

# ONS Guidelines™ to Support Patient Adherence to Oral Anticancer Medications

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**PURPOSE:** This evidence-based guideline intends to support patients, clinicians, and others regarding interventions and processes to support patient adherence to oral anticancer medications (OAMs).

**METHODOLOGIC APPROACH:** A panel of healthcare professionals and patient representatives developed a clinical practice guideline to support patients taking OAMs. GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology and criteria for trustworthy guidelines were followed. Risk of bias was assessed using the Cochrane Risk of Bias 2 tool. A quantitative or narrative synthesis of the evidence was completed. Certainty of the evidence was assessed using GRADE.

**FINDINGS:** The panel agreed on recommendations and suggested an adherence risk assessment, education addressing adherence, ongoing assessment, proactive follow-up, coaching, and motivational interviewing in addition to usual care. The panel suggested the implementation of a structured OAM program.

**IMPLICATIONS FOR NURSING:** As cancer treatment shifts from clinic to home settings, interventions and programs to support patients on OAMs are needed.

**KEYWORDS** guideline; oral anticancer medication; medication adherence; oncology nursing; pharmacy

Oral anticancer medications (OAMs) have changed the oncology treatment landscape for patients and clinicians. OAM use is growing annually, accounting for 40%–50% of new cancer treatments in development (U.S. Food and Drug Administration, 2021). Shifting treatment from a controlled clinical setting to a patient's home has advantages paired with potential challenges for the patient and healthcare team. Medication adherence, the process by which patients take their medications as prescribed (Vrijens et al., 2012), is increasingly recognized as a critically important factor in the new OAM treatment paradigm. Vrijens et al. (2012) described the following as critical components of medication adherence: treatment initiation (when the patient takes the first prescribed dose), implementation of the dosing regimen (extent to which the dose taken aligns with the prescribed regimen), and discontinuation (the end of therapy).

Adherence to any medication has been identified as the single most important modifiable factor that affects treatment outcomes (World Health Organization, 2003). As more cancer treatments are being administered via pill, adherence has garnered increasing attention among interprofessional cancer care professionals. Nonadherence can occur when patients intentionally or unintentionally delay or do not start a prescribed medication, take less than the prescribed dose, or stop taking a

prescribed medication (Vrijens et al., 2012). Although patient-related factors certainly influence adherence, factors beyond the patient's direct sphere of influence are also reported to considerably affect adherence, including socioeconomic-, therapy-, and condition-related, and health system factors (World Health Organization, 2003). For patients on OAMs, factors influencing adherence may also include challenging administration schedules, beliefs about the effectiveness of the medications, adverse events, and forgetfulness (Dowling et al., 2019; Greer et al., 2016; Jacobs et al., 2017), as well as costs, insurance issues, and difficulty in obtaining the medication (Ruddy et al., 2009). Suboptimal adherence can negatively affect treatment efficacy, disease outcomes, and overall survival while also increasing toxicities (e.g., from over adherence) and healthcare costs, which makes support for adherence a critical clinical priority (Arthurs et al., 2015). Interventions are needed to support patients taking OAMs at home.

Nurses and pharmacists are uniquely positioned to support optimal adherence in patients with cancer. Using evidence-based interventions to inform best practices for supporting patients taking OAMs is important. To address this need, the Oncology Nursing Society (ONS) developed this clinical practice guideline on interventions to support patients prescribed OAMs.

### **Aim of the Guideline and Specific Objectives**

This guideline aims to provide evidence-based recommendations to support adherence among patients on OAM regimens. The recommendations are intended to inform practice, identify research gaps, and promote policy and advocacy. A systematic review (Waseem et al., 2022) was conducted to explore various interventions and effects on patients' adherence to OAMs, and serves as the foundation of evidence for this guideline.

### **Guideline Development Methods**

The ONS vetted and appointed individuals to the guideline panel. The membership of the interprofessional panel included oncology nurses, pharmacists, and patient representatives. The panel was coordinated by the manager of evidence-based practice at ONS (P.K.G.), with collaboration from a GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodologist (R.L.M.). The body of evidence for this guideline was based on a rigorous systematic review and meta-analysis, as well as a scoping review (Waseem et al., 2022; Sivakumaran et al., 2022). The panel completed its work via online

meetings, during which the evidence was reviewed and recommendations were formulated.

The guideline panel graded the evidence and developed the recommendations according to the GRADE approach (Guyatt, Oxman, Sultan, et al., 2011). The guideline development process—including panel formation, management of conflicts of interest, internal and external review, and organizational approval—was guided by policies and procedures derived from the Guideline International Network McMaster Guideline Development Checklist (<http://cebgrade.mcmaster.ca/guidecheck.html>), and the National Academies of Science, Engineering, and Medicine criteria for trustworthy guidelines (Institute of Medicine, 2011; Schünemann et al., 2013).

At the time of appointment and again at the recommendations meeting, financial and intellectual disclosures of interest for all panelists were collected and managed according to ONS policies and the recommendations of the Guideline International Network and the National Academies of Science, Engineering, and Medicine (Institute of Medicine, 2011; Schünemann et al., 2013). The guideline panel had no relevant conflicts of interests.

### **Formulation of Specific Clinical Questions and Determining Patient-Important Outcomes**

The panel met via weekly remote meetings to discuss and prioritize questions for this guideline starting in January 2021. Panelists were instructed to identify clinically relevant questions about adherence to OAMs, which were framed as PICO (patient, intervention, comparator, and outcome) questions (Huang et al., 2006). The panel decided to include all patients on OAMs (inclusive of all cancer sites, treatments, and stages) and all phases of adherence in this guideline. It identified patient-important outcomes (to which clinicians could respond) and prioritized those deemed critical or important for patient decision-making using the GRADE approach (Guyatt, Oxman, Kunz, et al., 2011). The panel rated the following outcomes as critical for clinical decision-making across the PICO questions: adherence, cancer-related morbidity, quality of life, patient satisfaction, self-efficacy to manage medications, patient self-efficacy about treatment, patient knowledge of regimen, adherence to laboratory monitoring, time to obtain medication, and patient financial toxicity. The panel discussed that no standard of care currently exists for the management of adherence to OAMs and decided the reference for comparison would be usual care.

### Synthesis of Evidence and Development of Recommendations

A systematic review and meta-analysis were conducted to identify the evidence base to inform

this guideline (Waseem et al., 2022). The evidence from the systematic review was evaluated using the GRADE framework and presented to the panel. The certainty (quality) of the evidence, assessed risk of

**TABLE 1. GRADE Definitions on Strength of Recommendation and Guide to Interpretation**

Strength of Recommendation	Wording in the Guideline	For the Patient	For the Clinician	For Policymakers	For Researchers
Strong	“The ONS Guidelines™ panel recommends . . .”	Most individuals in this situation would want the intervention, and only a small proportion would not.	Most individuals should receive the intervention. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	In most cases, the recommendation can be adopted as policy. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	This recommendation is supported by credible research or other convincing judgments that make additional research unlikely to alter the recommendation. On occasion, a strong recommendation is based on low or very low certainty in the evidence. In such instances, further research may provide information that alters the recommendation.
Conditional	“The ONS Guidelines panel suggests . . .”	Most individuals in this situation would want the suggested intervention, but many would not.	Different choices will be appropriate for different individuals. Decision aids may be useful to help individuals make decisions consistent with their values and preferences. Clinicians should expect to spend more time with individuals when working toward a decision.	Policymaking will require substantial debate and involvement of various stakeholders.	This recommendation is likely to be strengthened by additional research. An evaluation of the conditions and criteria (and the related judgments, research evidence, and additional considerations) that determined the conditional recommendation will help identify possible research gaps.
Research and/or knowledge gap	“The ONS Guidelines panel recommends the intervention only in the context of a clinical trial.”	A discussion of benefits/harms and alternatives is warranted.	Clinicians should look for clinical trials testing this intervention, if individuals are interested.	–	Available evidence is insufficient to determine true effect, and this recommendation may be appropriate for research.

GRADE—Grading of Recommendations Assessment, Development and Evaluation; ONS—Oncology Nursing Society  
**Note.** Based on information from Guyatt, Oxman, Akl, et al., 2011; Guyatt, Oxman, Kunz, et al., 2011; Guyatt, Oxman, Sultan, et al., 2011.  
**Note.** From “ONS Guidelines™ for Cancer Treatment–Related Hot Flashes in Women With Breast Cancer and Men With Prostate Cancer,” by M. Kaplan, P.K. Ginex, L.B. Michaud, et al., 2020, *Oncology Nursing Forum*, 47(4), p. 376 (<https://doi.org/10.1188/20.ONF.374-399>). Copyright 2020 by Oncology Nursing Society. Reprinted with permission.

bias, inconsistency, indirectness, imprecision, and publication bias of the estimate of the effect was summarized in evidence profiles (Guyatt, Oxman, Sultan, et al., 2011). Both randomized controlled trials and nonrandomized evidence started at an initial rating of high. Risk of bias in randomized controlled trials was assessed using the Cochrane Risk of Bias 2 tool, and nonrandomized studies were assessed using the Risk of Bias in Nonrandomized Studies of Interventions (Sterne et al., 2016, 2019). In addition to the certainty assessment, the panel considered benefits and harms, patients' values and preferences, resources, equity, acceptability, and feasibility to develop recommendations for each PICO question. The panel agreed on the recommendations, remarks, and qualifications by consensus. The final guideline, including recommendations, was reviewed and approved by all members of the guideline panel.

### Interpretation of Recommendations

The recommendations in this guideline are labeled as strong, conditional, no recommendation, or knowledge gap. Table 1 provides GRADE's interpretation of the recommendations by patients, clinicians, healthcare policy makers, and researchers (Guyatt, Oxman, Alk, et al., 2011; Guyatt, Oxman, Kunz, et al., 2011; Guyatt, Oxman, Sultan, et al., 2011). The recommendations are summarized in Table 2.

### Document Review

Draft recommendations were reviewed and approved by all members of the guideline panel, then opened for public comment on November 8, 2021. In addition, a targeted comment was requested from clinical and research experts. The goal of soliciting public and targeted comments was to obtain direct feedback on the draft recommendations and recommendations for disseminating the final guideline to practitioners.

**TABLE 2. Summary of Recommendations: ONS Guidelines™ for Adherence to OAMs in Patients With Cancer**

Recommendation	Strength of Recommendation	Quality of Evidence
In patients starting a new OAM, the ONS Guidelines panel suggests an adherence risk assessment in addition to usual care rather than usual care alone.	Conditional	Very low
In patients taking OAMs, the ONS Guidelines panel suggests education addressing adherence in addition to standard education rather than standard education alone.	Conditional	Very low
In patients taking OAMs, the ONS Guidelines panel suggests ongoing assessment of adherence in addition to usual care rather than usual care alone.	Conditional	Very low
In patients with additional risk factors for nonadherence taking OAMs, the ONS Guidelines panel suggests proactive follow-up addressing adherence in addition to usual care rather than usual care alone.	Conditional	Very low
In patients taking OAMs, the ONS Guidelines panel suggests coaching in addition to usual care rather than usual care alone.	Conditional	Very low
In patients taking OAMs, the ONS Guidelines panel suggests motivational interviewing in addition to usual care rather than usual care alone.	Conditional	Low
The ONS Guidelines panel makes no recommendation for the use of technology, either interactive or noninteractive, based on a knowledge gap.	No recommendation; knowledge gap	–
The ONS Guidelines panel suggests implementation of a structured OAM program rather than no structured OAM program.	Conditional	Very low

OAM—oral anticancer medication; ONS—Oncology Nursing Society

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Frequent comments included acknowledging the limitations of the evidence, the need for specific tools and standards to implement the recommendations, and the complexity of needs for a variety of patients and treatments. Following public and targeted comment, the document was revised to address pertinent comments and clarify text where needed; however, no changes were made to the recommendations. The ONS Board reviewed and approved the guideline methodology and process. The guidelines were then submitted to the *Oncology Nursing Forum* as a manuscript for peer review.

### How to Use These Guidelines

ONS Guidelines™ are intended to assist clinicians in making decisions about treatments, interventions for symptoms, and supportive care for patients with cancer throughout the treatment trajectory. ONS Guidelines are intended to inform practice, identify research gaps, and promote policy and advocacy. ONS Guidelines are not medical advice and do not replace care by a cancer care clinician. Using a shared decision-making process, clinicians make decisions with patients, including discussion of patients' values and preferences with respect to their current situation. ONS Guidelines may not include all available treatments or interventions for an individual patient. Treatments and interventions described in the ONS Guidelines may not be appropriate for all patients or in all scenarios. Following these ONS Guidelines does not guarantee improvement or a successful outcome.

### Recommendations, Key Evidence, and Qualifying Statements

Each recommendation includes a description of the total analysis (network meta-analysis, pairwise meta-analysis, and narrative summaries) in the GRADE Evidence-to-Decision frameworks (Alonso-Coello, Oxman et al., 2016; Alonso-Coello, Schünemann, et al., 2016). The narrative following each recommendation parallels the organization of the GRADE Evidence-to-Decision. First, a summary of the evidence is presented, followed by a description of the potential benefits and harms considered by the panel members, including a statement about the certainty of the evidence. Additional factors from the evidence-to-decision discussions are then summarized in a section labeled "other evidence-to-decision criteria and considerations." Lastly, a final summary of the recommendation is presented, considering any overarching remarks made by the panel. Evidence profiles for each PICO question are presented in the appendices.

### Risk/Barrier Assessment

#### Should an assessment for adherence risk/barriers be completed in addition to usual care rather than usual care alone in patients starting a new OAM?

In patients starting a new OAM, the ONS Guidelines panel suggests an adherence risk assessment in addition to usual care rather than usual care alone (conditional recommendation, very low certainty of evidence).

### Summary of the Evidence

One study conducted a risk assessment (barriers or facilitators to adherence) and provided a tailored plan to improve adherence; however, the contribution of a risk assessment could not be isolated from the additional tailored intervention in this trial (Schneider et al., 2014). Nine studies reported on a variety of risk assessment instruments, including those that measured depression or anxiety, or evaluated the association between patient demographics and non-adherence (Berry et al., 2015; Decker et al., 2009; Dos Santos et al., 2019; Jacobs et al., 2017; Krikorian et al., 2019; Krolop et al., 2013; Timmers et al., 2015; Wickersham et al., 2013; Yusuf et al., 2020).

### Benefits

Risk assessment, along with a tailored intervention, improved adherence in comparison to usual care alone. Schneider et al. (2014) showed that the 25 participants who received risk assessment along with a tailored intervention had an adherence rate of 95%, whereas the 20 participants in the control arm had an adherence rate of 82%.

### Harms and Burdens

No harms were identified; however, it should be noted that there was limited existing research available on this topic.

### Certainty in the Evidence of Effects

There is very low certainty in the evidence due to concerns with indirectness and imprecision.

### Other Evidence-to-Decision Criteria and Considerations

The panel acknowledged a desirable effect where standardized risk assessment may inform patient care; however, it could not identify one standardized assessment instrument that was currently being used in the field. The panel recognized that an undesirable effect could occur if risk assessment findings did not yield consistent clinician follow-up. In addition, the panel discussed the potential patient burden of

additional assessments if they are not integrated into care processes. The panel also acknowledged that the cost of risk assessments would be dependent on the burden and length of time needed to complete the assessment. The panel highlighted that the use of standardized risk assessments may increase health equity. Although the panel acknowledged that some degree of risk assessment is already being used in clinical settings, and acceptability of this intervention may not present a challenge, feasibility considerations should be investigated further (e.g., the capacity to process, triage, and utilize results of these assessments).

### Conclusions

Based on the available evidence, the ONS Guidelines panel issued a conditional recommendation suggesting the use of risk assessment rather than no risk assessment in patients starting a new OAM regimen.

### Education

#### Should medication education that addresses adherence be used in addition to standard education rather than standard education alone in patients on an OAM?

In patients taking OAMs, the ONS Guidelines panel suggests education addressing adherence in addition to standard education rather than standard education alone (conditional recommendation, very low certainty of evidence).

### Summary of the Evidence

This PICO question was informed by 16 studies (Berry et al., 2015; Byrne et al., 2018; Gönderen Çakmak & Kapucu, 2021; Hendricks, 2015; Krikorian et al., 2019; Krolop et al., 2013; Lin et al., 2020; Morgan et al., 2017; Patel et al., 2016; Ribed et al., 2015; Schneider et al., 2014; Simons et al., 2010; Suttman et al., 2020; Vacher et al., 2019; Zerbit et al., 2020; Ziller et al., 2013). With respect to patient population, there was heterogeneity in type of cancer and regimen among studies. Educational programs were delivered in a variety of ways and were accompanied by co-interventions in some cases.

### Benefits

Educational programs may improve adherence rates in comparison to usual care (mean difference [MD] = 10.61%, 95% confidence interval [CI] [7.21, 14.01], very low certainty of evidence); however, the evidence is unclear (Krolop et al., 2013; Simons et al., 2010; Vacher et al., 2019; Zerbit et al., 2020). Self-reported adherence may also improve in patients receiving

educational programs (risk ratio [RR] = 1.16, 95% CI [1.01, 1.33], moderate certainty of evidence) (Berry et al., 2015; Suttman et al., 2020). Patient knowledge on dosage and frequency (RR = 1.26, 95% CI [1.03, 1.52], very low certainty of evidence), management of missed doses (RR = 1.51, 95% CI [1.16, 1.98], very low certainty of evidence), and dosage schedule (RR = 1.31, 95% CI [1.06, 1.62], very low certainty of evidence) may improve with the help of educational programs (Byrne et al., 2018).

### Harms and Burdens

No harms were identified resulting from educational programs; however, it should be noted that there was limited existing research available on this topic.

### Certainty in the Evidence of Effects

There is very low certainty in the evidence due to concerns with risk of bias, indirectness, and imprecision.

### Other Evidence-to-Decision Criteria and Considerations

The panel did not identify any undesirable effects from additional adherence education given to patients on OAM regimens. Based on clinical experience, the panel discussed that additional education should occur at each clinical encounter with consideration of the patient's medication cost. In addition, further research is needed to understand how this education should be delivered. The panel highlighted that the development of a standardized educational program or checklist to provide consistency within and across centers would be useful.

### Conclusions

Based on the available research, the ONS Guidelines panel suggests adherence education in addition to standard education rather than standard education alone in patients on OAMs.

### Ongoing Assessment

#### Should ongoing assessment of adherence in addition to usual care rather than usual care alone be used for patients on an OAM?

In patients taking OAMs, the ONS Guidelines panel suggests ongoing assessment of adherence in addition to usual care rather than usual care alone (conditional recommendation, very low certainty of evidence).

### Summary of the Evidence

Twelve identified studies addressed this PICO question (Bordonaro et al., 2014; Boulefour et al., 2021;

Dennison et al., 2021; Eldeib et al., 2019; Greer et al., 2020; Lin et al., 2020; Mir et al., 2020; Muluneh et al., 2018; Spoelstra et al., 2015, 2017; Suttman et al., 2020; Zerbit et al., 2020). Several studies did not base enrollment on cancer type or regimen. The interventions among studies also varied in method and frequency of delivery because the timing of ongoing assessment for this PICO question was broad. Frequency of delivery varied in the identified studies. Some included weekly follow-ups; others used check-ins at baseline and 3-, 6-, 12-, and 24-week marks; and some conducted ongoing assessments months or cycles apart.

### Benefits

Ongoing assessment may improve adherence in comparison to usual care (MD = 7%, 95% CI [0.66, 13.34], very low certainty of evidence), however, the evidence is very unclear (Zerbit et al., 2020). Ongoing assessment may also improve quality of life in comparison to usual care (MD = 15.7 points, 95% CI [8.84, 22.56], low certainty of evidence) (Bordonaro et al., 2014). In addition, patient satisfaction scores may be higher in patients receiving ongoing assessment in comparison to those receiving only usual care (RR = 1.32, 95% CI [1.02, 1.72], very low certainty of evidence) (Dennison et al., 2021).

### Harms and Burdens

No harms were identified in the existing literature pertaining to this topic.

### Certainty in the Evidence of Effects

There is very low certainty in the evidence due to concerns with risk of bias and imprecision.

### Other Evidence-to-Decision Criteria and Considerations

The panel did not identify any undesirable effects of ongoing assessment of adherence; however, the need for further research was discussed. Noted next steps to better inform clinical practice included considering the complexity of ongoing interventions and developing a standard for ongoing assessment. The panel highlighted that the frequency of ongoing assessment, personnel needed to execute the assessment, and coordination with the patient would affect cost and resource considerations. With respect to frequency of the assessment, there is variability in when and how often these assessments should be delivered based on diverse clinical experiences. The panel recognized that toxicities may contribute to

nonadherence, and that assessment of adherence could reasonably occur during toxicity assessments. The panel discussed the importance of early assessment and recurring assessments at periodic intervals, and that these assessments' occurrence in the treatment timeline would be an important topic for future research to explore.

### Conclusions

Based on the available evidence, the ONS Guidelines panel issued a conditional recommendation suggesting the use of ongoing assessment of adherence in addition to usual care, rather than usual care alone.

### Proactive Follow-Up

#### Should proactive follow-up outside of routine medical visits be done rather than usual care for patients on an OAM who have additional risk factors?

In patients with additional risk factors for nonadherence taking OAMs, the ONS Guidelines panel suggests proactive follow-up addressing adherence in addition to usual care, rather than usual care alone (conditional recommendation, very low certainty of evidence).

### Summary of the Evidence

Three studies reported on strategies for proactive follow-up for patients on OAMs (Eldeib et al., 2019; Hendricks, 2015; Vacher et al., 2019). There was heterogeneity among study populations in type of cancer and type of cancer regimen. Additional risk factors varied between studies as well. Two studies had patients more at risk for nonadherence as they were on complex medication regimens or were on oral chemotherapies considered emetogenic. Another study chose a subpopulation that was found to be nonadherent based on adherence scores less than 80% and provided those patients with proactive follow-up. Delivery of the interventions differed across studies.

### Benefits

Proactive follow-up in patients with additional risk factors may improve adherence in comparison to usual care (MD = 17.8 %, 95% CI [6.43, 29.17], very low certainty of evidence), however, the evidence is very uncertain (Vacher et al., 2019).

### Harms and Burdens

Although no harm was detected, it should be noted that the body of evidence available for this topic is very limited.

### Certainty in the Evidence of Effects

There is very low certainty in this evidence due to concerns with risk of bias and imprecision.

### Other Evidence-to-Decision Criteria and Considerations

Due to the limited literature available, the panel was not able to identify undesirable or desirable effects of proactive follow-up in patients with additional risk factors. The panel discussed the importance of an individualized approach, as some patients with risk factors may need more support while others would value less follow-up. Because risk factors may vary, it is important to identify a broad spectrum of factors and tailor follow-up in accordance with these risk factors.

### Conclusions

Using the available evidence, the ONS Guidelines panel suggests active follow-up in addition to usual care, rather than usual care alone in patients with additional risk factors for nonadherence on OAMs.

## Coaching

### Should coaching interventions be used in addition to usual care rather than usual care alone for patients on OAMs?

In patients taking OAMs, the ONS Guidelines panel suggests coaching in addition to usual care, rather than usual care alone (conditional recommendation, very low certainty of evidence).

### Summary of the Evidence

Eight studies reported on coaching interventions—a partnership between a patient and clinician that involves setting goals, identifying values and strengths, and facilitating the development of healthy routines and behaviors—for patients on OAMs (Bordonaro et al., 2014; Komatsu et al., 2020; Krikorian et al., 2019; Lam & Cheung, 2016; Middendorff et al., 2017; Muluneh et al., 2018; Patel et al., 2016; Schneider et al., 2014; Vacher et al., 2019). There was heterogeneity in type of cancer and OAM regimens among studies. The coaching intervention delivery varied among studies, but all included dedicated contact with a nurse or pharmacist for OAM management. Examples include therapeutic education, tailored adherence plans, patient-centered medication self-management and supportive care. Although usual care also varied across studies, all studies entailed only routine instructions and no additional counseling follow-up. Due to differences in how outcomes were reported, not all the study data could be pooled.

### Benefits

Coaching may improve adherence rates in patients with cancer in comparison to usual care alone (MD = 17.8% higher, 95% CI [6.43, 29.17], very low certainty of evidence) (Vacher et al., 2019). Coaching may also improve medication-possession ratio in patients with cancer in comparison to usual care alone (MD = 2.98%, 95% CI [2.95, 3.01], very low certainty of evidence) (Lam & Cheung 2016; Middendorff et al., 2017).

### Harms and Burdens

No harms were identified; however, it should be noted that there was limited existing research available on this topic.

### Certainty in the Evidence of Effects

There is very low certainty in the evidence due to concerns with risk of bias, indirectness, and imprecision.

### Other Evidence-to-Decision Criteria and Considerations

The panel discussed coaching broadly, acknowledging that coaching is a patient-centered, collaborative intervention where goals are identified and plans are defined to build self-efficacy to promote healthy behaviors (Olsen & Nesbitt, 2010; Wolever & Eisenberg, 2011). The panel was unable to judge the desirable and undesirable effects of coaching due to the lack of literature available. However, patient representatives and panel members discussed the benefits of providing baseline education and follow-up to improve patient adherence. The panel underscored the benefits of providing patients with symptom management and adherence strategies as part of coaching interventions. The panel highlighted that over time there may be a dip in patient adherence, and patients may value a coaching intervention that offers symptom management after six or nine months of treatment.

### Conclusions

Based on the available evidence, the ONS Guidelines panel issued a conditional recommendation suggesting the use of coaching, rather than usual care alone in patients on an oral anticancer regimen.

## Motivational Interviewing

### Should motivational interviewing be used in addition to usual care rather than usual care alone for patients on OAMs?

In patients taking OAMs, the ONS Guidelines panel suggests motivational interviewing in addition to



usual care rather than usual care alone (conditional recommendation, low certainty of evidence).

### Summary of the Evidence

Four studies were eligible for this PICO question (Gönderen Çakmak & Kapucu, 2021; Ribed et al., 2015; Spoelstra et al., 2017; Ziller et al., 2013). Although one study focused solely on patients with breast cancer, the remaining papers all had diverse patient populations with respect to cancer type and medication regimen. Motivational interviewing—collaborative and goal-oriented communication designed to enhance personal motivation and commitment to behavior change—included individualized education and strategies for adherence and was delivered in each of the four studies by a nurse or pharmacist. Motivational interviewing was implemented alongside co-interventions like cognitive behavioral therapy or education materials. The usual care among studies was also heterogeneous.

### Benefits

Motivational interviewing may improve adherence rates in comparison to usual care in patients on an oral anticancer regimen (MD = 3.23%, 95% CI [0.45, 6.02], low certainty of evidence) (Ziller et al., 2013). In addition, patient self-efficacy about their treatment may improve with motivational interviewing in comparison to usual care alone (MD = 9.9 points, 95% CI [9.68, 10.12], low certainty of evidence) (Gönderen Çakmak & Kapucu, 2021).

### Harms and Burdens

No harms were identified; however, it should be noted that there was limited existing research available on this topic.

### Certainty in the Evidence of Effects

The outcome of adherence drove the recommendation for motivational interviewing. There is low certainty in this evidence due to concerns with risk of bias and imprecision.

### Other Evidence-to-Decision Criteria and Considerations

The panel discussed motivational interviewing as an evidence-based methodology to promote behavior change. They discussed that definitions for motivation interviewing vary, but the technique is based on communication that strengthens personal motivation and empowers the patient toward a specific goal (Miller & Rollnick, 2013). The panel also discussed benefits

seen with motivational interviewing for adherence to medications in other chronic diseases. The panel was unable to judge the desirable and undesirable effects of motivational interviewing due to the lack of literature available. The panel discussed the value of motivational interviewing for patients to prevent lags in adherence over time. In addition, the panel discussed how the intervention could be beneficial to patients for symptom management purposes and ensuring they are taking their medication appropriately.

### Conclusions

Based on the available evidence, the ONS Guidelines panel issued a conditional recommendation suggesting the use of motivational interviewing in addition to usual care rather than usual care alone in patients on an oral anticancer regimen.

### Technology

#### Should technological interventions be used in addition to usual care instead of usual care alone for patients on OAMs? Should interactive technology rather than noninteractive technology be used for patients on OAMs?

The ONS Guidelines panel makes no recommendation for the use of technology, either interactive or noninteractive, based on a knowledge gap.

### Summary of the Evidence

Thirteen studies reported on the use of technological interventions for patients on OAMs (Collado-Borrell et al., 2020; Fischer et al., 2018; Greer et al., 2020; Hershman et al., 2020; Kim et al., 2018; Krok-Schoen et al., 2019; Mauro et al., 2019; McKay et al., 2019; Mir et al., 2020; Sikorskii et al., 2018; Spoelstra et al., 2013, 2015, 2016). There was heterogeneity in the type of cancer and OAM regimens between studies. Technological interventions varied, encompassing webpages, applications, text messaging, voicemails, and emails. Interactive technology entailed patients inputting a response using technology that was then addressed by a primary healthcare worker, whereas noninteractive technology provided automated reminders alone.

### Benefits

Technology may improve adherence rates in comparison to usual care (MD = 8.23%, 95% CI [2.9, 13.55], very low certainty of evidence) (Greer et al., 2020; Mauro et al., 2019); however, it should be noted that this improvement was seen when technology was accompanied by additional primary healthcare

follow-up. Technology may also improve medication possession ratio in cancer patients in comparison to those receiving usual care (MD = 4.7% higher, 95% CI [1.19, 8.2], very low certainty of evidence) (Collado-Borrell et al., 2020). Quality of life may improve in patients receiving technological interventions in comparison to usual care (SMD = 1.44, 95% CI [1.15, 1.74], very low certainty of evidence) (Greer et al., 2020; Kim et al., 2018).

### Harms and Burdens

No harms were identified in the literature; however, the panel acknowledged that this is a knowledge gap and more research is needed in this area. The panel did discuss the potential burden of costs to the patient and healthcare institution along with the institutional resources needed to implement a technology intervention.

### Certainty in the Evidence of Effects

There is very low certainty in the evidence due to concerns with risk of bias, imprecision, and inconsistency.

### Other Evidence-to-Decision Criteria and Considerations

The panel was unable to judge the desirable and undesirable effects of technological interventions due to the lack of literature available on co-interventions given alongside technology in the studies. Although the evidence suggested potential for benefit, there was very low certainty in the evidence, and the interventions used in the supporting evidence were coupled with additional follow-up, therefore there was not enough information available to make a judgment. In addition, patient values and preferences may vary based on whether patients have the willingness or skills needed to use technology in this capacity.

### Conclusions

Based on the paucity of direct evidence about the use of technological interventions for patients on OAMs, the ONS Guidelines panel identified this topic as a knowledge gap in need of further research.

## Structured Programs

### Should structured OAM programs be used by institutions providing care to patients on an OAM rather than no structured OAM programs?

The ONS Guidelines panel suggests implementation of a structured OAM program rather than no structured OAM program (conditional recommendation, very low certainty of evidence).

## Summary of the Evidence

This PICO question was informed by 14 studies (Bordonaro et al., 2012, 2014; Curry et al., 2020; Dennison et al., 2021; Gebbia et al., 2013; Khandelwal et al., 2012; Krolop et al., 2013; Lam & Cheung, 2016; Middendorff et al., 2017; Muluneh et al., 2018; Ribed et al., 2015; Stokes et al., 2017; Tschida et al., 2012; Vacher et al., 2019) in a scoping review (Sivakumaran, 2022). There was heterogeneity in the types of structured OAM programs used across studies; there were home-, clinical-, and pharmacy-based programs. Programs also varied with respect to what they offered. Some of the components that programs included were home visits, patient education, toxicity and adverse event monitoring, follow-up, and adherence monitoring/support. Similarly, the comparator within the studies also varied because some used pre- or postcomparisons, and others used a reference group without a program as the comparator.

### Benefits

Adherence may increase in patients in an OAM program in comparison to those receiving only usual care (MD = 12.22 higher, 95% CI [9.19, 15.24], versus MD = 6% higher, 95% CI [4, 8] [measured using Medication Event Monitoring System and medication-possession ratio, respectively], very low certainty of evidence) (Gebbia et al., 2013; Krolop et al., 2013; Lam & Cheung, 2016; Middendorff et al., 2017; Stokes et al., 2017; Tschida et al., 2012; Vacher et al., 2019). In addition, cancer-related morbidity may also improve in patients in an OAM program in comparison to those only receiving usual care (MD = 11.1 points, 95% CI [7.45, 14.75], very low certainty of evidence) (Bordonaro et al., 2014). Quality of life may also increase in patients in an OAM program compared to those only receiving usual care (MD = 15.7 points, 95% CI [12.7, 18.7], very low certainty of evidence) (Bordonaro et al., 2014). Similarly, patients in an OAM program are more likely to have increased satisfaction compared to those receiving usual care (RR = 1.32, 95% CI [1.02, 1.72], very low certainty of evidence) (Bordonaro et al., 2014).

### Harms and Burden

No harms were identified in the existing literature pertaining to this topic.

### Certainty in the Evidence of Effects

There is very low certainty in the evidence due to concerns with risk of bias, imprecision, and indirectness.

### Other Evidence-to-Decision Criteria and Considerations

The panel determined that the net benefit was in favor of a structured OAM program. However, the panel noted that resources required will include personnel, cost, and time. The panel discussed that the use of structured OAM programs may increase health equity as it could be used to help advocate for patients. Although the panel acknowledged that there may be variability in the acceptability of a program, it is in terms of who would be responsible for it (e.g., the institution and/or an additional responsibility on the patient). In addition the panel discussed questions about feasibility, specifically in terms of smaller versus larger practices, since there may be concerns with who would be responsible for it (e.g., one person or a whole department), who pays for it, and what kind of training would be needed.

### Conclusions

Based on available evidence, the ONS Guidelines panel issued a conditional recommendation suggesting the

use of a structured OAM program rather than no structured OAM program for patients on an OAM regimen.

### Discussion

The recommendations within this clinical practice guideline serve as a first step toward developing a framework for clinicians to support patients who are receiving an OAM treatment regimen. Recommendations encompass the full trajectory of treatment, from initial risk assessment to ongoing monitoring and follow-up, and are intended for all patients with cancer receiving any OAM. Research continues to emerge, and priorities for research were identified while developing this guideline (see Figure 1). A recent randomized controlled trial of intensified clinical pharmacy care (e.g., medication management, patient counseling, ongoing assessment) found lower side effects, decreased discontinuation of therapy, improvement in self-reported medication adherence, and improvement

#### FIGURE 1. Research Priorities Identified by the ONS Guidelines™ Panel

- In a climate where resources are finite, resources should be targeted toward populations identified as being most at risk for nonadherence.
- Understanding potential bidirectional relationships between financial hardship and adherence is critical, including points across the treatment trajectory where vulnerabilities may be exacerbated.
- Policies and system support are needed to bolster patients' ability to obtain and pay for OAMs to maintain adherence.
- Additional research is needed to develop and test valid, reliable, practical, and common subjective and objective measures of medication adherence to allow for analysis across multiple studies.
- Studies that include a subjective and objective measure of adherence as outcomes
- Studies that assess the timing of interventions and its impacts on outcomes
- Studies investigating the impact of financial difficulties on adherence rates and interventions aimed at providing patients with financial support
- Implementation studies that assess time, personnel, acceptability concerns, and resources to implement adherence interventions
- Studies to assess multicomponent interventions aimed at improving patient adherence
- Revisions of quality metrics should occur as new data become available, and studies should focus on metrics that are measurable and result in positive patient outcomes so practices can use these metrics to identify gaps and see improvement.
- Additional quality improvement reports of existing OAM adherence programs are needed and should include cost/benefit analyses and discussion of key low-cost and high-yield components.
- Studies assessing the needs and barriers of implementing OAM programs within community sites along with opportunities for improving access (e.g., partnership, funding by payers) should be explored.
- Studies should include analyses of interventions for those who are medically underserved with goals of eliminating disparities, achieving health equity, and improving health of all groups.
- Studies should identify, examine, and target interventions toward mechanisms (e.g., environment, social determinants, racism) that contribute to and exacerbate health inequities.
- Studies should increase focus on and ensure inclusion of populations historically underrepresented in research.
- Interprofessional research and cross-discipline clinical collaboration are needed to improve medication adherence.

OAM—oral anticancer medication; ONS—Oncology Nursing Society

in patient satisfaction between the control and intervention groups (Dürr et al., 2021). An oral chemotherapy management program (i.e., standardized management and documentation of patients receiving OAMs) recently reported significantly lower overall incidence of adverse events, decreased emergency department visits and hospitalizations, and improved medication adherence (Nhean et al., 2021). These recent studies, published after this review, support adherence education, ongoing assessment, and the benefits of having a structured OAM program. This review and guideline focused on OAMs, and there is a significant amount of literature on interventions to improve adherence to non-oncologic oral medications. As these recommendations are operationalized for patient care, considering the broad adherence literature may be informative to create best practices for patients on OAMs.

In the future, research may identify specific interventions that are targeted to specific patients or specific regimens. Research is also needed on patient and system factors that are related to adherence, such as financial toxicity. However, with the number of OAMs being developed, and the number of cancers being treated with OAMs, healthcare systems should be supporting patients now, while additional research is ongoing. Good clinical practice and expert consensus with patient stakeholders may be the best approach to operationalizing these recommendations. In addition, clinical infrastructure that involves a dedicated team of clinicians, information technology, and electronic health record pathways are important tools to address adherence to OAMs. Strategies such as a gap analysis using a quality improvement approach can help clinical sites to prioritize what needs to be changed and built on well-working structures that are already in place. Many of the reported studies involved nursing and pharmacy, and the DNP and PharmD roles are well positioned to lead this change in practice.

#### **Other Guidelines on Adherence to OAMs**

To the panel's knowledge, this is the first clinical practice guideline focused specifically on OAM adherence. These guidelines build on consensus practice guidance from national organizations in oncology care (Hematology/Oncology Pharmacy Association, ONS, American Society of Clinical Oncology [ASCO], National Community Oncology Dispensing Association, Société Internationale d'Oncologie Gériatrique). The Hematology/Oncology Pharmacist Association published pharmacy practice

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#### **SUPPLEMENTARY MATERIAL AVAILABLE ONLINE**

All appendices mentioned within this article can be accessed online at <https://bit.ly/3vph3Ag>.

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standards for the management of oral oncolytic therapy (Mackler et al., 2019). Included in the standards was prescribing, educating, dispensing and distributing, monitoring, and following up. In 2013, ONS and ASCO published standards for the safe administration and management of oral chemotherapy (Neuss et al., 2013). The standards included workflow from the selection of regimen to monitoring of response including staffing, documentation, practice and prescribing standards, patient consent and education, administration, monitoring, and assessment. ASCO and the National Community Oncology Dispensing Association published patient-centered standards for medically integrated dispensing of OAMs that included recommendations for education, tools, and policies to maximize adherence, documentation, and safety (Dillmon et al., 2019). The Société Internationale d'Oncologie Gériatrique convened a taskforce to develop recommendations on adherence to oral cancer therapy in older adults (Mislant et al., 2017). The taskforce identified advantages and disadvantages of oral therapy in older adults and outlined management considerations when initiating treatment with oral cancer agents. The Multinational Association of Supportive Care in Cancer's Oral Agent Teaching Tool is a clinical tool to assess patient knowledge of oral agents and guide patient education (Kav et al., 2009), and can be used at the point of care to implement the educational component recommended by these guidelines.

#### **Implications for Practice and Conclusion**

When cancer treatment is administered intravenously, patients interact with healthcare professionals at set intervals before, during, and after treatment. Standards and processes are in place to optimize patient care and outcomes during these visits. It is necessary to have similar guidelines and processes in place for patients managing their treatment at home on OAMs to optimize patient care. Successful implementation also requires adequate reimbursement to provide this additional care and follow-up. Staff resources to provide this heightened level of care are difficult to justify (particularly for community practices) without reimbursement for the care provided. Healthcare policy needs to

acknowledge the trend toward OAM treatment to ensure these important services can be provided. Although additional work is needed to define and operationalize these recommendations, they provide evidence-based guidance for oncology healthcare professionals to build upon, and clinicians should translate them into practice.

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