



Introduction and presentation of the basic notions of Health-related quality of life

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Health-related quality of life

WHO (1948) « *health is a complete physical, mental and social well-being and not merely the absence of disease or infirmity* »



WHO (1994) « **Quality of life** is an individual's perception of his position in life in the context of culture and value systems in which they live, in relation to their goals, expectations, standards and concerns »



Health-related quality of life (HRQoL)

Multidimensional concept including at least **physical, mental and social dimensions** as well as symptoms due to disease and treatment

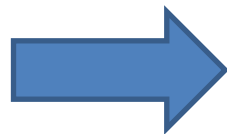
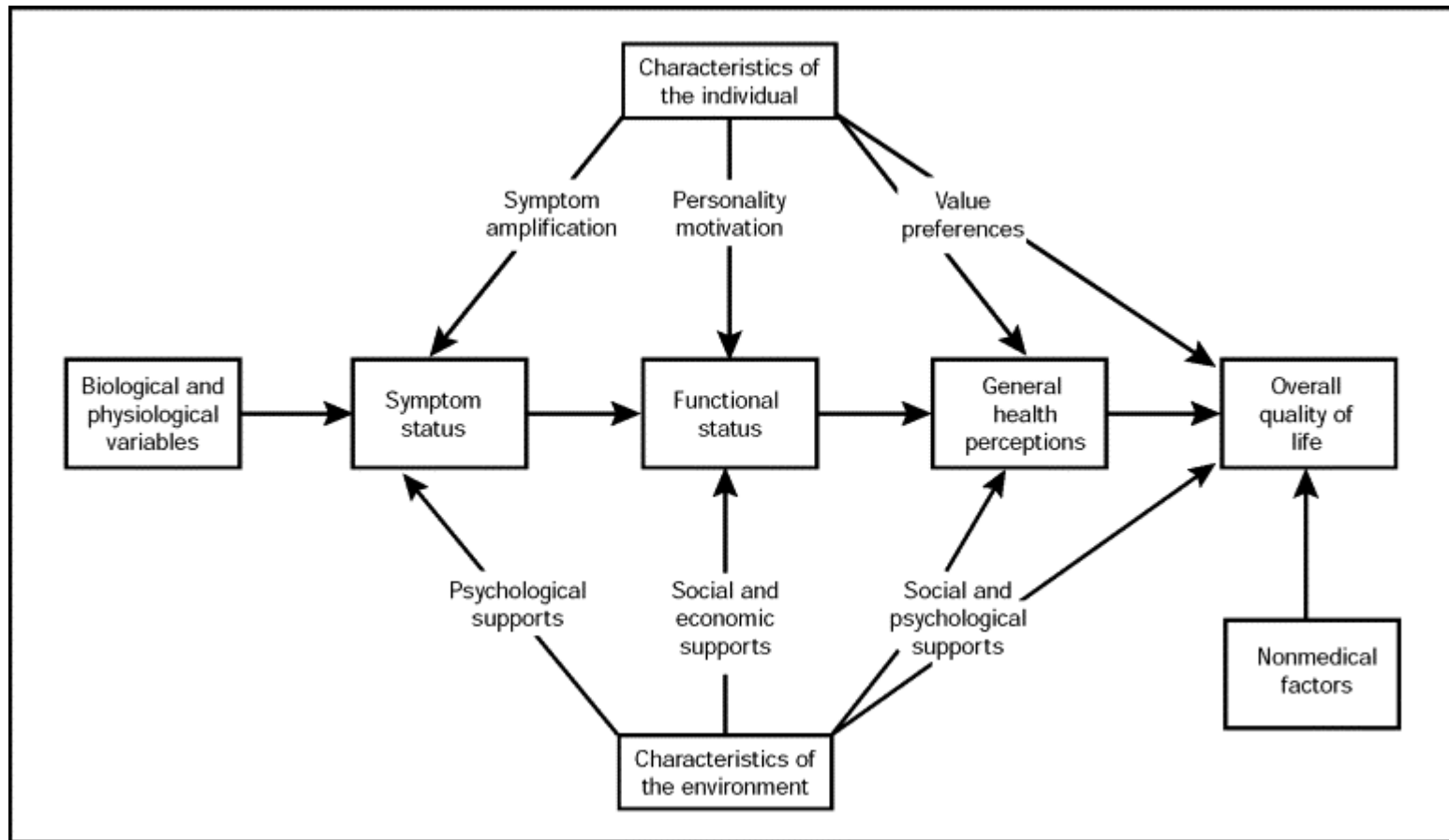
Patient-reported outcomes

- HRQoL falls within the “patient-reported outcomes”
- PRO = Health outcome directly reported by the patient who experienced




Dynamic relationship between 5 endpoints in health

Revised model of Wilson et Cleary {1995}.



A subjective and dynamic concept

How to assess HRQoL?

- **Qualitative assessment using interview**
- **Quantitative assessment using validated questionnaires**
 - Auto-assessment when it is possible
 -  Hetero-assessment for end of life (ALIM-K), elderly patients
 - Generic or specific HRQoL questionnaires



EORTC QLQ-C30 (version 3)

Nous nous intéressons à vous et à votre santé. Répondez vous-même à toutes les questions en entourant le chiffre qui correspond le mieux à votre situation. Il n'y a pas de "bonne" ou de "mauvaise" réponse. Ces informations sont strictement confidentielles.

Merci de préciser:

Vos initiales:

Date de naissance (jour/mois/année):

La date d'aujourd'hui (jour/mois/année):

31									

	Pas du tout	Un peu	Assez	Beaucoup
1. Avez-vous des difficultés à faire certains efforts physiques pénibles comme porter un sac à provisions chargé ou une valise?	1	2	3	4
2. Avez-vous des difficultés à faire une <u>longue</u> promenade?	1	2	3	4
3. Avez-vous des difficultés à faire un <u>petit</u> tour dehors?	1	2	3	4
4. Etes-vous obligée de rester au lit ou dans un fauteuil pendant la journée?	1	2	3	4
5. Avez-vous besoin d'aide pour manger, vous habiller, faire votre toilette ou aller aux toilettes?	1	2	3	4

Au cours de la semaine passée:

	Pas du tout	Un peu	Assez	Beaucoup
6. Avez-vous été gênée pour faire votre travail ou vos activités de tous les jours?	1	2	3	4
7. Avez-vous été gênée dans vos activités de loisirs?	1	2	3	4
8. Avez-vous eu le souffle court?	1	2	3	4
9. Avez-vous ressenti de la douleur?	1	2	3	4
10. Avez-vous eu besoin de repos?	1	2	3	4
11. Avez-vous eu des difficultés pour dormir?	1	2	3	4
12. Vous êtes-vous sentie faible?	1	2	3	4
13. Avez-vous manqué d'appétit?	1	2	3	4
14. Avez-vous eu des nausées (mal au coeur)?	1	2	3	4
15. Avez-vous vomi?	1	2	3	4

Au cours de la semaine passée:

Au cours de la semaine passée:					Pas du tout	Un peu	Assez	Beaucoup
16.	Avez-vous été constipée?				1	2	3	4
17.	Avez-vous eu de la diarrhée?				1	2	3	4
18.	Etiez-vous fatiguée?				1	2	3	4
19.	Des douleurs ont-elles perturbé vos activités quotidiennes?				1	2	3	4
20.	Avez-vous eu des difficultés à vous concentrer sur certaines choses par exemple pour lire le journal ou regarder la télévision?				1	2	3	4
21.	Vous êtes-vous sentie tendue?				1	2	3	4
22.	Vous êtes-vous fait du souci?				1	2	3	4
23.	Vous êtes-vous sentie irritable?				1	2	3	4
24.	Vous êtes-vous sentie déprimée?				1	2	3	4
25.	Avez-vous eu des difficultés pour vous souvenir de certaines choses?				1	2	3	4
26.	Votre état physique ou votre traitement médical vous ont-ils gênée dans votre vie <u>familiale</u> ?				1	2	3	4
27.	Votre état physique ou votre traitement médical vous ont-ils gênée dans vos activités <u>sociales</u> (par exemple, sortir avec des amis, aller au cinéma...)?				1	2	3	4
28.	Votre état physique ou votre traitement médical vous ont-ils causé des problèmes financiers?				1	2	3	4
9.	Comment évalueriez-vous votre <u>état de santé</u> au cours de la semaine passée?							
	1	2	3	4	5	6	7	
Très mauvais							Excellent	
10.	Comment évalueriez-vous l'ensemble de votre <u>qualité de vie</u> au cours de la semaine passée?							
	1	2	3	4	5	6	7	
Très mauvaise							Excellente	

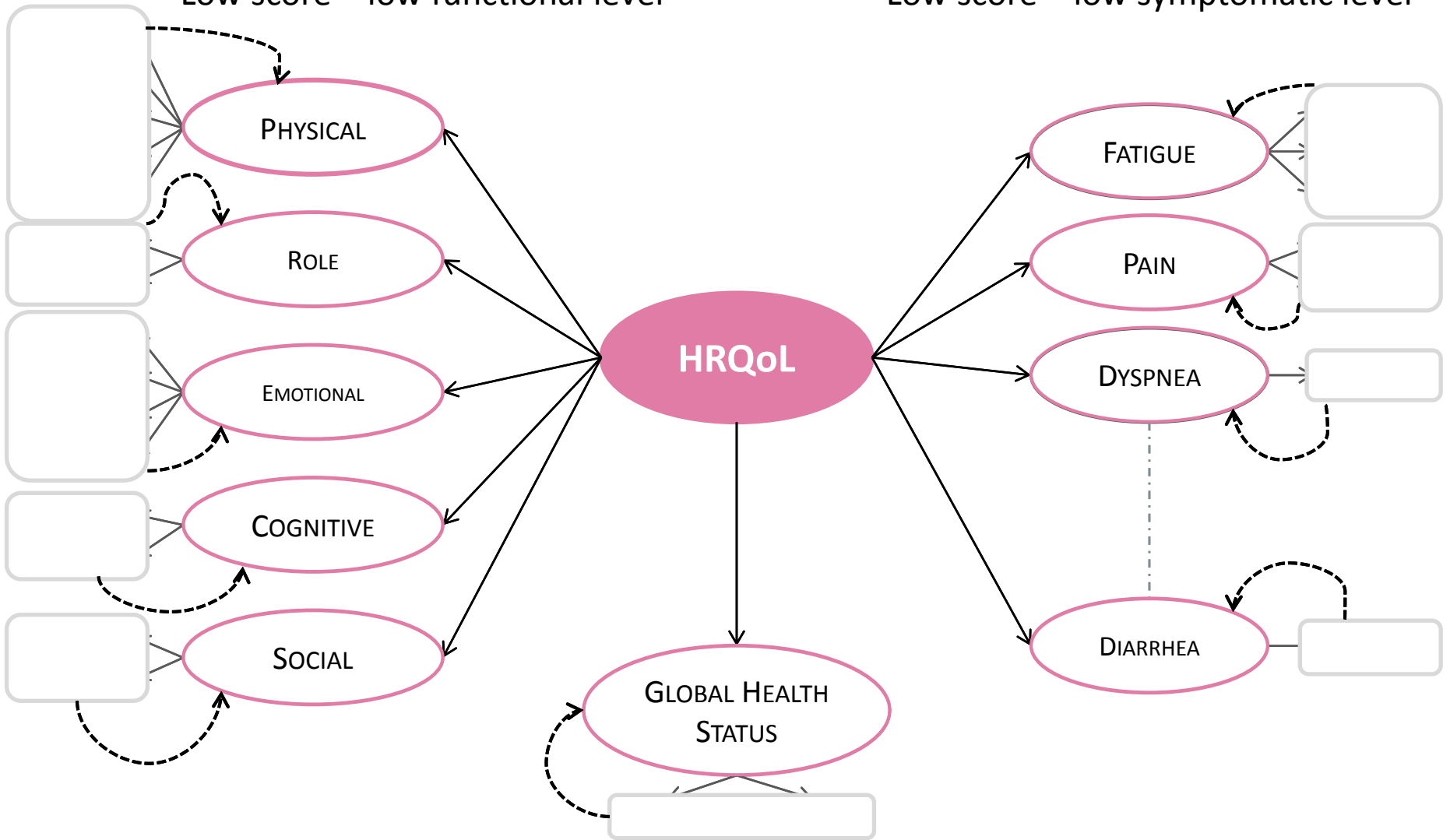
QLQ-C30

FUNCTIONS

Low score = low functional level

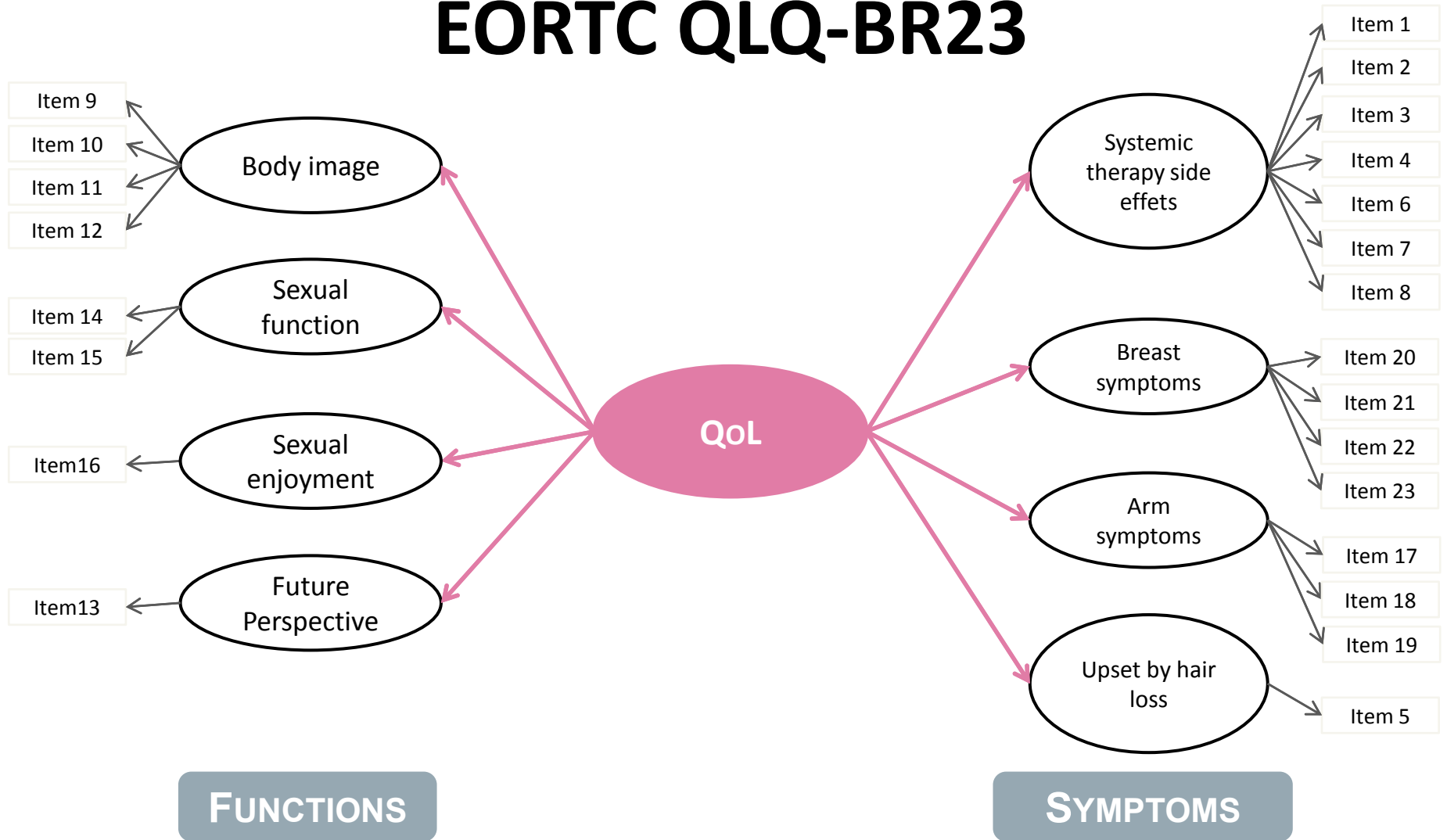
SYMPTOMS

Low score = low symptomatic level



15 scores varying on a 0 to 100 scale

EORTC QLQ-BR23



Low score = low functional level

Low score = low Symptomatic level

Mode of administration

Qual Life Res
DOI 10.1007/s11136-015-1110-8



SPECIAL SECTION: PROS IN NON-STANDARD SETTINGS (BY INVITATION ONLY)

Mode of administration does not cause bias in patient-reported outcome results: a meta-analysis

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Holly Rice³ • Liam Gabb⁴ • Madeleine King^{1,2}



A combination of electronic and paper self-completion and assisted completion methods can be used in the clinic and at home, based on patient preference for mode. To fill the

We can use all types of assessment methods without bias

Endpoints in oncology clinical trials



- **Clinical endpoints**

Reflect what the patient perceives of a function or survival

➡ Overall Survival; HRQoL; Patient-reported outcomes

- **Biological/tumor endpoints**

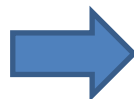
Quantitative and objective measure

➡ Progression Free Survival; Disease Free Survival

- **Surrogate endpoints:**

Biological endpoint which must predict the clinical benefit of treatments evaluated less patients & evaluated earlier than OS

Alternative



tumor endpoint such as PFS
+ HRQoL to ensure the clinical benefit

Table 1. A Comparison of Important Cancer Approval Endpoints

Endpoint	Regulatory Evidence	Study Design	Advantages	Disadvantages
Overall Survival	Clinical benefit for regular approval	<ul style="list-style-type: none"> Randomized studies essential Blinding not essential 	<ul style="list-style-type: none"> Universally accepted direct measure of benefit Easily measured Precisely measured 	<ul style="list-style-type: none"> May involve larger studies May be affected by crossover therapy and sequential therapy Includes noncancer deaths
Symptom Endpoints (patient-reported outcomes)	Clinical benefit for regular approval	<ul style="list-style-type: none"> Randomized blinded studies 	<ul style="list-style-type: none"> Patient perspective of direct clinical benefit 	<ul style="list-style-type: none"> Blinding is often difficult Data are frequently missing or incomplete Clinical significance of small changes is unknown Multiple analyses Lack of validated instruments
Disease-Free Survival	Surrogate for accelerated approval or regular approval*	<ul style="list-style-type: none"> Randomized studies essential Blinding preferred Blinded review recommended 	<ul style="list-style-type: none"> Smaller sample size and shorter follow-up necessary compared with survival studies 	<ul style="list-style-type: none"> Not statistically validated as surrogate for survival in all settings Not precisely measured; subject to assessment bias, particularly in open-label studies Definitions vary among studies

1st: Overall survival
2nd: PRO/HRQoL

Guidance for Industry Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics

Table 1, continued

Endpoint	Regulatory Evidence	Study Design	Advantages	Disadvantages
Objective Response Rate	Surrogate for accelerated approval or regular approval*	<ul style="list-style-type: none"> Single-arm or randomized studies can be used Blinding preferred in comparative studies Blinded review recommended 	<ul style="list-style-type: none"> Can be assessed in single-arm studies Assessed earlier and in smaller studies compared with survival studies Effect attributable to drug, not natural history 	<ul style="list-style-type: none"> Not a direct measure of benefit Not a comprehensive measure of drug activity Only a subset of patients who benefit
Complete Response	Surrogate for accelerated approval or regular approval*	<ul style="list-style-type: none"> Single-arm or randomized studies can be used Blinding preferred in comparative studies Blinded review recommended 	<ul style="list-style-type: none"> Can be assessed in single-arm studies Durable complete responses can represent clinical benefit Assessed earlier and in smaller studies compared with survival studies 	<ul style="list-style-type: none"> Not a direct measure of benefit in all cases Not a comprehensive measure of drug activity Small subset of patients with benefit
Progression-Free Survival (includes all deaths) or Time to Progression (deaths before progression censored)	Surrogate for accelerated approval or regular approval*	<ul style="list-style-type: none"> Randomized studies essential Blinding preferred Blinded review recommended 	<ul style="list-style-type: none"> Smaller sample size and shorter follow-up necessary compared with survival studies Measurement of stable disease included Not affected by crossover or subsequent therapies Generally based on objective and quantitative assessment 	<ul style="list-style-type: none"> Not statistically validated as surrogate for survival in all settings Not precisely measured; subject to assessment bias particularly in open-label studies Definitions vary among studies Frequent radiological or other assessments Involves balanced timing of assessments among treatment arms

Call for Clarity in the Reporting of Benefit Associated With Anticancer Therapies

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and Elizabeth A. Eisenhauer*

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Despite its original definition, in the modern era of targeted therapy clinical benefit is often used in this journal and elsewhere to describe a decrease in tumor size or stable disease for a minimum period of time.⁵⁻⁸ We suggest that whether such patients experience true clinical benefit depends on whether they also have improvement in the duration and/or quality of survival.

Ultimately, the goal of all of our therapies is to improve either the quality or quantity of survival for patients with cancer. We hope that the *Journal of Clinical Oncology* and other investigators consider the proposed changes in language in an effort to more clearly communicate the true benefits of our therapies to patients, clinicians, and policy makers.



**The real objective of the treatment is to improve
Survival duration and/or Quality of life**

How health-related quality of life assessment should be used in advanced colorectal cancer clinical trials

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Suggestions for future mCRC trials

Considering the above, we propose the following for future mCRC clinical trials:

1. HRQoL should be strongly considered as a co-primary end point alongside a tumor-based parameters such as PFS in the first-line and later settings [60, 105]. Appropriate investment and strategies to ensure completion of data collection and minimization of drop out is critical.
2. HRQoL could be used as a composite end point with tumor parameters when: treatment effects on each component of end point is expected to be of similar efficacy, treatment is expected to have long-term negative effects on patients HRQoL, and treatment effects are estimated to be small, but clinically meaningful. This approach would ensure adequate sample size for meaningful HRQoL assessments.

- Well accepted as an important endpoint, validated by the FDA and ASCO
- Actual researches concern the application of HRQoL in routine clinical practice, which allow the patient to have an active role in his disease treatment