

THE ECOSYSTEM OF EVIDENCE

Lessons learned in the pandemic era and future challenges

10* International Conference for EBHC Teachers and Developers 10* Conference of the International Society for EBHC Taoming, 25*- 29* October 2023

#EBHC2023

The impact of evidencebased practice guidelines adherence on clinical outcomes in patients with cancer A systematic review and meta-analysis

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Clinical practice guidelines (CPGs) are developed to standardize care by providing physicians and decision makers with evidencebased recommendations which are based on the systematic review of available evidence. There are currently about 3000 CPGs available worldwide in different languages according to the Guidelines International Network Library.

About 30% of these CPGs are oncology guidelines.









CPG Adherence Definition

- Conformity in fulfilling or following official, recognized, or institutional requirements, recommendations, protocols, pathways, or other standards (U.S. National Library of Science).
- Adherence to CPGs is expected to result in better patient outcomes.

Aims

To analyze the effects of guideline adherence versus non-adherence to CPGs (i.e., usual care without guideline adherence) on clinical outcomes in patients with cancer.







Methods



Databases searched:

MEDLINE

through April 2022

Search Period:

EMBASE

PsychINFO

CINAHL

Cochrane Controlled Trials Register

- Population: adult cancer patients being managed in healthcare centers
- Intervention: adherence to CPGs
- **Comparison:** usual care without use of adherence to CPGs
- Outcome: patient related outcomes (OS, DFS, incidencebased mortality, and quality of life)
- Study Designs: systematic reviews, RCTs, and observational studies (cohort, before and after and case control)

Abbreviations: OS, Overall Survival; DFS, Disease Free Survival; RCTs, Randomized Control Trial





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Title and abstract screening- 5039

Full text screening – 104

Included studies – 60

Included

Identific<mark>ation</mark>

Screening

Eligibility

Records identified through database searching N = 5807

Additional records identified through other sources N = 0

Records after duplicates removed N = 5039

> Records screened N = 5038

Records excluded N = 4934

Full-text articles assessed for eligibility N = 104

Studies included in qualitative synthesis N = 31

Studies included in quantitative synthesis (meta-analysis) N = 29

Full-text articles excluded, with reasons N = 44Does not include a study population of interest (N = 8) Does not include intervention of interest (N = 14) Does not include outcomes of interest (N = 9) Is not an included study design (reviews, case ... (N = 13)



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Study Population

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Study Location





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Study Designs



Guidelines Used

Guidelines	Number
National Comprehensive Cancer Network	17
German National Consensus S3 Guideline	11
European Association of Urology	5
Comprehensive Cancer Center Middle Netherlands	3
Barcelona Clinic Liver Cancer Guideline	3
European Society for Medical Oncology	2
Australian Cancer Council guidelines	2
American College of Surgeons	2
American Thyroid Association Guidelines	2
Japan Society of Gynecologic Oncology	2
National Dutch Guideline	2
Standardized treatment protocol	2
Others	11
Not specified	5



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Adherence Rate by Disease Site





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- Adherence to CPG may have little or no effect on OS in all disease sites (hazard ratio [HR]=0.96 (95%) confidence interval [CI]: 0.84-1.10); p=0.57, I²:98%; very low CoE).
- DFS and RFS analysis also showed similar findings (HR=0.84 (95% CI: 0.36-0.1.97); p=0.69, I²:91%; low CoE and HR=0.91 (95% CI: 0.60-1.39); p=0.67, I²:97%; very low CoE) respectively.
- Analysis by disease site showed similar results except in thoracic cancer (HR=0.79 (95% CI: 0.64-0.97); p<0.02, I²:80%; low CoE).

and a subscription of the		in the second second	Plazard Ratio	The start	
Study or Subgroup log	(Hazard Ratio) SE	Weight	IV, Random, 95% CI	IV, Rando	m, 95% CI
1.1.1 Breast					0
Andreano 2017	-0.4155 0.093	4.4%	0.66 [0.55, 0.79]	+	1
Krienenberg 2018	-0.2877 0.073	4.58	0.75 [0.65, 0.87]	-	1
Rocque 2018	-0.1625 0.1064	4.38	0.85 [0.69, 1.05]	+	
Sacerdote 2013	-0.0619 0.2643	2.8%	0.94 [0.56, 1.58]		
Schwentner 2012.1	1.0296 0.3322	2.3%	2.80 [1.46, 5.37]		
Schwentner 2012.2	0.9203 0.4303	1.7%	2.51 [1.08, 5.83]		
Schwartter 2013.1	1.0613 0.3225	2.3%	2,89 [1,54, 5,44]		
Schwartter 2013 2	-0 1393 0.0966	4 4%	0.87 10 72 1.051	14	
mm 2022	0 5247 0 1378	4.0%	1.69 [1 29 2 21]		
Varma 2010	1 5530 0 7536	0.7%	4 73 11 08 20 721		
Almmer 2010	-0.4463 0.1685	3.7%	0 64 10 46 0 801		
metal 2010 1	0.0450 0.1583	4.00	3 6 7 11 06 2 5 91		
Southern 2010	0.9439 0.1362	4.30	2.37 [1.90, 3.37]		
acideniager 2016	-0.4155 0.1119		0.00 [0.33, 0.82]		1
Applers 2015	-0.7765 0.0713	4.58	0.46 [0.40, 0.53]		
subtotal (95% C0		47.8%	1.11 (0.84, 1.48)		•
Heterogeneity: Tau* = 0.2	4; Ch# = 214.64, df = 1	30 < 0.0	0001); * = 94%		
fest for overall effect: Z =	0.73 (7 = 0.47)				
1.1.2 Gastrointestinal					
Regarde 2018	-0.3011 0.014	4.5%	0.74 [0.72, 0.76]		
Guarino 2015	0.6043 0.3621	2.1%	1.83 [0.90, 3.72]		
aap 2018	-0.6349 0.0097	4.6%	0.53 [0.52, 0.54]	*C	
Zhao 2018	0.5596 0.2463	3.0N	1.75 [1.08, 2.84]		
Subtotal (95% CD		14.6%	0.85 [0.64, 1.12]	-	
Heterogenetty: Tau ⁴ = 0.0	6: Chr = 413.26, df = 3	0 < 0.00	001); r = 95%		
Test for overall effect: Z =	1.15 (* = 0.25)				
1.1.3 Gynaecological					
Chiew 2017	-1 5141 0 5843	1.1%	0 22 10 07 0 691		
House & 2000	-0 1393 0 1109	4 79	0 87 10 20 1 081		
Inches 2000	0.1393 0.1109	3.00	0.07 (0.70, 1.00)		
OCHUM 2021	0.7608 0.2465	3.08	2.14 [1.32, 3.47]		
aneved 2006	-0.1054 0.4675	1.58	0.90 (0.36, 2.25)		
Shipeta 2017	-0.1165 0.0806	4.58	0.89 (0.76, 1.04)	-	
Subtotal (95% CO		14.3%	0.96 [0.67, 1.37]		
Heterogeneity: Tau* = 0.1 Test for overall effect: Z =	0; CNP = 18.15, df = 4 (0.25 (P = 0.80)	# = 0.001); (* = 78%		
1.1.4 Thoracic			Service and the service of the servi		
Duggan 2016	-0.8916 0.2524	2.9%	0.41 [0.25, 0.67]		
ohn 2021	-0.1165 0.0175	4.6%	0.89 [0.86, 0.92]	0.	
fue 2014	-0.1744 0.0786	4.58	0.84 [0.72, 0.98]	-	
Subtotal (95% CI)		12.2%	0.79 [0.64, 0.97]	•	
Heterogenetty: Tau ⁴ = 0.0	2: Chr = 9.84, df = 2 (f	- 0.007)	P - BON		
Test for overall effect: 2 -	2.25 (7 = 0.02)				
T C Back & Back					
LLS HEAD & NECK		1000	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		
Adam 2015	0.1484 0.0638	4.6%	1.16 [1.02, 1.31]		-
Schwam 2016	0.3784 0.0792	4.58	1.46 [1.25, 1.71]		-
Subtotal (95% CI)		9.1%	1.30 [1.03, 1.62]		•
Heterogeneity: Tau ⁴ = 0.0 Test for overall effect: Z =	2; Ch# = 5.11, df = 1 (# 2.25 (# = 0.02)	- 0.02); 1	- 80%		
1.1.6 Genitourinary					
Cindolo 2019	-0.9163 0.1617	2.14	0.40 10.20 0.801		
Subtotal (95% CD	-0.9103 0.9537	2.19	0.40 10 20 0.80	-	
lateroone paller More another	100		anan larent argal		1
Test for overall effect Z =	2.59 (# = 0.010)				
		100.00	0.00.10.00.000		
The second design of the second se		1001025	0.96 10.84, 1.10		
Total (95% CI)	a series the series of the ser		and a second sec	NA. 201-00 100	21
Total (95% Cl) Heterogeneity: Tau ⁴ = 0.1	0; Chr = 1376.25, df =	28 (< 0	00001); # - 95N	0.01 01	10 1



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- Studies in breast cancer with an average of 5 years ٠ follow up showed adherence to guidelines may improve OS (HR=0.70 (95% CI: 0.64-0.77); p<0.001, I²:0%; low CoE).
- None of the studies evaluated OOL. .

Study or Subgroup log[Hazard Ratio] 5		SE	Hazard Ratio SE Weight IV, Random, 95% CI Year			Hazard Ratio IV, Random, 95% Cl			
Sacerdote 2013	~0.0619	0.2643	3.3%	0.94 [0.56, 1.58]	2013	8			
Andreano 2017	-0.4155	0.093	26.7%	0.66 [0.55, 0.79]	2017		-		
Krienenberg 2018	-0.2877	0.073	43.4%	0.75 [0.65, 0.87]	2018				
Wollschlager 2018	-0.4155	0.1119	18.5%	0.66 [0.53, 0.82]	2018		-		
Wimmer 2019	-0.4463	0.1685	8.1%	0.64 [0.46, 0.89]	2019				
Total (95% CI)			100.0%	0.70 [0.64, 0.77]					
Heterogeneity: Tau ² = 0.00; Chi ² = 3.08, df = 4 (P = 0.54); l ² = 0%					0.01	al.	1	100	
Test for overall effect: Z = 7.30 (P < 0.00001)					0.01	Favours CG adherence	Favours CG non adherence	100	

Summary of findings:

Adherence to CPG compared to non-adherence to CPG for patients with cancer

Patient or population: patients with cancer Settina: Intervention: adherence to CPG Comparison: non-adherence to CPG

	Anticipated ab (95%	solute effects* % CI)					
Outcomes	Risk with non- adherence to CPG	Risk with adherence to CPG	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments	
OS - All disease sites follow-up: range 1.3 years to 15 years	432 per 1,000ª	419 per 1,000 (378 to 464)	HR 0.96 (0.84 to 1.10)	111132 (29 observational studies) ^b		Adherence to CPG may have little to no effect on OS in all disease sites but the evidence is very uncertain.	
OS- Breast subgroup follow-up: median 5 years	267 per 1,000	195 per 1,000 (180 to 212)	HR 0.70 (0.64 to 0.77)	17964 (5 observational studies)		The evidence suggests adherence to CPG may improve OS in breast cancer disease subgroup.	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: confidence interval; HR: hazard Ratio

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.



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Limitations



Available studies that were pooled were all retrospective registry study design which are inherently subject to reporting and selection bias and issues with incomplete data.



None of the studies gathered any quality-of-life data on these patients or included any qualitative reporting on patients or clinicians' views on guideline adherence.



Meta-analysis showed very high I² ranging from 78-99%. Despite further subgroup analysis the I² was still high in most instances.



Issues affecting guideline adherence could also play a role in the effect sizes reported in the studies.









Conclusions

Clinician's adherence to CPG recommendations have little or no effects on outcomes.

However it may have some beneficial effect on outcomes in some disease areas that include breast and thoracic cancer.

Adherence to guideline recommendations should be implemented and encouraged.







