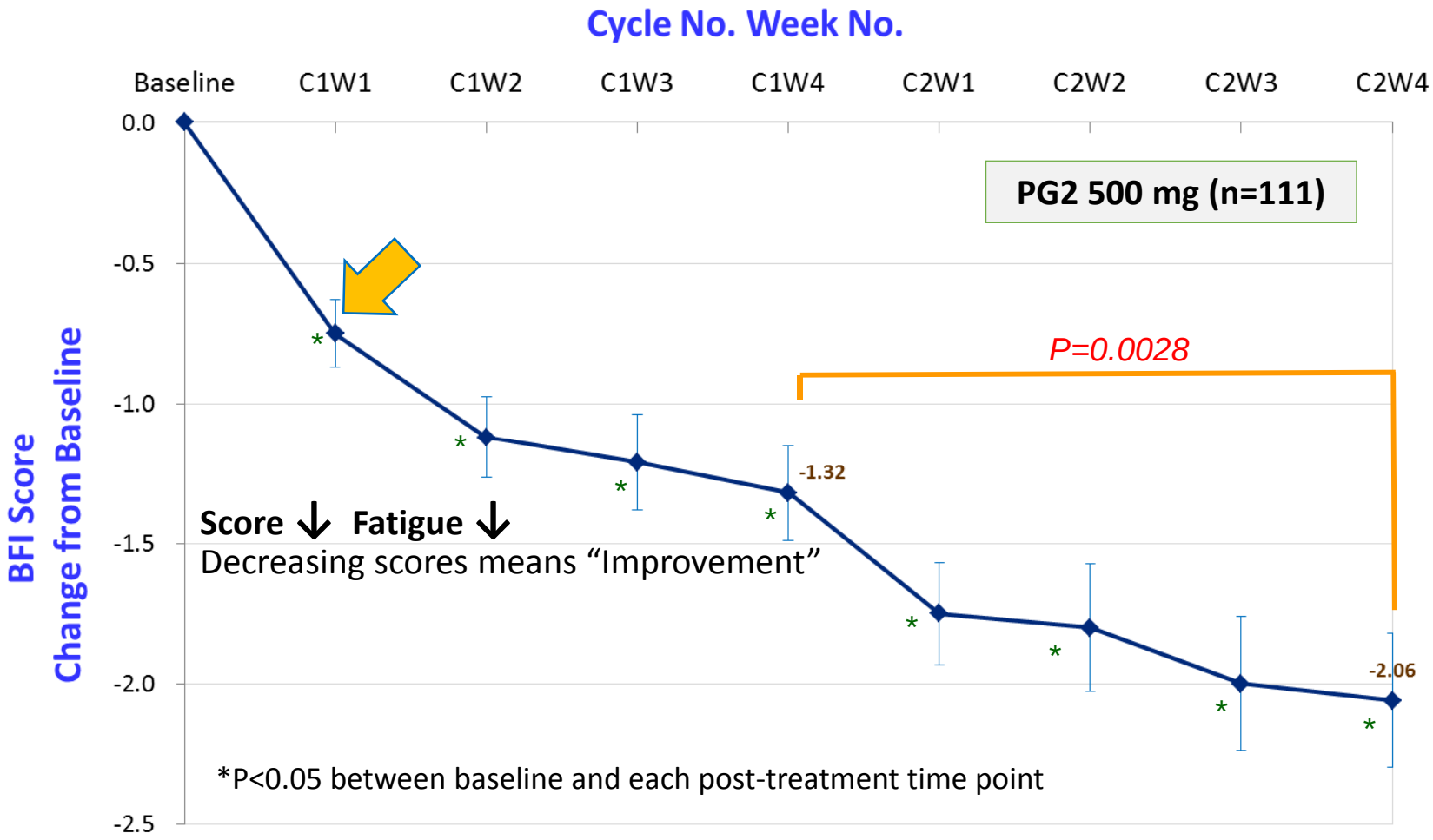
Mean BFI Score Change



- ✓ **PG2 treatment showed efficacy in relieving fatigue as early as the first week of treatment.**
- ✓ **PG2 is more effective at the end of cycle 2 compared to cycle 1.**

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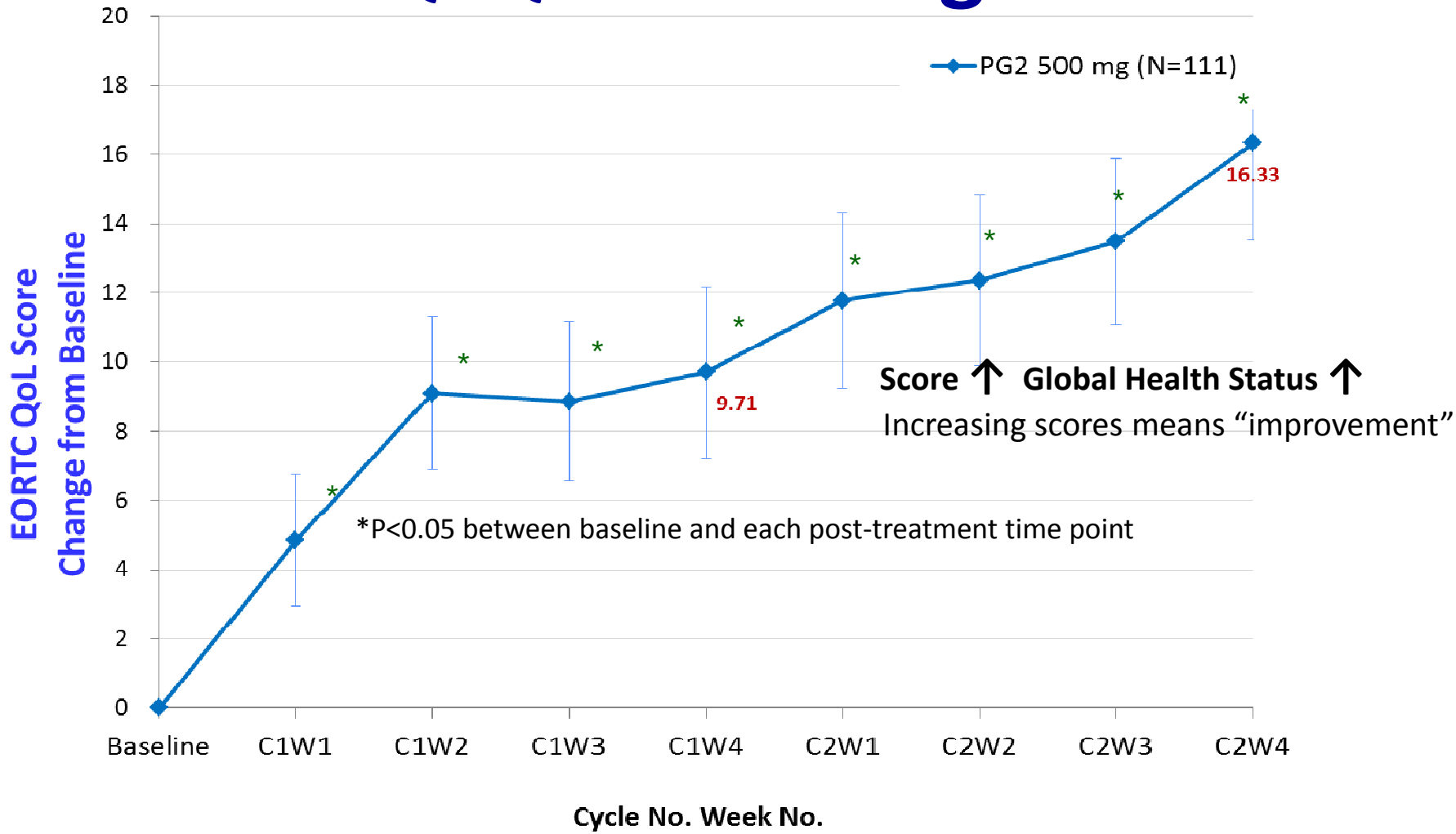
Global Health Status: EORTC-QLQ-C30 Change



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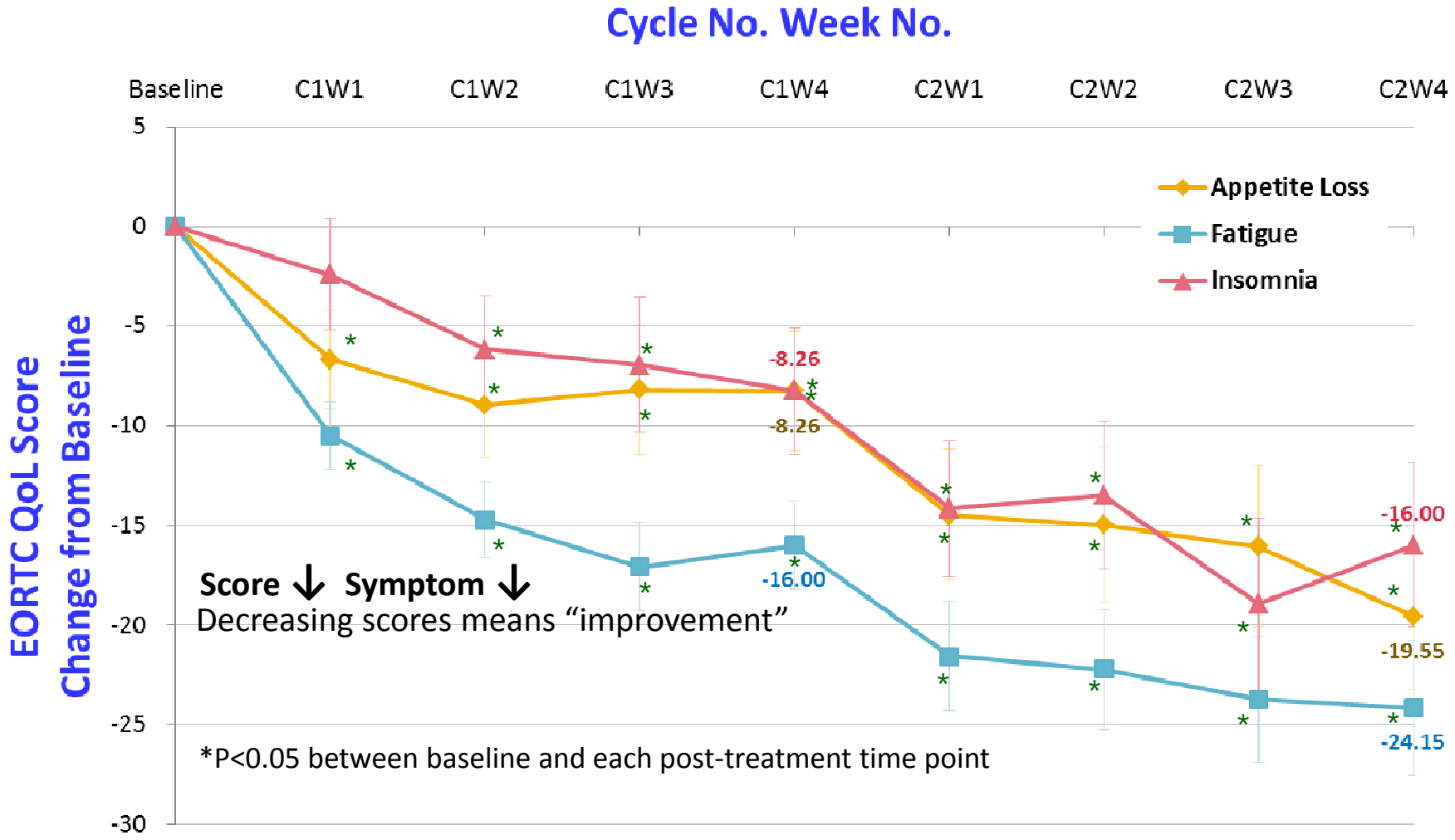
Global Health Status: domains with significant improvement



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cancers

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Article

Karnofsky Performance Status as A Predictive Factor for Cancer-Related Fatigue Treatment with Astragalus Polysaccharides (PG2) Injection—A Double Blind, Multi-Center, Randomized Phase IV Study

Cheng-Hsu Wang [1], Cheng-Yao Lin [2], Jen-Shi Chen [3,4], Ching-Liang Ho [5], Kun-Ming Rau [6,7,8], Jo-Ting Tsai [9,10], Cheng-Shyong Chang [11], Su-Peng Yeh [12], Chieh-Fang Cheng [13] and Yuen-Liang Lai [14,15,*]

Received: 22 October 2018; Accepted: 15 January 2019; Published: 22 January 2019

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Cancers **2019**, *11*, 128; doi:10.3390/cancers11020128

www.mdpi.com/journal/cancers

Multivariate analysis for responders and non-responders to PG2

- Patients with **higher KPS** responded **better to PG2**.
- Identified **KPS as a promising predictive factor** for the therapeutic efficacy of PG2.

Table 3. Multivariate analysis for responders and non-responders to Astragalus Polysaccharides (PG2) injection.

All Subjects	Cut-off Points = 10%			Multivariate Analysis	
Variable/Status	Responder (*N* = 140)	Non-Responder (*N* = 74)	Univariate Analysis *p*-value *	Odds Ratio (95% CI)	*p*-value **
Baseline KPS score					
30–50	22 (15.71%)	31 (41.89%)	<0.0001 [C]	0.253 (0.126, 0.504)	<0.0001
60–90	118 (84.29%)	43 (58.11%)			
4–6	72 (51.43%)	41 (55.41%)	0.5794 [C]	0.885 (0.475, 1.647)	0.6998
7–10	68 (48.57%)	33 (44.59%)			
Cancer Type: three categories					
Lung cancer	22 (15.71%)	12 (16.22%)	0.2876 [C]		
Breast cancer	22 (15.71%)	6 (8.11%)		1.297 (0.343, 4.905)	0.7020
other	96 (68.57%)	56 (75.68%)		0.957 (0.414, 2.208)	0.9173
Albumin (g/dL)					
<3.0	20 (14.29%)	11 (14.86%)	0.9088 [C]	1.272 (0.518, 3.124)	0.5997
≥3.0	120 (85.71%)	63 (85.14%)			
Hemoglobin (g/dL)					
<10	48 (34.29%)	30 (40.54%)	0.3659 [C]	0.767 (0.405, 1.452)	0.4148
≥10	92 (65.71%)	44 (59.46%)			
Peripheral blood TLC (/μL)					
<700	46 (32.86%)	18 (24.32%)	0.1947 [C]	1.709 (0.846, 3.452)	0.1353
≥700	94 (67.14%)	56 (75.68%)			

* The Wilcoxon rank-sum test [W] was used to compare the difference between responders and non-responders for continuous variables; the Chi-squared test [C] was used to compare the difference between responders and non-responders for categorical variables. ** A logistic regression model was used to compare the differences between responders and non-responders.

Baseline KPS score	Responder %
30-50 (N=53)	22 (42%)
60-90 (N=161)	118 (73%)

Cancers 2019, 11, 128; doi:10.3390/cancers11020128

Summary of PG2® Phase IV Study

- **Fatigue improvement**

✓ PG2® treatment showed efficacy in relieving fatigue as early as the first week of treatment.

✓ Clinically meaningful fatigue improvement (≥ 10%) was observed in more than 65% of subjects receiving PG2® after the cycle 1 treatment when compared to baseline.

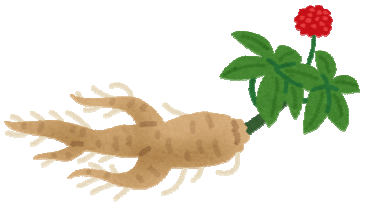
✓ Patients with higher KPS showed better chance to respond to PG2 treatment in BFI-T score.

2018 ASCO Annual Meeting, Poster Presentation

使用蔘類應諮詢醫療團隊的專業建議

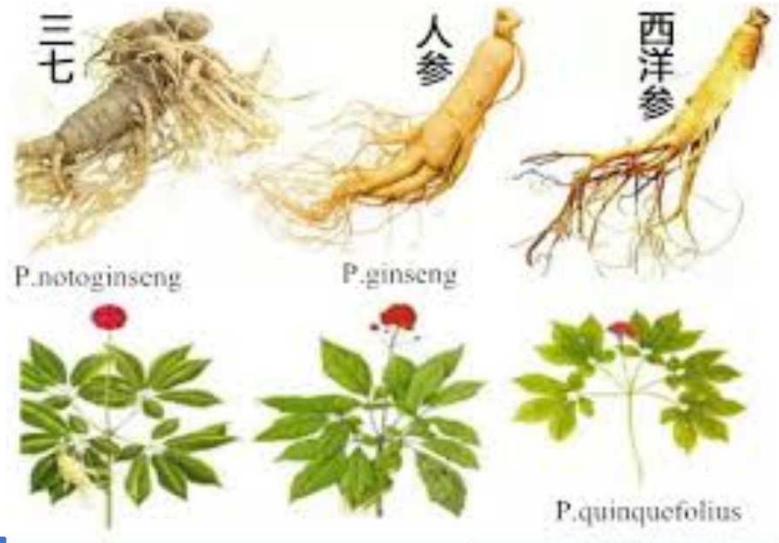
使用蔘類的關鍵可能在於[1]:

- **試驗使用含有至少3%人蔘皂苷的標準化粉末**
- **療程較長**
- 蔘類可能會**和抗凝血劑warfarin有交互作用**[2]
- 中草藥在使用上會因**原料形式、製備方法、或服用期間而影響療效**
- **使用前應先諮詢醫療團隊的專業建議，並依其指示服用**



1. Thomas GB et al. J Fam Pract 2014; 63:270-2.
2. Yuan CS et al. Ann Intern Med 2004; 141:23-7.

蔘類的類型、劑量、和療程非常關鍵



蔘類 (分為亞洲蔘和西洋蔘)

傳統功效

- 可補血補氣
- 有補氣救脫、益血復脈、養心安神等功效

試驗簡介	每日平均治療劑量	療程	結果
Yennurajalingam et al., 2017[1] (n = 112)	亞洲蔘 (Panax ginseng) 800 mg	4週	疲憊較嚴重 、憂鬱傾向 、男性病人才明顯優於對照
Kim et al., 2017[2] (n = 438)	紅蔘 (蒸製並乾燥後的亞洲蔘) 2,000 mg	16週	顯著改善疲憊程度
Barton et al., 2010[3] (n = 290)	西洋蔘 (Panax quinquefolius) 750 mg、1,000 mg、2,000 mg	8週	1,000、2,000 mg組疲憊改善幅度優於其他組別
Barton et al., 2013[4] (n = 364)	西洋蔘 2,000 mg	8週	疲憊改善幅度優於對照組

1. Yennurajalingam S et al. J Natl Compr Canc Netw 2017; 15:1111-20.
2. Kim YH et al. J Clin Oncol 2017; 35(15_suppl):10008, Abstract 10008
3. Barton DL et al. Support Care Cancer 2010; 18:179-87.
4. Barton DL et al. J Natl Cancer Inst 2013; 105:1230-8.

Bruera E

- **A Double-Blind, Randomized, Placebo-Controlled Trial of *Panax Ginseng* for Cancer-Related Fatigue in Patients With Advanced Cancer.**

Yennurajalingam S[1], Tannir NM[1], Williams JL[1], Lu Z[1], Hess KR[1], Frisbee-Hume S[1], House HL[1], Lim ZD[1], Lim KH[1,1], Lopez G[1], Reddy A[1], Azhar A[1], Wong A[1], Patel SM[1], Kuban DA[1], Kaseb AO[1], Cohen L[1], Bruera E[1].

- **Conclusions:**
- ***Panax Ginseng*** was

  not significantly superior to placebo after 4 weeks of treatment.
- There is NO justification to recommend the use of Panax Ginseng for CRF.

J Natl Compr Canc Netw. 2017 Sep;15(9):1111-1120

癌因性疲憊症規律評估

2018-10-15

台灣癌症安寧緩和醫學會
Taiwan Society of Cancer Palliative Medicine

癌因性疲憊症日記

2017年台灣癌症安寧緩和醫學會與台灣腫瘤護理學會共同制定並發行『癌因性疲憊症之臨床治療指引』提高對此之關注，並做為臨床醫護人員治療時之使用參考。2018年台灣癌症安寧緩和醫學會發展『疲憊日誌』，提供給癌症病人了解癌因性疲憊症及評估紀錄疲憊分數的工具，希望結合病人及臨床醫護人員的投入，一起共同增進癌症治療照護的品質。

問：什麼是癌因性疲憊症？

答：癌因性疲憊症 (Cancer-related fatigue, CRF)是指因癌症或癌症治療所引起的主觀且長時間感到難以遏止的精疲力竭。身、心、靈持續缺乏能量，而造成情緒、認知及體能的負擔，並影響日常生活。癌症病人的疲憊與活動量沒有直接的關係，且無法透過休息獲得緩解。

問：『疲憊日誌』要如何填寫使用？

答：疲憊、缺乏活動力、注意力不集中、失眠或嗜睡、食慾不振、憂鬱、對生活及人與人相處缺乏興趣等，都是癌因性疲憊症常見的症狀。您可利用手冊中的「疲憊量尺」選出最符合您當下疲憊感受的分數，每天規律的評估，寫下您的疲憊分數和處置方法在『疲憊日誌』中，並即時向醫護人員反應和討論您的疲憊狀況。

問：『疲憊日誌』可以幫助我什麼呢？

答：疲憊時容易產生負面想法，對於疾病治療感到無力，或想放棄治療。藉由『疲憊日誌』評估和紀錄您的疲憊分數，及時主動向醫護人員反應，協助您與醫護人員更有效的溝通，也讓醫護團隊了解您的疲憊，根據您的疲憊狀況，提供最適合的治療方式，讓您的疲憊獲得改善和治療，以避免因疲憊造成療程延遲或中斷，影響治療成效。

附件下載

- 6周記錄表- 疲憊日誌
- 完整版-疲憊日誌

癌因性疲憊症規律評估

3 疲憊量尺

0 1 2 3 4 5 6 7 8 9 10

以0分為沒有疲憊，10分為想像中最嚴重的疲憊，請您根據自身疲憊的感覺指出對應的疲憊分數。或選擇最能代表您疲備狀態的圖像及其對應的分數。

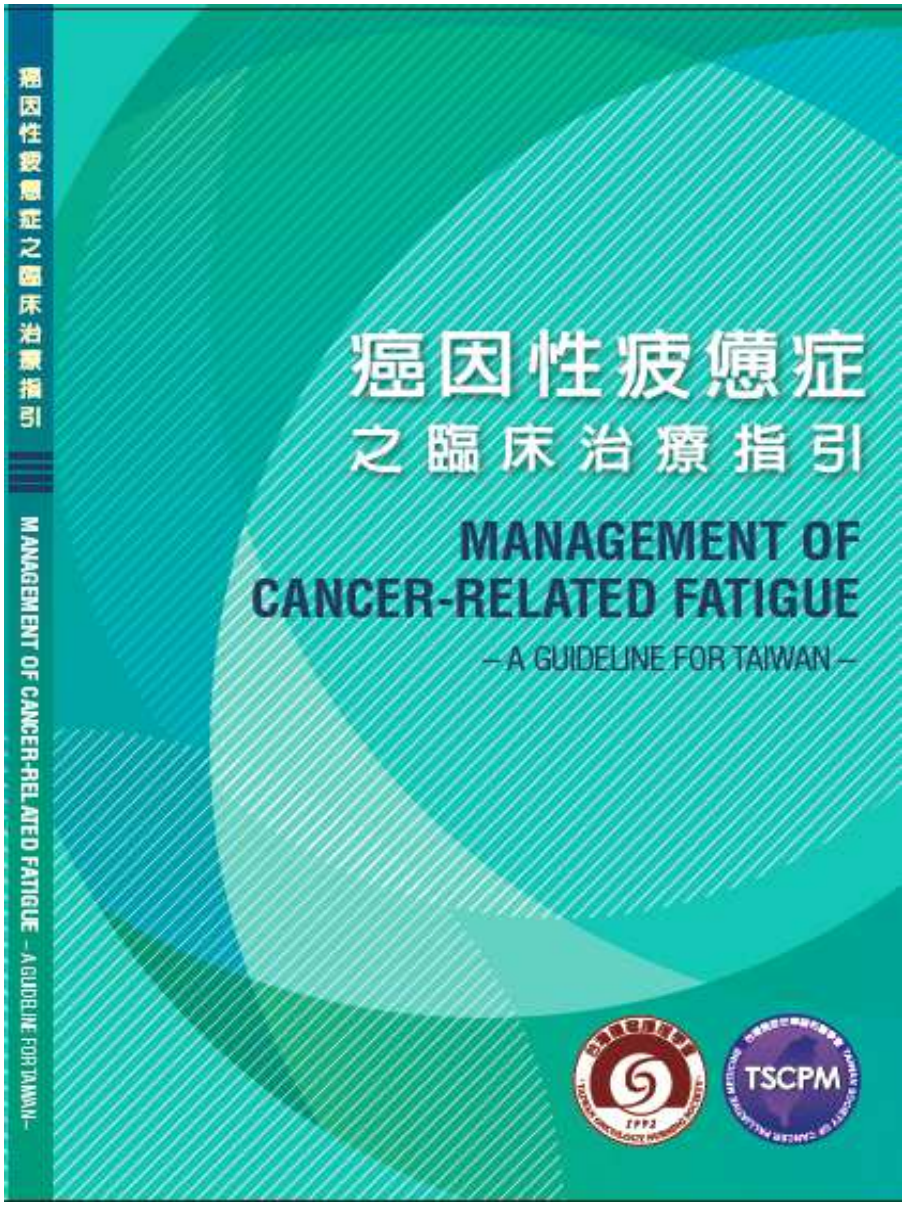
疲憊日誌

每天規律的評估、記錄疲憊分數或處置方法，這些資料有助您的醫療團隊更有效的提供處置方案。

	非藥物處置	藥物處置
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____

	非藥物處置	藥物處置
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____
日期 疲憊分數	□運動 □睡眠衛生 □輔助治療 □心理社會措施 □營養處置 □其他____	□精神刺激藥物 □類固醇 □黃耆多醣注射劑 □中草藥藥物 □其他____

♥ 貼心小叮嚀 ♥
遵照醫護人員的指示，配合治療方式調整生活，按時複診，如果藥物的幫助不大，或是有副作用，請告訴醫護人員。請記住，您的疲憊是可以緩解的！



癌因性疲憊症之臨床治療指引電子版連結由此去

”Cure sometimes, treat often, comfort always“

Hippocrates