ONS Guidelines ™ to Support Patient Adherence to Oral Anticancer Medications

13 **Table 1. Study characteristics of additional studies for PICO 1**

Study	Country	Study Design	N subjects (intervention/comparator)	% female	Age mean (SD) / Median (IQR)	Type of cancer regimen	Tools/methods used to assess risk	Timing of risk assessment	Findings from the risk assessment	Funding Source
Berry/ 2015	US	RCT	70 (49/21)	40	Median: 61 Range: 34-80	Diverse cancers on chemotherapy and hormonal therapy	Measured odds of low/medium adherence on Symptom distress: SDS-15, Depression: PHQ-9; demographic characteristics	Demographic characteristics at baseline. Unknown when depression and symptom distress assessments were taken.	Symptom distress: OR: SDS-15+1 vs SDS-15a 1.1 (1.0–1.2) Depression: Demographic characteristics: Lack of a spouse/ partner, symptom distress, younger age, not working at the start of therapy, female sex, and oral chemotherapy vs oral hormonal medications	N/A

									NS association with low/medium adherence: cancer stage, working status, education, minority identification, age, married/partner status, time on regimen	
Decker/2009	US	Cohort	30 (23/7)	94	Mean (SD): 59.93 (12.03) Range: 21-71+	Diverse cancers on diverse treatments	Depression: CESD-20;, Functional ability: SF-12	Baseline and end of study (at the exit interview)	Functional ability (SF-12): NS btw adherence and nonadherence group Depression (CESD-20): lower scores at baseline (10.91 vs 13.13) and end of study (8.67 vs 11.0) in adherence group (NS)	N/A
DosSantos/2019	France	Cohort	129	40%	Median: 70	Renal cell, lung, prostate, colorectal, breast	Depression: CES-D, Anxiety: STAI-Trait (score range, Global	Baseline (before initiation of treatment)	Significant negative association between depression and non-adherence	N/A

						cancers treated with targeted therapy, chemotherapy, and chemoradiotherapy	cognitive status: MoCA, Digit memory: WAIS-III, Information processing speed: TMT, Autonomy: IADL			
Jacobs/ 2017	US	Cohort	90	55.6	Mean (SD): 58.06 (13.08) Range: 28-88	Diverse cancers on oral chemotherapy	Symptom distress: Symptom Distress Scale, Anxiety and depressive symptoms: Hospital Anxiety and Depression Scale, Cancer-specific psychological distress: Cancer	Baseline and post-assessment (12 weeks)	- Demographic: Women had greater adherence than men (93.48% vs 83.90%) (S) - Significant associations with better adherence: improvements in symptom distress (-0.79), depressive symptoms (-1.57), quality of life (0.38), - Improvements in patient-reported symptom distress (23.94	Massachusetts General Hospital Cancer Center

							Worries Inventory (CWI)		at baseline and -0.22 change from baseline), depressive symptoms (4.23 at baseline and 0.37 change from baseline), satisfaction with clinician communication and treatment (92.68 at baseline and -2.84 change from baseline), and perceived burden to others (5.04 at baseline and -0.04 change from baseline) were associated with better adherence. No association between anxiety and adherence	
Krikorian/ 2019	US	RCT	200 (101/99)	77	Intervention - Mean (SD): 61.8 (11.5) Control -	Diverse cancers on oral antineoplastic medication	Beliefs about medicines: BMQ	Assessment taken at baseline. Demographic forms were	Non-adherence was associated with forgetfulness, wanting to avoid side-effects, being depressed or overwhelmed, falling asleep before taking	N/A

					Mean (SD): 61.9 (12)			updated at later time points.	medication. **Numbers not provided. Supplement only provides the questions in BMQ.** Statistically significant correlations associated with non-adherence were forgetfulness (p = 0.009), wanting to avoid side effects (p = 0.02), feeling depressed or overwhelmed (p = 0.032), or falling asleep before taking medication (p = 0.048) in both groups	
Krolop/2013	Germany	Cohort	73	74	N/A	Breast cancer, colorectal cancer, and esophageal cancer treated	N/A	Separated into initially non-adherent and adherent after	Found no associations between age, gender, any sociodemographic or disease-related characteristics to	Supplementary grant was

						with capecitabine in combination or monotherapy		first follow-up	adherence. **No numbers reported.**	provided by Roche, Basel
Timmers/ 2015	Netherlands	Cohort	62	47	Mean: 63.5	Non small cell lung cancer on erlotinib	Demographic characteristics, smoking, co-medications, Quality of life: SF-12, Attitude(s) towards medication: BMQ, Illness perception: Brief IPQ, and symptoms (likert scale)	Collected at baseline	Relationships with incorrect intake were: older age (OR 1.10, 95 % CI 1.00–1.21), MARS < 25 (OR 4.83, 95 % CI 1.06–21.99), oculair symptoms (OR 3.13, 95 % CI 1.11–8.82) and stomatitis (OR 6.59, 95 % CI 1.77–24.60) **BMQ and Brief IPQ can be found in Table 8**	Roche, The Netherlands
Wickersham	US	Cohort	198 (162/36)	100	Mean (SD): 59.1 (7.5)	Breast cancer treated with	Sociodemographic variables: University	Information on predictor	Depressive symptoms, fatigue, gastrointestinal symptoms,	National

/2013					Range: 39-75	Anastrozole, Letrozole, Examestane, Tamoxifen	of Pittsburgh, School of Nursing Center for Research in Chronic Disorders Sociodemographic Questionnaire, Depressive symptoms: Beck Depression Inventory-II, Anxiety: Profile of Mood States (POMS) Tension-Anxiety subscale, Side effects of hormonal therapy: BCPT	variables was measured pre-treatment	cognitive symptoms, weight concerns, gynecological symptoms, musculoskeletal pain, and total BCPT score were identified as linear predictors of nonadherence. **Numbers are not reported**	Institute for Nursing
Yusuf	US	Cohort	73 (54/19)	100	Mean (SD):	Breast cancer on	Depression: The	All measured at	Psychological and menopause	N/A

ov/ 2020					55 (10.1)	tamoxifen and aromatase inhibitors	Patient Health Questionnaire (PHQ-8), Tendency to perceive normal visceral or somatic sensations as being dangerous, abnormal, intense, or potentially harmful The Somatosensory Amplification Scale (SSAS), Anxiety: The Generalized Anxiety Disorder (GAD-7), Sleep: The Insomnia Severity Index (ISI),	baseline	symptoms (depression, generalized anxiety, insomnia, somatosensory amplification, hot flash frequency, and hot flash-related interference) were assessed pre-AET initiation as predictors of subsequent non-adherence Adherent vs non-adherent: Anxiety: 3.1(4.2) vs 4.1(4.6) Depression: 3.4 (3.3) vs 6.0 (3.9) Insomnia (subthreshold): 7.5 (5.3) vs 7.7(4.6) Hot flash related interference: 6.2 (15.2) vs 7.4(14.1) Somatosensory Amplification: 22.3(6.5) vs 26.5(8.5)	

							Hot flash related interference: The Hot Flash-Related Daily Interference Scale (HFRDIS)		Hot flash frequency: 1.1(2.0) vs 2.0(3.0)	

14

Table 2. Evidence Profile for PICO 1

Question: Standardized assessment for risk/barriers compared to standard of care for Patients starting a new oral anti-cancer medication regimen

Setting: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	standardized assessment for risk/barriers	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 4 months; assessed with: self-report)												
1 [1]	randomised trials	not serious [a]	not serious	serious [b]	very serious [c,d]	none	25 participants who received risk assessment plus tailored intervention had an adherence rate of 95.1% vs 20 participants in the control arm with an adherence rate of 82.4%.				⊕◯◯◯ VERY LOW	CRITICAL
Self-efficacy to manage medications - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Health-related Quality of Life and Patient-reported Outcomes (HRQOL/PROs) - not reported												

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

Patient satisfaction - not reported

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval

Explanations

a. Minimal information provided about randomization and allocation concealment.

b. Intervention included tailored coaching intervention in addition to risk assessment.

c. Sample doesn't meet optimal information size. Concerns with fragility.

d. The possibility of no difference cannot be excluded due to limited information.

References

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Table 3. Evidence Profile for PICO 2

Question: Educational programs compared to standard of care for patients starting a new oral anticancer medication regimen

Setting: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	educational programs	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 3-12 weeks; assessed with: self-report and pill count)												
2 [1,2]	randomised trials	serious [a]	not serious	not serious	very serious [b,c]	none	215	156	-	MD **0.4 % higher** (1.87 lower to 2.68 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Adherence rate (follow up: 2-24 weeks; assessed with: self-report and medication event monitoring system pillboxes)												
4 [3,4,5,6]	observational studies	very serious [d]	not serious	not serious	serious [b]	none	83	100	-	MD **10.61 % higher** (7.21 higher to 14.01 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Proportion with high adherence (follow up: 14-24 weeks; assessed with: MMAS-4 and MMAS-8)												

2 [7,8]	randomised trials	serious [e]	not serious	not serious	not serious	none	222/391 (56.8%)	175/354 (49.4%)	**RR 1.16** (1.01 to 1.33)	**79 more per 1,000** (from 5 more to 163 more)	⊕⊕⊕◯ MODERATE	CRITICAL

Patient satisfaction (assessed with: Helpfulness of meeting with specialty pharmacist and medication navigator - % "very")

1 [9]	observational studies	very serious [f,g]	not serious	not serious	very serious [c,h]	none	30/39 (76.9%)	32/37 (86.5%)	**RR 0.89** (0.72 to 1.10)	**95 fewer per 1,000** (from 242 fewer to 86 more)	⊕◯◯◯ VERY LOW	CRITICAL

Patient satisfaction (assessed with: Helpfulness of medication info sheet - % "very")

1 [9]	observational studies	very serious [f,g]	not serious	not serious	very serious [c,h]	none	25/39 (64.1%)	28/37 (75.7%)	**RR 0.85** (0.63 to 1.14)	**114 fewer per 1,000** (from 280 fewer to 106 more)	⊕◯◯◯ VERY LOW	CRITICAL

Patient satisfaction (assessed with: Helpfulness of check-in with medication navigator - % very")

1 [9]	observational studies	very serious [f,g]	not serious	not serious	serious [b]	none	27/39 (69.2%)	34/37 (91.9%)	**RR 0.75** (0.60 to 0.95)	**230 fewer per 1,000** (from 368 fewer to 46 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

Patient knowledge of regimen (follow up: 2 cycles; assessed with: Dosage and frequency)

1 [10]	observat	very	not serious	not serious	serious	none	29/29	23/29	**RR 1.26**	**206 more per 1,000**	⊕◯◯◯	CRITICAL

	ional studies	serious [i]			[b]		(100.0%)	(79.3%)	(1.03 to 1.52)	(from 24 more to 412 more)	VERY LOW	

Patient knowledge of regimen (follow up: 2 cycles; assessed with: How to manage missed doses)

1 [10]	observational studies	very serious [i]	not serious	not serious	serious [b]	none	29/29 (100.0%)	19/29 (65.5%)	**RR 1.51** (1.16 to 1.98)	**334 more per 1,000** (from 105 more to 642 more)	⊕◯◯◯ VERY LOW	CRITICAL

Patient knowledge of regimen (follow up: 2 cycles; assessed with: Dosage schedule)

1 [10]	observational studies	very serious [i]	not serious	not serious	serious [b]	none	29/29 (100.0%)	22/29 (75.9%)	**RR 1.31** (1.06 to 1.62)	**235 more per 1,000** (from 46 more to 470 more)	⊕◯◯◯ VERY LOW	CRITICAL

Quality of life - not reported

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio

Explanations

a. Some concern with measurement of outcome due to subjectivity in self-report. Serious concern with missing outcome data and selection of the reported result.

b. Small sample, concerns with fragility.

c. The 95% CI cannot exclude the potential for no difference.

d. Critical concern with confounding and missing data. Serious concern with bias in the selection of participants.

e. Some concerns with randomization, effect of assignment to intervention, missing outcome data and measurement of the outcome.

f. Critical concern with confounding, moderate concern in selection of participants and measurement of outcome.

g. Not measuring satisfaction before and after intervention, instead looks at satisfaction a little after start of intervention and end of intervention.

h. Few events reported do not meet the optimal information size and suggest fragility of the estimate.

i. Critical concern with confounding.

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70 **Table 4. Evidence Profile for PICO 3**

71 **Question**: Standardized, periodic/ongoing assessment of adherence compared to usual care for patients on an oral anti-cancer medication

72 regimen

73 **Setting**: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	standardized, periodic/ongoing assessment of adherence	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 12 weeks; assessed with: electronic pill caps)												
1 [1]	randomised trials	not serious	not serious	not serious	very serious [a,b]	none	75	83	-	MD **2.34 % higher** (5.58 lower to 10.26 higher)	⊕⊕◯◯ LOW	CRITICAL
Adherence rate (follow up: 6 months; assessed with: self-report)												
1 [2]	observational studies	very serious [c]	not serious	not serious	serious [a]	none	34	51	-	MD **7 % higher** (0.66 higher to 13.34 higher)	⊕◯◯◯ VERY LOW [d]	CRITICAL

Adherence (follow up: 21-28 days; assessed with: relative dose intensity)

1 [3]	randomised trials	serious [e]	not serious	not serious	very serious [a,b]	none	31	37	-	MD **0.32 % higher** (0.08 lower to 0.72 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Quality of life (follow up: 12 weeks; assessed with: FACT-G; higher=better; MID 5-7; Scale from: 0 to 108)

1 [1]	randomised trials	not serious [f]	not serious	not serious	serious [a]	none	77	85	-	MD **2.28 points higher** (1.93 higher to 2.63 higher)	⊕⊕⊕◯ MODERATE	CRITICAL

Quality of life (follow up: 3 months; assessed with: EORTC; higher=better; MID 4-11)

1 [4]	observational studies	serious [g]	not serious	not serious	serious [a]	none	56	56	-	MD **15.7 points higher** (8.84 higher to 22.56 higher)	⊕⊕◯◯ LOW	CRITICAL

Patient satisfaction (follow up: 3 months; assessed with: self-report (single question on satisfaction))

1 [5]	observational studies	very serious [h]	not serious	not serious	very serious [i]	none	20/20 (100.0%)	15/20 (75.0%)	**RR 1.32** (1.02 to 1.72)	**240 more per 1,000** (from 15 more to 540 more)	⊕◯◯◯ VERY LOW	CRITICAL

Cancer-related morbidity (follow up: 24 weeks; assessed with: global toxicity score; higher=worse; Scale from: 0 to 36)

1 [6]	randomised trials	serious [j]	not serious	not serious	very serious [a,b]	none	92	91	-	MD **1 points higher** (1.72 lower to 3.72 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Cancer-related morbidity (follow up: 21-28 days; assessed with: Symptom Experience Inventory; higher=worse; Scale from: 0 to 190)

1 [3]	randomised trials	serious [e]	not serious	not serious	very serious [a,b]	none	31	37	-	MD **1.75 points lower** (9.48 lower to 5.98 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Cancer-related morbidity (follow up: 8 weeks; assessed with: Symptom Experience Inventory; higher=worse; Scale from: 0 to 190)

1 [7]	observational studies	very serious [k]	not serious	not serious	serious [a]	none	24	30	-	MD **4.78 points lower** (7.8 lower to 1.76 lower)	⨁◯◯◯ VERY LOW	CRITICAL

Self-efficacy (follow up: 21-28 days; assessed with: MASES-R; higher=better; Scale from: 1 to 4)

1 [3]	randomised trials	serious [e]	not serious	not serious	very serious [a,b]	none	31	37	-	MD **0.51 points lower** (1.3 lower to 0.28 higher)	⨁◯◯◯ VERY LOW	IMPORTANT

Self-efficacy (follow up: 8 weeks; assessed with: MASES; higher=better; Scale from: 1 to 4)

1 [7]	observa	very	not serious	not serious	very serious	none	24	30	-	MD **0.01 points lower**	⨁◯◯◯	IMPORTANT

	tional studies	serious [k]			[a,b]					(0.36 lower to 0.34 higher)	VERY LOW	

Adherence to supportive care/lab monitoring - not reported

-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

CI: Confidence interval; **MD:** Mean difference; **MID:** Minimally important difference; **RR:** Risk ratio; **MASES-R:** Medication Adherence Self-Efficacy Scale – Revision

Explanations

a. Small sample, concerns with fragility.

b. 95% CI cannot exclude the possibility of no effect.

c. Moderate concern with confounding. and measurement of outcome due to subjective measure. Serious concern with missing data.

d. An additional study reported a risk ratio of 0.92; 95% CI: 0.54, 1.56 comparing on-going assessment to no assessment measured with self-reported adherence at 3 months.

e. Some concerns due to deviations from the intended interventions.

f. Self-reported outcome measurement could lead to some concerns with risk of bias but not serious.

g. Critical concern with confounding and serious concern with subjectivity of outcome.

h. Critical concern for confounding and moderate concern with measurement of outcome due to self-report.

i. Few events reported do not meet the optimal information size and suggest fragility of the estimate.

j. Some concerns due to deviations from the intended interventions and self-reported outcome measurement.

k. Serious concern with confounding, bias in selection of participants, missing data and measurement of outcome. Moderate concern with deviations from intervention.

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112 **Table 5. Evidence Profile for PICO 4**

113 **Question**: Active follow-up compared to usualcare for patients on an oral anticancer medication regimen who have additional risk factors

114 **Setting**: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	active follow-up	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 6 cycles; assessed with: MEMS (medication event monitoring system) pillboxes)												
1 [1]	observational studies	very serious [a]	not serious	not serious	very serious [b]	none	10	10	-	MD **17.8 % higher** (6.43 higher to 29.17 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Cancer-related morbidity - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Quality of life - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
Patient satisfaction - not reported												

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

Patient self-efficacy about treatment - not reported

-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

CI: Confidence interval; **MD:** Mean difference

Explanations

a. Critical concern with confounding.

b. Small sample, concerns with fragility.

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123 **Table 6. Evidence Profile for PICO 5**

124 **Question**: Coaching compared to usual care for patients on an oral anti-cancer medication regimen who have additional risk factors

125 **Setting**: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Coaching	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 3-4 weeks; assessed with: pill count)												
1 [1]	randomised trials	serious [a]	not serious	not serious	very serious [b,c]	none	101	99	-	MD **0.8 % higher** (2.24 lower to 3.84 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Adherence rate (follow up: 2 educational sessions every three cycles; assessed with: MEMS pillboxes)[d]												
1 [2]	observational studies	very serious [e]	not serious	not serious	serious [c]	none	10	10	-	MD **17.8 % higher** (6.43 higher to 29.17 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Adherence (follow up: 3 months; assessed with: MPR greater than or equal to 90%)												
1 [3]	random	serious [f]	not serious	serious [g]	very serious	none	59/64	54/59	**RR 1.01**	**9 more per 1,000**	⨁◯◯◯	CRITICAL

	ised trials				[b,h]		(92.2%)	(91.5%)	(0.91 to 1.12)	(from 82 fewer to 110 more)	VERY LOW	

Adherence (follow up: 6-31.9 months; assessed with: MPR)

2 [4,5]	observational studies	very serious [i]	serious [j]	serious [g]	serious [c]	none	84	281	-	MD **2.98 % higher** (2.95 higher to 3.01 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Cancer-related morbidity -Symptom severity (follow up: 3 months; assessed with: 13 item M.D. Anderson Symptom Inventory; higher=worse; MID 1.0 per 10 point scale; Scale from: 0 to 130)

1 [3]	randomised trials	serious [f]	not serious	not serious	very serious [b,c]	none	64	62	-	MD **0 points** (0.55 lower to 0.55 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Patient self-efficacy (follow up: 3 months; assessed with: General self-efficacy scale; higher=better; Scale from: 1 to 40)

1 [3]	randomised trials	serious [f]	not serious	not serious	very serious [b,c,h]	none	64	62	-	MD **1.8 points higher** (0.01 lower to 3.61 higher)	⊕◯◯◯ VERY LOW	IMPORTANT

Quality of life (follow up: 3 months; assessed with: FACT-B; higher=better; MID 7-8 points; Scale from: 0 to 144)

1 [3]	random	serious [f]	not serious	not serious	very serious	none	64	62	-	MD **0.2 points higher**	⊕◯◯◯	CRITICAL

	ised trials				[b,c]					(6.18 lower to 6.58 higher)	VERY LOW	

Patient satisfaction (follow up: 3 months; assessed with: self-designed scale; higher=better; Scale from: 0 to 5)

1 [3]	random ised trials	serious [f]	not serious	not serious	very serious [b,c]	none	64	62	-	MD **0.1 points higher** (0.9 lower to 1.1 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference; **MEMS:** Medication event monitoring system; **MPR:** Medication possession ratio; **RR:** Risk ratio;

MID: Minimally important difference

Explanations

a. Serious concern with missing outcome data and selection of the reported result.

b. The 95% CI cannot exclude the potential for no difference.

c. Small sample, concerns with fragility.

d. Reflects the mean of the daily adherence scores which correspond to the proportion of pills actually taken (recorded opening by MEMS) in comparison with prescribed amounts (expected openings).

e. Critical concern with confounding and missing outcome data.

f. Serious concerns with missing outcome data.

g. MPR is surrogate for adherence.

h. Few events reported do not meet the optimal information size and suggest fragility of the estimate.

i. Critical concern with confounding.

j. Concerns with heterogeneity due to I2 value of 100%.

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153 **Table 7. Evidence Profile for PICO 6**

154 **Question**: Motivational interviewing compared to usual care for patients on an oral anti-cancer medication regimen who have additional risk

155 factors

156 **Setting**: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	motivational interviewing	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 12 weeks; assessed with: self-report)												
1 [1]	randomised trials	not serious	not serious	not serious	very serious [a,b]	none	57	114	-	MD **3.23 % higher** (0.45 higher to 6.02 higher)	⨁⨁◯◯ LOW	CRITICAL
Cancer-related morbidity - Summed symptom severity (follow up: 8 weeks; assessed with: Symptom Experience Inventory; Higher=worse; Scale from: 0 to 190)												
1 [2]	observational studies	very serious [c]	not serious	not serious	serious [a]	none	24	30	-	MD **4.78 points lower** (7.8 lower to 1.76 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Patient-self efficacy about treatment (follow up: 12 weeks; assessed with: MASES; higher=better; Scale from: 1 to 96)												

1 [3]	randomised trials	serious [d]	not serious	not serious	serious [a]	none	40	40	-	MD **9.9 points higher** (9.68 higher to 10.12 higher)	⨁⨁◯◯ LOW	IMPORTANT

Patient-self efficacy about treatment (follow up: 8 weeks; assessed with: MASES; higher=better; Scale from: 1 to 4)

1 [2]	observational studies	very serious [c,e]	not serious	not serious	serious [a,f]	none	24	30	-	MD **0.01 points lower** (0.36 lower to 0.34 higher)	⨁◯◯◯ VERY LOW	IMPORTANT

Quality of life - not reported

-	-	-	-	-	-	-	-	-	-	-	-	

Patient satisfaction - not reported

-	-	-	-	-	-	-	-	-	-	-	-	

CI: Confidence interval; **MD:** Mean difference; **MASES:** Medication Adherence Self-Efficacy Scale

Explanations

a. Small sample reported does not meet the optimal information size and suggests fragility of the estimate.

b. Cannot exclude no meaningful improvement in adherence.

c. Serious concern with confounding, selection of participants, missing data and measurement of outcome. Moderate concerns due to deviations from intended interventions.

d. Some concerns with bias due to subjectivity of outcome measurement and limited information provided about analysis used to estimate the effect of assignment to intervention.

e. Scale used to measure outcome not specified.

f. CI does not have meaningful difference thus not docked down for CI.

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175 **Table 8. Evidence Profile for PICO 7**

176 **Question**: Technology compared to usual care for patients on an oral anti-cancer medication regimen

177 **Setting**: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	technology	standard of care	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 3-6 months; assessed with: self-report and smart bottle openings)												
2 [1,2]	randomised trials	serious [a]	serious [b]	not serious	serious [c]	none	91	99	-	MD **8.23 % higher** (2.9 higher to 13.55 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Adherence rate (follow up: 6 months; assessed with: MPR)												
1 [3]	observational studies	very serious [d]	not serious	not serious	serious [c]	none	50	51	-	MD **4.7 % higher** (1.19 higher to 8.21 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Adherence - Relative dose intensity (follow up: 3-13 weeks; assessed with: pill counts)												
2 [4,5]	rando	serious	not serious [f]	not serious	very serious	none	149	152	-	MD **0.01 % lower**	⨁◯◯◯	CRITICAL

	mised trials	[e]			[c,g]					(0.04 lower to 0.02 higher)	VERY LOW	

Cancer related morbidity - Summed symptom severity (follow up: 21 days; assessed with: Symptom Experience Inventory; higher=worse; Scale from: 0 to 190)

1 [6]	rando mised trials	not serious	not serious	not serious	very serious [c,g]	none	49	26	-	MD **3.5 points lower** (12.48 lower to 5.48 higher)	⊕⊕◯◯ LOW	CRITICAL

Quality of Life (follow up: 3-12 weeks; assessed with: FACT-G and WHO Quality of Life-BREF Scale; higher=better)

2 [1,7]	rando mised trials	serious [a]	serious [h]	not serious	serious [c]	none	77	85	-	SMD **1.44 SD higher** (1.15 higher to 1.74 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Quality of Life (follow up: 6 months; assessed with: assessed using the EuroQol-5D (EQ-5D); MID 0.061; higher=better)

1 [3]	observ ational studies	very serious [d]	not serious	not serious	serious [c]	none	50	51	-	MD **0.13 points higher** (0.07 lower to 0.2 higher)	⊕◯◯◯ VERY LOW	CRITICAL

Patient satisfaction (follow up: 6 cycles (ranging from 21 day to 90 day cycles); assessed with: FACIT-TS-PS; higher=better; Scale from: 0 to 73)

1 [8]	randomised trials	serious [i]	not serious	not serious	very serious [c,g]	none	56	33	-	MD **0 points** (1.31 lower to 1.31 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **MD:** Mean difference; **MPR:** Medication possession ratio; **SMD:** Standardised mean difference

Explanations

a. Limited information on effect of assignment to intervention and some concerns with measurement of the outcome.

b. Rated down due to I2 value of 74%.

c. Small sample, concerns with fragility.

d. Critical concerns with confounding. Serious concerns with missing data.

e. Some concerns with bias due to deviations from the intended interventions.

f. I2 value is 61%; however, rating down for imprecision accounts for the variability between study findings.

g. 95% CI cannot exclude the possibility of no effect.

h. Rated down due to the I2 value of 95%.

i. Some concerns with effect of assignment to intervention and measurement of outcome.

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213 **Table 9. Evidence Profile for PICO 8**

214 **Question**: Interactive technology compared to non-interactive technology for patients on an oral anti-cancer medication regimen

215 **Setting**: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interactive technology	non-interactive technology	Relative (95% CI)	Absolute (95% CI)		
Adherence (follow up: 8 weeks; assessed with: only adherence rate ≥80%)												
1 [1]	randomised trials	very serious [a]	not serious	not serious	very serious [b,c]	none	56/79 (70.9%)	33/40 (82.5%)	**RR 0.86** (0.70 to 1.05)	**116 fewer per 1,000** (from 248 fewer to 41 more)	⨁◯◯◯ VERY LOW	CRITICAL
Cancer related morbidity - Exit symptom severity (follow up: 8 weeks; assessed with: Symptom Experience Inventory range 0-150; higher = worse)												
1 [1]	randomised trials	serious [d]	not serious	not serious	very serious [b,e]	none	79	40	-	MD **4.12 points higher** (0.4 lower to 8.64 higher)	⨁◯◯◯ VERY LOW	CRITICAL

Health-related Quality of Life and Patient-reported Outcomes (HRQOL/PROs) - not reported

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

Patient satisfaction - not reported

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. Serious concerns with randomization, measurement of outcome and bias in selection of the reported result.

b. 95% CI cannot exclude no difference.

c. Few events reported do not meet the optimal information size and suggest fragility of the estimate.

d. Serious concerns with randomization.

e. Small sample, concerns with fragility.

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Table 10. Evidence Profile for PICO 9

Question: Structured oral anti-cancer medication program compared to no structured oral anti-cancer medication program for institutions providing care to patients on an oral anti-cancer medication regimen

Setting: Outpatient

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	structured oral anti-cancer medication program	no structured oral anti-cancer medication program	Relative (95% CI)	Absolute (95% CI)		
Adherence rate (follow up: 6 cycles; assessed with: medication event monitoring system)												
2 [1,2]	observational studies	very serious [a]	not serious	not serious	serious [b]	none	18	29	-	MD **12.22 % higher** (9.19 higher to 15.24 higher)	⨁◯◯◯ VERY LOW	CRITICAL
Adherence rate (follow up: 6 months - end of treatment; assessed with: medication possession ratio)												
4 [3,4,5,6]	observat	very	not serious	serious [d]	not serious	none	12536	31123	-	MD **6 %**	⨁◯◯	CRITICAL

	ional studies	serious [c]								**higher** (4 higher to 8 higher)	◯ VERY LOW	

Adherence (follow up: end of treatment; assessed with: pill counting)

1 [7]	observational studies	very serious [e]	not serious	serious [d]	very serious [b,f]	none	87/100 (87.0%)	38/50 (76.0%)	**RR 1.14** (0.96 to 1.36)	**106 more per 1,000** (from 30 fewer to 274 more)	⊕◯◯ ◯ VERY LOW	CRITICAL

Cancer-related morbidity - Physical functioning (follow up: 1 year; assessed with: EORTC QoL physical function; higher = better; MID 6 points; Scale from: 0 to 100)

1 [8]	observational studies	very serious [e]	not serious	serious [g]	serious [b]	none	56	56	-	MD **11.1 points higher** (7.45 higher to 14.75 higher)	⊕◯◯ ◯ VERY LOW	CRITICAL

Quality of Life (follow up: 1 year; assessed with: EORTC Health/QoL Global; higher = better; MID 4 to 11 points; Scale from: 0 to 100)

1 [8]	observational studies	very serious [e]	not serious	not serious	serious [b]	none	56	56	-	MD **15.7 points higher** (12.7 higher to 18.7 higher)	⊕◯◯ ◯ VERY LOW	CRITICAL

Patient satisfaction (follow up: once during or after treatment; assessed with: telephone survey)

1 [9]	observational studies	very serious [h]	not serious	not serious	serious [b]	none	20/20 (100.0%)	15/20 (75.0%)	**RR 1.32** (1.02 to 1.72)	**240 more per 1,000** (from 15 more to 540 more)	⊕◯◯ ◯ VERY LOW	CRITICAL

Patient financial toxicity (follow up: 1 year; assessed with: EORTC financial difficulties; higher = worse; Scale from: 0 to 100)

1 [8]	observational studies	very serious [e]	not serious	not serious	very serious [b,f]	none	56	56	-	MD **0** (1.57 lower to 1.57 higher)	⊕◯◯ ◯ VERY LOW	CRITICAL

Time to obtain medication - not reported

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

OCM model/value-based care - not reported

-	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

CI: Confidence interval; **MD:** Mean difference; **RR:** Risk ratio

Explanations

a. Critical concerns with confounding and missing data. Moderate concern with measurement of outcome.

b. Small sample, concerns with fragility.

c. Critical concerns with confounding. Moderate concerns with selection of participants.

d. Indirect measure of adherence.

e. Critical concerns with confounding.

f. The 95% CI cannot exclude the potential for no difference.

g. Indirect measure of morbidity.

h. Critical concerns with confounding. Serious concerns with selection of participants.

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