

Depression moderates the positive impact of early palliative care on survival among advanced cancer patients.

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## I. Background

We previously demonstrated improved depression and survival in advanced cancer patients participating in two palliative care RCTs. ENABLE II (EII; N=322) compared intervention vs. usual care and ENABLE III (EIII; N=207) compared immediate vs. delayed intervention. The interventions were similar (e.g. in-person PC consultation, weekly phone sessions facilitated by a nurse coach, and monthly follow-up calls) except in EIII there was a delayed intervention group (beginning 12 weeks after enrollment) and a caregiver intervention. The Center for Epidemiologic Studies-Depression (CES-D) was collected at baseline and approximately every 12 weeks until death or study completion.

II. Research Objective: To determine whether baseline depression moderates the effect of the intervention on survival in the combined RCTs' sample (N=529; intervention n=368; usual care n=161).

## III. Methods

A Cox proportional hazard analysis was conducted with (a) intervention (as a time-varying covariate), (b) baseline CES-D scores, and (c) their interaction, entered simultaneously.

## IV. Results

There was a significant effect of the interaction (intervention x CES-D) on mortality risk ( $P=.035$ ), indicating a moderating role of depression. To clarify the nature of this interaction, we classified patients as depressed (baseline CES-D > 16) or not, and conducted a separate Cox analysis within each depression group that included intervention as the sole predictor variable. Among depressed patients, receiving the intervention was associated with lower mortality risk (HR = 0.65, CI: 0.44-0.95,  $P = .029$ ), but this relationship was not significant among non-depressed patients (HR = 0.89, CI: 0.65-1.21,  $P = .45$ ).

## V. Conclusions

The ENABLE intervention effect of reduced mortality risk was moderated by baseline depression such that the magnitude of the intervention effect increased as baseline depression scores worsened. This finding provides initial insight into one mechanism of early PC.

## VI. Implications for research, policy or practice

This finding warrants further study; however given limited PC resources, it may be most beneficial to target early PC for depressed patients.